PHYSICAL METHODS

IN

ORGANIC CHEMISTRY

by

John Hamilton Bowie

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STATEMENT

The thesis consists of sixty five reprints of published works. Fifty one of the papers describe the candidate's contribution to mass spectrometry, five to nuclear magnetic resonance spectroscopy, and nine to the use of these physical techniques to aid the structure elucidation of naturally-occurring compounds. A short description of the most important facets of this work is contained in the summary (below).

My major contributions to organic chemistry lie in the field of organic mass spectrometry. Pioneering work on skeletal-rearrangement processes (see especially papers 37, 38, 40, 41, 43-49, 51-53, 55, 59, and 61-64) has led to the discovery of many such processes in a variety of systems.

The thesis is divided into three sections:- (A) Structure-Elucidation of Natural Products - (i) Aphid Constituents, (ii) Miscellaneous Natural Products; (B) Solvent-Shifts in Nuclear Magnetic Resonance Spectroscopy, and (C) Mass Spectrometry.

Papers 1-7 in section A describe the elucidation of the structures of aphid constituents. This work was carried out by myself during the tenure of an I.C.I. Post-Doctoral Fellowship at Emmanuel College, Cambridge University (U.K.), in collaboration with Dr. D.W. Cameron, who directed all research related to aphid colouring matters.

Publications 8, 12-15 and 17-32 give accounts of researches in structure determination, nuclear magnetic resonance spectroscopy and mass spectrometry respectively, also completed while I was an I.C.I. Fellow at Cambridge University. This research was undertaken jointly

with Dr. D.H. Williams, who leads a large research school working in these fields. Paper 33 describes work carried out at Cambridge in collaboration with Dr. A.F. Thomas.

Papers 34-65 describe fundamental researches in mass spectrometry, while 9-11 are concerned with structure determination, and 16 with nuclear magnetic resonance spectroscopy. This work was performed at the University of Adelaide. All projects were planned and directed by myself. I wrote all the papers, except 55, which describes a joint project, carried out at Adelaide, but written by Dr. D.H. Williams. Many projects resulted in joint publications. The co-authors were: Professors, G.M. Badger, J.C. Earl, A.W. Johnson, Drs. I.R.C. Bick, D.W. Cameron, G.E. Gream, S.-O. Lawesson, G.E. Lewis, J.W.W. Morgan, R.H. Prager, H.J. Rodda, and T.M. Spotswood. Where Dr. R.G. Cooks appears in the list of authors, he performed the high-resolution measurements listed in that paper. This was due to the non-availability of facilities for performing high-resolution studies at Adelaide for the period 1966-1967.

This thesis does not contain any material that I have previously submitted for a degree in any University.

J.H. BOWIE

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SUMMARY

Papers have been set out essentially in chronological order within each section of the thesis. This constitutes a logical sequence for sections A and B. Subdivision of section C has not been undertaken, because of the difficulty of classifying papers on the basis of skeletal-rearrangement or normal fragmentation processes (many papers contain accounts of both types of fragmentation), and of further subdivision within a group (certain papers describe more than one type of rearrangement process).

(A) Structure-Elucidation of Natural Products

The great potential of mass spectrometry and N.M.R. spectroscopy for the determination of structure is exemplified by the following studies.

(i) Aphid Constituents

Papers 2-5 describe the elucidation of the structures of the dactynaphin and rhodoaphin pigments, while papers 1 and 6 are records of the chemistry of aphid constituents. Paper 7 gives an account of the mass spectra of known aphin derivatives, a knowledge of which was vital for the interpretation of the mass spectra of the dactynaphins and rhodoaphins.

The rhodoaphin and dactynaphin pigments are among the most complicated quinones yet isolated from natural sources. Only very small amounts of these compounds were available for study. High-resolution mass spectrometry and N.M.R. spectroscopy allowed complete

structural formulations for the pigments. On the basis of these formulations, chemical experiments were designed which would either support or negate such structures. Electron-impact induced ring cleavage of the dactynaphins split each molecule into two known species which were readily identified by their known breakdown patterns. Chemical confirmation of the dactynaphin structures was obtained by reductive and hydrolytic cleavage of the molecules to produce either known compounds, or compounds which were readily synthesised from compounds of known structure. The mass spectrum of rhodoaphin was very similar to a known aphin derivative, dihydroxyerythroaphin-*fb*. This indicated that the only difference between the two compounds was stereochemical in nature. As the N.M.R. spectrum showed rhodoaphin to be symmetrical, only one structure was possible for the molecule. This structure was confirmed chemically by acid-catalysed epimerisation of rhodoaphin to dihydroxyerythroaphin-*fb*.

(ii) Miscellaneous Natural Products

The aphin problem described a situation where physical methods were successfully applied in the initial stages of structure elucidation. In the determination of the structure of the alkaloid repanduline (paper 8) the converse was true. The chemical investigation of repanduline had continued over a period of two decades, and was virtually at a standstill. The elemental composition of the molecule was unknown, as were its more important structural features. The problem was solved by the successive application of high-resolution mass spectrometry followed by N.M.R. spectroscopy. A successful synthesis of a degradation product has since partially confirmed the structure.

Other examples of the application of physical techniques are the determination of the structures of the antibiotic ochromycinone (paper 9), maesopsin degradation products (10), and the alkaloid moschatoline (11). Mass spectrometry clearly indicated the presence of a 3-methyl-1-tetralone moiety in ochromycinone, and allowed the determination of the relative positions of hydroxyl and methoxyl groups in moschatoline, because of the highly characteristic losses of methyl radicals from the 1- and 3- but not 2-methoxyl groups of alkaloids of this type.

(B) Solvent-Effects in N.M.R. Spectroscopy

It is widely accepted that 'solvent-shifts' of proton resonances in N.M.R. spectra may be used to aid structure elucidation of organic compounds, particularly those containing methyl or methoxyl groups. The 'solvent shift' is the difference between the chemical shifts of proton resonances measured in a 'complexing' solvent (e.g. benzene) and a 'non-complexing' solvent (e.g. carbon tetrachloride or cyclohexane). It is assumed that benzene forms a complex with a positive-centre in the solute, thus altering the chemical shift with respect to that obtained using a 'non-complexing' solvent. Controversy exists concerning the nature of the complex, and there is even doubt whether a complex is formed at all. Nevertheless, this approach may be used empirically in certain cases to determine the positions of methyl or methoxyl groups in a molecule. This is demonstrated for quinones (paper 12), anisole derivatives (13 and 14), flavones (15) and

α-diketone derivatives (16). Paper 16 questions the nature of the 'complex' formed between benzene and the α-diketone system.

(C) Mass Spectrometry

The original aims of this research were threefold.

(i) To investigate the normal fragmentation modes of a variety of organic systems. Knowledge of this work is essential for the organic chemist to be able to interpret spectra of such systems.

(ii) To discover and investigate skeletal-rearrangement processes in mass spectra. As skeletal-rearrangement processes involve the migration of groups other than hydrogen, the presence of fragment ions resulting from such processes cannot be explained in terms of the structure of the intact molecule. The recognition of such processes and a knowledge of the structures of the rearrangement ions are not only of vital interest to the mass spectrometrist, but are also essential if the organic chemist is to use mass spectrometry to determine the structures of organic compounds. This field of research is one of the most actively pursued in organic mass spectrometry at the present time, and is likely to continue to be so until such processes can be predicted with certainty, and until the mechanisms of the rearrangement processes are fully understood. The relative non-predictability of rearrangement processes at the present time also severely limits the important application of computor-aided mass spectrometry to structure elucidation.

(iii) In cases where extensive rearrangement (cf. ii) occurs in positive-ion mass spectra, interpretation is difficult because of the presence of the rearrangement ions. Negative-ion mass spectrometry should provide a viable alternative under these conditions, even though little development of this technique has previously occurred.

Papers 17-65 go some way to fulfilling these aims, and present work is directed towards the mechanism of rearrangement processes, the structures of ions, and the development of negative-ion mass spectrometry.

Papers 17-33 are the result of research performed at Cambridge and may be roughly divided into normal fragmentations of organic molecules upon electron impact (19-23, 25, 29, 31 and 33) and skeletal-rearrangement processes (17, 18, 24, 26-28, 30 and 32). The latter group contain examples of some of the first rearrangement processes encountered in mass spectrometry.

The publications 34-65 of section C comprise my major contribution to organic chemistry. Publications 34-36, 39, 42, 44, 50, 54, 56, 57, 58 and 60 record the basic fragmentations of a variety of aliphatic, aromatic and heterocyclic systems upon electron impact. Deuterium-labelling and high-resolution studies were necessary for many of the projects. Papers 37, 38, 40, 41, 43, 45-49, 51-53, 55, 59, 61-64 describe a multitude of new and novel skeletal-rearrangement processes as well as normal fragmentations which occur upon electron impact. The most notable of the rearrangements are those which occur in the spectra of compounds containing the $-\overset{+}{N}=O^{-}$ group, organo-sulphur compounds, and heterocyclic systems containing diphenyl substituents. For example, specific but complex rearrangement of the molecular ions

of azoxybenzenes (43,45), nitrones (59,62) and N-oxides (47) are observed. All involve carbon-oxygen bond formation. Reorganisation of the molecular ion is also observed for sulphinylanilines (41), thio[18]annulenes (49), mercapto esters (46,51) and sulphonamides (52,53). Migrations to carbonium-ion centres are apparent in the spectra of thioglycollates (64). Many examples of the general rearrangement ABC → AC + B have been discussed; e.g. azobenzenes (40), azoxybenzenes (43,45), nitrones (59,62), sulphonamides (52,53) and anils (61). A remarkable rearrangement which occurs in the spectra of diphenyl heterocyclic systems (55,61) has been studied with the aid of extensive deuterium labelling.

The potential of negative-ion mass spectrometry is clearly demonstrated in paper 65. The positive-ion spectra of compounds containing the $-\overset{+}{N}=O^{-}$ group are complicated by pronounced rearrangement fragments. The corresponding negative-ion spectra are simple, diagnostic, contain pronounced molecular anions, and are devoid of rearrangement peaks.

CONTENTS

Section B. SOLVENT-EFFECTS IN N.M.R. SPECTROSCOPY

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1050. *Colouring Matters of the Aphididae. Part XXV.*[1] *A Comparison of Aphid Constituents with those of their Host Plants. A Glyceride of Sorbic Acid*

By J. H. Bowie and D. W. Cameron

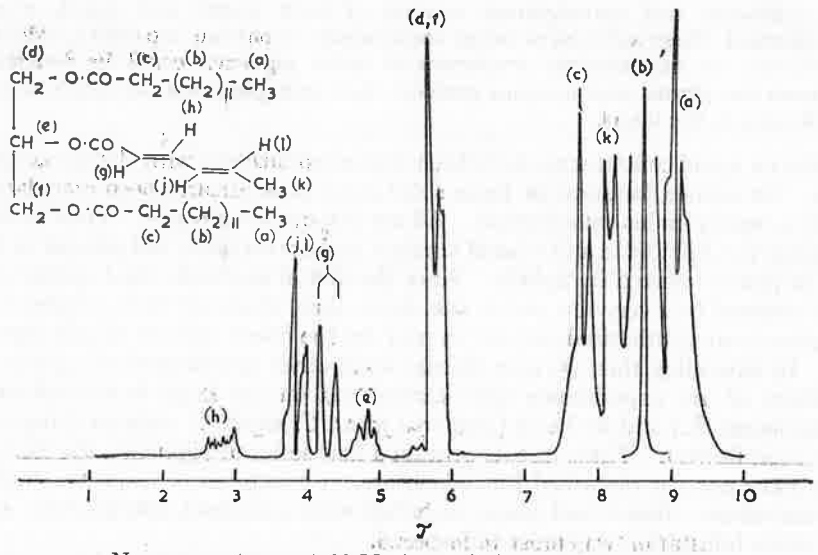
The aphid *Dactynotus jaceae* (L.) contains 2-*trans*,*trans*-sorbo-1,3-dimyristin as its major triglyceride (65%). This compound is the first glyceride of sorbic acid to be reported. Hydrolysis of other aphid glycerides also gives sorbic acid, in quantities that vary with species, together with saturated fatty acids, chiefly myristic. The fat of four *Centaurea* species, hosts of *D. jaceae*, is quite different, however, and contains no sorbic acid. A similar difference between this aphid and its hosts is observed in flavonoid content. The latter contain substantial amounts of the flavonol jaceidin and related compounds, whilst in the former no flavonoids were found. However, the amino-acid and carbohydrate content of both plants and insect were identical, these substances being constituents of phloem sap which aphids ingest: no naphthalenic precursors of aphid pigments could be isolated from the plants, and it seems probable that such pigments are synthesised *de novo* in the insect.

Our studies on aphid constituents have been concerned hitherto with the chemistry of their pigments. Structures for some of these substances have already been elucidated,[2] while others are currently under examination. All are polycyclic quinones. They have not been found outside the Aphididae and related families, and are certainly not present in detectable amounts in plants infested by aphids. Since the diet of any individual species of aphid is generally confined to a very few plants this shows that, whatever their detailed biogenesis, aphid pigments are synthesised, at least in part, by the insect and not simply ingested from its host. In extending this, we now discuss some other constituents of aphids and their hosts. Many of our experiments were carried out on the large bronze-coloured aphid *Dactynotus jaceae* (L.) and its hosts *Centaurea jacea*, *C. nigra*, *C. scabiosa* (knapweed), and *C. cyanus* (cornflower). These insects contain a new series of pigments, the dactynaphins, which we have not yet described but which are, in a number of respects, similar to the aphins themselves. Insect and plant materials were examined concurrently in the late summer, when infestation was most widespread.

In common with many other aphid species, *D. jaceae* yields a fat-soluble fraction, which solidifies readily and amounts to 5—6% of the live insect weight.* An extensive previous survey [3] of aphid fatty acids showed them to be mixtures of saturated compounds, with myristic acid as the chief component. However, the crude extract of *D. jaceae* absorbed strongly at 261 mμ. This is characteristic neither of unbranched conjugated dienes, αβ-unsaturated esters, nor of previously reported aphid constituents. Thin-layer chromatography on silicic acid showed the presence of two major components, one of which was identical with trimyristin. Conversion into methyl esters and vapour-phase chromatography confirmed that myristic acid (87%) was indeed the only saturated acid present to any significant extent. It could be isolated, by chromatography of the free acids on silicic acid, together with a second component (13%) having $\lambda_{max.}$ 254 mμ, readily identified as *trans*,*trans*-sorbic acid. This, surprisingly, appears to have been reported from only one other natural source [4] (in 1859), never as a glyceride, and never from the animal kingdom. The unsaponified fat was fractionated on silicic acid and yielded the two major components trimyristin (35%) and a new triglyceride (65%) having $\lambda_{max.}$ 261 mμ. This is formulated as a *trans*,*trans*-sorbodimyristin since, on saponification, it yields the two acids in correct

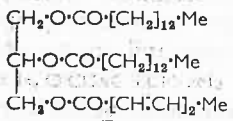
* From *Eriosoma lanigerum* (Hausmann), the woolly apple aphid, which surrounds itself with an extensive waxy secretion, the corresponding yield was 34%.

proportion and in agreement with its nuclear magnetic resonance (n.m.r.) spectrum (Figure). This was virtually a summation of the spectra of *trans,trans*-sorbic acid in the 0—10 τ region, and of trimyristin, and its peaks were of the correct relative intensities. It remains to distinguish between the two possible structures (I) and (II) for this new substance. Both were synthesised. Reaction of 1,2-*O*-isopropylideneglycerol with *trans,trans*-sorboyl chloride, followed by removal of the protecting groups [5] gave 1-sorbin as an oil. Treatment with two moles of myristoyl chloride then gave compound (I). The symmetrical analogue (II), was prepared by treatment of 1,3-dimyristin [5,6] with an excess of *trans,trans*-sorboyl chloride in pyridine under forcing conditions. Both compounds (I) and (II) had virtually the same melting point as the natural glyceride which was, however, identified as (II) by mixed melting point and infrared and n.m.r. spectra. This structure supports the observation, made on vegetable fats, that, in mixed saturated–unsaturated triglycerides, an unsaturated residue generally esterifies the central hydroxyl of the glyceryl unit.[7a] Other short-chain acids of natural fats include butyric from milk fats [7b] and isovaleric from marine sources, *e.g.*, dolphins.[7c] Sorbic acid could of course be

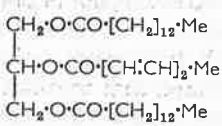


N.m.r. spectrum at 60 Mc./sec. of glyceride (II) in CCl_4

derived *via* the normal fatty-acid pathway from acetate–malonate units. Alternatively, as it is a six-carbon acid only two oxidation levels lower than glucose, which *D. jaceae* ingests (see below) in relatively enormous quantities, the possibility of direct conversion cannot be excluded.



(I)



(II)

Other species of aphids also were examined (Table 1). In only one other case, *Tuberolachnus salignus*, was a substantial quantity of sorbic acid observed. All species, however, contained material having $\lambda_{max.}$ 261 mμ, formulated, by analogy, as sorboyl glycerides. Methyl sorbate was, in such cases, detected by vapour-phase chromatography. Most of these aphid species were not examined in Strong's more extensive survey,[3] but the general trend of his results and ours is the same. Myristic acid is the most commonly occurring fatty acid, together with smaller amounts of palmitic and lauric acids in that order, and

traces of other even-numbered saturated acids. One elution peak, assigned by Strong to an iso C_6-ester, has a relative retention time similar to methyl sorbate and, in view of our results, the possibility of this latter assignment being more correct must be considered.

TABLE 1

Aphid triglycerides (% of fatty acid in saponification mixture)

Aphid	$E^{1\%}_{1\,cm}$ (261 mμ) †	Sorbic † (0·50)	C_6 (0·36)	C_8 (1·08)	C_{10} (2·07)	C_{12} (4·09)	C_{14} (7·32)	C_{16} (20·40)	C_{18} (41·40)
Dactynotus jaceae	252	13	tr.	—	—	tr.	87	—	—
Tuberolachnus salignus	311	16	tr.	tr.	—	3	81	—	—
Eriosoma lanigerum	41	2	tr.	tr.	tr.	17	70	11	tr.
Aphis sambuci	26	1	tr.	—	—	tr.	50	49	—
Aphis fabae.....	24	1	tr.	—	—	tr.	51	48	—
Macrosiphoniella artemisiae	26	1	2	—	—	5	63	29	—
Brevicoryne brassicae.....	14	tr.	1	—	—	2	57	40	—

* Pure compound (II) has $E^{1\%}_{1\,cm}$ (261 mμ) 402. † Retention times (min. sec.) are given in parentheses.

The only other discrepancy is that, in contrast to Strong, we did not observe any C_9-acid in the hydrolysates. This may be due to the fact that his results were obtained on total fats whereas our experiments were carried out on solids obtained by low-temperature crystallisation which may well have largely eliminated trace or liquid components from the mixture. Finally, it is noteworthy that, in the species we examined, a high content of scorbic acid appears to be associated with a low content of palmitic acid, and *vice versa*. The reason for this, and whether any relationship exists between fat and pigment content of aphids is, at present, a matter for speculation.

A similar examination of the fats from the four *Centaurea* species mentioned earlier as hosts of *D. jaceae*, showed compositions almost identical with one another but substantially different from that of the insect. Thin-layer chromatography on silicic acid indicated at least fifteen different components. Column chromatography showed that 65% of the fat-soluble components were triglycerides. Conversion into methyl esters and vapour-phase chromatography indicated the presence of myristate (4·5%), palmitate (32·5%), stearate (63%), and no sorbate.

Centaurea species also contain flavonoid material in considerable quantity. Previous workers have reported the presence of glycosides of the following flavonols; apigenin (III; $R^1 = R^2 = R^3 = H$, $R^4 = OH$) from flowers of *C. scabiosa* and *C. cyanus*,[8] scutellarein (III; $R^1 = R^3 = H$, $R^2 = R^4 = OH$) from leaves of *C. scabiosa*,[9] and jaceidin (III; $R^1 = R^2 = R^3 = OMe$, $R^4 = OH$) from leaves and stems of *C. jacea*.[10] In the course of examining these species for precursors of aphid pigments, we observed these compounds not only as glycosides but also as the free aglycones in yields given in Table 2. The

TABLE 2

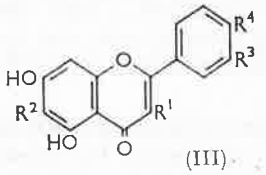
Percentages of flavonoids in Centaurea species

Plant	Jaceidin		Apigenin		Scutellarein	
	Aglycone	Glycoside	Aglycone	Glycoside	Aglycone	Glycoside
C. scabiosa (stems)	0·5	0·3	—	—	—	0·1
C. jacea (whole plant)	0·2	0·2	0·1	tr.	0·05	tr.
C. nigra (leaves)	6·1	0·5	—	—	0·2	—
(stems)	0·1	0·4	—	—	—	—
(flowers)	0·4	0·2	0·2	0·3	—	—
C. cyanus (whole plant) ...	—	tr.	0·12	0·29	—	—

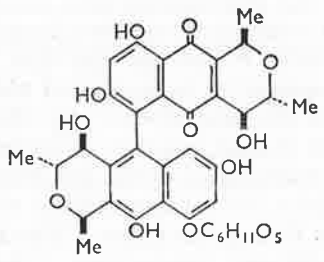
aglycone jaceidin does not appear to have been found in Nature before, although the possibility that it arose in our experiments by enzymic hydrolysis during preparation of plant material for extraction cannot be excluded. All species were extracted at the same time of year. The high yield of jaceidin in the leaves of *C. nigra* is particularly noteworthy. We had

begun structural work on this substance before becoming aware of the recently reported studies of Farkas *et al.*,[10] which established structure (III; $R^1 = R^2 = R^3 = OMe$, $R^4 = OH$) both by degradation and synthesis. In addition to compounds described therein, jaceidin was readily converted into a triacetate, whilst spectroscopic methods gave support to its structure. For example, its ultraviolet spectrum [11] undergoes a bathochromic shift on addition of sodium acetate, indicative of a free 7-hydroxy-group, and a further bathochromic shift in sodium ethoxide, indicating a free 4′-hydroxy-group. Aluminium chloride also causes a bathochromic shift consistent with a 5-hydroxy-group, while boric acid has no effect, indicating the absence of *o*-dihydroxy-groups. The nuclear magnetic resonance spectra of a number of derivatives showed a single peak, due to the C-8 proton, which ranged from 2·71 to 3·44 τ depending on substituents, together with an ABX or ABC system due to the protons of ring C. As has been found previously with other flavonoid systems,[12] the C-5 proton is observed at higher field (2·80—2·97 τ) than either the 2′- or 6′-protons, both of which in this system are found at 2·22—2·32 τ.

A careful examination of *D. jaceae*, on the other hand, showed no detectable quantity of flavonoid material to be present. Such compounds, therefore, would seem not to be ingested by the insect. (The possibility of rapid and complete degradation following ingestion cannot be excluded but seems less likely.)



(III)



(IV)

Examination of the amino-acid content of *D. jaceae* by two-dimensional paper chromatography showed the presence of aspartic acid, glycine, serine, alanine, tyrosine, valine, phenylalanine, leucine, and several peptides which on hydrolysis produce no further amino-acids. An identical mixture was obtained from stems of the host *C. scabiosa*. Similarly, examination for free sugars has shown glucose to be the only detectable constituent of both plant and stored insect, both before and after hydrolysis. Traces of other components were also detected, but in very much smaller amount. A similar correspondence in amino-acid and sugar content has previously been observed between honeydew from the aphid *Tuberolachnus salignus* and its host *Salix acutifolia*.[13] Such compounds were shown to be major constituents of phloem sap, which aphids ingest, and their presence unchanged in the insect therefore can readily be explained. Fats and flavonoids are elaborated elsewhere in the plant and are not transferred to the aphid.

These observations have an indirect bearing on the origin of aphid pigments. These, *e.g.*, protoaphin-*fb* (IV), are alike in consisting of two naphthalenic units coupled together. Our studies on the dactynaphins, from *D. jaceae*, suggest that they are no exceptions to this. We have seen that pigments must be synthesised, at least in part, by the insect, since they are not found in host plants. Our attempts to obtain direct evidence on this point by tracer experiments on the bean aphid *Aphis fabae* were unsuccessful, because of experimental difficulties in rearing this insect on synthetic media.[14] The structure of protoaphin-*fb* (IV), which *A. fabae* produces, is consistent with biogenesis by the acetate–malonate pathway. What is not obvious is whether this occurs *de novo* in the insect, or whether colourless precursors, *e.g.*, naphthalenic systems, are ingested from the plant and subsequently coupled. Indirect evidence on this comes from the results on *D. jaceae* and its hosts. Any such naphthalenic precursor of aphid pigments would be expected to occur in the phloem sap. None to date have been observed. Similarly, a careful examin-

ation of whole plants of the four *Centaurea* species and of *Sambucus nigra*, the host of *A. sambuci*, did not indicate the presence of any obvious aphin precursor. This does not, of course, exclude the possibility that such substances are present in small amounts, but we regard this as less likely, and conclude that aphid pigments are probably synthesised in their entirety within the insects. Certain compounds, *e.g.*, isoeleutherin,[15] which structurally resemble possible precursors, have indeed been isolated from the plant kingdom, but their occurrence is restricted to a few species. We would have expected any true precursor to be widespread, because of the large range of plants that act as hosts to pigment-containing aphids.

Experimental

Unless otherwise stated, infrared (i.r.) spectra were measured in KBr discs and ultraviolet (u.v.) spectra in 95% ethanol. Nuclear magnetic resonance (n.m.r.) spectra were measured at 60 Mc./sec. with tetramethylsilane as internal reference. Light petroleum refers to the fraction having b. p. 40—60°. Silicic acid refers to Mallinckrodt 2847.

Examination of Triglycerides.—Insects were macerated with light petroleum, the extracts evaporated to 10 ml., allowed to solidify, and filtered, and the solid was redissolved in warm methanol (1 g. in 20 ml.), and the solution refrigerated at −15° for several weeks. This method gave a 95% (or better) recovery of crystalline triglycerides, all of which had melting ranges 45—50° and $\lambda_{max.}$ 261 mμ. Each (1 g.) was refluxed for 3·5 hr. with a mixture of methanol (10 ml.) and aqueous sodium hydroxide (10 ml.; 2·5N). Methanol was then removed by evaporation, the mixture acidified with hydrochloric acid, diluted with water to 100 ml., and extracted with ether (2 × 25 ml.). The extracts were dried, and treated with an excess of diazomethane in ether. The solution of esters was then concentrated to 10 ml. and subjected to routine vapour-phase chromatography, with results shown in Table 1. Samples (1 μl.) were applied to an F and M 720 instrument having a 6-in. column of 20% silicone rubber Se 30 on 60—80P, flow rate 120 ml./min., oven temperature 175°, bridge current 150 mA.

Triglycerides from D. jaceae.—(*a*) Crude triglycerides (3·41 g.) were isolated and saponified as above. The resulting acids were dissolved in hexane (20 ml.) and chromatographed on a column of silicic acid (40 × 5 cm.). Elution with hexane–ether (4 : 1) gave myristic acid (2·52 g.), which after crystallisation from methanol formed colourless needles, m. p. 63—64°, undepressed in admixture with authentic material, having identical i.r. spectrum and, after methylation, identical behaviour on vapour-phase chromatography. Elution with hexane–ether (1 : 1) gave *trans,trans*-sorbic acid (405 mg.), which was recrystallised from the same solvent, as colourless blades, m. p. 133—134°, and identified by comparison with authentic material as for myristic acid above; $\lambda_{max.}$ 254 mμ (log ε 4·45).

(*b*) Crude triglyceride (0·75 g.) was chromatographed on silicic acid (40 × 5 cm.) in hexane–ether (15 : 1), collecting fractions of 25 ml. Fractions 22—30 were recrystallised from methanol (5 ml.), crystallisation being allowed to proceed at −15° for several weeks. This yielded trimyristin (232 mg.), m. p. 33—34° (lit. γ-form, 33°), and had i.r. and n.m.r. spectra identical with authentic material. Conversion into its methyl ester gave a product identical on vapour-phase chromatography with methyl myristate.

Fractions 34—51 on recrystallisation from methanol (5 ml.) gave colourless rosettes of 2-trans,trans-*sorbo*-1,3-*dimyristin* (II), m. p. 54—54·5° [Found: C, 73·5; H, 10·8%; *M* (thermistor drop method), 596. $C_{37}H_{66}O_6$ requires C, 73·3; H, 11·0%; *M*, 607]; $\lambda_{max.}$ 261 mμ (log ε 4·38); $\nu_{max.}$ 1736 (saturated ester C=O), 1719 (αβ-unsaturated ester C=O), 1648, 1620 cm.$^{-1}$ (C=C); n.m.r. in CCl_4 (Figure 2·77 (1H, multiplet, =CHCO), 3·77, 3·90, 4·14, 4·40 (3H, multiplets, =CH), 4·77 (1H, multiplet, R_2CH–O), 5·75, 5·84 (4H, multiplet, RCH_2–O), 7·70 (4H, multiplet, $-CH_2CO-$), 8·12 (3H, doublet J = 4·5 c/sec., MeCH:), 8·72 (44H, composite peak, $-CH_2-$), 9·12 τ (6H, muliplet, $MeCH_2-$). This substance was identified by m. p. and mixed m. p. with synthetic material (below). U.v., i.r., and n.m.r. spectra for the two compounds were identical.

1-*Sorbo*-2,3-*dimyristin* (I).—To a mixture of 1,2-*O*-isopropylideneglycerol (8 g.) and pyridine (5 ml.) was added *trans,trans*-sorboyl chloride (8 g.), the temperature being maintained at 0° during the addition. The mixture was stirred at room temperature for 2 hr., then treated with ice-cold dilute sulphuric acid (60 ml. of 0·5N) and ether (100 ml.). The ethereal extract was further washed with ice-cold sulphuric acid (2 × 60 ml.), saturated aqueous sodium hydrogen

carbonate (3 × 50 ml.), and water (50 ml.), then dried and evaporated. The resulting oil was dissolved in ether (70 ml.) and concentrated hydrochloric acid was slowly added, the temperature being kept below 5°. After 30 min. the mixture was diluted with water (300 ml.) and extracted with ether (3 × 200 ml.). The extract was washed with water, dried, and evaporated to yield 1-sorbin (11·0 g., 95%) as a colourless liquid. Without purification this was mixed with quinoline (15 g.), and myristoyl chloride (30 g.) was added at 0° with stirring. After 1 hr. at room temperature the mixture was worked up as above to yield 1-trans,trans-*sorbo*-2,3-*dimyristin* (I) (33·8 g., 94%), which after recrystallisation from methanol formed colourless rosettes, m. p. 55·5—56°, mixed m. p. with the glyceride from *D. jaceae* 48—51° (Found: C, 73·6; H, 10·9. $C_{37}H_{66}O_6$ requires C, 73·3; H, 11·0%); $\lambda_{max.}$ 261 mμ (log ε 4·44); $\nu_{max.}$ 1732, 1708, 1645, 1619 cm.$^{-1}$; n.m.r. in CCl_4 virtually identical with that of compound (II) except for reproducible differences of a " fingerprint " kind.

2-trans,trans-*Sorbo*-1,3-*dimyristin*.—1,3-Dimyristin was synthesised by literature methods.[5,6] It had m. p. 64—65° (lit., 63·8—64·4°). To a solution of 1,3-dimyristin (2 g.) in pyridine (10 ml.) was added *trans,trans*-sorboyl chloride (3 g.) at room temperature, the mixture stirred for 24 hr., and then heated at 50° for 30 min. It was then worked up in the usual way and chromatographed in hexane on silicic acid (40 × 5 cm.), fractions of 50 ml. being collected. Concentration of fractions 19—32 gave 2-*trans,trans*-sorbo-1,3-dimyristin (1·2 g., 45%), which crystallised from methanol as colourless rosettes, m. p. 54—54·5°, identified with the natural glyceride as described previously.

Identification of Amino-acids and Sugars.—A sample of *D. jaceae* was extracted with acetone and then with water. The aqueous extract was examined for amino-acids by two-dimensional chromatography on Whatman 3 MM paper. Systems used were n-butanol–acetic acid–water (4 : 1 : 5, top layer); phenol–water–ammonia (77·5 : 21·5 : 1). Spots were developed with ninhydrin. The extract was also examined for sugars by chromatography in the first system above, spraying with aniline hydrogen phthalate.

Examination of the four *Centaurea* species for amino-acids and sugars was carried out as above, on aqueous extracts obtained as indicated below.

Extraction of Centaurea *species*.—Air-dried plants were extracted (Soxhlet) successively with light petroleum, acetone, and water with the exception of *C. scabiosa*, which was extracted in the reverse order. The petroleum extract of all species was shown to contain the same components by thin-layer chromatography on silicic acid, developing with hexane–ether–acetic acid (95 : 4 : 1), spraying the dried chromatogram with sulphuric acid (50%), and heating at 250° for 15 min.

Stems of *C. scabiosa* (2 kg.) gave a petroleum-soluble fraction (25 g.), which after chromatography on silicic acid (18 × 0·75 cm.) gave a triglyceride fraction (16·2 g.). Alkaline hydrolysis and methylation as before gave a mixture which was shown by vapour-phase chromatography to contain myristate (4·5%), palmitate (32·5%), and stearate (63%) esters.

A similar examination of the complete petroleum-solubles from *C. nigra* leaves showed the presence of myristate (19%), palmitate (21%), and stearate (53%) esters.

Solutions of the acetone-soluble components from the plants were evaporated and extracted with benzene, and the resulting extract was chromatographed on silicic acid, eluting with chloroform–methanol mixtures. Flavonols were eluted in the order jaceidin, apigenin, scutellarein. The last two were identified and determined by their absorption spectra. The benzene-insoluble material from the acetone extract was combined with the aqueous extract and refluxed with hydrochloric acid (2·5N) for 30 min. The aglycones so formed were extracted into chloroform and analysed by chromatography as above.

Jaceidin.—Crude jaceidin from chromatography above, was crystallised from acetone–water (1 : 1) as yellow needles, m. p. 99—100°. From benzene it formed rosettes of needles, m. p. 111—112°, and after drying at 125°/10^{-6} mm. had m. p. 165—166°; on standing, it absorbed water, giving m. p. 99—100°. It was identical in i.r. and u.v. spectra with an authentic specimen (lit., m. p. 127—135°) [10] (Found: C, 57·3; H, 4·7. Calc. for $C_{18}H_{16}O_8,H_2O$: C, 57·1; H, 4·8%); $\lambda_{max.}$ (*a*) in ethanol 255, 270, 354 mμ (log ε 4·25, 4·19, 4·35) (*b*) in ethanol containing sodium ethoxide (0·1N) 275, 330, 400 mμ (log ε 4·11, 4·17, 4·34), (*c*) in ethanol containing aluminium chloride (5%) 245, 265, 385 mμ (log ε 4·00, 4·21, 4·31), (*d*) in ethanol saturated with sodium acetate 273, 316, 374 mμ (log ε 4·33, 4·09, 4·22), (*e*) in ethanol saturated with sodium acetate and boric acid 273, 316, 374 mμ (log ε 4·33, 4·08, 4·22); $\nu_{max.}$ 3582, 3280 (OH), 1655, 1610, 1600, 1578, 1558, 1516 cm.$^{-1}$ (C=O, C=C); n.m.r. in $CDCl_3$, −2·86 (C_5–OH), 2·30 ($C_{2'}$–H),

2·32 ($C_{6'}$–H), 2·95 ($C_{5'}$–H), 3·41 (C_8–H), 5·96, 6·03, 6·14 τ (OMe), (J_{ortho} = 9·0 c/sec., J_{meta} = 2·0 c./sec., J_{para} = 0).

Jaceidin dimethyl ether, m. p. 158—159°, identified by comparison with an authentic specimen,[10] had n.m.r. in $CDCl_3$, −3·05 (C_5–OH), 2·22 ($C_{6'}$–H), 2·27 ($C_{2'}$–H), 2·97 ($C_{5'}$–H), 3·44 (C_8–H), 6·00, 6·05, 6·14 τ (OMe, 3 : 1 : 1), J as above.

Jaceidin trimethyl ether, m. p. 142—143°, identified by comparison with an authentic specimen,[10] had n.m.r. in $CDCl_3$ 2·24 ($C_{6'}$–H), 2·25 ($C_{2'}$–H), 2·96 ($C_{5'}$–H), 3·21 (C_8–H), 5·98, 6·04, 6·08. 6·12 τ (OMe, 1 : 3 : 1 : 1), J as above.

Jaceidin Triacetate.—Jaceidin (504 mg.) was acetylated with acetic anhydride (5 ml.) and pyridine (1 ml.) at room temperature for 4 hr. The resulting *triacetate* (650 mg.) was crystallised from ethanol as pale yellow needles, m. p. 159—160° (Found: C, 59·5; H, 4·8. $C_{24}H_{22}O_{11}$ requires C, 59·3; H, 4·5%); $\lambda_{max.}$ 248, 325 mμ (log ε 4·29, 4·17); $\nu_{max.}$ 1769, 1645 cm.$^{-1}$; n.m.r. in $CDCl_3$ *ca.* 2·30 ($C_{2'}$–H, $C_{6'}$–H), *ca.* 2·80 ($C_{5'}$–H), 2·71 (C_8–H), 6·08, 6·11, 6·17 (OMe), 7·56, 7·61, 7·63 τ (OAc).

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Colouring Matters of the Aphididae. Part XXXII.[1,2] Rhodoaphin

By J. H. Bowie and D. W. Cameron, University Chemical Laboratory, Cambridge

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Colouring Matters of the Aphididae. Part XXXII.[1,2] Rhodoaphin

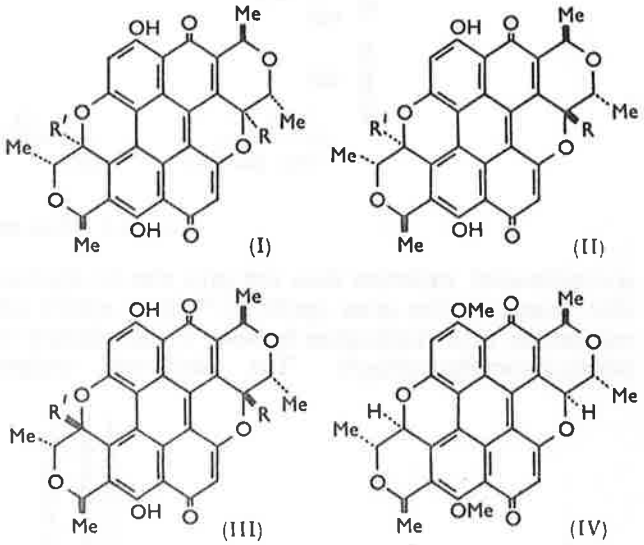
By J. H. Bowie and D. W. Cameron, University Chemical Laboratory, Cambridge

Re-investigation of the pigments of *Hormaphis* (*Hamamelistes*) species shows that rhodoaphin-*be* is a dihydroxyerythroaphin, structurally analogous to dihydroxyerythroaphin-*fb* but stereochemically belonging to the -*tt* series. This follows both from spectroscopic considerations, and its epimerisation to dihydroxyerythroaphin-*fb* on mild treatment with acid and is consistent with its behaviour on catalytic hydrogenolysis. Rhodoaphin is the first derivative of erythroaphin-*tt* to be obtained from natural sources. Its precursor, heteroaphin, which occurs in the living insect is consistent, spectroscopically, with being a simple rhodoaphin glycoside but has not been examined in detail. The triglyceride content of *H. betulina* is similar to that of other aphids. Myristate is the major component together with smaller amounts of palmitate and laurate.

FOLLOWING the completion of structural studies on the aphins [3-5] our attention has lately been directed towards groups of non-aphin pigments. Some of these have been found co-occurring with aphins; others are apparently restricted to specific aphid genera, although the possibility that they may be more widely distributed cannot be excluded, in view of the geographical limitations that usually attended collection of material. A preliminary examination [1] has shown that aphid pigments, in general, possess considerable structural and presumably biogenetic similarities. They invariably occur in the insects as glycosides, hydrolysis of which leads to C_{30} aglycones, usually polycyclic quinones. All can be visualised as being formed by oxidative coupling of two C_{15} units related to 1,3,8-trihydroxynaphthalene, processes for which close parallels *in vitro* have recently been found.[2,6,7]

In this Paper we are concerned with pigments, found in the genus *Hormaphis* (previously known as *Hamamelistes*). These were first described in detail by MacDonald,[8] who obtained them from the British *H. betulina* (Horvath) (previously *H. betulae*), which parasitises birch, and from the North American *H. spinosus* (Shimer). Such insects contained, instead of protoaphin,[3] a red glycosidic heteroaphin, which, on post mortem enzymic action or on treatment with acid, gave a red fluorescent aglycone, rhodoaphin. The suffixes -*be* or -*sp*, derived from the species of origin, were appended to their names where appropriate, following the system employed in naming aphins, *e.g.*, erythroaphins -*fb*, -*sl*, and -*tt* (I, II, III; R = R′ = H, respectively).

Re-examination of this problem in the light of recent work on the aphins [3-5] has been in progress for some years but has been impeded by the scarcity of *H. betulina* in the Cambridge area. *Hormaphis spp.* are members of the Thelaxidae, no other examples of which have been examined chemically. Their distinctive appearance has been described previously.[8] The nature of their pigments reflects this taxonomic difference from aphin-containing species. They were found in successive seasons on only the same few trees and they colonised relatively slowly. The work described in this Paper was carried out on material collected during each of the years 1963—1965. This led to a combined yield of 16 g. of insects from which *ca.* 50 mg. of rhodoaphin-*be* could be obtained.



MacDonald [8] concluded that rhodoaphins were dihydroxyerythroaphins having a further oxygen atom with some other function. This was consistent with their partition behaviour and light absorption. The latter was identical in character with that of dihydroxyerythroaphin-*fb* (I; R = R′ = OH) [9] having a slight bathochromic shift (1—2 mμ). Like dihydroxyerythroaphin-*fb*, rhodoaphin underwent reduction with zinc and acetic acid. Whereas the former compound yielded erythroaphin-*fb* under these conditions,[4] the latter gave an erythroaphin-like product which could not be obtained homogeneous. Our results are in considerable agreement with these observations and conclusions. In addition, the mass spectrum of rhodo-

[1] Part XXXI, J. H. Bowie, D. W. Cameron, J. A. Findlay, and J. A. K. Quartey, *Nature*, 1966, **210**, 395.
[2] Part XXX, G. M. Blackburn, D. W. Cameron, and H. W.-S. Chan, *J. Chem. Soc.* (*C*), 1966, 1836.
[3] D. W. Cameron, R. I. T. Cromartie, D. G. I. Kingston, and Lord Todd, *J. Chem. Soc.*, 1964, 51.
[4] D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, P. M. Scott, and Lord Todd, *J. Chem. Soc.*, 1964, 62.
[5] A. Calderbank, D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, E. Haslam, D. G. I. Kingston, Lord Todd, and J. C. Watkins, *J. Chem. Soc.*, 1964, 80.
[6] D. W. Cameron and H. W.-S. Chan, *J. Chem. Soc.* (*C*), 1966, 1825.
[7] D. W. Cameron, H. W.-S. Chan, and E. M. Hildyard, *J. Chem. Soc.* (*C*), 1966, 1832.
[8] S. F. MacDonald, *J. Chem. Soc.*, 1954, 2378.
[9] B. R. Brown, A. W. Johnson, S. F. MacDonald, J. R. Quayle, and A. R. Todd, *J. Chem. Soc.*, 1952, 4928.

aphin-*be* (Figure 1) contains a molecular ion (*m/e* 542), shown by exact mass measurement to correspond to $C_{30}H_{22}O_{10}^{+}$. This is isomeric with dihydroxyerythroaphin-*fb* (I; R = R′ = OH). Moreover, the spectra of these two compounds are identical in the region above *m/e* 500. (Below this point the spectrum of the *-fb* derivative, which has been analysed previously,[10] is non-reproducible due to thermal decomposition which accompanies fragmentation as a consequence of its extreme involatility.) Since in aphin derivatives, absent from specimens analysed immediately after drying, *i.e.*, the true molecular formula is $C_{30}H_{22}O_{10}$. The alternative possibility, that the extra oxygen is covalently bound to the system in such a way as to be eliminated rapidly from the molecular ion in the mass spectrometer is inconsistent with nuclear magnetic resonance (n.m.r.) studies described below.

The n.m.r. spectrum of rhodoaphin-*be* (Figure 2) is remarkably simple and permits the assignment of every proton in the molecule, hydroxyls apart. Each of the

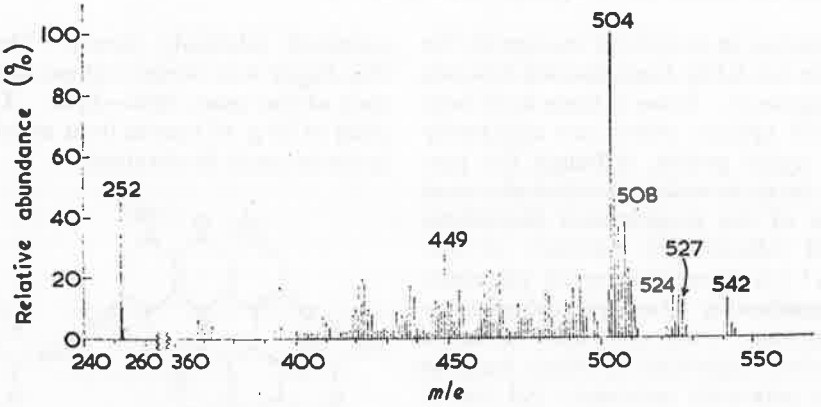


FIGURE 1 Mass spectrum of rhodoaphin-*be*

stereochemical variation does not give rise to appreciable change in the mass spectrum,[10] these results are compatible with rhodoaphin-*be* being a stereoisomer of dihydroxyerythroaphin-*fb*. The additional oxygen

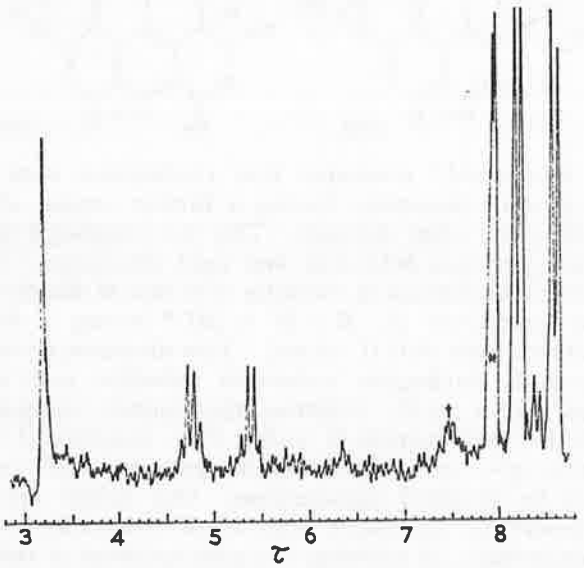


FIGURE 2 Nuclear magnetic resonance spectrum (100 Mc./sec.) of rhodoaphin-*be* in perdeuterioacetone at 80° (* resonances due to partially deuterated solvent; † resonances due to water or hydroxyl groups).

atom, found by MacDonald[8] and confirmed by us on combustion analysis of crystalline rhodoaphin, is doublets in the methyl region interacts with a quartet due to methine protons (J = 6·5 c./sec.). These signals and that in the aromatic region are all observed at chemical shifts appropriate to aphin derivatives.[11] If it is now assumed, as will subsequently be confirmed, that rhodoaphins indeed contain the same carbon skeleton as erythroaphins, the only possible formulation consistent with this spectrum is a stereochemical modification of dihydroxyerythroaphin-*fb* (I; R = R′ = OH), which also is in agreement with the mass spectroscopic evidence above. (The n.m.r. spectrum of the *-fb* isomer was not available for comparison with Figure 2, because of this compound's relative insolubility.) The simplicity of Figure 2 suggests that the rhodoaphin chromophore is symmetrically substituted, unlike derivatives of erythroaphin-*sl*, for example, whose spectra[11] are complex. Irradiation of the low-field quartet caused collapse of the low-field doublet to a singlet and *vice versa*. This is consistent with assignments previously made for erythroaphin derivatives,[11] namely, that resonances due to the benzylic ·$CHCH_3$ occur at lower field both in the methine and methyl regions of the spectrum.

Preliminary experiments to confirm these conclusions chemically began with the reductive conversion of rhodoaphin-*be* into an erythroaphin, as reported by MacDonald.[8] On the basis of the structure discussed above, this reaction would involve removal of hydroxyl groups which are not only benzylic but which also form part of hemiketal systems, a process described

[10] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.* (*B*), 1966, 684.

[11] D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, P. M. Scott, N. Sheppard, and Lord Todd, *J. Chem. Soc.*, 1964, 90.

previously for other erythroaphin derivatives.[9] Catalytic hydrogenolysis proved the most satisfactory method of reduction. Applied first to dihydroxyerythroaphin-*fb* (I; R = R′ = OH) as a model compound, it gave an erythroaphin fraction consisting mainly of the *-fb* isomer (I; R = R′ = H), accompanied by a minor component, chromatographically indistinguishable from erythroaphin-*sl* (II; R = R′ = H), *i.e.*, hydrogenolysis proceeded largely, but not completely, with retention of configuration, an observation of importance to the work that follows. Additionally, in view of the fact that erythroaphin-*tt* (III; R = R′ = H) cannot be detected chromatographically in the presence of appreciably larger quantities of the *-sl* isomer, because of the closeness of their R_f values, it is probable that the former compound is also present in the reduction product. (Reaction conditions were such that epimerisation of erythroaphins, once formed, would not have occurred.) When rhodoaphin-*be* was hydrogenolysed under the same conditions, an erythroaphin fraction, as shown by its light absorption following elution, was also obtained. This was resolved chromatographically into components indistinguishable from those obtained above. In this case, however, the major product was clearly erythroaphin-*tt* (III; R = R′ = H). A smaller amount of the *-fb* isomer (I; R = R′ = H) was readily detected and of the *-sl* (II; R = R′ = H) inferred from considerations already discussed. This suggests that rhodoaphin-*be* is a dihydroxyerythroaphin-*tt* (III; R = R′ = OH), which is, of course, consistent with spectroscopic observations. However, the reductions described in this paragraph were accompanied by formation of appreciable amounts of by-products of low R_f, so that the overall yield of erythroaphins was low. In view of the small quantity of rhodoaphin available and the successful epimerisation described below, no attempt was made to confirm these tentative conclusions on a preparative scale. It is worth noting, however, in agreement with the structure proposed, that mild reduction of rhodoaphin-*be* gave a fraction whose light absorption was identical with that of hydroxyerythroaphin-*fb* (I; R = OH, R′ = H).[9] This consisted of two chromatographically distinguishable components, one present in much larger quantity than the other. Assuming, as implied above, that hydrogenolysis proceeds largely but not completely with retention of configuration, the major product would correspond to compound (III; R = OH, R′ = H) and the minor to compound (II; R = OH, R′ = H).

Confirmation of structure (III; R = R′ = OH) for rhodoaphin-*be* was provided by acid-catalysed epimerisation. Although both rhodoaphin and dihydroxyerythroaphin-*fb* (I; R = R′ = OH) are decomposed by strong mineral acids, brief treatment of the former with trifluoroacetic acid resulted in conversion to the latter in 70% yield, the product being identified by comparison with an authentic specimen.[9] The greater thermodynamic stability of derivatives of erythroaphin-*fb* over *-tt* or *-sl* is attested to by many reactions.[4,12] The acid-catalysed epimerisation of rhodoaphin at the hemiketal group is therefore unexceptional. Comparison of the product with authentic material would also, in theory, enable determination of the absolute configuration of rhodoaphin-*be*. However, the sparing solubility of dihydroxyerythroaphin-*fb*, coupled with its strong absorption over much of the spectral range has not yet permitted this to be done.

In the course of this work, a quantity of *H. spinosus*, collected in Ontario, was made available to us through the courtesy of the Canadian Department of Forestry. This yielded rhodoaphin-*sp*, which proved to be spectroscopically and chromatographically identical with rhodoaphin-*be* confirming MacDonald's conclusion[8]. Rhodoaphin is the first derivative of erythroaphin-*tt* to be obtained from natural sources. Compounds of the *-tt* series have previously been made by photochemical isomerisation of *-fb* or *-sl* derivatives.[12] Rhodoaphin, however, is not accessible by synthetic methods at present available; introduction of hydroxyl groups into positions R and R′ in compound (III) by such methods leads exclusively to products of the *-fb* series.[4]

The non-availability of *H. betulina* during 1966 has precluded a systematic investigation of heteroaphin to date. Small scale experiments have, however, confirmed MacDonald's data for this compound.[8] It is worth noting that its visible spectrum ($\lambda_{max.}$ 443, 515, 551 mμ) is similar in character to that of the erythroaphin dimethyl ether (IV)[13] ($\lambda_{max.}$ 435, 498, 531 mμ) and bathochromically shifted. This is consistent with heteroaphin being a simple glycoside of rhodoaphin, the glycosidic linkage being at one of the hydroxyl groups *peri* to the quinone carbonyls. Confirmation of this hypothesis will be sought when further supplies of insects become available.

In addition to these studies, the composition of the triglyceride fraction of *H. betulina* has also been determined. Saponification, methylation, and gas chromatographic analysis of the resulting esters showed that myristic (74%) was the major fatty acid component together with lesser amounts of palmitic (23%) and lauric acids (3%). This is consistent with results obtained from the fats of other species of aphids.[14] It is noteworthy that no glyceride of sorbic acid was detected, despite its presence in substantial amounts in *Tuberolachnus salignus* and *Dactynotus jaceae*.[15] There is no obvious correlation between pigmentation and fat content in aphid species that have been examined up to the present.

EXPERIMENTAL

The mass spectrum was determined by the direct insertion technique using an A.E.I. MS9 mass spectrometer

[12] D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, B. S. Joshi, P. M. Scott, and Lord Todd, *J. Chem. Soc.*, 1964, 72.
[13] D. W. Cameron and H. W.-S. Chan, unpublished results.
[14] F. E. Strong, *Hilgardia*, 1963, **34**, no. 2, 43.
[15] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.*, 1965, 5651.

operating at 70 ev, with a source temperature of 375°. Exact mass measurement was carried out at a resolution of 15,000 (10% valley definition) to an accuracy of 10 p.p.m.; heptacosafluorotributylamine was used to provide reference mass. The term " light absorption " refers to u.v. and visible absorption spectra.

Collection of H. betulina.—Birch leaves infested with *H. betulina* were collected and the insects gently dislodged with a small metal spatula. For extraction of heteroaphin they were worked up on the same day; for rhodoaphin, they could be stored for at least a year at −15° without appreciable loss of pigment.

Rhodoaphin-be.—Specimens of *H. betulina* (5·5 g.) were ground in phosphate buffer at pH 6·0 (*ca.* 10 ml.) in a large centrifuge tube and the mixture set aside for 30 min. at room temperature, to permit enzymic action. Acetone was then added to dissolve the pigment, the mixture centrifuged and the intensely red supernatant liquors collected. A further portion of acetone was added to complete the extraction; it is important that the total volume be kept to a minimum. Sufficient ether and water were then added to form a two-phase system. The red ether-solubles were collected, washed well with water, dried (Na_2SO_4), and solvent evaporated to dryness under reduced pressure. The residue was chromatographed on silica gel (B.D.H., for chromatography). Benzene eluted a pale yellow fraction containing fats and a trace of carotene hydrocarbon, as evidenced by its light absorption. Benzene–ether mixtures yielded rhodoaphin-*be* as the only other component. After evaporation of solvent, the residue was warmed gently with light petroleum (b. p. 40—60°) to remove residual fat and then recrystallised from ethanol to form deep red crystals (14 mg.). Re-chromatography of the mother-liquors followed by recrystallisation gave a further 2 mg. A sample was dried at 80° for 4 hr. and analysed immediately (Found: C, 66·7; H, 4·3. $C_{30}H_{22}O_{10}$ requires C, 66·4; H, 4·1%), $\lambda_{max.}$ (in $CHCl_3$) 428, 454, 491, 527, 568·5, 596 mμ (log ε 4·37, 4·50, 3·79, 4·02, 4·16, 3·70); $\nu_{max.}$ (KBr disc, OH region obscured) 1630, 1570, 1480, 1448, 1420, 1375, 1288, 1250, 1230, 1172, 1155, 1110, 1070, 1040, 972, 940, 880, 850, 830, 760, 728 cm.$^{-1}$; n.m.r. (Figure 2), singlet at τ 3·18, quartets at 4·75, 5·39, doublets at 8·21, 8·60. Chromatography on Whatman 3MM paper in the system chloroform saturated with water: R_f values for rhodoaphin and dihydroxyerythroaphin-*fb ca.*, 0·9 and 0·5, respectively.

Similar extraction of *H. spinosus* gave rhodoaphin-*sp*, indistinguishable from the product above in light absorption and R_f value.

Heteroaphin-be.—Live *H. betulina* (1000 insects, 350 mg.) were macerated with acetone (5 ml.). This inactivates the enzyme responsible for the conversion of heteroaphin to rhodoaphin. The extract was separated by centrifuging and sufficient ether and water added to form a two-phase system. The red water-soluble fraction, containing most of the colour was repeatedly extracted with ether to remove acetone completely and then extracted with n-butanol. The extract was washed with water and solvent evaporated *in vacuo* to yield crude heteroaphin. Redissolved in ethanol, the product had, $\lambda_{max.}$ 443, 515, 551 mμ. The spectrum indicated no detectable quantity of aphinin [1] to be present, though this remains to be confirmed when larger amounts of material become available. On brief warming with dilute hydrochloric acid, heteroaphin was converted into rhodoaphin,[8] identified by light absorption.

Triglycerides.—The fat-containing fractions from the extraction of *H. betulina* were combined, solvent evaporated and the residue re-chromatographed on silica gel. The product showed only end absorption in the u.v. It was analysed [15] and shown to contain myristate (74%), palmitate (23%), and laurate (3%).

Dihydroxyerythroaphin-fb.—A solution of rhodoaphin-*be* (2·5 mg.) in trifluoroacetic acid (3 drops) was left at room temperature for 30 min. (Prolonged standing or evaporation of solvent caused extensive decomposition.) Dilution with light petroleum (b. p. 40—60°) gave a deep red precipitate. This was filtered off, washed with petroleum and recrystallised from ethanol to yield dihydroxyerythroaphin-*fb* (1·8 mg.), identical with an authentic specimen in light absorption, i.r. spectrum and R_f value.

Hydrogenolysis of Rhodoaphin-be.—(*a*) A solution of rhodoaphin-*be* (0·5 mg.) in dioxan in the absence of light and the presence of Adams catalyst (2 mg.) was hydrogenated for 3 hr. The mixture was filtered and the filtrate, containing products in the hydroquinone form, set aside to reoxidise (3 hr.) at room temperature. Solvent was evaporated at 40° and the product chromatographed on Whatman 3MM paper in benzene–light petroleum (2 : 1). The main product was eluted with chloroform. Its light absorption ($\lambda_{max.}$ 424, 450, 488, 524, 565, 591 mμ) corresponded to that of hydroxyerythroaphin-*fb*.[9] Rechromatographed, it gave two incompletely resolved spots, the major having R_f 0·40, the minor, R_f 0·28. Hydroxyerythroaphin-*fb*, erythroaphins, and dihydroxyerythroaphin-*fb* in this system had R_f values 0·25, > 0·9, < 0·1, respectively.

(*b*) A minor product of the reduction above was an erythroaphin fraction. This was obtained in larger quantity when hydrogenolysis of rhodoaphin-*be* was carried out for 12 hr. No hydroxyerythroaphin was obtained under these conditions but appreciable amounts of by-product having R_f 0 were present. The erythroaphin fraction was eluted with chloroform ($\lambda_{max.}$ 421, 447, 486, 542, 563, 588·5 mμ). On re-chromatography in light petroleum–benzene (4 : 1) it was resolved into a major and a minor component having R_f values 0·40 and 0·12, respectively, indistinguishable from erythroaphins-*tt*, and -*fb*. The spot due to the former component tailed, obscuring the region where erythroaphin-*sl* (R_f = 0·34) would have been observed.

Dihydroxyerythroaphin-*fb* was reduced similarly, with results reported in the Discussion.

We are grateful to Professor Lord Todd for encouragement. We thank H. L. G. Stroyan for identification of insects, and S. F. MacDonald and the Canadian Department of Forestry for a supply of *H. spinosus*. The award of an I.C.I. Fellowship (to J. H. B.) is gratefully acknowledged.

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Colouring Matters of the Aphididae. Part XXXIII [1]. Dactynaphins

By J. H. Bowie and D. W. Cameron, University Chemical Laboratory, Cambridge

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Colouring Matters of the Aphididae. Part XXXIII [1]. Dactynaphins

By J. H. Bowie and D. W. Cameron, University Chemical Laboratory, Cambridge

Aphids of several *Dactynotus* species contain a distinct group of pigments termed dactynaphins. Like the aphins, these substances occur in living insects as glycosides. Following the insects' death, they are enzymically converted into a mixture of red and yellow aglycones consisting chiefly of the isomeric, interconvertible rhodo- and xantho-dactynaphins-*jc*-1, $C_{30}H_{28}O_{12}$. Smaller quantities of a similar pair of isomers, rhodo- and xantho-dactynaphins-*jc*-2, $C_{30}H_{28}O_{11}$, are also present. Preliminary investigation shows these compounds to be structurally related to the aphins.

In addition to the aphins [2-4] and *Hormaphis* pigments,[1] a third group of aphid constituents has also been examined. Its occurrence has so far been confined to seven *Dactynotus* species,[5] for which reason its members have collectively been termed dactynaphins. The term "aphin" is restricted to the proto-, xantho-, chryso-, and erythro-aphins.

In the earliest survey [6,7] carried out in this laboratory, it was observed that the bronze coloured *D. jaceae* L. and *D. cirsii* L. contained non-aphin pigments. These insects parasitise knapweed and thistles, respectively, during the late summer. (The latter species is notable in that individuals frequently attain relatively large dimensions, *e.g.*, a weight of 8 mg.; this is ten to twenty times as heavy as an average specimen of *Aphis fabae*.) Aphins were absent from *D. cirsii* but a small amount of protoaphin was reported from *D. jaceae*.[6] Re-examination of this species in the present investigation has resulted in the isolation of erythroaphin-*fb*.[3] While this might indeed arise from protoaphin in the living insect, the yield was so minute (*ca.*, 0·001%) that it is more likely to be due to contamination of the sample with a small quantity of aphin-containing insects. Contamination to this extent is unavoidable in large-scale collection; on the small scale, homogeneity of species can usually be guaranteed. Both species were collected during 1963—1965 inclusive and a total of *ca.* 300 g. of insects obtained. Most of the structural work described here was carried out with *D. jaceae*, the more readily available of the two. There was, however, no detectable difference in pigment composition between it and *D. cirsii* as indicated by spectroscopic and chromatographic comparison of their respective extracts. Different subspecies of *D. jaceae* or specimens of the same subspecies obtained from different host plants were also chemically indistinguishable. Those examined were *D. jaceae sensu stricto*, from both the knapweed *Centaurea nigra* or cornflower *C. cyanus*, and *D. jaceae* subsp. *henrichi* Börner from the greater knapweed *C. scabiosa*.

In common with other aphid pigments, dactynaphins occur in the living insects as glycosides. Following the insects' death or on treatment with acid, these substances are converted into a mixture of aglycones a process which also has been effected enzymically *in vitro* using aqueous extracts of *D. jaceae*. Full discussion of the glycosidic precursors is reserved for a subsequent Paper.[8] The aglycones were obtained in crude form as a pink coloured solid in yield of up to 0·75% of the live insect weight. Thin-layer chromatography (t.l.c.) showed this to be a mixture consisting essentially of two red and two yellow components. These compounds, as will be seen, are inter-related. Accordingly, they are termed rhodo-dactynaphin-*jc*-1 and -*jc*-2, and xanthodactynaphin-*jc*-1 and -*jc*-2, respectively, each of them derived from a glycosidic protodactynaphin.[8] Following a system of nomenclature employed for the aphins,[6] a suffix-*jc*, indicative of species of origin is included. However, the occurrence of dactynaphins differs from that of aphins in one significant respect, necessitating the further differentiation implicit in the suffixes -1 and -2. In the former group, minor structural or stereochemical variation, such as distinguishes aphins-*fb* from aphins-*sl*, is not characteristic of a particular species of origin but has been found in all *Dactynotus* species examined, *i.e.*, whereas *A. fabae* and *Tuberolachnus salignus* contain only aphins-*fb* and -*sl*, respectively, *D. jaceae* and the other *Dactynotus* species contain both dactynaphins-*jc*-1 and -*jc*-2.

Following the initial observations on *D. jaceae* and *D. cirsii* further work [9] at Cambridge showed that *D. tanaceti* L. and *D. taraxaci* Kaltenbach also contained non-aphin pigments qualitatively similar to dactynaphins but not examined in detail. More recently while the present work was in progress, Weiss and Altland [10] reported some preliminary observations on two red substances derived from the North American species *D. rudbeckiae* Fitch and *D. ambrosiae* Thomas. Through the courtesy of Dr. U. Weiss, we were enabled to compare extracts of these and of a further North American species, *D. nigrotuberculatus* Thomas Olive, with that of *D. jaceae*. All contained the same four components, evidenced by chromatographic behaviour. Weiss and Altland's

[1] Part XXXII, J. H. Bowie and D. W. Cameron, preceding Paper.
[2] D. W. Cameron, R. I. T. Cromartie, P. M. Scott, and Lord Todd, *J. Chem. Soc.*, 1964, 51.
[3] D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, P. M. Scott, and Lord Todd, *J. Chem. Soc.*, 1964, 62.
[4] A. Calderbank, D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, E. Haslam, D. G. I. Kingston, Lord Todd, and J. C. Watkins, *J. Chem. Soc.*, 1964, 80.
[5] J. H. Bowie, D. W. Cameron, J. A. Findlay, and J. A. K. Quartey, *Nature*, 1966, **210**, 395.
[6] H. Duewell, J. P. E. Human, A. W. Johnson, S. F. MacDonald, and A. R. Todd, *Nature*, 1948, **162**, 739.
[7] H. Duewell, J. P. E. Human, A. W. Johnson, S. F. MacDonald, and A. R. Todd, *J. Chem. Soc.*, 1950, 3304.
[8] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.* (C), 1967, 720.
[9] B. S. Joshi, Ph.D. Thesis, Cambridge (1955).
[10] U. Weiss and H. W. Altland, *Nature*, 1965, **207**, 1295.

rhododactynaphins A and B were indistinguishable from rhododactynaphins-*jc*-2 and -*jc*-1, respectively. In the case of the -*jc*-2 (A) isomers, chromatographic comparison was supplemented by the identity of their i.r. and nuclear magnetic resonance (n.m.r.) spectra.

Despite the fact that dactynaphins are susceptible to base-catalysed decomposition, samples of *D. jaceae* can be stored at −15° for a year without appreciable loss of pigments or change in composition. Preparative-scale extraction followed by chromatography on silicic acid led to the isolation of three of the four compounds already described. A mixture of rhodo- and xantho-dactynaphins-*jc*-2 was eluted first. The latter being present in small quantity, could not be separated from the mixture; it has not been obtained in greater than spectroscopic amounts. Further elution then yielded a mixture of the two -*jc*-1 isomers. They were obtained in *ca.* ten times the amount of the -*jc*-2, and in quantity sufficient for their separation by fractional crystallisation. All these compounds form solvates readily, as evidenced both by elemental analysis and n.m.r. spectroscopy. Rhododactynaphin-*jc*-1, was shown thereby to solvate stoicheiometrically with 1 mole of chloroform or of benzene. In the former case, solvent could not completely be removed even on prolonged drying. Exact mass measurements of their respective molecular ions established molecular formulæ as $C_{30}H_{28}O_{12}$ for both rhodo- and xantho-dactynaphins-*jc*-1 and $C_{30}H_{28}O_{11}$ for rhododactynaphin-*jc*-2. Xantho-dactynaphin-*jc*-2, in the light of experiments described in the following paragraphs, was assumed to be isomeric with the corresponding rhodo-compound.

A close structural relationship between the -*jc*-1 and -*jc*-2 series is shown by their general similarity both in physical properties and simple chemical behaviour. Both rhodo-compounds were presumed to be quinones because on mild catalytic hydrogenation they were converted into pale yellow quinols which readily underwent atmospheric reoxidation. The xantho-compounds on the other hand were stable to mild reduction. All four compounds were relatively stable in solution in organic solvents. In aqueous buffer of pH 6, however, rhododactynaphin-*jc*-1 underwent a striking reaction. (Solutions of dactynaphins at this pH are readily prepared, since these substances contain relatively acidic hydroxyl groups.) Within ½ hr. at room temperature the colour of the solution, initially red, had faded and a nearly quantitative conversion to xanthodactyn-aphin-*jc*-1 resulted. The two compounds being isomeric, it is concluded that in aqueous but not organic media, equilibration between them proceeds at an appreciable rate and favours the xantho-compound. Changing the pH of the solution does not substantially affect the rate of equilibration or position of equilibrium. (However, the extent of variation possible is limited by the compounds' instability at extremes of pH.) The process was unaffected by being carried out in the absence of light. The reverse conversion was most readily demonstrated chromatographically. Xanthodactynaphin-*jc*-1 was adsorbed on thin-layer plates coated with Kieselgel, left to stand for 8 hr. at room temperature and the chromatograms then developed. Substantial conversion to the analogous rhodo-compound resulted. Chromatograms developed immediately after adsorption, on the other hand, contained only starting material. The nature of this adsorptive isomerisation was not examined in detail. It serves, however, to confirm the close relationship between rhodo- and xantho-compounds, a factor that has facilitated structural work. Since separation of the two isomers by fractional crystallisation is of limited efficiency, the conversion of mixtures

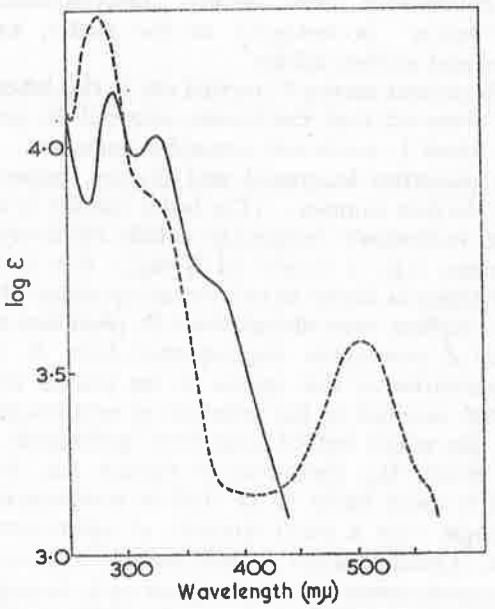


FIGURE 1 Absorption spectra of rhododactynaphin-*jc*-1 (– – – –) and xanthodactynaphin-*jc*-1 (——) in ethanol

of the two into essentially pure xantho-compounds is useful also in allowing considerable economy of material.

Similar interconversions have been observed involving the two dactynaphins-*jc*-2, although in this case the rate in either direction is noticeably lower than for the -*jc*-1 series.

The similarity in molecular formulæ between dactyn-aphin aglycones and the fluorescent aphins [3,4] together with the fact that both series of compounds are derived from glycosidic precursors suggests that they may possess structural elements in common. This is supported by spectroscopic evidence. The n.m.r. spectra [11] of dactynaphins are resolvable in the methyl region into four partly overlapping doublets as in an unsymmetrical aphin derivative.[12] In the i.r. their most prominent peaks are due to hydroxyl and H-bonded carbonyl groups. The ultraviolet–visible absorption spectra of the -*jc*-1 series are shown in Figure 1; those of the two -*jc*-2 isomers are indistinguishable from them.

[11] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.* (*C*), following Paper.

[12] D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, P. M. Scott, N. Sheppard, and Lord Todd, *J. Chem.*, 1964, 90.

Experiments aimed at structure elucidation were directed first towards the rhodo-compounds in the hope of establishing the chromophore responsible for their absorption at 504 mμ. Reductive acetylation of rhododactynaphin-*jc*-1 was carried out on a spectroscopic scale. It led to a pale yellow product whose highest absorption band was an inflection at *ca.* 340 mμ. This suggests that the rhodo-compounds are not polycyclic quinones and that chromophorically they are no more complex than naphthalene derivatives. Few oxygenated naphthaquinones absorb above 500 mμ. Notable exceptions are those which contain two oxygen substituents *peri* to the quinone carbonyl groups, *e.g.*, naphthazarin or

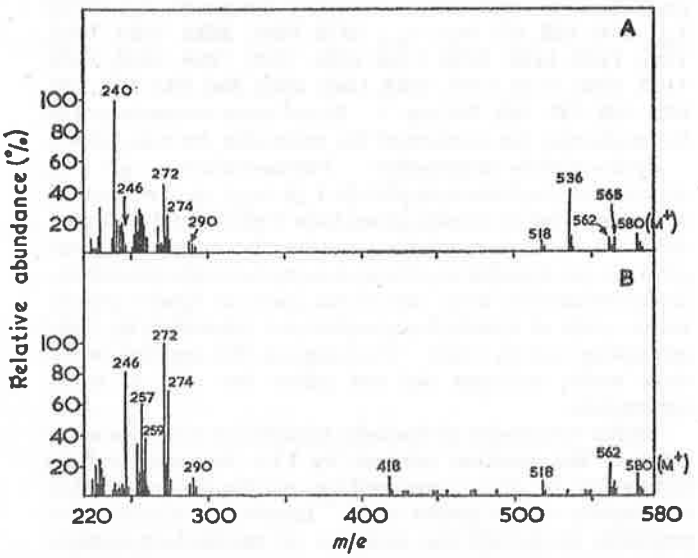
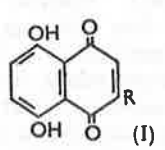


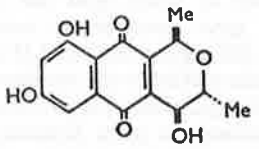
FIGURE 2 Mass spectra of (A) xanthodactynaphin-*jc*-1 and (B) rhododactynaphin-*jc*-1

naphthopurpurin (I; R = H, R = OH, respectively). Both these substances in organic solvents absorb in the same spectral region as rhododactynaphins but with some differences in the character of the absorption band. However, the visible spectrum of rhododactynaphin-*jc*-1 boroacetate, prepared at room temperature, was almost identical with that of naphthazarin. In sulphuric acid, on the other hand, the dactynaphin was spectroscopically almost indistinguishable from naphthopurpurin. While these observations do not permit detailed definition of the chromophore, they nevertheless suggest strongly that it is closely related to system (I; R = oxygen substituent). This has amply been confirmed by subsequent experiments.

The mass spectra of the two dactynaphins-*jc*-1 (Figure 2) are (apart from a few additional peaks in the spectrum of the xantho-compound), very similar, consistent with the ease with which they undergo chemical interconversion. Certain fragmentations of the molecular ion are evident, characteristic of systems containing the aphin side chain, *e.g.*, loss of methyl, water, and acetaldehyde. The most interesting fragmentation process in both spectra, however, leads to an ion having *m/e* 290, *i.e.*, half the molecular weight. Its subsequent fragmentation pattern is strikingly similar to that of the molecular ion (*m/e* 290) derived from the quinone A (II),[2,13] a degradation product of protoaphin-*fb*. (This excludes differences of intensity unexceptional in spectra



(I)



(II)

obtained at high temperatures using the direct insertion technique.) The simplest explanation of this process is that the dactynaphins-*jc*-1, although chromophorically related to the system (I), undergo mass spectroscopic cleavage to give an ion derived from quinone A (II) or stereoisomers thereof, as the only product, *i.e.*, the dactynaphins are, formally, dimerisation products of this system. Confirmation of this conclusion and determination of the mode of dimerisation follow from the degradative experiments described in the following Paper.

EXPERIMENTAL

Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Light petroleum refers to the fraction having b. p. 40—60°, silicic acid to Mallinckrodt 2847. Unless otherwise stated, i.r. spectra were measured as KBr discs and u.v. and visible spectra in 95% ethanol. The term " light absorption " refers to u.v. and visible spectra. N.m.r. spectra were measured at 100 Mc./sec. in per deuterioacetone (unless otherwise specified) using tetramethylsilane as internal reference. Mass spectra were determined on an A.E.I. MS 9 mass spectrometer, by the direct insertion technique, with the source temperature at approximately 300°. Exact mass measurements were carried out at a resolution of 15,000 (10% valley definition), using heptacosafluorotributylamine to provide reference masses, and were correct to 10 p.p.m.

Isolation of Dactynaphin Aglycones.—Specimens of *D. jaceae* (150 g., stored at −15° for 3 months) were macerated in citrate–phosphate buffer of pH 6·5 (500 ml.) and set aside for 1 hr. at room temperature. The mixture was centrifuged, the supernatant liquors kept to one side (see below) and the solid residue extracted with acetone (2 × 250 ml.). The combined extracts were kept at −15° for 30 min. to deposit triglyceride [14] (4·5 g.). The filtrate was then evaporated to dryness *in vacuo*. The oily residue was redissolved in warm methanol (250 ml.) and after cooling at −15°, deposited further triglyceride (3·6 g.). Evaporation of solvent *in vacuo* then gave an oil which was redissolved in chloroform (solution A).

The original buffer extract of *D. jaceae* (above) was extracted with chloroform (500 ml.) and the resulting emulsion centrifuged to separate the phases. The tan-coloured aqueous liquors were used as the source of enzyme in subsequent experiments. The chloroform extract was combined with solution A, washed with water (100 ml.),

[13] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.* (*B*), 1966, 684.

[14] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.*, 1965, 5651.

dried (Na_2SO_4), and the solvent evaporated under reduced pressure to give a red oil. This was triturated with light petroleum (5 × 10 ml.) to remove a further quantity of triglyceride (2·3 g.). The pink residue (925 mg.) consisted of crude dactynaphins, which were then chromatographed on a column of silicic acid (30 × 5 cm.). Elution with chloroform gave successively residual fats (100 mg.), a brown gum (55 mg.), a red band (1 mg.) identical in R_f value and light absorption with erythroaphin-*fb*, and a further discrete red band containing *rhododactynaphin*-jc-2 (27 mg. after crystallisation from benzene) together with a little xanthodactynaphin-*jc*-2 which was detected by t.l.c. but not isolated. Elution with chloroform–ethanol (50 : 1) gave a mixture of xantho- and rhodo-dactynaphins-*jc*-1 (312 mg.). This was dissolved in hot chloroform (25 ml.), crystallisation proceeded rapidly and the product, *xantho-dactynaphin*-jc-1 (95 mg.), filtered off before the mixture had cooled to room temperature. The filtrate was concentrated successively to 15, 10, and 7 ml. and further crops of the xantho-compound (42 mg.) obtained in the same way. The final filtrate on standing overnight then deposited a mixture of the xantho- and rhodo-compounds (75 mg.). Concentration of the filtrate to 5 ml. followed by slow crystallisation at room temperature during several days gave *rhododactynaphin*-jc-1(33 mg.). Evaporation of the filtrate and crystallisation of the residue from benzene gave a further quantity of the rhodo-compound (68 mg.).

T.l.c. examination of crude de-fatted extracts showed that the four dactynaphins described above were the only components present in significant quantity. A similar observation was made for crude extracts of *D. cirsii*, *D. rudbeckiae*, *D. ambrosiae*, and *D. nigrotuberculatus*. For rhododactynaphin-*jc*-1, -2, xanthodactynaphin-*jc*-1, -2, R_f in chloroform–methanol (19 : 1) 0·45, 0·58, 0·20, 0·22, respectively, in chloroform–methanol (9 : 1) 0·95, 0·95, 0·47, 0·53, respectively.

Rhododactynaphin-jc-2.—Rhododactynaphin-*jc*-2 (27 mg.) was recrystallised from benzene to form rosettes of red needles, darkening at 230—240° and decomposing at 290°. A sample was dried at 50°/10^{-3} mm. for 3 hr. (Found: C, 63·7; H, 5·0. $C_{30}H_{28}O_{11}$ requires C, 63·8; H, 5·0%), $\lambda_{max.}$ 277, 504 mμ (log ε 4·28, 3·57); $\lambda_{infl.}$ 325, 390, 560 mμ (log ε 3·88, 3·24, 3·25). Its light absorption in boroacetic anhydride and in sulphuric acid were indistinguishable from those of rhododactynaphin-*jc*-1 (*q.v.*), $\nu_{max.}$ 3340, 3240, 2968, 2927, 2915, 1616, 1606, 1585, 1541, 1400, 1381, 1363, 1310, 1281, 1258, 1240, 1200, 1163, 1148, 1134, 1112, 1104, 1073, 1060, 1046, 1017, 970, 957, 932, 907, 880, 858, 835, 813, 798, 786, 768, 741, 732, 707 cm.$^{-1}$. Exact mass measurement of the molecular ion confirmed the molecular formula above.

Xanthodactynaphin-jc-1.—Xanthodactynaphin-*jc*-1 (137 mg.) was recrystallised from chloroform as silky yellow needles decomposing at 250°. A sample was dried at 50°/10^{-4} mm. for 3 hr. (Found: C, 62·1; H, 4·9. $C_{30}H_{28}O_{12}$ C, 62·1; H, 4·9%), $\lambda_{max.}$ 232, 289, 326 mμ (log ε 4·23, 4·10, 4·02); $\lambda_{infl.}$ 245, 382 mμ (log ε 4·22, 3·86); in aqueous buffer of pH 5·0 $\lambda_{max.}$ 289, 323 mμ (log ε 4·09, 3·93), $\lambda_{infl.}$ 380 mμ (log ε 3·65); in aqueous 0·2M-disodium hydrogen phosphate $\lambda_{max.}$ 252, 341, 406 mμ (log ε 3·98, 4·21, 3·80); $\nu_{max.}$ 3400, 3000, 2958, 2902, 1665, 1632, 1483, 1460, 1375, 1355, 1333, 1295, 1275, 1200, 1171, 1156, 1126, 1100, 1088, 1068, 1026, 1003, 967, 930, 889, 860, 845, 813, 786, 755, 705 cm.$^{-1}$. Exact mass measurement of the molecular ion confirmed the molecular formula above.

Rhododactynaphin-jc-1.—Rhododactynaphin-*jc*-1 (100 mg.) was recrystallised from chloroform as rosettes of red needles, decomposing at 232° and from benzene as deep red needles decomposing above 300°. The latter sample was dried at 50°/10^{-3} mm. for 3 hr. (Found: C, 62·4; H, 4·7. $C_{30}H_{28}O_{12}$ requires C, 62·1; H, 4·9%), $\lambda_{max.}$ 277, 504 mμ (log ε 4·27, 3·57), $\lambda_{infl.}$ 325, 390, 560 mμ (log ε 3·87, 3·25, 3·28); in sulphuric acid $\lambda_{max.}$ 528, 564 mμ, $\lambda_{infl.}$ 496 mμ; in acetic anhydride $\lambda_{max.}$ 276, 390, 510 mμ, $\lambda_{infl.}$ 325, 570 mμ; in acetic anhydride containing boroacetic anhydride $\lambda_{max.}$ 500, 533, 577 mμ; $\nu_{max.}$ 3316, 2984, 2935, 1629, 1612, 1580, 1495, 1450, 1408, 1384, 1325, 1292, 1268, 1246, 1208, 1175, 1165, 1120, 1077, 1062, 1045, 1015, 960, 935, 900, 886, 858, 819, 793, 753, 710 cm.$^{-1}$. Exact mass measurement of the molecular ion confirmed the molecular formula above.

Rhodo–Xantho-dactynaphin Interconversions.—(*a*) A solution of rhododactynaphin-*jc*-1 (5 mg.) in methanol (1 ml.) was added to citrate–phosphate buffer of pH 6 (5 ml.). After 30 min. at room temperature the orange coloured solution was brought to pH 3 and extracted with chloroform. Recrystallisation from chloroform gave an almost quantitative yield of xanthodactynaphin-*jc*-1 identified by light absorption and R_f value. Carrying out this reaction in the dark under nitrogen did not affect the rate of interconversion.

Similar treatment of rhododactynaphin-*jc*-2 and examination of the reaction mixture by t.l.c. demonstrated its conversion to the corresponding xantho-compound but less rapidly and in poorer yield. Insufficient material was available to permit the isolation of xanthodactynaphin-*jc*-2 on a preparative scale but a sample eluted from a chromatogram possessed light absorption identical with that of the -*jc*-1 isomer.

(*b*) Prolonged standing of xanthodactynaphin-*jc*-1 in buffer as for the rhodo-compound in (*a*), followed by extraction with chloroform (no acidification), yielded a trace of rhododactynaphin-*jc*-1, identified by its light absorption.

(*c*) Xanthodactynaphin-*jc*-1 was applied to a thin-layer chromatogram (Kieselgel), set aside for 8 hr., and then the chromatogram developed. Comparison with reference specimens chromatographed immediately after application, showed a substantial conversion to rhododactynaphin-*jc*-1, verified by the identity of its light absorption, following elution with methanol, with that of authentic material.

A similar reaction was observed for xanthodactynaphin-*jc*-2 but the extent of conversion to the corresponding rhodo-compound was much lower.

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Colouring Matters of the Aphididae. Part XXXIV [1]. Rhodo- and Xantho-dactynaphins

By J. H. Bowie and D. W. Cameron, University Chemical Laboratory, Cambridge

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By J. H. Bowie and D. W. Cameron, University Chemical Laboratory, Cambridge

Rhodo- and xantho-dactynaphins undergo fission to form naphthaquinone derivatives related to the aphin pigments. Two different modes of fission occur, one under reductive conditions, the other on treatment with base. Structures are proposed for xantho- and rhodo-dactynaphins-*jc*-1. They resemble those of the aphins in consisting of two naphthalenic units coupled together but differ from them in that coupling is effected through carbon–oxygen rather than carbon–carbon bonds. The smooth rhodo ⇌ xantho interconversion is explained in terms of the reactivity towards nucleophiles of the 8-position in derivatives of 5,7-dihydroxy-1,4-naphthaquinone. Dactynaphins-*jc*-2 differ from the -*jc*-1 isomers in lacking a benzylic hydroxyl group. They contain the same non-aromatic side chain as the plant pigment, isoeleutherin.

EXPERIMENTS described in the preceding Paper [1] establish that the four dactynaphin aglycones are closely related to one another. Determination of their structures requires the solution of two largely independent problems, the relationship between rhodo- and xantho-dactynaphins and that between the -*jc*-1 and -*jc*-2 series. It is in this order that they are considered here.

Like the protoaphins,[2,3] the two dactynaphins-*jc*-1 undergo reductive fission to give a mixture of naphthalene derivatives. Essentially, the same mixture was obtained from both isomers, apart from small but chromatographically detectable quantities of the respective starting materials. This shows that the dactynaphins-*jc*-1 consist essentially of coupled naphthalenic units, that they possess no readily reducible olefinic double bonds other than may be involved in the fission process itself, and that, despite the substantial chromophoric difference between them, they possess a considerable number of structural elements in common. This last point was already evident from their ease of interconversion and the similarity of their mass spectra.[1] The optimal conditions for reduction involved prolonged catalytic hydrogenolysis in ethanolic solution. Although protoaphin undergoes hydrogenolysis much more rapidly in aqueous than in alcoholic media,[3] the former was considered undesirable in the present case because of the rapidity of the rhodo- ⟶ xantho-dactynaphin conversion that would result. In ethanol, on the other hand, this conversion does not occur to a detectable extent and the results of reduction therefore are structurally meaningful for both dactynaphin isomers. The main product under these conditions, following aerial re-oxidation of quinols to quinones, was the quinone A (I; R = OH, R′ = H) (0·8 mole), previously obtained by reduction of protoaphin-*fb* [2] and also implicated [1] in mass spectroscopic fragmentation of both dactynaphins. It was also obtained when neutral aqueous sodium dithionite was used as the reducing agent. The remaining products of hydrogenolysis were unstable to air. One of them was obtained colourless and crystalline (0·4 mole) but proved too unstable for proper characterisation. However, its u.v. absorption both in neutral media and in the striking hyperchromic shift that accompanied basification, closely resembled that of 2,4-dihydroxyacetophenone (Figures 1 and 2). Moreover, this same compound was also obtained in some-

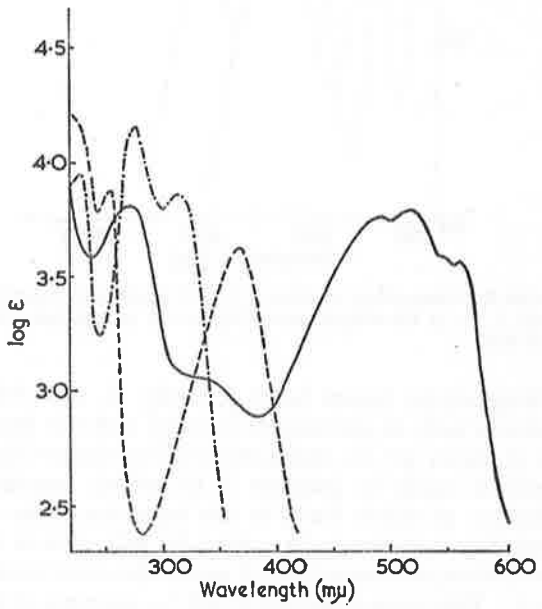


FIGURE 1 Absorption spectra of (——) naphthazarin, (– – –) 2,5-, and (— · — · —) 2,4-dihydroxyacetophenone in ethanol

what lower yield by direct reduction of quinone A under the same prolonged conditions as for the dactynaphins. It was therefore presumed to be the tetralone derivative (II; R = OH or possibly R = H). Oxidative aromatisation leading to a labile 1,3,8-trihydroxynaphthalene system [2] would account for its instability.

Varying the conditions of reduction did not increase the yield of quinone A at the expense of the tetralone beyond the optimal values quoted here. Milder conditions, for example, resulted in the recovery of substantial amounts of unreduced dactynaphins. Since hydrogenation of quinone A must accompany the initial reductive fission, determination of the primary products of hydrogenolysis, essential to the ensuing structural argument, is not straightforward. Taken together, the

[1] Part XXXIII, J. H. Bowie and D. W. Cameron, preceding Paper.
[2] D. W. Cameron, R. I. T. Cromartie, D. G. I. Kingston, and Lord Todd, *J. Chem. Soc.*, 1964, 51.
[3] D. W. Cameron and H. W.-S. Chan, *J. Chem. Soc.* (*C*), 1966, 1825.

two products [(I) and (II)] amount to more than 1 mole per mole of starting material. Both are C_{15} compounds derived from a C_{30} precursor. They therefore represent between them both halves of the dactynaphin molecule. Two alternative processes are possible. Either the

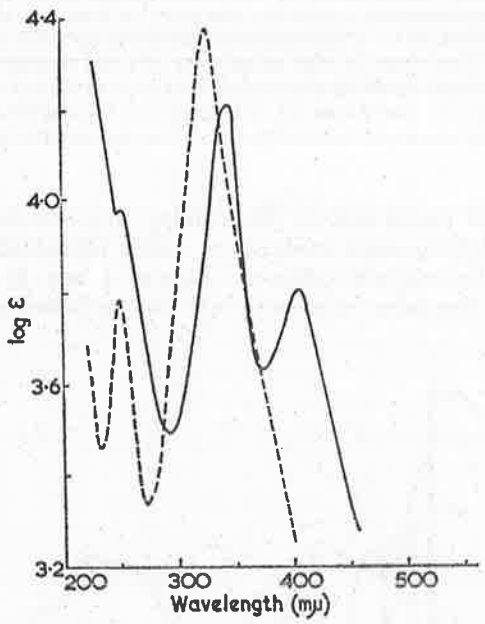
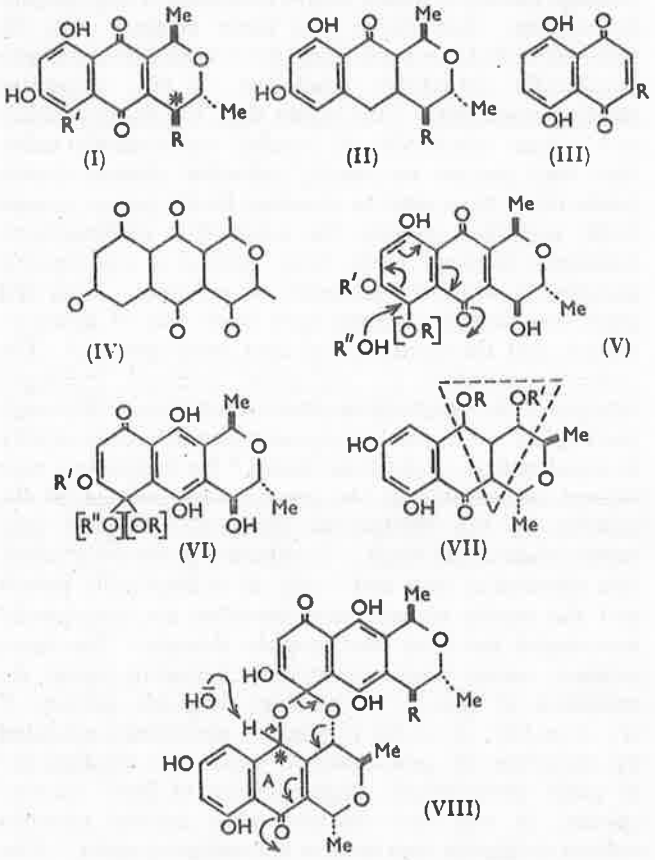


FIGURE 2 Absorption spectra of (——) xanthodactynaphin-*jc*-1 and (– – – –) 2,4-dihydroxyacetophenone in aqueous buffer of pH 8·5

hydrogenolytic fission leads formally to two different products such as quinone A (1 mole) and the tetralone (II) (1 mole) (or to others reductively convertible into them) or solely to quinone A (2 moles), concomitant reduction of which leads to the tetralone. The latter possibility is shown to be correct by reference to reduction of rhododactynaphin-*jc*-2 under the same conditions (*q.v.*). This gives a mixture of *two* C_{15} quinones in a combined yield of 0·9 mole and in approximately equal amounts. Between them these compounds clearly represent both halves of the original molecule which, unlike the *jc*-1 isomer, is formally derivable from two structurally dissimilar units. The stoicheiometry of reductive fission of rhodo- and xantho-dactynaphins-*jc*-1 is therefore assumed to be ($C_{30}H_{28}O_{12} + 2H_2 \longrightarrow 2C_{15}H_{16}O_6$). Quinone A, of course, is present in the reducing medium as the corresponding quinol ($C_{15}H_{16}O_6$). This relationship is important in that it accounts for all carbon and oxygen atoms of the original compounds. In the absence of rearrangement within the naphthalenic units during reduction, a process that is considered unlikely both on general grounds and in view of the physical evidence to be presented, the two dactynaphins-*jc*-1, therefore consist essentially of a combination of two C_{15} units having the same carbon and oxygen skeleton as quinone A (I; R = OH, R′ = H).

An alternative mode of decomposition occurs on treatment with base. When rhododactynaphin-*jc*-1 is dissolved in aqueous sodium hydroxide a blue colour is observed initially and then fades rapidly. This is due presumably to anion formation, cf. the blue anion of naphthazarin (III; R = H), accompanied by isomerisation to xanthodactynaphin, whose anion is yellow. The presence of the latter compound in the solution is readily established spectroscopically and chromatographically. Further standing of the alkaline solution in air gives rise to substantial decomposition resulting in intractable products. Under nitrogen, on the other hand, the solution turns red and controlled decomposition occurs leading, within half an hour at room temperature, to two major products, one red (0·7 mole) and the other orange (0·6 mole), together with a trace of quinone A (I; R = OH, R′ = H) (less than 0·1 mole). Although both major products are acidic the former is appreciably more so, separation being effected by its selective extraction from chloroform by aqueous buffer of pH 6. The molecular formulæ of these two compounds, confirmed by exact mass measurements on their respective molecular ions were $C_{15}H_{14}O_7$ (red) and $C_{15}H_{14}O_5$



(orange), (cf. quinone A, $C_{15}H_{14}O_6$). Since they were obtained in combined yield greater than 1 mole they represent both halves of the dactynaphin molecule. Moreover, summation of their molecular formulæ $C_{30}H_{28}O_{12}$, gives rise to that of dactynaphins-*jc*-1, *i.e.*, the change brought about by base is essentially one of isomerisation.

The light absorption of the red product both in neutral and in basic media was very similar to that of naphthopurpurin (III; R = OH). This chromophore would also account for its considerable acidity, described in the preceding paragraph. Like naphthopurpurin, it underwent reductive C–O bond fission,[4] either on catalytic hydrogenolysis in neutral aqueous solution or on treatment with neutral aqueous sodium dithionite. The product that resulted was spectroscopically and chromatographically identical with quinone A (I; R = OH, R′ = H). These obervations strongly suggest that the red product is the naphthopurpurin derivative (I; R = R′ = OH) (or tautomer thereof). This was confirmed by its nuclear magnetic resonance (n.m.r.) spectrum which in the aromatic –CH region contained only a singlet (τ 3·72) due to one proton. The remainder of the spectrum was consistent with the presence of an aphin side-chain and is described in the Experimental section. Finally, the red product was synthesised. Treatment of quinone A with dimethylamine resulted in ready nucleophilic addition and the formation of an intermediate (I; R = OH, R′ = NMe_2), hydrolysis of which led to the naphthopurpurin derivative (I; R = R′ = OH) identical with the dactynaphin degradation product. (Direct nucleophilic addition of hydroxide ion to quinone A could not be effected, base-catalysed decomposition occurring instead.) The nature of the novel amination process is not discussed at length here since it is the subject of an independent study.[5] It is worth noting, however, as an example of the considerable reactivity of the 8-position of 5,7-dihydroxy-1,4-naphthaquinone derivatives towards nucleophiles or reducing agents. Other examples include the nucleophilic addition of phenols at this centre,[6] and the reductive fission of 8 C–O bonds, as in naphthopurpurins [4] or of certain 8 C–C bonds, as in the protoaphins.[2] Similar reactivity will be invoked in due course to account for the ready interconversion of rhodo- and xanthodactynaphins. The purple product described by Weiss and Altland [7] as arising from the action of ammonia on rhododactynaphin-*jc*-2 is identical in light absorption with the intermediate (I; R = OH, R′ = NMe_2). Although we have not examined this reaction in detail it seems likely that it represents a further example of the reactivity towards nucleophiles described above.

The light absorption of the orange product, $C_{15}H_{14}O_5$ in both neutral and basic media, was virtually identical with that of quinone A. Its n.m.r. spectrum in the aromatic region consisted of two doublets at τ 3·01 and 3·41 (J = 2·5 c./sec.), corresponding to two protons *meta* to one another. It also contained a multiplet (2H) centred at τ 7·5 and two methyl doublets at 8·46, 8·69. The general resemblance of this region of its spectrum to that of the plant product isoeleutherin [8] suggests that the orange product possesses structure (I; R = R′ = H). This was confirmed by synthesis. Reductive removal of the benzylic hydroxyl group from quinone A (I; R = OH, R′ = H) was smoothly effected with alkaline sodium stannite. The product was identical with that derived from the dactynaphins either by treatment with base as already described, or by direct reduction with the alkaline reducing agent above. It was also identified chromatographically from similar reduction of the quinone A′ (I; R = OH, R′ = H, epimeric at C*), related to protoaphin-*sl*.[2] (It has not previously been noted, however, that an epimeric mixture of quinones A and A′ results when either of them is subjected to treatment with aqueous sodium hydroxide under anaerobic conditions.)

The reductive and alkaline degradations of the dactynaphins-*jc*-1 afford two complementary modes of fission. Formal recombination of the fission products to accommodate the properties of the original substances should result in their structures. For this purpose the reductive process is the more useful of the two, since it has been shown to affect both rhodo- and xantho-compounds in the same way. The alkaline reaction, on the the other hand, is carried out under conditions where these two compounds are in equilibrium. It will be shown subsequently that this process is specifically a reaction of xanthodactynaphin-*jc*-1, which is by far the major component of the equilibrium mixture under the conditions of reaction. Both dactynaphins have been shown to be directly related to 2 mols. of quinone A, *i.e.*, they each must be represented by combination of 2 units having the same carbon–oyxgen skeleton (IV). Subsequent paragraphs set out to determine the nature of attachment of these units to one another.

Simple observations on rhododactynaphin-*jc*-1 establish that the chromophore responsible for its absorption maximum at 504 mμ [1] has partial structure (V). [The groups R and R′ are temporarily undefined; the parenthesis indicates an oxygen substituent which must stem from the second unit (IV).] The similarity of its absorption to that of napthazarin and naphthopurpurin (III; R = H and OH, respectively) has already been described,[1] hence two oxygen substituents *peri* to the quinone carbonyl groups are present. One of these substituents is a free hydroxyl group because of the appreciable change in visible absorption that accompanies treatment with boroacetic anhydride. Ionisation of this group presumably accounts for the transient blue colour that accompanies the alkaline degradation already described. The n.mr. spectrum of rhododactynaphin-*jc*-1 (Figure 3) confirms the presence of an aromatic C–H group (singlet, τ 3·38). The methyl region of this spectrum is resolvable into four partly overlapping doublets centred in the region τ 8·3—8·7 and characteristic of an aphin side chain.[8] The presence of a free alcoholic hydroxyl group in the side chain is inferred from the chemistry of rhododactynaphin-*jc*-2, which was in-

[4] J. F. Garden and R. H. Thomson, *J. Chem. Soc.*, 1957, 2483.
[5] H. W.-S. Chan, Ph.D. Thesis, Cambridge, 1966, p. 214.
[6] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.* (*B*), 1966, 684.
[7] U. Weiss and H. W. Altland, *Nature*, 1965, **207**, 1295.
[8] D. W. Cameron, D. G. I. Kingston, N. Sheppard, and Lord Todd, *J. Chem. Soc.*, 1964, 98.

dependently shown to lack this oxygen substituent altogether. Since the properties of the *-jc*-1 and -2 series are qualitatively similar, it is improbable that in the former, linkage between the two units (IV) would be effected through the oxygen in question.

These considerations indicate that the main chromophore (V) of rhododactynaphin-*jc*-1 is linked to the remainder of the molecule solely *via* the oxygen substituents RO–, R'O–. In addition, this chromophore is clearly not substantially extended by absorption due to

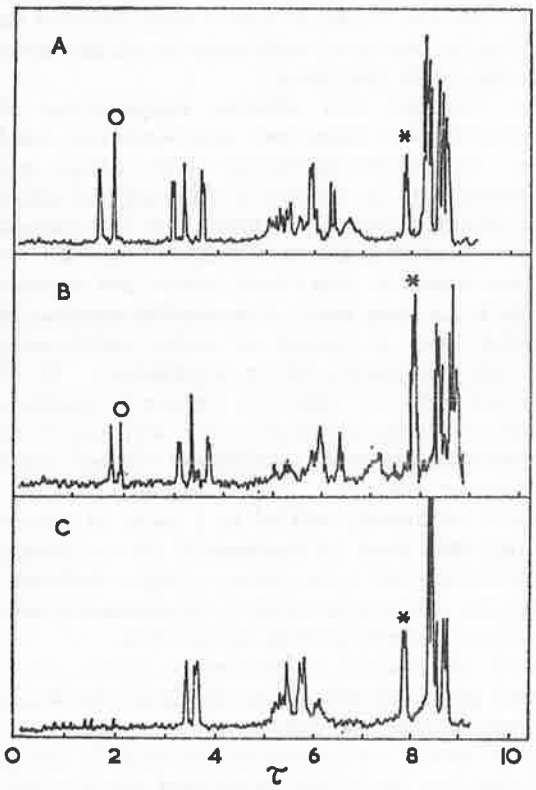


FIGURE 3 N.m.r. spectra at 100 Mc./sec. of (A) rhododactynaphin-*jc*-1, (B) rhododactynaphin-*jc*-2, (C) xanthodactynaphin-*jc*-1 in perdeuterioacetone (* resonances due to solvent, O resonances due to chloroform solvation)

the rest of the molecule, *i.e.*, the spectrum overall can probably be visualised as a summation of the spectra of the two C_{15} units comprising the molecule as a whole. This was suggested initially by the results of reductive acetylation [1] and the general similarity in visible absorption of rhododactynaphin [1] and naphthazarin (III; R = H) (Figure 1) the latter compound being the closest model of system (V) that was available.

Before discussing the remainder of the rhododactynaphin structure it is necessary to consider the corresponding xantho-compound. The isomerisation of the former compound into the latter proceeds under very mild conditions but involves a substantial change in chromophore, including destruction of the quinonoid grouping. Nonetheless, the skeleton of xanthodactynaphin must remain a combination of the two C_{15} units (IV). The points of linkage of chromophore (V) to the remainder of the rhododactynaphin molecule having been determined, structural modification leading to the xantho-compound probably occurs in their vicinity. There is nothing in system (V) to account for its ready isomerisation by means of intermolecular processes under such mild conditions, and it is concluded that some group in the remainder of the molecule is suitably positioned to attack it intramolecularly. The properties of xanthodactynaphin are most satisfactorily accounted for if this takes the form indicated in structure (V) with a hydroxyl group, represented as R''OH, effecting nucleophilic addition at a position already shown to be susceptible to attack. (Other processes also have been considered, *e.g.*, direct attack at the quinonoid carbonyl group; this leads to a structure containing an eight-membered ring, which does not account for the base-catalysed isomerisation described earlier.) The resulting system (VI) would therefore depict the chromophore of the xantho-compound, parentheses as before, representing oxygen substituents derived from the second unit (IV) and the groups R and R' not necessarily the same as in structure (V). Its n.m.r. spectrum (Figure 3) is consistent with this formulation in containing a singlet (τ 3·46) in the aromatic C–H region and being resolvable in the methyl region into four overlapping doublets as for the rhodo-compound. A suitable spectroscopic model for this chromophore is 2,5-dihydroxyacetophenone. [Since the non-aromatic enolic double bond in structure (VI) is in cross-conjugation with this chromophore, its auxochromic effect would be expected to be small.] Its light absorption (Figure 1) is in good agreement with the longest wavelength band in the spectrum of xanthodactynaphin-*jc*-1 (370 mμ).[1] From this and evidence below, it is inferred that the latter spectrum, like that of the rhodo-compound is essentially a summation of its two component C_{15} units.

The remainder of the xanthodactynaphin molecule is readily shown to include the system (VII), the groups within the triangle not being amenable to direct analysis. The absorption spectrum of the xantho-compound contains two peaks at 289 and 326 mμ. At pH 8·5 these are replaced by a single peak at 341 mμ (Figure 2) with considerable enhancement of intensity. [The band at 370 mμ, associated with the chromophore (VI) is also bathochromically shifted as will be discussed subsequently.] Remarkably parallel behaviour was noted earlier in the corresponding spectra of 2,4-dihydroxyacetophenone (Figures 1 and 2). Moreover, the spectrum of xanthodactynaphin in ethanol satisfactorily resembles a summation of those of 2,4- and 2,5-dihydroxyacetophenone, together with a small bathochromic shift. At pH 8·5, ionisation would involve only the non-bonded phenolic hydroxyl group in 2,4-dihydroxyacetophenone; the corresponding group in xanthodactynaphin is therefore free. At pH values high enough to ionise the bonded hydroxyl group in system (VII), base-catalysed decomposition processes occur, complicating the analysis. However, the presence

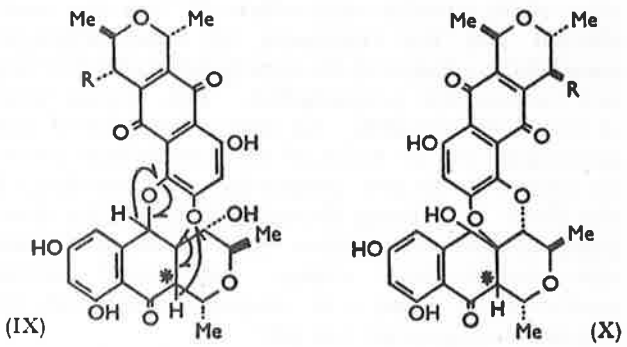
of a free hydroxyl group at this position in the xantho-compound is inferred, because it is on this oxygen that the glucose residue in protodactynaphin-*jc*-1 will independently be shown to reside;[9] no rearrangement occurs following its hydrolysis. The remaining details of structure (VII) follow from n.m.r. spectroscopic considerations (Figure 3). Two highly unsymmetrical doublets of an AB system at τ 3·62 and 3·67 ($J = 2$ c./sec.) represent two aromatic C–H groups *meta* to one another; the methyl region has already been discussed.

The presence of the same unit (VII) in rhododactynaphin-*jc*-1 is also inferred from a pair of doublets (τ 3·17 and 3·85; $J = 2$ c./sec.) in its n.m.r. spectrum (Figure 3) in addition to methyl resonances already mentioned. The presence of a shoulder at 325 mμ in its u.v. absorption spectrum[1] is also consistent with this view, *i.e.*, its spectrum resembles a summation of the spectra of naphthazarin and 2,4-dihydroxyacetophenone. Its absorption at pH 8·5 could not be measured because of the rate at which it underwent conversion to xantho-dactynaphin under these conditions.

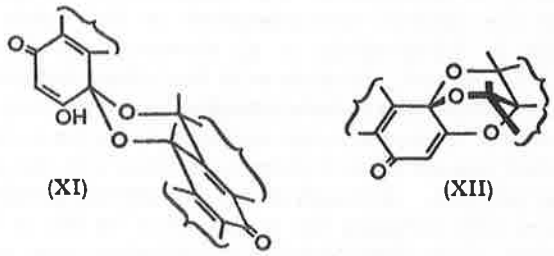
Despite these points of similarity, rhodo- and xantho-dactynaphins-*jc*-1 differ in one important respect. The latter compound is much the more acidic. It is almost completely extracted from chloroform solution by aqueous buffer of pH 6, the former compound remaining in the organic phase under these conditions. The ionisation is accompanied by a bathochromic shift (*ca.* 36 mμ) of the band attributable to the chromophore (VI), whence it is concluded that in this system, R′ = H. (The auxochromic influence of the enolate system becomes significant following ionisation despite its being in cross conjugation with the main chromophore, cf. the relative absorption of 2,5-dihydroxy-1,4-naphthaquinone and its anion.[2]) The spectrum of rhododactynaphin-*jc*-1 at pH 8·5, measured immediately after dissolution, showed no shift in the peak at 504 mμ due to chromophore (V) other than rapid lowering of intensity associated with xanthodactynaphin formation. This means that in this system, R′ ≠ H; a free hydroxyl group at this position would certainly ionise under these conditions with a substantial accompanying bathochromic shift. The most acidic group in the molecule is therefore the non-bonded phenolic hydroxyl group in the unit (VII).

Combination of structures (VI) and (VII) to give the xanthodactynaphin skeleton is now readily effected. The former structure contains two oxygen substituents introduced from the latter; the latter has two oxygen substituents unaccounted for. Stereochemical considerations apart, they can be linked only as shown in structure (VIII). Direct linkage of these units would lead to a structure containing two hydrogen atoms more than xanthodactynaphin, *i.e.*, one element of unsaturation must be introduced within the triangle in system (VII) in such a way as not to affect the earlier arguments based on u.v. absorption spectra. Although the precise form that this takes cannot be determined directly, the properties of xanthodactynaphin are best satisfied by a double bond positioned as in structure (VIII; R = OH) which is tentatively proposed for the -*jc*-1 isomer.

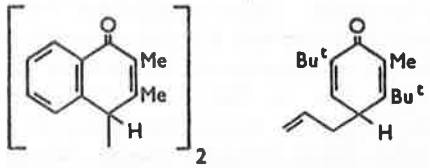
The structure of rhododactynaphin-*jc*-1 is similarly derived by combination of two systems (V) and (VII). Only one of the oxygen substituents OR, OR′ of the latter system is introduced into the former, thereby affording two possible structures (IX, X; R = OH). Since the group R′ in system (V) is not hydrogen, it must represent a second point of attachment to system (VII). Its arrangement as in structures (IX) and (X) is



(IX) (X)



(XI) (XII)



(XIII) (XIV)

determined by mechanistic considerations to be discussed and strongly supported by the presence in the n.m.r. spectrum of rhododactynaphin-*jc*-1 (Figure 3) of a doublet (τ 6·38, $J = 6$ c./sec.) well separated from other resonances in the methine region and completely absent from the spectrum of the xantho-compound. This is assigned to the proton attached to the asterisked carbon atom in structures (IX, X; R = OH). One of these structures is considered to represent rhododactynaphin-*jc*-1 but their close similarity has not permitted unequivocal differentiation between them. Because we have a marginal preference for the former, we shall use it in subsequent discussion. Unless otherwise stated, any remarks concerning it may readily be extrapolated to structure (X). These conclusions relating to the xantho- and rhodo-dactynaphins are, necessarily, tentative. The complexity of the structures proposed means that

[9] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.* (*C*), following Paper.

rigorous proof, other than by *X*-ray methods which have not yet fully been investigated, would require considerably more of the pure components than the limited amounts available to us [rhodo- (50 mg.), xantho- (100 mg.)].

In both these structures the two component C_{15} units are linked *via* two oxygen bridges. In either case, reactive groups are suitably juxtaposed to permit the formation of a third bridge through which their interconversion is visualised as proceeding. One stereoisomer of the 1,3-dioxan ring in xanthodactynaphin is represented in formula (XI), the two C_{15} systems being approximately at right angles to one another. Formation of the unstable intermediate (XII) is then readily effected and the conversion to rhododactynaphin completed by fission of the appropriate ketal C–O bond and concomitant aromatisation. This process would, of course, be reversible. An alternative mode of interconversion, *viz.*, by fission of the ketal linkage followed by closure of the new oxygen bridge is considered far less likely. In passing through a singly, rather than a triply bridged intermediate there would be considerable conformational change, and almost certainly aromatisation of ring A in compound (VIII) with subsequent decomposition (see below).

If it is assumed, as will subsequently be proved, that the absolute stereochemistry of the aphin side chain in dactynaphins is as shown in the formulæ (VIII)—(X), *viz.*, the same as in the aphins themselves,[2] the structure of rhododactynaphin involves three new centres of asymmetry and xanthodactynaphin a closely related element of asymmetry associated with the spiro-ring junction. Although it has not proved possible to assign with certainty the configuration at any of these centres, some stereochemical observations may nevertheless be made. Since equilibrium between xantho- and rhodo-dactynaphins is rapid, elements of asymmetry created as a consequence of the process will almost certainly give rise to the most stable configurational possibility, *e.g.*, the benzodioxan ring in rhododactynaphin (IX), being virtually planar, would almost certainly be *cis*-fused to the remainder of the system. Similarly, the geometrical requirements involved in forming a tricyclic intermediate, *e.g.*, (XII) would place restrictions on configurational variation in its vicinity. Finally, the configuration at the asterisked carbon in rhododactynaphin (IX) is closely related to the magnitude of its vicinal proton coupling constant ($J = 6$ c./sec.). However, in view of the complexity of the fused ring system of which it is a part, and the consequent lack of knowledge as to its conformation, configurational assignment at this stage would be hazardous.

The xanthodactynaphin-*jc*-1 structure (VIII; R = OH) contains both quinone ketal [10] and cyclohexadienone systems. That the latter does not tautomerise more readily to form a phenolic ring is attributed to the asterisked carbon forming part of a 1,3-dioxan which can readily be represented in the chair form, *e.g.*, (XI). Aromatisation would result in the carbon in question becoming trigonally hybridised, causing flattening of the dioxan ring. This conformational change, it is argued, to some extent would offset the increased stability otherwise associated with aromatisation. Other examples of cyclohexadienone systems, possessing enhanced relative stability due to steric factors include compounds (XIII) and (XIV).[11,12] In both these cases, aromatisation may readily be effected either directly or during the formation of derivatives. Xanthodactynaphin is no exception. Its reaction with alkali to form quinones (I; R = R′ = OH, R = R′ = H) is thought to involve such a process and is depicted formally on structure (VIII). Base-catalysed removal of the proton attached to C* causes aromatisation *via* the phenolate anion. The system is then effectively a mono-alkyl ether of a readily oxidisable quinol. Both naphthalenic units become naphthaquinones in the process shown, following tautomerisation of the product initially formed. The reaction as a whole is mechanistically unexceptional though it possesses, to our knowledge, no obvious analogy. It is to be noted that neither (IX) structure nor (X) for rhododactynaphin would be expected to give rise to a similar reaction. Hence the high yields of products observed probably stem from the xantho-compounds, by far the major component of the equilibrium. At the same time structures (IX) and (X) could readily be envisaged as leading to quinone A (I; R = OH, R′ = H) under these conditions. This would involve displacement of the group OR in structure (V), followed by elimination, and may account for the small quantity of this quinone which accompanies the major products of reaction.

Reduction of both dactynaphins-*jc*-1 to yield quinone A (2 mols.) is readily interpretable in terms of structures (VIII) and (IX). Reaction involves fission of a ketal and of a reducible carbon–oxygen bond [4] of the naphthopurpurin system, together with, in the case of rhododactynaphin, a ready elimination. The reaction was used to establish the absolute configuration of the two component quinone A units. Since both halves of a dactynaphin molecule have been shown to contribute to the quinone A actually isolated, the optical purity of this product was examined. Circular dichroism measurement of a small positive maximum at *ca.* 300 mμ established its optical identity, within experimental error, with authentic quinone A whose absolute configuration has been determined independently.[2] Although the complete stereochemistry of dactynaphins remains unknown, they are thereby shown to belong to the same series as the aphins themselves. Their mass spectrometric fission to quinone A as the sole product is also readily explicable in terms of known fragmentation processes [13] as depicted formally in

[10] *E.g.*, W. Ried and W. Radt, *Annalen*, 1965, **688**, 170.
[11] B. R. Brown and A. H. Todd, *J. Chem. Soc.*, 1963, 5564.
[12] B. Miller, *J. Amer. Chem. Soc.*, 1965, **87**, 5515.
[13] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, San Francisco, 1964, 175, 177.

structure (IX). Similar processes accompanied by an intermolecular H-transfer reaction such as occurs in the mass spectrometric conversion of quinones to quinols[6] would account for formation of the same product also from structures (VIII) and (X).

The n.m.r. spectra of dactynaphins (Figure 3) have already been discussed to some extent. Examination of the complex methine regions (τ 5—7) shows them to be consistent with the structures proposed and with the spectra of known aphin derivatives.[8] Detailed analyses are not presented, since the complexity of the spectra prevents them from being made unequivocally. Spin decoupling gives evidence of mutual coupling between methyl doublets and specific parts of the methine region thereby facilitating analysis and confirming the presence of aphin side chains. It also confirms the assignment of the doublet (τ 6·38) in the spectrum of the rhodo-compound as due to the proton attached to C* in formula (IX). The vicinal proton to which this is coupled also interacts with a methyl group with approximately the same coupling constant ($J = 6$ c./sec.), so that it appears as a quintet (τ 5·31), only the three main peaks of which are clearly resolved. When the doublet at τ 6·38 was irradiated, these were replaced by two peaks, presumably the major peaks of a quartet. Conversely, irradiation of the quintet caused collapse of the doublet to a singlet.

In addition to those discussed above, the spectra of all dactynaphins contain two well-defined singlet peaks below τ −2. Because of this low chemical shift, they are assumed to be due to the two phenolic hydroxyl groups bonded to carbonyls. The proton of a further hydroxyl group is also evident in the spectra of rhodo-dactynaphins-*jc*-1 and -2 (τ 1·68 and 1·72, respectively) but not in that of the xantho-compound. It disappeared on addition of D_2O to the perdeuterioacetone solvent and is presumed to be due to the new alcoholic hydroxyl group formed in the xantho–rhodo conversion. The presence of broad hydroxyl signals in the methine region also is inferred from minor changes there following deuteration.

Given these structures for dactynaphins-*jc*-1, those of the corresponding -*jc*-2 isomers are readily determined. Work on this series was carried out almost exclusively with the rhodo-compound which was, however, availably only in a relatively small quantity. It differs from the -*jc*-1 isomer in lacking one oxygen,[1] although it possesses the same light absorption and undergoes similar transformations, apart from its conversion to the corresponding xantho-compound which proceeds more slowly. It is concluded therefore that the two series differ only in the presence of a non-chromophoric oxygen atom which is not involved in linking the two C_{15} units. The n.m.r. spectra of the two rhodo-compounds resemble one another closely except for a slight difference in the methine region and the presence in the -*jc*-2 isomer of signals in the region τ 7·0—7·5. Their pattern possesses similarities to that of the methylene protons in the plant product isoeleutherin,[8] suggesting loss of a benzylic hydroxyl group from one of the aphin side chains of dactynaphins-*jc*-1. Since one of these hydroxyls is involved in xanthodactynaphin formation it is concluded that rhododactynaphin-*jc*-2 is represented by (IX, X; R = H) and the corresponding xantho-compound by (VIII; R = H).

Application of degradation processes devised for the -*jc*-1 isomers confirms these conclusions. Catalytic hydrogenolysis of rhododactynaphin-*jc*-2, or treatment with neutral sodium dithionite, gave rise to a mixture of two quinonoid products in approximately equal amounts and in combined yield, estimated spectrophotometrically, of 0·9 mole. On chromatographic analysis they were indistinguishable from quinone A (I; R = OH, R′ = H) and the orange quinone (I; R = R′ = H). (Not surprisingly, the latter compound was the sole product of reduction with alkaline sodium stannite.) As in the -*jc*-1 series, the presence of products of further reduction was observed but the small scale on which experiments were carried out did not permit further examination. Treatment of rhododactynaphin-*jc*-2 under anaerobic conditions with aqueous sodium hydroxide gave, as in the -*jc*-1 series, a mixture of a red and an orange product. The latter was identical with quinone (I; R = R′ = H). The former was identified chromophorically and by partition behaviour as a derivative of naphthopurpurin (III; R = OH). It differed from the naphthopurpurin derivative (I; R = R′ = OH) and was more mobile on chromatograms. Although insufficient was available for proper characterisation it seems highly probable on the basis of foregoing evidence that this product is the deoxyquinone (I; R = H, R′ = OH). Mass spectroscopic fragmentation of rhododactynaphin-*jc*-2 is also consistent with fission into quinones (I; R = OH, R′ = H) and (I; R = R′ = H) by processes analogous to those described for the -*jc*-1 isomer.

The stereochemistry of dactynaphins-*jc*-2 has not been considered in detail. It would be surprising if it differed from that of the -*jc*-1 series. The former compounds are the first aphid constituents shown to contain the (iso)eleutherin side chain.[14] Their co-occurrence with derivatives containing the aphin side chain is biogenetically interesting since the oxygen atom which differentiates the two series is "introduced" into the normal acetate–malonate pattern. Wider aspects of their biogenesis including relationship with the aphins will be discussed in the following Paper [9] when the nature of the protodactynaphins has been considered.

EXPERIMENTAL

Experimental conditions are the same as given in the preceding Paper.[1]

Reduction of Dactynaphins-jc-1.—(*a*) A solution of rhododactynaphin-*jc*-1 (9 mg.) in ethanol (10 m.) was hydrogenated for 2 days in the presence of Adams catalyst (10 mg.). After filtering off the catalyst, the filtrate was set

[14] H. Schmid and A. Ebnöther, *Helv. Chim. Acta*, 1951, **34**, 1041.

aside for 1 hr. in air to enable re-oxidation of quinols to quinones. Solvent was then evaporated and the residue chromatographed on silicic acid. Elution with chloroform gave an orange fraction (3·5 mg.) which after crystallisation from benzene–chloroform (1 : 1) formed orange-brown crystals decomposing at 200°, undepressed on admixture with quinone A and having identical light absorption, infrared and mass spectrum, and R_f value. Elution with chloroform–ethanol (9 : 1) gave a second product (2 mg.). After crystallisation from chloroform this compound had m. p. 246—248°, undepressed on admixture with the tetralone (II; R = H or OH) and having identical light absorption).

The same products were obtained in the same proportions on similar reduction of xanthodactynaphin-*jc*-1; c.d. (in 95% EtOH), for authentic quinone A (*c* 0·76 mg./ml.) λ 300 mμ (Δε + 9·04); for quinone A obtained by reduction of rhododactynaphin-*jc*-1 (*c* 0·25), λ 300 mμ (Δε + 8·54).

Reduction of quinone A (9·5 mg.) under the same conditions gave a mixture of starting material (4·5 mg.) and the tetralone (II; R = OH or H) (1·5 mg.), m. p. 246—248°. This compound darkened to give intractable material after standing for a few hours in air. In the mass spectrometer, no peaks corresponding to the molecular ion could be obtained; in 3N-hydrochloric acid $\lambda_{max.}$ 286 mμ, $\lambda_{infl.}$ 320 mμ; in saturated aqueous sodium hydrogen carbonate $\lambda_{max.}$ 336 mμ; in 3N-sodium hydroxide $\lambda_{max.}$ 334, 540 mμ; n.m.r. at 60 Mc./sec. in perdeuterioacetone, doublets at τ 3·15, 3·73, J = 2·5 c./sec. (2 × ArH) were the only resolvable peaks.

(*b*) Rhododactynaphin-*jc*-1 (6·5 mg.) in methanol (1 ml.) was added to a solution of sodium dithionite (40 mg.) in citrate–phosphate buffer of pH 6·0 (15 ml.) and the resulting solution set aside for 1 hr. under nitrogen. The pH was brought to 2 and the mixture immediately extracted with ether. Working up as for (*a*) above then yielded quinone A (1·5 mg.) identified by comparison of light absorption and R_f value with authentic material. A similar quantity (40—50%) of quinone A was recovered after treating either quinone A itself or xanthodactynaphin-*jc*-1 with dithionite under the same conditions.

(*c*) A solution of sodium stannite was prepared by mixing a warm solution of stannous chloride (2·5 g.) in concentrated hydrochloric acid (5 ml.) with one of sodium hydroxide (7·5 g.) in water (15 ml.). To this solution (3 ml.) was added rhododactynaphin-*jc*-1 (6·0 mg.) and the resulting nearly colourless mixture heated on a steam-bath for 30 min. It was then cooled, brought to pH 4, extracted with chloroform, and set aside in the air for several hours until oxidation of quinols was complete. Crystallisation from chloroform–benzene (1 : 1) then gave quinone (I; R = R′ = H) (3 mg.), m. p. 207·5—209° with decomposition, as the sole product. This was undepressed in admixture with authentic material and was identical with it in light absorption, infrared, n.m.r. and mass spectra, and in R_f value.

The same product was obtained on similar reduction of xanthodactynaphin-*jc*-1.

Quinone (I; R = R′ = H).—Quinone A (30 mg.) was reduced with aqueous sodium stannite as for rhododactynaphin-*jc*-1 above. The crude product was chromatographed on silicic acid in chloroform to yield *quinone* (I; R = R′ = H) (20 mg.) orange-red needles, m. p. 207·5—209° (decomp.) after crystallisation from chloroform (Found: C, 66·0; H, 5·2. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·2%), $\lambda_{max.}$ 270, 438 mμ (log ε 4·14, 3·59), $\lambda_{infl.}$ 289 mμ (log ε 3·84); $\nu_{max.}$ 3260, 2960, 2903, 1653, 1631, 1609, 1585, 1560, 1524, 1510, 1500, 1460, 1446, 1420, 1400, 1383, 1367, 1330, 1266, 1210, 1181, 1162, 1140, 1125, 1104, 1084, 1065, 1052, 1034, 1013, 926, 870, 864, 855, 824, 802, 764, 705, 700 cm.$^{-1}$; n.m.r. at 60 Mc./sec. in perdeuterioacetone τ −2·1 (OH, broad), 3·01 (ArH, doublet J = 2·5 c./sec.), 3·46 (ArH, doublet J = 2·5 c./sec.), 5·1 (MeCH, multiplet), 6·0 (MeCH, multiplet), 7·5 (CH_2, multiplet), 8·46 (CH_3, doublet J = 6·8 c./sec.), 8·69 (CH_3, doublet J = 6·5 c./sec.). Exact mass measurement of the molecular ion confirmed the formula above. Its mass spectrum has been discussed previously.[6] R_f value on Kieselgel in the system chloroform–methanol (19 : 1) 0·75. Corresponding values for quinones A and A′ are 0·65 and 0·41, respectively.

Alkaline Degradation of Dactynaphins-jc-1.—To a solution of xanthodactynaphin-*jc*-1 (11 mg.) in methanol (10 ml.) in an atmosphere of nitrogen was added aqueous 3N-sodium hydroxide (3 drops).

With 15 sec. the solution became red. It was kept under nitrogen for 25—30 min. A shorter reaction time than this resulted in the presence of a considerable quantity of unchanged starting material which impeded purification of the products; a longer time gave rise to base-catalysed decomposition. The reaction solution was brought to pH 3 with dilute hydrochloric acid, being kept under nitrogen throughout the addition. It was immediately extracted with chloroform (2 × 15 ml.). This extract, in turn, was extracted with buffer of pH 6·0 (4 × 20 ml.). The residual chloroform liquors were treated as described below. The aqueous extract was re-acidified to pH 3, re-extracted into chloroform (2 × 15 ml.), dried, and concentrated to 0·5 ml. On slow evaporation *quinone* (I; R = R′ = OH) (4 mg.) was deposited as deep red-purple needles which did not melt and charred above 250°. This was identical with an authentic specimen [5] in light absorption, i.r. spectra, and in R_f values; $\lambda_{max.}$ 229, 303, 500 mμ (log ε 4·29, 3·92, 3·86); $\lambda_{infl.}$ 476, 523, 538 mμ (log ε 3·83, 3·73, 3·63); $\nu_{max.}$ 3430, 1613, 1412, 1330, 1260, 1208, 1159, 1128, 1105, 1075, 1058, 1042, 990, 965, 948, 924, 885, 863, 840, 813, 755 cm.$^{-1}$; n.m.r. in $CDCl_3$ 3·72 (ArH, singlet), 5·06 (MeCH, quartet, J = 6·4 c./sec.), 5·47 (ArCHOH, doublet, J = 6·4 c./sec.), 6·00 (MeCH, multiplet), 6·32 (OH, singlet), 8·34 (CH_3, doublet, J = 6·4 c./sec.), 8·62 (CH_3, doublet, J = 5·6 c./sec.). Exact mass measurement of the molecular ion confirmed its molecular formula. The spectrum also contained peaks corresponding to loss of water, a methyl group, carbon monoxide, and acetaldehyde, fragmentations characteristic of quinones containing an aphin side chain.[6]

The chloroform liquors remaining after extraction with buffer of pH 6·0 were dried (Na_2SO_4), solvent evaporated, and the residue chromatographed on silicic acid (15 × 1 cm.) in chloroform to yield quinone (I; R = R′ = H) (3 mg.), decomposing at 208° after crystallisation from benzene–chloroform. Its m. p. was undepressed on admixture with authentic material and was identical in light absorption, i.r. spectra, and in R_f value. A trace of quinone A (<0·5 mg.) identified by light absorption and R_f value was also eluted.

Reduction of Rhododactynaphin-jc-2.—In the experiments (*a*)—(*c*) below, reaction products were identified by thin-layer chromatographic comparison with authentic material and by light absorption because of the small amounts of rhododactynaphin-*jc*-2 available for degradative studies.

(*a*) Hydrogenolysis of rhododactynaphin-*jc*-2 (2 mg.) as for the -*jc*-1 isomer gave a mixture of quinone A and

quinone (I; R = R = H) in approximately equal amounts and in overall yield, estimated spectrophotometrically, of 45%.

(*b*) Reduction with sodium dithionite as for the *-jc*-1 isomer gave the same results as in (*a*) but in poorer yield.

(*c*) Treatment of rhododactynaphin-*jc*-2 (2 mg.) with alkaline sodium stannite as for *-jc*-1 yielded quinone (I; R = R′ = H) (1·3 mg.), estimated spectrophotometrically.

Alkaline Degradation of Dactynaphins-jc-2.—Rhododactynaphin-*jc*-2 (5 mg.) was treated with alcoholic sodium hydroxide as for the *-jc*-1 isomer. The more acidic product was presumably the naphthopurpurin derivative (I; R = H, R′ = OH) (1·5 mg.) but insufficient was available for proper characterisation $\lambda_{max.}$ 298, 475, 492, 526, 542 mμ. Chromatographed on Kieselgel in chloroform–ethanol, it formed a discrete spot (R_f 0·75) whereas quinone (I; R = R′ = OH) in the same system streaked considerably and had R_f 0·55.

The less acidic reaction product was shown to consist exclusively of quinone (I; R = R′ = H) (1 mg.) by comparison of its light absorption and R_f value with those of authentic material.

We are grateful to Professor Lord Todd for encouragement. We wish to thank Professor R. C. Cookson for circular dichroism measurements. The award of an I.C.I. Fellowship (to J. H. B.) is gratefully acknowledged.

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Colouring Matters of the Aphididae. Part XXXV.[1] Protodactynaphin

By J. H. Bowie and D. W. Cameron, University Chemical Laboratory, Cambridge

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Colouring Matters of the Aphididae. Part XXXV.[1] Protodactynaphin

By J. H. Bowie and D. W. Cameron, University Chemical Laboratory, Cambridge

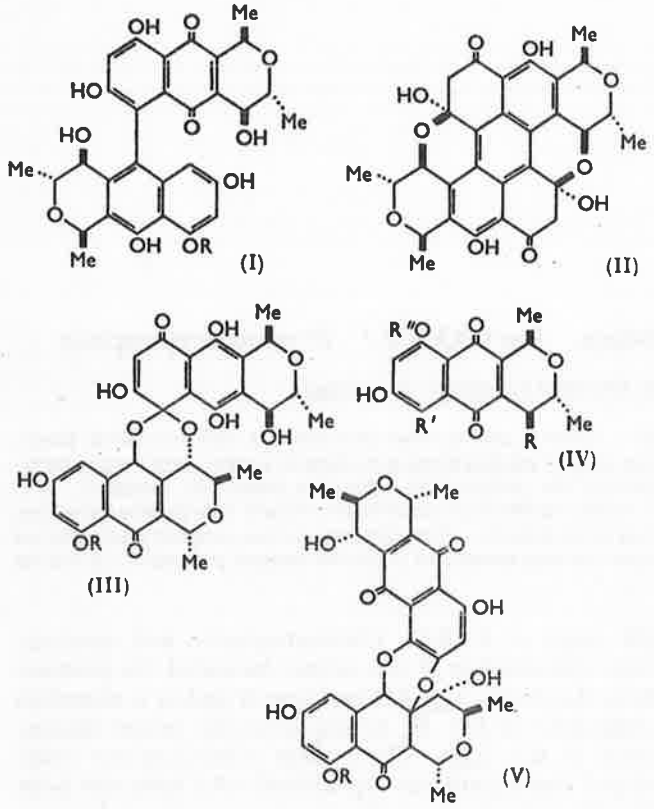
Living specimens of the aphid, *Dactynotus jaceae* L. contain, among other glycosides, a new substance, protodactynaphin-*jc*-1, which is converted by enzymic or acidic hydrolysis into a mixture of xantho- and rhodo-dactynaphins-*jc*-1. It is shown to be a simple glucoside of the dactynaphin aglucones previously discussed. It is presumed to exist in the living insect in the form of a xantho ⇌ rhodo equilibrium mixture, though only the isomer corresponding to the former (major) component has been isolated. Structural similarities between dactynaphins and other aphid pigments are discussed. Enzyme-containing extracts of *D. jaceae* convert protoaphin-*fb* into its aglucone rather than into xanthoaphin-*fb*.

In common with other series of aphid pigments,[2,3] the dactynaphins already described [1,4] do not occur in living insects as such but in the form of water-soluble precursors. Conversion into rhodo- and xantho-dactynaphins is an enzymic process that occurs following the death of the insects. This has been established for the cases of *Dactynotus jaceae* and *D. cirsii* and is presumed to apply also to other dactynaphin-containing species.[4] In the aphin series the change brought about by enzymes present in the living insect, *viz.*, conversion of protoaphin-*fb* (I; R = glucose) to xanthoaphin-*fb* (II) is complex, involving hydrolysis of the glucosidic linkage followed by substantial rearrangement. For pigments derived from *Hormaphis* species [3] the change is thought to involve the hydrolytic step only.

In order to inactivate the enzymes responsible for such processes, living specimens of *D. jaceae* were crushed in acetone. The resulting extract then contained only traces of aglycones. Washing the insects from infested plant material with hot water, a method used in the isolation of protoaphins [2] could not be employed in the present case because of the relative thermal instability of *Dactynotus* glucosides. By modifying a work-up procedure devised for isolation of the green aphid constituent, aphinin,[5] a crude mixture of *Dactynotus* glucosides was readily obtained. The process as a whole required *ca.* 2 hr., ambient temperature, and a pH range of 3—8·5. Chromatographic and spectroscopic examination of the extract indicated the presence both of aphinin ($\lambda_{max.}$ 645 mμ, broad) and of a colourless component of low R_f, having intensely yellow fluorescence in u.v. light. Both these substances are widespread throughout the Aphididae,[5] and have not been directly related chemically to dactynaphin aglycones. However, a third constituent was obtained by a simple but somewhat inefficient partition procedure, its acidity being intermediate between those of the other two. It was obtained in yield of 0·1% of the live insect weight as a light brown hygroscopic powder. On treatment with extracts of *D. jaceae* or of *Aphis fabae* it gave a mixture of rhodo- and xantho-dactynaphins-*jc*-1 (55%) as the only products. It was therefore considered to be their precursor and termed protodactynaphin-*jc*-1. It is difficult to detect in the presence of the other two glycosidic components, being masked on chromatograms by their respective colour and fluorescence. No other constituent was detected in the glycosidic extract. It is probable, however, that the mixture also contains a smaller quantity of a protodactynaphin-*jc*-2 to account for this series of aglycones.[1] Failure to obtain it is not surprising in view of the limited methods available for fractionating structurally similar glycosides of such complexity. So far as can at present be judged, the

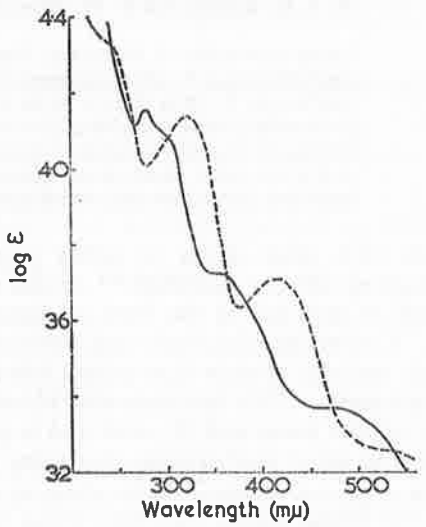
[1] Part XXXIV, J. H. Bowie and D. W. Cameron, preceding Paper.
[2] D. W. Cameron, R. I. T. Cromartie, D. G. I. Kingston, and Lord Todd, *J. Chem. Soc.*, 1964, 51.
[3] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.* (*C*), 1967, 704.
[4] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.* (*C*), 1967, 708.
[5] J. H. Bowie, D. W. Cameron, J. A. Findlay, and J. A. K. Quartey, *Nature*, 1966, **210**, 395.

polycyclic glycosidic components of *D. jaceae* differ from those of *A. fabae* only in the absence of protoaphin-*fb* from the former and its replacement by protodactynaphin. It is worth noting that *D. jaceae* appears to be abnormal in one other respect, *viz.*, the unusually high proportion of sorboyl glycerides it contains.[6]



The molecular formula of protodactynaphin-*jc*-1, $C_{36}H_{38}O_{17},H_2O$, corresponds to a glycoside of the corresponding rhodo- or xantho-compound. This was confirmed by acid hydrolysis which yielded glucose as the only sugar, together with traces of rhodo- and xanthodactynaphins-*jc*-1. The low yield of aglucones is accounted for by their decomposition accompanying hydrolysis. Since protodactynaphin-*jc*-1 is also hydrolysed by extracts of *A. fabae*, it is probable that the nature and configuration of its sugar is the same as in protoaphin-*fb*.[7]

The u.v. absorption of aqueous solutions of protodactynaphin-*jc*-1 (Figure) is strikingly similar to that of the xantho-compound (III; R = H)[1] both at pH values of 4 and 8·5. (The spectrum also contains a broad band of relatively low intensity in the region 450—550 mμ which will be discussed in a subsequent paragraph.) Since for the most part these spectra are hypsochromically shifted relative to those of xanthodactynaphin, the sugar residue is inferred to be attached to one of its phenolic hydroxyl groups. The spectrum of xanthodactynaphin is essentially the summation of spectra of its two component C_{15} units.[1] In protodactynaphin, both these component spectra undergo substantial bathochromic shifts in going to the higher pH (Figure). Hence the sugar cannot be attached to the two acidic non-bonded hydroxyl groups of structure (III) which are ionised at this pH. The actual point of attachment is suggested by the extent to which each band in the protodactynaphin spectrum is shifted from the corresponding band in that of xanthodactynaphin. The comparison is best made at pH 8·5 where clearly defined maxima rather than points of inflection are observed. The longest wavelength maximum (415 mμ) of the proto-compound is hypsochromically shifted by 22 mμ relative to that of the xantho-compound. Since this band is associated almost entirely with the lower of the C_{15} units depicted in structure (III), it suggests placement of the sugar as in structure (III; R = glucose). This was confirmed by degradation as described below. The corresponding shift of the band at 319 mμ is smaller as expected but not negligible (9 mμ bathochromic). That any shift at all is observed is regarded as being due



Absorption spectra of protodactynaphin-*jc*-1 in aqueous buffer (——) and at pH 8·5 (– – – –)

to the fact that, in this region of the spectrum, both C_{15} components contribute appreciably to the overall absorption even though only one of them absorbs maximally.

Treatment of protodactynaphin-*jc*-1 with alkali as described for the xantho-compound [1] gave two products, only one of which was soluble in organic solvents. It was readily identified as the naphthopurpurin derivative (IV; R = R′ = OH, R″ = H) by comparison with authentic material obtained from xanthodactynaphin. The other, though not available in amount sufficient for characterisation readily yielded the deoxyquinone (IV; R = R′ = R″ = H) after treatment with extracts of *D. jaceae*. This compound was also identified by comparison with authentic material. It is concluded

[6] J. H. Bowie and D. W. Cameron, *J. Chem. Soc.*, 1965, 5651.
[7] D. W. Cameron, H. W.-S. Chan, and D. G. I. Kingston, *J. Chem. Soc.*, 1965, 4363.

that its water-soluble precursor was the glucoside (IV; R = R′ = H, R″ = glucose). Following the chemistry of xanthodactynaphin, these results can only be interpreted in terms of structure (III; R = glucose) for the proto-compound.

There is no obvious reason for this compound not being in equilibrium in aqueous media with an analogous rhododactynaphin glucoside (V; R = glucose), cf. interconversion of the corresponding aglucones.[1] It is suggested that a small quantity of such a component accounts for the inflection in the absorption spectra (Figure) in the region 450—550 mμ. Since the yellow form is much the more abundant at equilibrium it is this which is isolated in the solid phase. The likelihood of separating a minor constituent corresponding to structure (V; R = glucose) is small in view of the limited methods available for fractionation of these systems. Its presence is supported, however, by the formation of rhododactynaphin-*jc*-1 as well as the xantho-compound on both acidic or enzymic hydrolysis. Whether the enzyme system has any effect on the relative proportions of these two isomers has not been carefully investigated. At present there is nothing to suggest that it does. It is concluded that in living *D. jaceae* there exists an equilibrium (III ⇌ V; R = glucose), the former being present in much the larger amount, probably together with smaller quantities of an analogous pair of compounds corresponding to dactynaphin-*jc*-2.

Comparison of the structures of protodactynaphin and protoaphin reveals a number of interesting similarities some of which have already been discussed.[5] Both systems can be regarded as derived by formal coupling of two similar naphthalenic units but differ in that the former involves carbon–oxygen rather than carbon–carbon bond formation. Several related examples of the latter kind have been effected *in vitro* either by oxidative coupling[8] or by nucleophilic addition processes.[9,10] Carbon–oxygen bond formation has not, however, been observed in these reactions and attempts to generate system (III) or (V), *e.g.*, by self-coupling of quinone A (IV; R = R″ = H, R′ = OH) or coupling a mixture of the naphthopurpurin derivative (IV; R = R′ = OH, R″ = H) with the deoxyquinone (IV; R = R′ = R″ = H) under a variety of conditions have to date been uniformly unsuccessful.

A further point of similarity between protodactynaphin and protoaphin lies in the attachment of the sugar residue to corresponding oxygen atoms in the two compounds. Arising out of this is an interesting observation concerning the reaction of both compounds with enzyme-containing solutions. Extracts of both *A. fabae* and *D. jaceae* convert protodactynaphin to the corresponding aglucones. Whereas those of *A. fabae* convert protoaphin into xanthoaphin (III) *via* the aglucone (I; R = H),[7] extracts of *D. jaceae* convert it into this aglucone and no further. The product was identified by the similarity of its absorption spectrum to that of protoaphin, its partition behaviour and the fact that on standing in air it underwent oxidative decomposition and could be converted no longer into xanthoaphin. This confirms the conclusion[7] that two separate enzymic functions are involved in the proto-xanthoaphin conversion and suggests that they may be due to distinct separable enzymes. It is recalled that *D. jaceae* contains no detectable quantity of protoaphin. It is intriguing that it also lacks the enzyme involved in xanthoaphin formation.

[8] D. W. Cameron, H. W.-S. Chan, and E. M. Hildyard, *J. Chem. Soc.* (*C*), 1966, 1832.

EXPERIMENTAL

Unless otherwise stated, m. p.s were measured on a Kofler hot-stage apparatus and are uncorrected. Light petroleum refers to the fraction having b. p. 40—60°. Infrared spectra were measured as KBr discs and u.v. and visible spectra in 95% ethanol. Silicic acid refers to Mallinckrodt 2847.

Protodactynaphin-jc-1.—Knapweed infested with *D. jaceae* was collected. These insects, unlike many aphid species, are readily detached undamaged from their host by tapping it with a metal spatula over a large funnel. Living specimens (80 g.) so obtained were macerated with acetone (3 × 75 ml.) within 4 hr. of collection. The supernatant liquors were separated by centrifuging. To this extract was added water (150 ml.) and the mixture washed with ether (10 × 500 ml.) to remove fats [6] and the small quantity of carotene that invariably accompanies them.[5] The aqueous phase was then extracted with n-butanol–ether (50 ml. of 1 : 1) and the extract washed with tap water (pH 7) until no more aphinin [5] in the form of its pale blue anion was removed. This was followed by extraction with 0·2M-disodium hydrogen phosphate (3 × 100 ml.), the fluorescent component remaining chiefly in the organic phase under these conditions. These aqueous liquors were then re-extracted with neat n-butanol (50 ml.). (This is a powerful solvent for glucosides of this kind, *e.g.*, it extracts protoaphin from its aqueous solution at pH 9 in the form of its violet-coloured anion.) The butanol extract was washed with water containing a few drops of acetic acid till the washings were faintly acidic, then once with water. Solvent was evaporated under reduced pressure to give *protodactynaphin*-jc-1 (III; R = glucose) (75 mg.) as a brown solid. After fractional precipitation from absolute ethanol with light petroleum, it was obtained as a light brown hygroscopic powder which decomposed above 200°. A sample was dried at room temperature and 10^{-4} mm. for 4 hr. (Found: C, 57·0; H, 5·8. $C_{36}H_{38}O_{17},H_2O$ requires C, 56·8; H, 5·4%); in phosphate–citrate buffer of pH 4·0, $\lambda_{max.}$ 275, 295 mμ (log ε 4·17, 4·05), $\lambda_{infl.}$ 360 mμ (log ε 3·71); in 0·2M-disodium hydrogen phosphate, $\lambda_{max.}$ 319, 415 mμ (log ε 4·16, 3·72) $\lambda_{infl.}$ 232 mμ (log ε 4·35); $\nu_{max.}$ 3420, 2936, 2862, 1611, 1580, 1450, 1376, 1368, 1313, 1263, 1177, 1060, 1024, 886, 840, 803 cm.$^{-1}$.

A small portion of crude aqueous liquors remaining after removal of fats was brought carefully to pH 3, extracted with n-butanol until no more colour was removed, and solvent evaporated under reduced pressure. The resulting pale green extract had $\lambda_{max.}$ 645 mμ (broad), similar to that of aphinin.[5] Thin-layer chromatography confirmed the

[9] D. W. Cameron and H. W.-S. Chan, *J. Chem. Soc.* (*C*), 1966, 1825.

[10] G. M. Blackburn, D. W. Cameron, and H. W.-S. Chan, *J. Chem. Soc.* (*C*), 1966, 1836.

presence of this compound by comparison with authentic material. The chromatogram also contained a further component, observed as a strongly yellow fluorescent streak near the origin. It was obtained following chromatography on cellulose in chloroform–n-butanol (1 : 1) and had $\lambda_{max.}$ 295, 307, 340, 350 mμ indistinguishable from similarly fluorescent naphthalene constituents of other aphid species.[5]

Hydrolysis of Protodactynaphin-jc-1.—Protodactynaphin-*jc*-1 (10 mg.) was boiled with 2N-sulphuric acid (5 ml.). The mixture was then cooled and extracted with chloroform. The aqueous phase was brought to pH 7 with aqueous barium hydroxide, centrifuged, and the supernatant liquors evaporated to dryness *in vacuo*. The residue was identified as glucose by paper chromatography against authentic material in the following solvent systems: (i) Whatman 3 MM ascending, n-butanol–acetic acid–water (4 : 1 : 5 top layer) R_f 0·22 (ii) Whatman 3 MM ascending, ethyl acetate–water–pyridine (2 : 2 : 1, top layer) R_f 0·31. Alkaline triphenyl tetrazolium chloride was used as developing agent and the treated chromatograms heated to 100°/5 mm.

The chloroform layer from the hydrolysis mixture was shown by thin-layer chromatography (t.l.c.) [4] to contain a mixture of rhodo- and xantho-dactynaphins-*jc*-1 in low yield.

Alkaline Degradation of Protodactynaphin-jc-1.—A solution of protodactynaphin-*jc*-1 (5 mg.) in water (5 ml.) under nitrogen was treated with saturated aqueous sodium hydroxide (3 drops). After 30 min. aqueous phosphate–citrate buffer of pH 4 (15 ml.) was added and the mixture extracted with chloroform (2 × 10 ml.). The extract was dried and solvent evaporated to yield purple needles of the naphthopurpurin derivative (IV; R = R′ = OH, R″ = H) (1 mg.). This was identical in light absorption, i.r. spectra, and R_f value with authentic material.[1]

The aqueous solution remaining after extraction with chloroform was carefully brought to pH 6 with 0·2M-disodium hydrogen phosphate. To it was added crude enzyme extract [4] of *D. jaceae* (2 ml.) and the mixture kept under nitrogen. After 1 hr. it was extracted with chloroform (5 ml.) and the extract dried and solvent evaporated to yield orange-coloured needles of quinone (IV; R = R′ = R″ = H) (0·8 mg. estimated spectrophotometrically). Repeating the reaction several times enabled this product to be obtained in sufficient quantity to be chromatographed on silicic acid and recrystallised from chloroform. It then melted at 208°, was undepressed on admixture with authentic material [1] and possessed identical light absorption, infrared spectra and R_f value.

Enzymic Hydrolyses.—(*a*) A solution of protodactynaphin-*jc*-1 (10 mg.) in citrate–phosphate buffer of pH 6 (2 ml.) was treated with extracts of *D. jaceae* [4] (2 ml.) and the mixture set aside at room temperature for 1 hr. It was then acidified to pH 2 and extracted immediately with chloroform (2 × 5 ml.), the extract dried (Na_2SO_4) and solvent evaporated to give a mixture of rhodo- and xantho-dactynaphins-*jc*-1 (4 mg., 55%) identified by t.l.c. and light absorption of the individual components after separation on a column of silicic acid. No rhododactynaphin-*jc*-2 was detected in the reaction mixture. Similar results were obtained with extracts of *A. fabae*.

(*b*) Treatment of protoaphin-*fb* (I; R = glucose) under similar conditions with extracts of *D. jaceae* followed, after acidification, by extraction of the product into ether gave an extract having $\lambda_{max.}$ 276, 345, 357, 450 mμ, $\lambda_{infl.}$ 310 mμ, representing the bulk of the starting material in the form of its aglucone. This spectrum was similar in character to that of protoaphin.[2] No xanthoaphin-*fb* (II) was detected in the extract.

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HAEMOLYMPH PIGMENTS OF APHIDS

By Dr. J. H. BOWIE, Dr. D. W. CAMERON, Dr. J. A. FINDLAY and Dr. J. A. K. QUARTEY
University Chemical Laboratory, Cambridge

SOME years ago, an extensive investigation[1,2] by Todd *et al.* directed attention to a range of remarkable colouring matters found in the haemolymph of various species of aphids. These substances were observed to fall into a number of groups, one of which has been investigated chemically in considerable detail and the structures of its components elucidated[3–5]. This group, termed aphins, is of comparatively wide occurrence, having been found in eighteen of the forty-two species of the Aphididae originally examined. Less attention has been paid until recently to the several non-aphin haemolymph pigments, which frequently occur in equally large proportions. This was due, in some cases, to their instability and in others to their relative inaccessibility. Despite these difficulties, enough of these substances has now been obtained for systematic chemical study, which is in progress. Though not yet complete, it has advanced sufficiently far to show interesting structural and biogenetic similarities affecting all groups of aphid pigments and to permit a limited survey of their occurrence to be made. We are concerned here with establishing what these similarities are. It is not proposed to discuss the chemistry of new compounds in detail except in so far as is necessary to characterize them adequately.

The chemistry of the aphins[3–5] was considered chiefly with reference to the aphins-*fb*, which were obtained from the bean aphid, *Aphis fabae* Scop., and from a number of other species. (Addition of the suffix *-fb* was used to distinguish them from the isomeric aphins *-sl*, obtained from the willow aphid *Tuberolachnus salignus* Gmelin.) These substances occur in the living insect as a glucoside, protoaphin-*fb* (I), $C_{36}H_{38}O_{16}$. After the death of the insect, this compound suffers enzymatic hydrolysis of the glucosidic linkage, together with extensive rearrangement, and is converted successively into xantho-, chryso-, and finally the stable, highly condensed erythroaphin-*fb* (II; $R = H$).

Careful examination of *A. fabae*, so as to avoid enzymatic decomposition processes, shows that, in addition to protoaphin-*fb*, two other glycosidic components are

present in substantial amounts. One of them is a dark blue-green substance, the presence of which was detected in earlier work[2] but which was not then investigated. For this we now propose the name 'aphinin'. The other is a colourless component which fluoresces strongly in ultra-violet light. Protoaphin and aphinin, between them, account for virtually the entire soluble pigment content of the insects. (The small amounts of yellow fat-soluble constituents[2], which are invariably found on extraction of aphids, correspond spectroscopically and in partition behaviour to carotene hydrocarbons. Usually they are present in such small amounts, typically 0·005 per cent of the live insect weight, that we have not examined them in detail.)

Other highly pigmented aphid species, for example, *A. sambuci* L. (elders), *A. rumicis* L. (dock), *A. farinosa* Gm. (*Salix*) and *A. corniella* HRL (dogwood), contain the same three glycosidic constituents as *A. fabae*, but not in the same proportions. In general, black-coloured aphids, for example, *A. fabae* and *A. rumicis*, seem to contain more protoaphin relative to aphinin than dark green species, for example, *A. sambuci*. Variation in pigment content can indeed occur between different individuals of the same species. *A. sambuci*, for example, shows considerable variability in colour, ranging from dark blue-green to reddish-brown, the proportion of each being dependent on external factors, for example, time of season or temperature[6]. Examination of specimens of each of these extreme colour forms shows them to differ only in the relative amounts of the three glycosides already mentioned. A more striking example of colour variation is found in *A. farinosa* which ranges from deep blue-green to dark yellow. Specimens of the former type contain all three glycosides in significant quantities; the latter differ in that the proportion of protoaphin is much reduced, while the amount of aphinin present is so small as to be scarcely detectable.

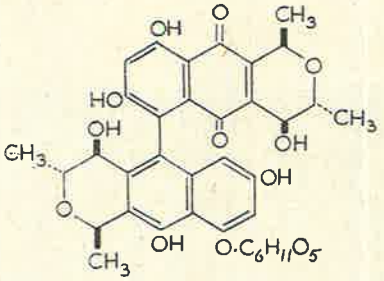
Relatively non-pigmented, pale green insects, for example, *Brevicoryne brassicae* L. (cabbage), *Hyalopterus pruni* Geoffr. (plum), *Macrosiphoniella artemisiae* (*Artemisia vulgaris*) and *Megoura viciae* Buckton (bean), chemically fall into the same category as those already discussed. Not surprisingly, they contain little protoaphin or aphinin. Indeed, the presence of the former cannot be detected; the latter, for which more sensitive methods of detection are available, is present to the extent of only *c.* 0·02 per cent of the live insect weight. The main component of such species is the colourless, fluorescent glycoside, chromatographically similar to that in *A. fabae* and present in substantial quantity (up to 1 per cent of the live insect weight).

A sufficient quantity of aphinin for chemical study is most conveniently obtained from *A. sambuci*, whence it

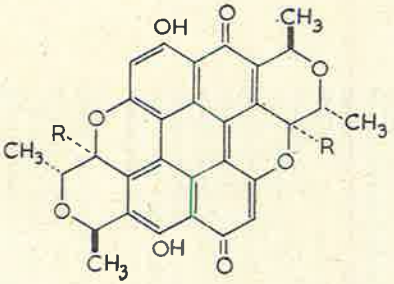
can be isolated to the extent of 0·2 per cent of the live insect weight. In the solid phase aphinin-*sm* is dark blue-green, almost black, and, in solution, absorbs strongly at 638 mμ. It is exceedingly unstable towards heat, light and most oxidizing conditions. It readily undergoes reversible reduction to a yellow hydroquinone. It can be separated from protoaphin by virtue of its greater acidity. On mild treatment with acid it is hydrolysed to the corresponding aglucone and glucose. Unlike protoaphin it is not hydrolysed enzymatically by extracts of crushed insects. Its probable molecular formula is $C_{36}H_{38}O_{16}$ and its structure almost certainly is based on the extended quinone (III; R = glucose). A compound based on the system (III; R=H) has been synthesized in connexion with other work[7]. It is spectroscopically almost identical with aphinin, and the chemistry of the two compounds, inasmuch as it affects their chromophores, is completely parallel. For example, very mild, controlled oxidation of either leads to the chromophore (IV). The product obtained from aphinin-*sm* in this way has the formula $C_{36}H_{36}O_{16}$ and absorbs at 590 and 628 mμ. The corresponding aglucone, $C_{30}H_{26}O_{11}$, being less unstable and more symmetrical than its precursors, is more suitable for further chemical study which is in progress. The nature of the non-aromatic residues which substitute the aphinin nucleus (III) has not been established. Spectroscopic considerations, however, strongly suggest that they are closely related to the aliphatic side-chains in protoaphin (I).

The colourless, fluorescent glycosidic component, which accompanies protoaphin and aphinin in the insect species so far considered, has as yet been examined only cursorily. It has not been obtained pure, nor has its homogeneity been established. It is most conveniently isolated from relatively non-pigmented species, for example, *H. pruni*. It is very unstable towards oxidation and less acidic than either of its congeners. Its light absorption is that of a hydroxylated naphthalene, being somewhat similar to the spectrum of derivatives of 1,3,8-trihydroxynaphthalene, obtained by degradation[3] of protoaphin (I).

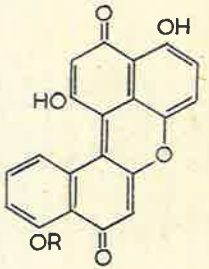
In addition to these substances, two other series of aphid pigments have been found. These were confined to specific genera, although the possibility that they may occur elsewhere cannot be excluded in view of the geographical limitations that attended collection of insects. The pigments derived from two species of *Hormaphis* (previously known as *Hamamelistes*) have already been described[8]. A red glycosidic heteroaphin, present in the living insects, is converted enzymatically after death into a red fluorescent aglycone, rhodoaphin. Recent work suggests that the latter has the molecular formula $C_{30}H_{22}O_{10}$ and confirms that it is closely related to dihydroxyerythroaphin-*fb* (II; R = OH).



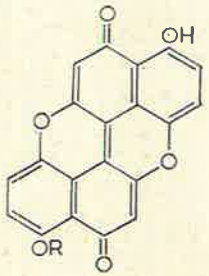
I



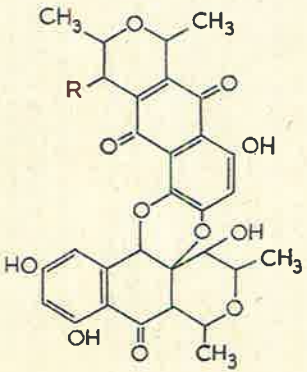
II



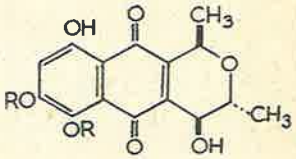
III



IV



V



VI

A second series of pigments is evidently restricted to the genus *Dactynotus*. They have been found in *D. jaceae* L. (knapweed), *D. cirsii* L. (thistle)[1,2], *D.* (*Uromelan*) *taraxaci* Kaltenbach, *D. tenaceti* L.[9] and in the North American species *D. rudbeckiae* Fitch and *D. ambrosiae* Thomas[10]. *D. jaceae* has been examined in greatest detail. It contains aphinin and a colourless fluorescent glycoside, but no protoaphin. Instead, a new glucoside and its enzymatically derived aglucones constitute a complex series of pigments for which we propose the name 'dactynaphins'. These amount to 0·75 per cent of the live insect weight. Using similar conventions of nomenclature as for the aphins, we refer to the glucosidic precursor as protodactynaphin-*jc*-1, $C_{36}H_{38}O_{17}$. This compound on enzymatic hydrolysis yields a mixture of two aglucones, a reddish orange rhododactynaphin-*jc*-1 and a yellow xanthodactynaphin-*jc*-1, each having the molecular formula $C_{30}H_{28}O_{12}$ and convertible one into the other. Smaller amounts of an analogous pair of aglucones are also isolable from *D. jaceae*. These are termed rhodo- and xantho-dactynaphins-*jc*-2, $C_{30}H_{28}O_{11}$. The properties of the former are similar to those reported for a substance, rhododactynaphin A, which was obtained by Weiss and Altland[10] from the two North American species mentioned. Through the courtesy of Dr. U. Weiss we have been enabled to compare these two compounds. They are indeed identical, as are rhododactynaphin-*jc*-1 and Weiss and Altland's rhododactynaphin *B*. Rhododactynaphins are readily and reversibly reduced to pale yellow hydroquinones; xanthodactynaphins, on the other hand, are stable to mild reduction. The chemistry of these substances is exceedingly complex and is not to be discussed at length here. Evidence is available, however, to support the structure (V; R = OH) for rhododactynaphin-*jc*-1 and (V; R = H) for -*jc*-2. Alkaline degradation of the former leads to the naphthaquinone (VI; R = H), the structure of which has been unambiguously established. For present purposes it is sufficient to note that the major chromophore in rhododactynaphin-*jc*-1 is (VI), linkage of which to a further C_{15} unit is effected through ethereal oxygen.

Despite the considerable structural variety in these haemolymph pigments, certain unifying features are, nevertheless, already apparent. All occur in the insects as glycosides, hydrolysis of which invariably leads to C_{30} aglycones. All are quinones or close relatives, as evidenced by their redox properties and general chemistry. All can be visualized as derived formally by oxidative coupling of two C_{15} naphthalenic units, in particular derivatives of 1,3,8-trihydroxynaphthalene. Indeed, the structural variety that occurs is evidently the result of the various possible ways that this coupling process can be effected. In the aphins, aphinin and rhodoaphin, coupling involves carbon–carbon bond formation, in the dactynaphins,

carbon–oxygen. In indirect support of these conclusions, similar reactions leading to syntheses of proto- (I) and erythroaphins (II) and several related systems have readily been effected *in vitro* under exceedingly mild conditions[7]. Further, the presence in aphids of colourless glycosides possessing hydroxynaphthalene spectra is of considerable interest. They may be regarded either as pigment precursors or as close relatives formed by similar processes. Besides testing these hypotheses, the completion of structural work in this general area may also provide a basis for speculation on a more fundamental question, namely, the function played by such substances in the insects themselves.

We are grateful to Lord Todd for his interest and encouragement in this work. We thank Mr. H. L. G. Stroyan for identification of aphid specimens and helpful advice, and also Fisons Pest Control, Ltd., Mr. R. N. B. Prior, and Dr. H. Descimon for specimens of *M. viciae*, *A. farinosa*, and *M. artemisiae*, respectively.

[1] Duewell, H., Human, J. P. E., Johnson, A. W., MacDonald, S. F., and Todd, A. R., *Nature*, **162**, 759 (1948).

[2] Duewell, H., Human, J. P. E., Johnson, A. W., MacDonald, S. F., and Todd, A. R., *J. Chem. Soc.*, 3304 (1950).

[3] Cameron, D. W., Cromartie, R. I. T., Kingston, D. G. I., and Lord Todd, *J. Chem. Soc.*, 51 (1964).

[4] Cameron, D. W., Cromartie, R. I. T., Hamied, Y. K., Scott, P. M., and Lord Todd, *J. Chem. Soc.*, 62 (1964).

[5] Calderbank, A., Cameron, D. W., Cromartie, R. I. T., Hamied, Y. K., Haslam, E., Kingston, D. G. I., Lord Todd, and Watkins, J. C., *J. Chem. Soc.*, 80 (1964.

[6] Markkula, M., and Pulliainen, E., *Ann. Ent. Fenn.*, **31**, 39 (1965).

[7] Cameron, D. W., Chan, H. W.-S., and Hildyard, E. M. (unpublished observations).

[8] MacDonald, S. F., *J. Chem. Soc.*, 2378 (1954).

[9] Joshi, B. S., thesis, Univ. Cambridge (1955).

[10] Weiss, U., and Altland, H. W., *Nature*, **207**, 1295 (1965).

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Colouring Matters of the Aphididae. Part XXVII.[1] Mass Spectra of Aphin Derivatives

By J. H. Bowie and D. W. Cameron

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Colouring Matters of the Aphididae. Part XXVII.[1] Mass Spectra of Aphin Derivatives

By J. H. Bowie and D. W. Cameron

The mass spectra of fifteen aphin derivatives and related compounds have been investigated. Their characteristic fragmentation processes, which have been substantiated both by exact mass measurements and by appropriate metastable ions, have been correlated with structures; stereochemical differences, on the other hand, are not distinguishable by this technique.

THIS Paper is concerned with the interpretation of the mass spectra (Table 1 and Figures 1—6) of a series of aphin derivatives and related systems (I—XV). The compounds studied consist of perylene derivatives and naphthaquinones related to the erythro- and proto-aphins, respectively. All have been described in earlier Parts. The investigation was undertaken to determine to what extent fragmentation of aphin derivatives could be correlated with their structures

[1] Part XXVI, D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, E. Haslam, D. G. I. Kingston, Lord Todd, and J. C. Watkins, *J. Chem. Soc.*, 1965, 6923.

TABLE 1 *

(III) †	*m/e*	502	503	504	505	506	507	508	509	510	511	524	526	527	528	542 (*M*)	543
	I (%)	12	12	100	41	36	12	36	18	18	9	10	8	18	7	28	9
(VII)	*m/e*	210	210·5	211	211·5	212	393	394	395	409	411	421	422	423	424	433	451
	I (%)	15	9	82	25	19	14	14	14	12	15	18	100	43	19	7	44
	m/e	452	453	466	467	468	469	470	484	485	495	496	510	511	528	529	546 (*M*)
	I (%)	13	8	82	32	7	20	8	55	16	17	7	60	19	18	7	8
(VIII)	*m/e*	465	466	479	495	509	510	511	524	551	553	554	566	567	568 (*M*)	569	570
	I (%)	12	7	7	7	67	24	10	7	7	39	16	14	7	100	38	11
(X)	*m/e*	203	231	246	247	257	259	273	274	275	285	287	289	300	302	303	318 (*M*)
	I (%)	11	12	54	11	7	18	8	100	25	6	5	5	5	5	5	2
(XIV)	*m/e*	197	199	201	199	211	213	214	215	225	227	228	229	230	231	239	240
	I (%)	7	7	7	7	8	10	14	12	7	9	10	18	9	7	21	8
	m/e	242	243	244	254	257	258	259	271	272 (*M*)		273	274				
	I (%)	14	42	14	7	72	14	13	7	100		20	9				
(XV)	*m/e*	197	199	201	211	213	214	215	227	228	229	230	239	242	243	244	254
	I (%)	6	6	6	8	9	19	11	8	10	16	9	19	16	41	18	7
	m/e	257	258	259	272 (*M*)		273	244									
	I (%)	80	12	11	100		20	8									

* All ions greater than 5% of the base peak (arbitrarily taken as 100%) are recorded. *M* = metastable.

† The extreme involatility of this compound is the cause of considerable thermal decomposition, accompanying normal fragmentation. This results in a non-reproducible spectrum below *m/e* 500, of much lower intensity than the base peak (*m/e* 504) and accordingly this region is not recorded.

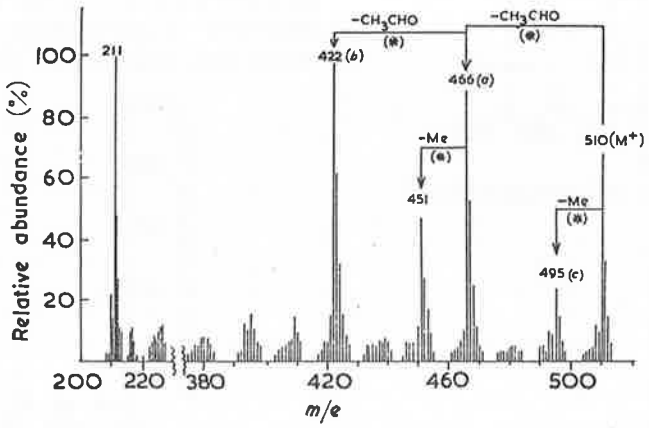


FIGURE 1 Mass spectrum of erythroaphin–*fb* (I)

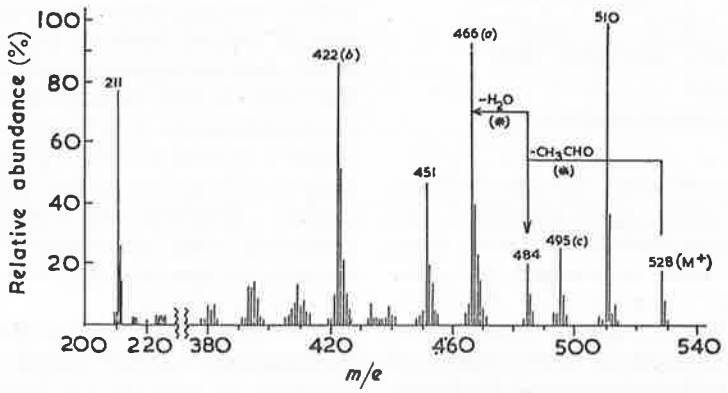


FIGURE 2 Mass spectrum of chrysoaphin–*fb* (VI)

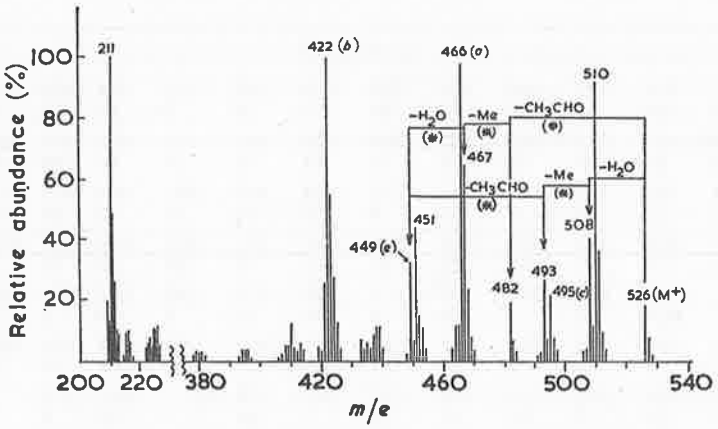


FIGURE 3 Mass spectrum of hydroxyerythroaphin–*fb* (II)

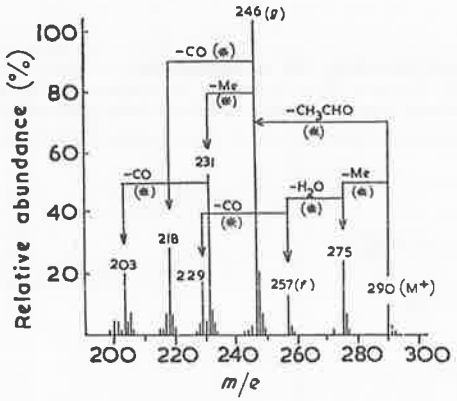


FIGURE 4 Mass spectrum of compound(XIII)

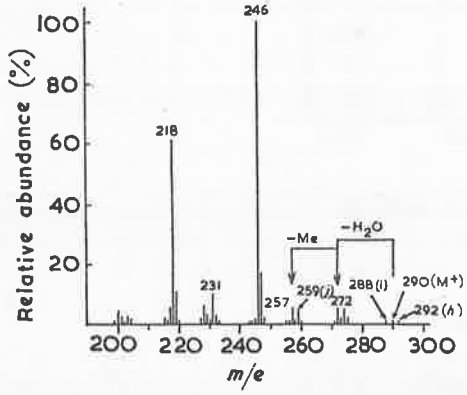


FIGURE 5 Mass spectrum of compound (IX)

and stereochemistry and also to assist structural studies, currently in progress, on other aphid pigments, *e.g.*, dactynaphins [2] and rhodoaphin-*be*.[2,3] Exact mass measurements have been used to confirm the compositions of many of the fragment ions described; specific structures have been assigned primarily to produce a self-consistent rationale for interpretation of the spectra and are to be regarded as formal representations only.

[2] J. H. Bowie and D. W. Cameron, unpublished results.
[3] S. F. MacDonald, *J. Chem. Soc.*, 1954, 2378.

The mass spectrum of erythroaphin-*fb* [4] (I) (Figure 1) is remarkably simple and is rationalised in Scheme 1. The compositions of the major ions (*m/e* 510, 495, 467, 466, 451, 423, and 422) have been established by high resolution (H.R.) measurements, and all fragmentation processes are substantiated by appropriate metastable ions [indicated by an asterisk (*)]. The molecular ion (*m/e* 510) fragments in two ways. Successive loss of two molecules of acetaldehyde gives *m/e* 422, possibly *b*, which may then lose an electron to form the stabilised

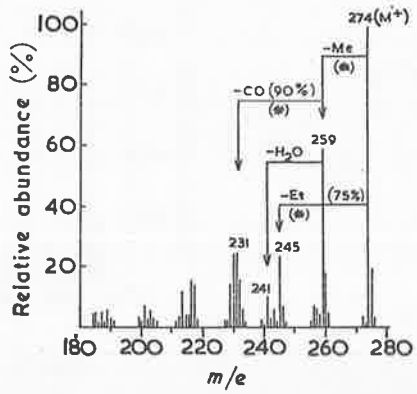


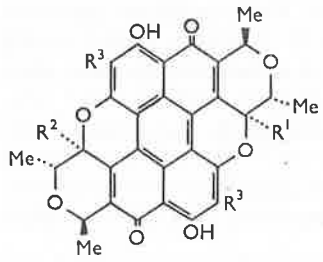
FIGURE 6 Mass spectrum of compound (XI)

doubly charged species *m/e* 211. Alternatively loss of a methyl radical leads to the stable cation *c* (*m/e* 495) which does not appear to undergo further fragmentation. This process has, throughout this Paper, been depicted as involving loss of a benzylic methyl group with consequent extension of conjugation. The possibility that an alternative methyl group is lost cannot be excluded. Similarly the formation of ions *a* and *b* is consistent with geometrical considerations and the stability of dication *m/e* 211 but these structures are necessarily tentative.

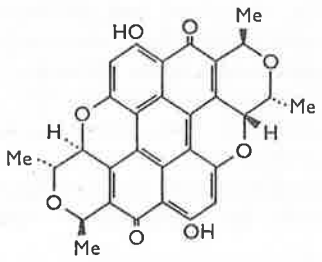
A similar mass spectrum (Figure 2) is obtained from chrysoaphin-*fb* (VI),[5] whose moleclar ion (*m/e* 528)

[4] D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, P. M. Scott, and Lord Todd, *J. Chem. Soc.*, 1964, 62.
[5] A. Calderbank, D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, E. Haslam, D. G. I. Kingston, Lord Todd, and J. C. Watkins, *J. Chem. Soc.*, 1964, 80.

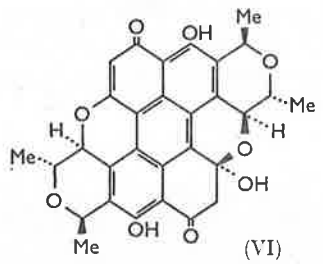
furnishes the erythroaphin molecular ion (*m/e* 510) by loss of water. Subsequent fragmentation of the latter ion then proceeds as already described. Alternatively, loss of acetaldehyde may occur directly from the chrysoaphin molecular ion leading to *m/e* 484, which then



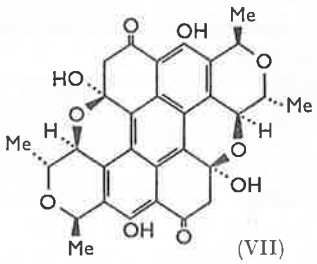
(I: $R^1 = R^2 = R^3 = H$)
(II: $R^1 = OH, R^2 = R^3 = H$)
(III: $R^1 = R^2 = OH, R^3 = H$)
(IV: $R^1 = R^2 = H, R^3 = Br$)



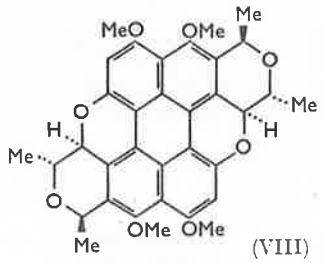
(V)



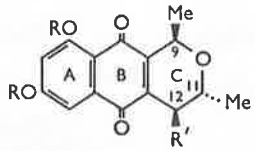
(VI)



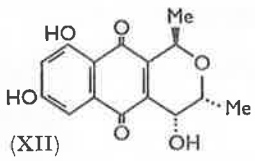
(VII)



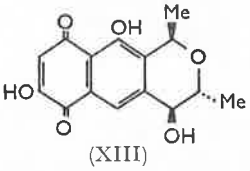
(VIII)



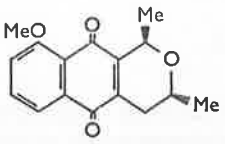
(IX: R = H, R′ = OH)
(X: R = Me, R′ = OH)
(XI: R = R′ = H)



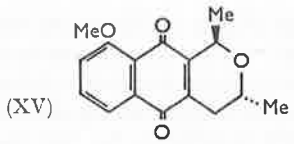
(XII)



(XIII)



(XIV)

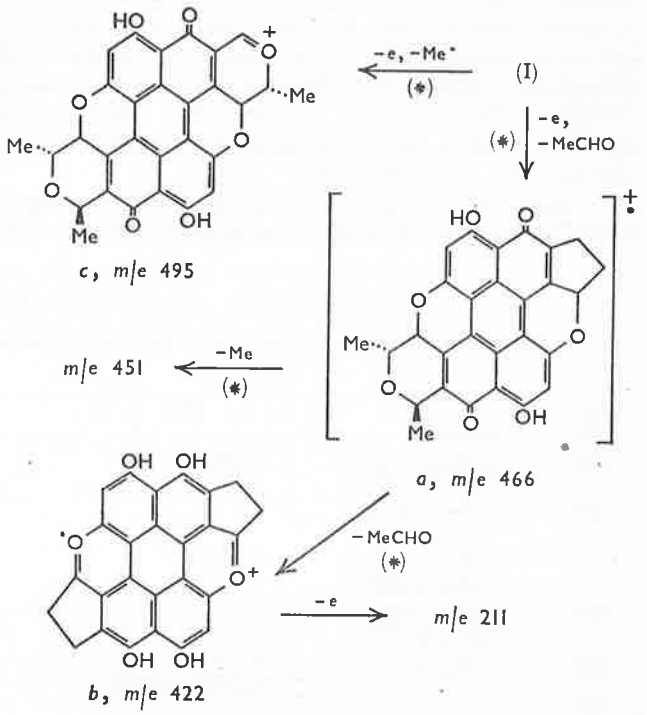


(XV)

oses water to form the ion *a* (*m/e* 466). An analogous situation is observed in the mass spectrum (Table 1) of xanthoaphin-*fb* (VII),[5] whose molecular ion (*m/e* 546) fragments by loss of water to produce the chrysoaphin molecular ion (*m/e* 528) which undergoes fragmentation as shown in Figure 2. Loss of acetaldehyde from the xanthoaphin *fb* molecular ion (*m/e* 546) is not observed.

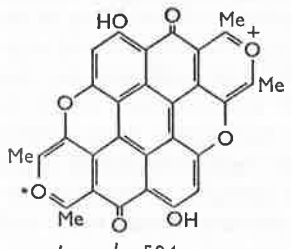
[6] J. H. Bowie, D. W. Cameron, and D. H. Williams, *J. Amer. Chem. Soc.*, 1965, **87**, 5094.
[7] J. H. Beynon and A. E. Williams, *Appl. Spectroscopy*, 1960, **14**, 156.

The general features of the erythroaphin spectrum are also retained in the mass spectrum of dibromoerythroaphin-*fb* (IV).[4] Alternatively, this compound may, on electron impact, like simpler halogenated

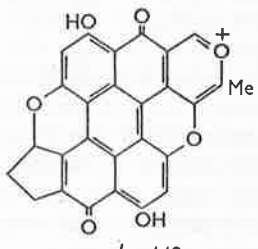


Scheme 1

quinones,[6-8] lose halogen radicals from the molecular ion. Subsequent fragmentation by this pathway is complex, *e.g.*, the base peak of the spectrum corresponds formally to $M - 2Br\cdot - 4H\cdot$ ($M - 164$). Further structural variation in the erythroaphin system is provided by the tetramethoxyperylene derivative[9] (VIII), whose spectrum (Table 1) shows major peaks corresponding to $M - 15$ ($M - Me\cdot$), $M - 59$ ($M - Me\cdot - CH_3CHO$) and $M - 103$ ($M - Me\cdot - 2CH_3CHO$) ions (metastable ions substantiate all processes). Significant loss of acetaldehyde from the molecular ion is not observed in this case, in contrast to the spectrum of erythroaphin.



d, *m/e* 504



e, *m/e* 449

Hydroxy- and dihydroxy-erythroaphins-*fb*[4] (II and III), on electron impact, behave very differently from

[8] J. H. Bowie, D. W. Cameron, R. G. F. Giles, and D. H. Williams, *J. Chem. Soc.* (*B*), 1966, 335.
[9] D. W. Cameron, R. I. T. Cromartie, Y. K. Hamied, B. S. Joshi, P. M. Scott, and Lord Todd, *J. Chem. Soc.*, 1964, 72.

one another and to some extent from the compounds already discussed. The molecular ion (*m/e* 542) of the latter (see Table 1) loses two molecules of water and two hydrogen radicals to form *m/e* 504 [$C_{30}H_{16}O_8^+$ (H.R.)] plausibly represented as the ion *d*; alternatively loss of a methyl radical from the molecular ion is observed, but no appreciable loss of acetaldehyde. The spectrum (Figure 3) of hydroxyerythroaphin-*fb* (II) is much more complex. The molecular ion (*m/e* 526) fragments to *m/e* 449, possibly the ion *e*, according to either of the schemes $M - CH_3{\cdot}CHO - Me{\cdot} - H_2O$ or
$M - H_2O - Me{\cdot} - CH_3{\cdot}CHO$ [high resolution measurements confirm the compositions of *m/e* 508, 567, and 449; *m/e* 467 is a doublet corresponding to $C_{28}H_{19}O_7^+$ (85%) and $C_{27}H_{15}O_8^+$ (15%)]. Alternatively, formal loss of an oxygen atom from the molecular ion leads to the erythroaphin molecular ion (*m/e* 510), as evidenced by the normal breakdown pattern of erythroaphin which is substantiated by appropriate metastable ions. How this process is effected has not been established (care was taken to ensure that the sample of hydroxyerythroaphin-*fb* used was not contaminated with the parent erythroaphin). Direct loss of an oxygen atom with rearrangement of hydrogen cannot be excluded; alternatively, disproportionation in the source may lead to the erythroaphin and dihydroxyerythrophin molecular ions. The spectrum of the latter would not be observed under these conditions because of its much lower volatility. (In support of the second possibility, pyrolysis of hydroxyerythroaphin-*fb* at 350° under vacuum does indeed produce detectable amounts of erythroaphin *fb*).

The spectra of naphthaquinones (IX—XV) are more complex than those of the perylene derivatives so far described and extensive high-resolution measurements have been necessary to interpret unequivocally their breakdown patterns. It is noteworthy that these processes always involve at least initially the non-aromatic rings in the compounds concerned; the general fragmentation pathways[6] established for simple hydroxy- and methoxy-naphthaquinones are unfavourable by comparison. Compound (XIII)[10] exhibits the simplest mass spectrum (Table 2, Figure 4) of the naphthaquinones examined. Its interpretation is summarised in Scheme 2 and is, in some respects, analogous to those of the erythroaphin derivatives already discussed. The molecular ion (*m/e* 290) fragments by two major pathways. Successive loss of a methyl radical and water can lead to the relatively stable cation *f* (*m/e* 257), which fragments further only by loss of carbon monoxide. Alternatively, loss of acetaldehyde results in an ion *m/e* 246, formulated as *g*, which may decompose either by loss of carbon monoxide or a methyl radical to form *m/e* 218 and 231, respectively.

Similar, and therefore diagnostic, processes are also observed when ring C is fused to a quinonoid rather than

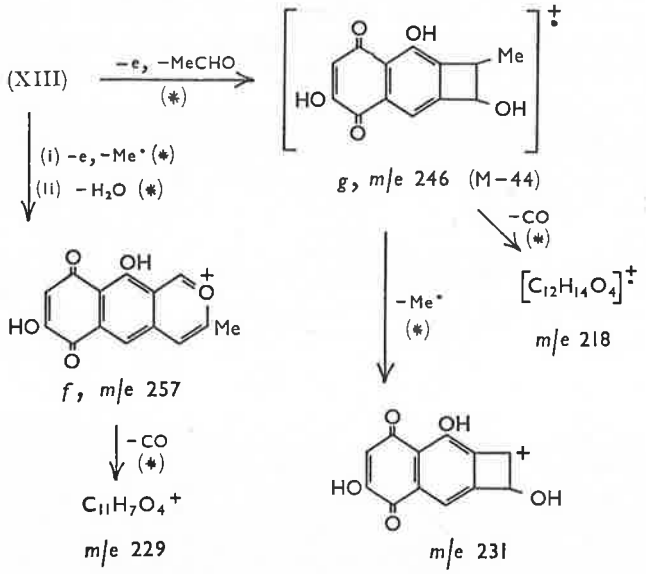
TABLE 2

High-resolution measurements of fragment ions in the mass spectra of the naphthaquinones (IX—XV)

	Compound				
m/e	(IX)	(XI)	(XIII)	(XIV)	(XV)
275	$C_{14}H_{11}O_6$		$C_{14}H_{11}O_6$		
274	$C_{14}H_{10}O_6$ (70%) $C_{15}H_{14}O_5$ (30%)	$C_{15}H_{14}O_5$			
272	$C_{14}H_8O_6$ (30%) $C_{15}H_{12}O_5$ (70%)		$C_{15}H_{12}O_5$		
259	$C_{14}H_{11}O_5$ (75%) $C_{15}H_{15}O_4$ (25%)	$C_{14}H_{11}O_5$			
257	$C_{14}H_9O_5$ (65%) $C_{15}H_{13}O_4$ (35%)		$C_{14}H_9O_5$	$C_{15}H_{13}O_4$	$C_{15}H_{13}O_4$
246	$C_{13}H_{10}O_5$	$C_{13}H_{10}O_5$ (75%) $C_{14}H_{14}O_4$ (25%)	$C_{13}H_{10}O_5$		
244				$C_{14}H_{12}O_4$ (90%) $C_{15}H_{16}O_3$ (10%)	$C_{14}H_{12}O_4$ (95%) $C_{15}H_{16}O_3$ (5%)
243				$C_{14}H_{11}O_4$ (80%) $C_{15}H_{15}O_3$ (20%)	$C_{14}H_{11}O_4$ (80%) $C_{15}H_{15}O_3$ (20%)
241		$C_{14}H_9O_4$			
239				$C_{15}H_{11}O_3$	$C_{15}H_{11}O_3$
231	$C_{12}H_7O_5$ (65%) $C_{13}H_{11}O_4$ (35%)	$C_{13}H_{11}O_4$ (90%) $C_{12}H_7O_5$ (10%)	$C_{12}H_7O_5$		
229	$C_{13}H_9O_4$ (55%) $C_{14}H_{13}O_3$ (45%)		$C_{13}H_9O_4$	$C_{14}H_{13}O_3$ (90%) $C_{13}H_9O_4$ (10%)	$C_{14}H_{13}O_3$ (85%) $C_{13}H_9O_4$ (15%)
228	$C_{13}H_8O_4$ (70%) $C_{14}H_{12}O_3$ (30%)			$C_{14}H_{12}O_3$ (80%) $C_{13}H_9O_4$ (20%)	$C_{14}H_{12}O_3$ (65%) $C_{13}H_9O_4$ (35%)
218	$C_{12}H_{10}O_4$		$C_{12}H_{10}O_4$		
217		$C_{12}H_9O_4$			
203			$C_{11}H_7O_4$		

[10] D. W. Cameron, R. I. T. Cromartie, D. G. I. Kingston, and Lord Todd, *J. Chem. Soc.*, 1964, 51.

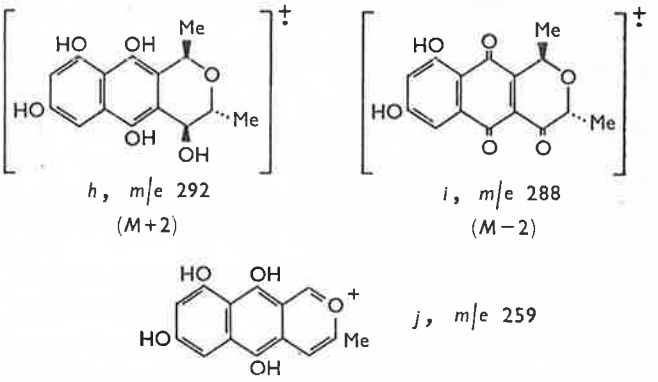
a benzenoid ring as in compound (IX) [10] (Figure 5). This mode of fusion leads to certain minor differences in fragmentation. For example, in the spectrum of compound (IX) loss of water is more pronounced than the loss of a methyl radical from the molecular ion, and is followed by the loss of a methyl radical, leading to an ion analogous to *f*. The molecular ion of compound (XIII), on the other hand, has little observable tendency to lose water and the ion *f* may be formed as shown in Scheme 2. The main difference between the



Scheme 2

spectra of compounds (IX) and (XIII), however, lies in the greater complexity of the former, as evidenced by high resolution measurements shown in Table 2. This complexity is due, at least in part, to the presence of significant $(M + 2)$ and $(M - 2)$ ions, not observed in the spectrum of the latter, which fragment independently of the molecular ion. These ions are neither due to impurity nor are they formed thermally, since the spectra determined by the direct insertion technique are independent of source temperature (60—200°) but dependent on source pressure. These ions are plausibly formulated as *h* and *i*, respectively, in support of which the former may fragment to give *j*, *m/e* 259 (70% H.R.), while no analogous fragmentation is observed from the latter. Their formulation is visualised as involving intermolecular collisions in the source.

Modification of compound (IX) by methylation of the phenolic hydroxyl groups as in compound (X) [10] leads to no significant change in fragmentation pattern (Table 1). Removal of the *C*(12) hydroxyl group, however, as in compound (XI),[2] causes a considerable modification (Tables 1 and 2, Figure 6). Its mass spectrum exhibits a pronounced molecular ion which, in contrast to the molecular ions from (IX), (X), and (XII), does not fragment by loss of acetaldehyde. It fragments principally by loss of a methyl radical and to a lesser extent of an ethyl radical to *m/e* 245(75% H.R.). Further decompositions are summarised in Figure 6. An analogous fragmentation is observed in the spectrum of isoeleutherin [11] (XV) (Tables 1 and 2), illustrating the ease with which this substitution pattern in ring C can be detected by mass spectrometry even with differing groups on ring A.



All the results, so far described, have been obtained on compounds which despite considerable variation in structure, possess the same stereochemistry. The effects of changing stereochemistry have also been studied whenever possible. Epimerisation at C(12), for example, has little effect on the mass spectra, as evidenced by the almost identical mass spectra exhibited by compounds (IX) and (XII) [10] and by erythroaphin-*fb* (I) and -*sl* [4] (V). Epimerisation at C(11) also is without effect since the spectrum of eleutherin [11] (XIV) is very similar to that of isoeleutherin (XV) (Tables 1 and 2). It is concluded, therefore, that mass spectrometry is of considerable utility for structural studies in this field, in particular in yielding valuable information regarding the nature of the non-aromatic side-chain but that epimeric structures cannot be differentiated by this technique.

EXPERIMENTAL

All spectra were measured with an A.E.I. MS 9 mass spectrometer, by use of the direct insertion technique, with source temperatures of *ca.* 150° for the naphthaquinones and 350—400° for the aphins. Exact mass measurements were carried out at a resolution of 14,000 (10% valley definition) and heptacosafluorotributylamine was used to provide reference masses.

We thank Dr. D. H. Williams for discussion, and Professor H. Schmid for samples of eleutherin and isoeleutherin. Part of this work was carried out during the tenure of an I.C.I. Fellowship (to J. H. B.).

UNIVERSITY CHEMICAL LABORATORY,
CAMBRIDGE. [5/1324 *Received, December 13th*, 1965]

[11] H. Schmid and A. Ebnöther, *Helv. Chim. Acta*, 1951, **34**, 1041.

Alkaloids of *Daphnandra* Species. Part VIII.[1] The Structure of Repanduline. The Evidence based on Mass Spectrometry and Nuclear Magnetic Resonance

By I. R. C. Bick, J. H. Bowie, John Harley-Mason, and D. H. Williams, University Chemical Laboratory Cambridge

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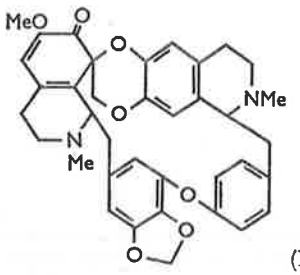
Alkaloids of *Daphnandra* Species. Part VIII.[1] The Structure of Repanduline. The Evidence based on Mass Spectrometry and Nuclear Magnetic Resonance

By I. R. C. Bick, J. H. Bowie, John Harley-Mason, and D. H. Williams, University Chemical Laboratory Cambridge

High resolution mass spectrometry has established the molecular formula of repanduline and its key degradation products. The highly characteristic breakdown patterns of bisbenzyltetrahydroisoquinoline alkaloids permit the chemically labile functional groups (enol-ether and carbonyl functions) to be located in a small portion of the repanduline skeleton. The relative location of the enol-ether and carbonyl functions is strongly supported by the n.m.r. spectra of repanduline and its reduction products, as are other unusual features of the repanduline skeleton.

THE chemical evidence upon which the structure of repanduline (I) or (Ia) is based was described in Part VII.[1] This Paper records the mass and n.m.r. spectra of repanduline and some of its key degradation products which support the proposed structures (I) or (Ia) in some detail, but do not permit differentiation between them. The reasons for regarding (I) as the more likely structure for repanduline were outlined in Part VII,[1] and details of the spectra are therefore discussed in terms of this structure only, for purposes of clarity.

The molecular formulae of repanduline [(I), $C_{37}H_{36}N_2O_7$], dihydrorepanduline [(II), $C_{37}H_{38}N_2O_7$], repandulinol [(III), $R^1 = R^2 = H$), $C_{37}H_{38}N_2O_7$], [$^2H_2$]-repandulinol [(III), $R^1 = R^2 = D$), $C_{37}H_{36}D_2N_2O_7$], dihydrorepandulinol [(IV), $C_{37}H_{40}N_2O_7$], and dihydrode-*O*-methylrepandulinol [(VI), $C_{36}H_{38}N_2O_7$] are established by molecular ions at appropriate integral values in all the mass spectra, in conjunction with exact mass measurements on the molecular ions from repanduline (I) and dihydrorepandulinol (IV). The presence of the unit $C_{15}H_{12}O_3$ in repanduline (I) and the transformation products (II)—(VI) is indicated by the occurrence of prominent $M - C_{15}H_{13}O_3$ ions ($M - 241$) in the spectra of repanduline (I) and of (II), (III), (IV), and (VI) (see Figures 1—5). In the light of the known fragmentation pattern of bisbenzyltetrahydroisoquinoline alkaloids,[2-4] the $M - C_{15}H_{13}O_3$ ion would *a priori* be assigned to the loss of the two benzyl groups with their three oxygen substituents and one extra carbon atom by double α-cleavage adjacent to nitrogen (with associated



(Ia)

hydrogen rearrangement to the neutral fragment). The appropriate ions are marked in Figures 1—5 and the cleavages summarised in the structural formulae (I)—(IV) and (VI).

In addition, analytically useful ions are formed by cleavage of the same bonds as in the formation of the $M - 241$ species, but without loss of a hydrogen atom from the incipient charged fragment and associated with overall loss of 2 electrons (*i.e.*, to form a doubly charged ion). This behaviour is also observed in other bisbenzyltetrahydroisoquinoline alkaloids,[2-4] and gives rise to *m/e* 191 (382^{2+}) from (II) and (III), *m/e* 192 (384^{2+}) from (IV), and *m/e* 185 (370^{2+}) from (VI). For example,

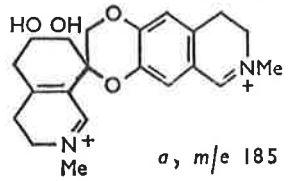
[1] Part VII, I. R. C. Bick, P. S. Clezy, J. Harley-Mason, A. S. Howard, W. I. Taylor, and M. J. Vernengo, preceding Paper.

[2] D. C. DeJongh, S. R. Shrader, and M. P. Cava, *J. Amer. Chem. Soc.*, 1966, **88**, 1052.

[3] M. Tomita, T. Kikuchi, K. Fujitani, A. Kato, H. Furukawa, Y. Aoyagi, M. Kitano, and T. Ibuka, *Tetrahedron Letters*, 1966, 857.

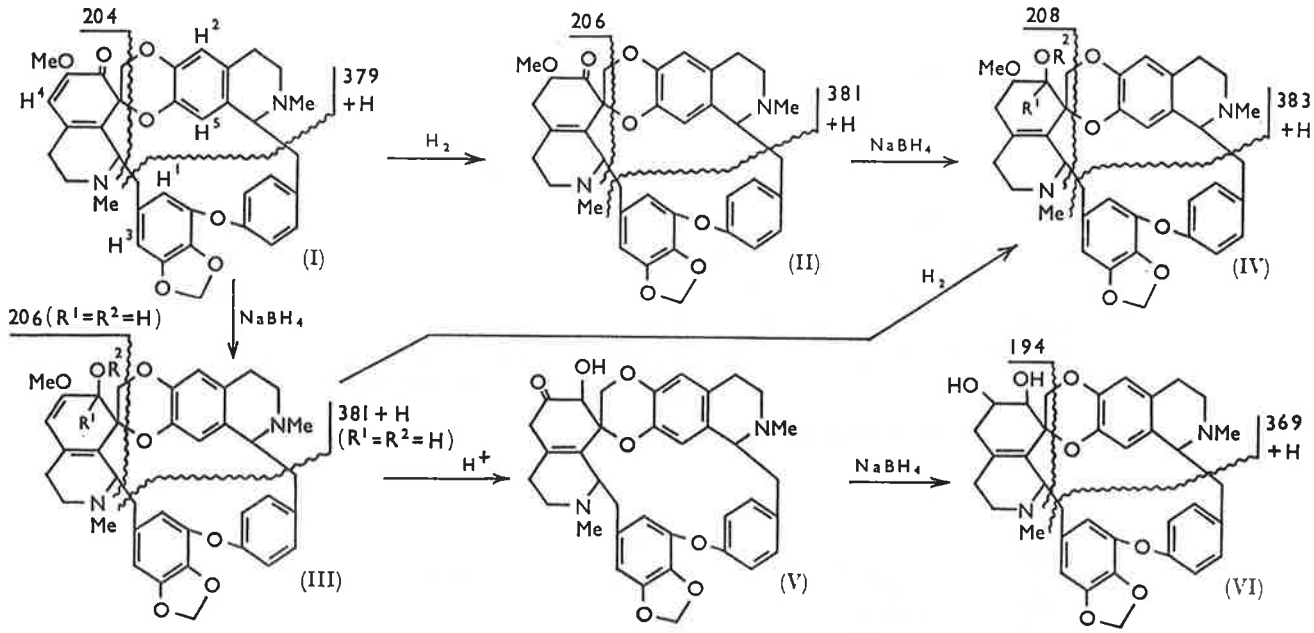
[4] J. Baldas, Q. N. Porter, I. R. C. Bick, and M. J. Vernengo, *Tetrahedron Letters*, 1966, 2059.

in the last case the fragment ion corresponds to *a* (*m/e* 185).



a, *m/e* 185

A third fragmentation reaction which is of great diagnostic value corresponds to the loss of 416 mass units from repanduline (I), dihydrorepanduline (II), resolution measurements on the spectra of (I) and (IV) establish the loss of 416 mass units as $M - C_{25}H_{22}NO_5$. The findings point to the presence of an intact $C_{25}H_{22}NO_5$ unit in repanduline (I) and its transformation products (II)—(VI), and to the occurrence of both chemical reductions (with borohydride or catalytically) and subsequent reactions in a small portion ($C_{12}H_{14}NO_2$) of the original repanduline (I) molecule. A formal mechanism by which *m/e* 204 ($C_{12}H_{14}NO_2^+$, base peak in Figure 1) may be derived from repanduline is indicated by the sequence (I) ⟶ *b* ⟶ *c* (for other examples of "retro-Diels–Alder" reactions in heterocyclic systems,



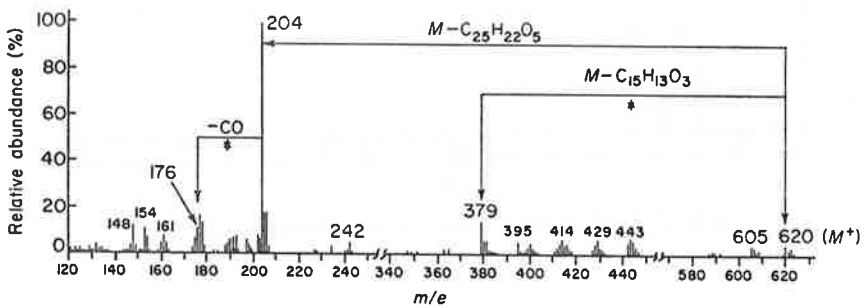


FIGURE 1 Mass spectrum of repanduline (I)

repandulinol (III; $R^1 = R^2 = H$), [$^2H_2$]repandulinol (III; $R^1 = R^2 = D$), dihydrorepandulinol (IV), and dihydrode-*O*-methylrepandulinol (VI) (see Figures 1—5). Appropriate metastable peaks in the spectra of (II), (III; $R^1 = R^2 = D$), (IV), and (VI) correspond to the genesis of $M - 416$ from the molecular ion,* and high see ref. 5). Although the isomerisation of *b* ⟶ *c* requires considerable reorganisation of the hydrogen atoms and is of course unproved, the importance of aromaticity is suggested by the more pronounced tendency of the corresponding $M - C_{25}H_{22}NO_5$ ions (*m/e* 206) from dihydrorepanduline (II) and repandulinol (III; $R^1 = R^2 = H$) to give peaks (*m/e* 204) due to the loss of two additional hydrogen atoms, since the

* It was pointed out recently that metastable peaks do not necessarily arise only from one-step processes, but that they can correspond also to consecutive transitions, *e.g.*, a two-step process, as is probable in the present case (see K. R. Jennings, *Chem. Comm.*, 1966, 283, and J. Seibl, *Helv. Chim. Acta*, 1967, **50**, 263).

[5] H. Budzikiewicz, J. Braumann, and C. Djerassi, *Tetrahedron*, 1965, **21**, 1855; D. C. DeJongh, S. C. Perricone, and W. Korytnyk, *J. Amer. Chem. Soc.*, 1966, **88**, 1233.

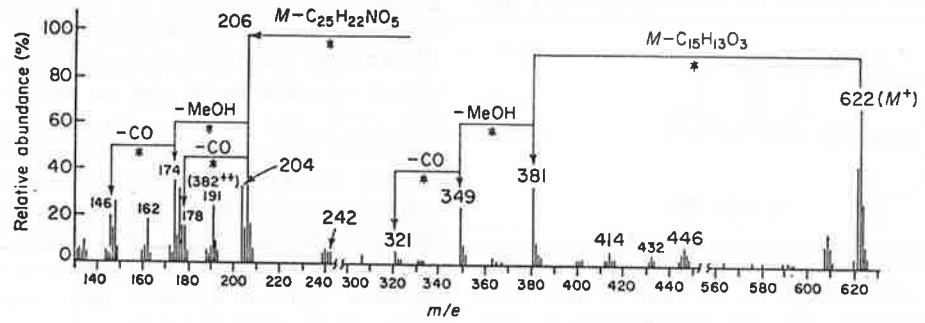


FIGURE 2 Mass spectrum of dihydrorepanduline (II)

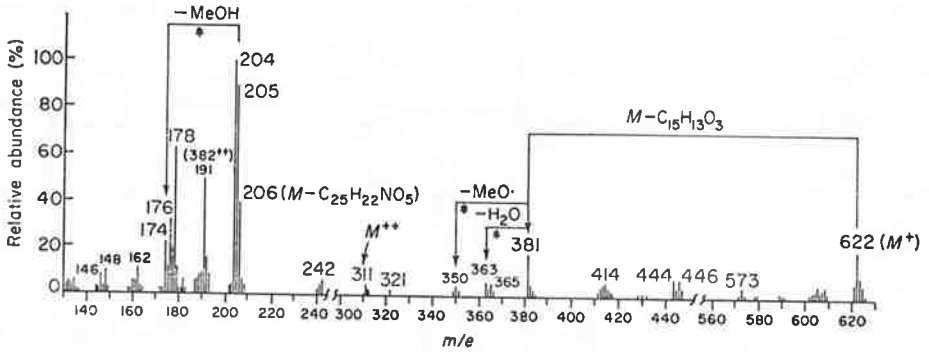


FIGURE 3 Mass spectrum of repandulinol (III; $R^1 = R^2 = H$)

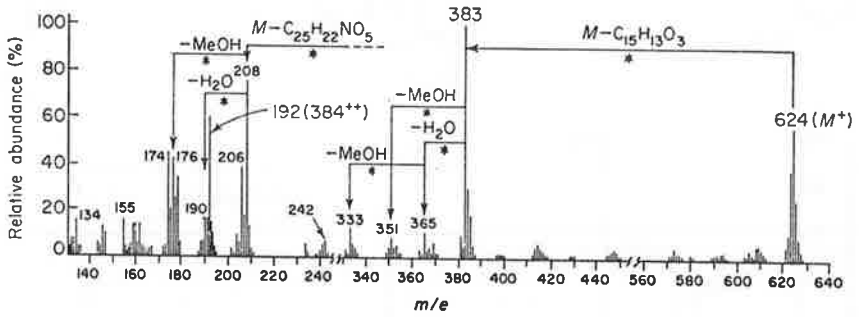


FIGURE 4 Mass spectrum of dihydrorepandulinol (IV)

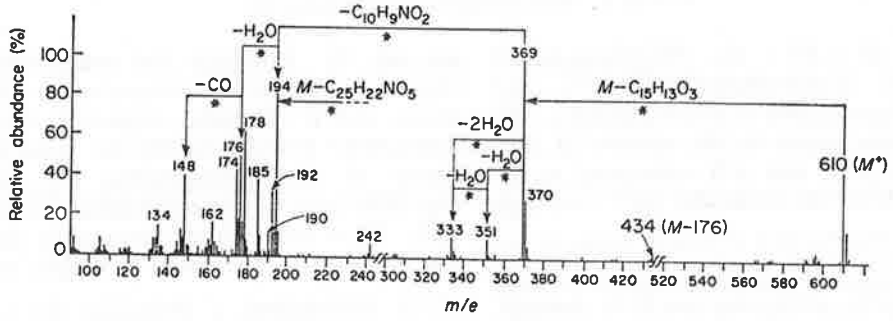
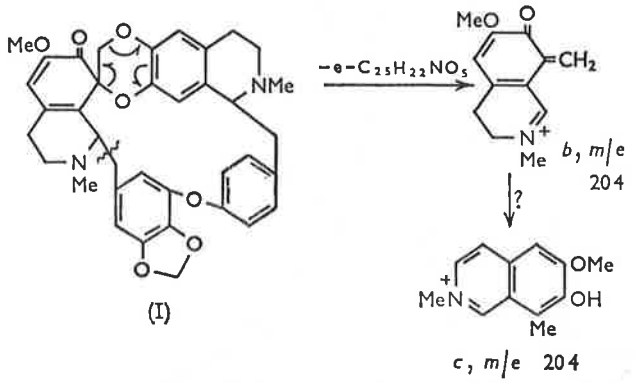


FIGURE 5 Mass spectrum of dihydrode-*O*-methylrepanduline (VI)

m/e 206 ions formally correspond to dihydroquinolinium ions [the *m/e* 204 ion which constitutes the base peak in the spectrum (Figure 3) of repandulinol (III; $R^1 = R^2 = H$) arises from *m/e* 206 by the successive losses of hydrogen radicals as established by appropriate metastable peaks]. When the $M - 416$ species correspond to tetrahydroisoquinolinium ions, the tendency to form quinolinium ions by loss of four hydrogen atoms is greatly reduced, *i.e.*, *m/e* 204 and 190 (in Figures 4 and 5, respectively) are of much smaller abundance than *m/e* 208 and 194. The ions which arise by the loss of 416 mass units are indicated in the structural formulae and the relative abundances of the ions may be seen in Figures 1—5.



(I)

The further decompositions of $M - 241$ and $M - 416$ ions, as established by high resolution measurements and appropriate metastable peaks, are of utility in establishing the nature of substituents in the portion of the molecule which exists as a blocked dienone in repanduline (I) itself. The breakdown of the $M - 241$ and $M - 416$ ions from dihydrorepanduline (II) and repandulinol (III; $R^1 = R^2 = H$) by losses of methanol and/or carbon monoxide (see Figures 2 and 3) are consistent with the presence of both methoxy- and carbonyl-groups in the modified tetrahydroisoquinoline nucleus. Moreover, the $M - 241$ and the $M - 416$ ions from dihydrorepandulinol (IV) break down by losses of water and/or methanol, suggesting the presence of methoxy- and hydroxy-groups as indicated in (IV), whereas the $M - 241$ ion from dihydrode-*O*-methylrepandulinol (VI) undergoes the concerted or stepwise elimination of 2 molecules of water, in complete accord with the presence of two hydroxy-groups in close proximity as in (VI).

The most comprehensive set of high resolution measurements have been obtained for the spectrum (Figure 4) of dihydrorepandulinol (IV). The results (Table 1) are in complete accord with the gross structure (I) for repanduline. The data in Table 1, in conjunction with metastable peaks, permit the detailed analysis of the spectrum (Figure 4).

The mass spectra of (I)—(IV) and (VI) * are of tremendous help in establishing the groupings of atoms in these molecules, whereas the n.m.r. spectra of (I)—(VI) are useful in indicating the relative orientations and environments of protons attached to double bonds or

TABLE 1

Composition of major fragment ions from dihydrorepandulinol (IV)

m/e	Composition	*m/e*	Composition
174	$C_{11}H_{12}NO$	191	$C_{11}H_{13}NO_2$
175	$C_{11}H_{13}NO$ (75%)	192	$C_{11}H_{14}NO_2$
	$C_{10}H_9NO_2$ (25%)	208	$C_{12}H_{18}NO_2$
176	$C_{11}H_{14}NO$ (50%)	242	$C_{15}H_{14}O_3$
	$C_{10}H_{10}NO_2$ (50%)	333	$C_{21}H_{21}N_2O_2$
177	$C_{10}H_{11}NO_2$	351	$C_{21}H_{23}N_2O_3$
178	$C_{10}H_{12}NO_2$	365	$C_{22}H_{25}N_2O_3$
190	$C_{12}H_{16}NO$ (70%)	383	$C_{22}H_{27}N_2O_4$
	$C_{11}H_{12}NO_2$ (30%)	624	$C_{37}H_{40}N_2O_7$

adjacent to oxygen atoms. The n.m.r. spectrum (Figure 6) of repanduline (I) indicates the presence of two non-equivalent *N*-methyl groups (2·38 and 2·62) † and one *O*-methyl group (3·58). An important feature which strongly supports the proposed structure (I) for repanduline is the AB quartet ($J = 11$ c./sec., $\delta_A = 4{\cdot}14$, and $\delta_B = 3{\cdot}88$) assigned to non-equivalent protons of the bridging CH_2O-group. The protons of the methylenedioxy-group are non-equivalent and resonate as a two-proton multiplet centred at 5·94. The four aromatic protons of the *p*-disubstituted benzene ring are all non-equivalent and the lines which would be anticipated in terms of a first-order analysis in which each of the four proton resonances is split by an *ortho*-interaction (8 c./sec.) and a *meta*-interaction (2 c./sec.) can be identified (see Figure 6). The three broadened singlets at 6·07, 6·48, and 6·77 are assigned to the protons designated as H^1, H^2, and H^3 in (I), though not necessarily respectively. The proton (H^4) on the enol–ether double bond resonates at 5·52. The singlet resonance at 5·12 is assigned to the aromatic proton (H^5) since molecular models indicate that this proton lies directly over the *p*-disubstituted benzene ring, in a region where strong shielding is expected.

The n.m.r. spectrum of dihydrorepanduline (II) differs from that of repanduline (I) in two important features. First the resonance at 5·52 in the spectrum of repanduline (I) is not present in the spectrum of dihydrorepanduline (II), since the enol–ether double bond is now saturated. Secondly, an upfield shift (0·27 p.p.m.) of the methoxy-resonance occurs on passing from repanduline (I) to dihydrorepanduline and this shift is perfectly consistent with saturation of the enol–ether double bond.

The spectrum of repandulinol (III; $R^1 = R^2 = H$) in the $\delta = 4{\cdot}0$—$7{\cdot}5$ p.p.m. region (Figure 7) differs most significantly from that of repanduline (I) in the appearance of a new broad singlet at 4·15. Also, there is an upfield shift of the enol–ether proton (H^4) from 5·52 in repanduline (I) to 4·53 in repandulinol (III; $R^1 = R^2 = H$); the upfield shift is associated with a change in multiplicity from a singlet (Figure 6) to a doublet ($J \sim 2$ c./sec.; Figure 7). Since the broad 4·15 singlet (Figure 7) does not disappear from the spectrum

* The mass spectrum of de-*O*-methylrepandulinol (V) was useful, but less helpful than those of (I)—(IV) and (VI) and therefore has not been reported.

† The quoted values correspond to p.p.m. on the δ scale.

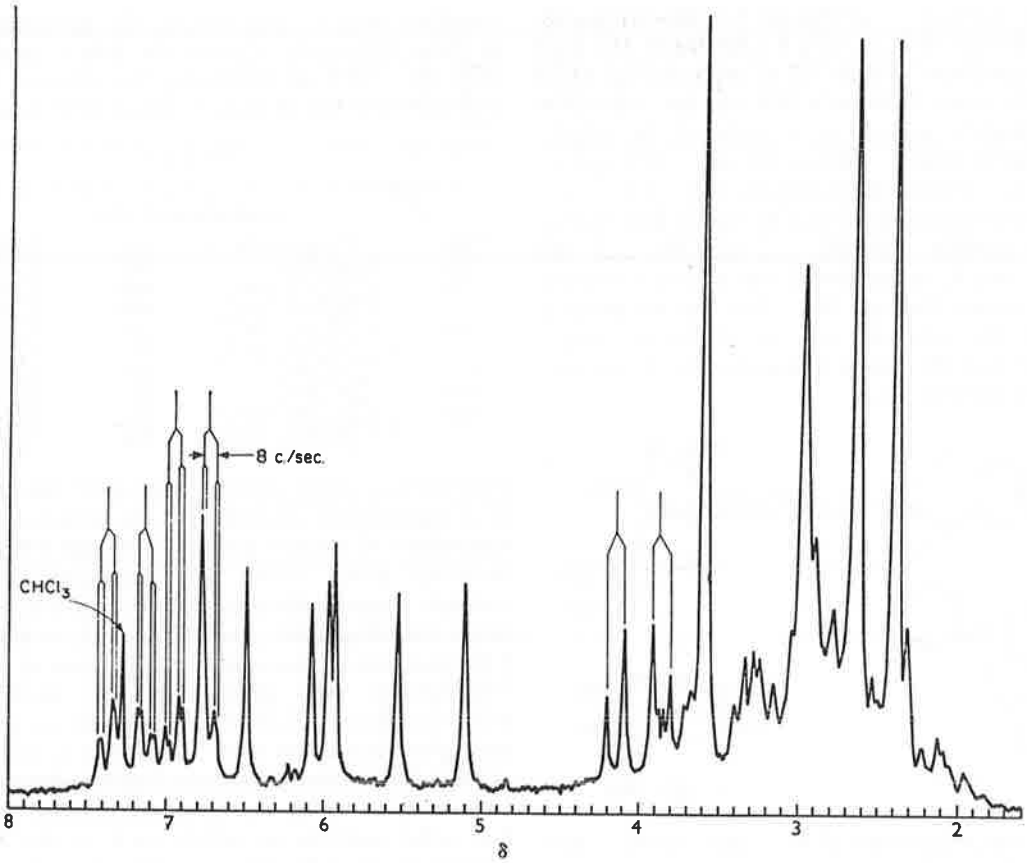


FIGURE 6 100 Mc./sec. n.m.r. spectrum of repanduline (I) in $CDCl_3$ solution

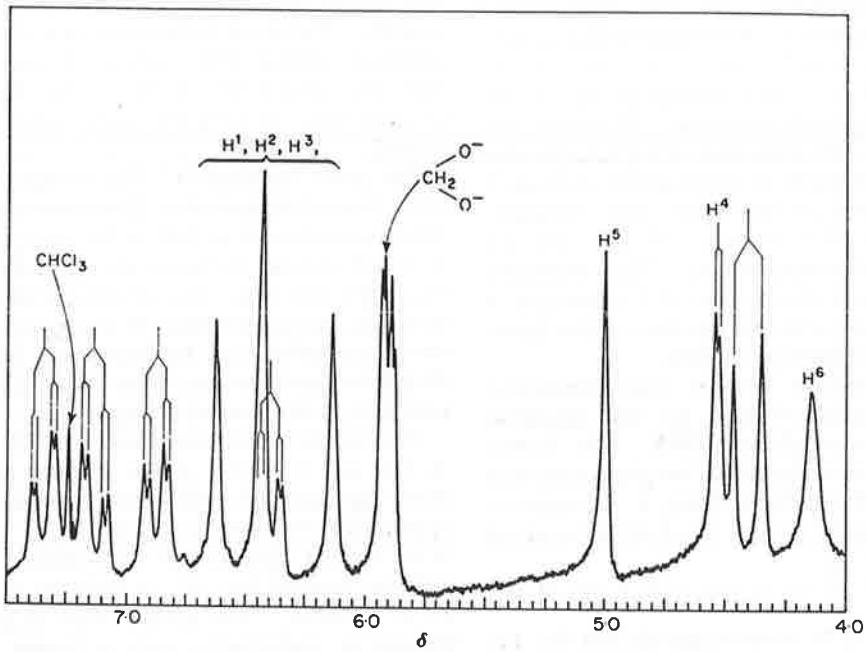
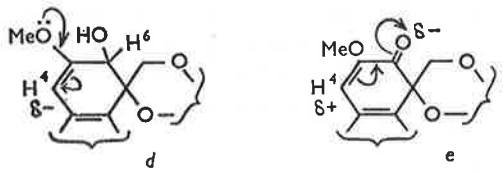


FIGURE 7 Partial 100 Mc./sec. n.m.r. spectrum (δ = 4·0—7·5 p.p.m.) of repandulinol (III; $R^1 = R^2 = H$) in $CDCl_3$ solution

on shaking the deuteriochloroform solution of repandulinol (III; $R^1 = R^2 = H$) with deuterium oxide, but is not present in the spectrum of [$^2H_2$]repandulinol (III; $R^1 = R^2 = D$), it must be associated with H^6 (see partial structure *d*). Moreover, the splitting (2 c./sec.) of the enol–ether proton H^4 (partial structure *d*) is absent in the spectrum of [$^2H_2$]repandulinol (III; $R^1 = R^2 = D$) and therefore $J_{H^4,H^6} \sim 2$ c./sec. The significant coupling between H^4 and H^6 confirms the close proximity of the enol–ether and carbonyl functions. In addition, the specific arrangement shown in partial structure *e* (of repanduline) is strongly supported by the upfield shift of H^4 on reduction of the carbonyl group, since the polarisation indicated in *e* is removed, leaving only the shielding polarisation indicated in *d* to operate.



d *e*

Other assignments in Figure 7 are either indicated in the figure or will be obvious by analogy to Figure 6, with the exception of the doublet resonance ($J = 11$ c./sec.) centred at 4·40. This signal is due to one of the protons of the bridging CH_2O-group. Apparently, the chemical shift between these methylene protons is increased upon reduction of the carbonyl function; the high field proton has been located by a double resonance experiment in which the doublet centred at 4·40 is collapsed to a singlet by irradiation at 3·66.

An acetyl derivative of repandulinol (III; $R^1 = R^2 =$ H) has been prepared.[1] Its spectrum is most noteworthy for the shift of the broad singlet observed at 4·15 in Figure 7 to 5·38; the change in δ value (1·23 p.p.m.) corresponds to a typical acetylation shift.[6] The methyl resonance of the acetyl group occurs at remarkably high field (1·65) and molecular models of acetylrepandulinol do indeed suggest that a marked shielding of the acetyl methyl group by the aromatic rings of this compound can occur.

[6] See, for example, J. N. Shoolery, and M. T. Rogers, *J. Amer. Chem. Soc.*, 1958, **80**, 5121.

[7] M. Ohashi, J. M. Wilson, H. Budzikiewicz, M. Shamma, W. A. Slusarchyk, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 2807.

The n.m.r. spectra of dihydrorepandulinol (IV), de-*O*-methylrepandulinol (V), and dihydrode-*O*-methylrepandulinol (VI) do not merit separate discussion, other than to point out that they are in perfect accord with the structures assigned to these compounds, and in particular that a methoxy-resonance is not found in the spectra of (V) and (VI). Also, the spectra of (V) and (VI) establish that the tetrasubstituted double bond of the dienone group in repanduline (I) does not migrate into conjugation with the carbonyl function of (V).

The remaining function of mass spectrometry and nuclear magnetic resonance in the structure elucidation of repanduline (I) has been to provide supporting evidence for the structure of a degradation product, hemirepanduline (VII) and its derived acetate (VIII), which contain only a portion of the skeleton of the intact alkaloid.

The mass spectrum (Figure 8) of hemirepanduline (VII) is that of a typical benzyltetrahydroisoquinoline.[7-9] High resolution measurements establish its molecular formula as $C_{20}H_{25}NO_3$. The base peak corresponds to ion *f* (*m/e* 206, $C_{12}H_{16}NO_2^+$, high resolution), which then decomposes further (as established by high resolution measurements and appropriate metastable peaks) as indicated in Figure 8. The presence of the methoxy-

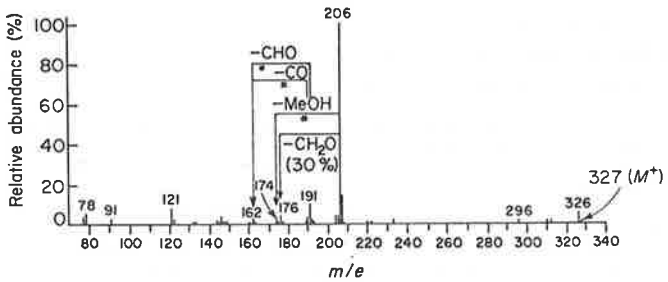
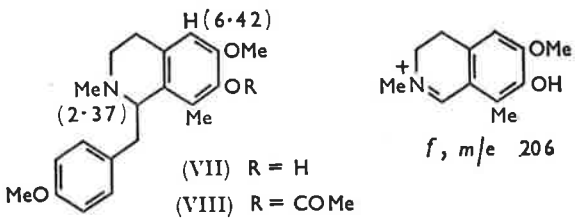


FIGURE 8 Mass spectrum of hemirepanduline (VII)

benzyl substituent is suggested by the ion at *m/e* 121 ($C_8H_9O^+$). As expected, the mass spectrum of the derived acetate (VIII) exhibits the molecular ion at *m/e* 369 and shifts of 42 mass units are observed relative to the corresponding ions from hemirepanduline (VII)



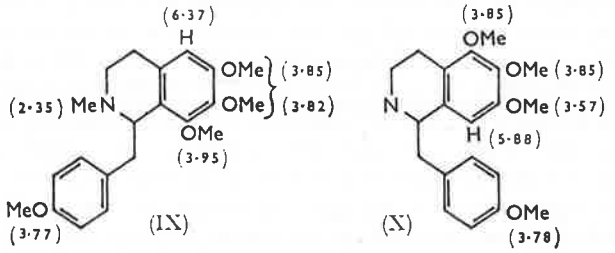
in those cases where the elimination of keten does not precede fragmentation. The n.m.r. spectrum of hemirepanduline establishes the presence of the methoxy-groups (two three proton singlets at 3·80 and 3·87), one *N*-methyl group (three proton singlet, at 2·42),

[8] F. R. Stermitz, L. Chen, and J. I. White, *Tetrahedron*, 1966, **22**, 1095.

[9] M. Tomita, H. Furukawa, T. Kikuchi, A. Kato, and T. Ibuka, *Chem. and Pharm. Bull.* (*Japan*), 1966, **14**, 232.

and one aromatic *C*-methyl group (three proton singlet at 2·18). Signals associated with a typical A_2B_2 system are centred at 6·83 and 7·17 and thus the methoxy-substituent of the benzyl group must be in the *para*-position. The remaining aromatic proton in the molecule resonates as a singlet at 6·42.

The relative orientation of the aromatic Me, OH, and OMe substituents was tentatively deduced in the following manner. First, it was known that the hydroxy-group was *meta* to the unsubstituted position in the aromatic ring, since hemirepanduline does not incorporate deuterium on equilibration with deuterium oxide under basic conditions.[1] Secondly, *O*-acetylhemirepanduline (VIII) gives án n.m.r. spectrum in which the singlet aromatic proton has shifted from 6·42 to 6·54, consistent with its location *meta* to the acetoxy-group.[10] Thirdly, there must be a substituent in the 8-position of the isoquinoline ring. This follows from the data of Tomita *et al.*,[11] who showed from the analysis of the n.m.r. spectra of a number of benzyltetrahydroisoquinolines that if a substituent is present in this position, the benzyl group adopts a conformation as in (IX), which results in shielding of the *N*-methyl protons, so that they resonate around 2·35. With no substituent at C-8, the benzyl group adopts a different conformation, as in (X), in which the *N*-methyl protons resonate at 2·50 or lower field; the H^8 proton is now shielded and resonates around 5·88; these observations have been supplemented by the data of Kubota *et al.*[12] [from whose work examples (IX) and (X) are taken] and by others.[13–15] Attention is drawn to the close correspondence of the *N*-methyl and aromatic proton chemical shifts in (IX) and (VII).



In the light of the above evidence, and biogenetic considerations [16] which lead one to expect oxygenation at C-6 and C-7 of the isoquinoline nucleus, structure (VII) is the most reasonable for hemirepanduline. As described in the following Paper,[17] this suggestion has now been confirmed by synthesis.

EXPERIMENTAL

Mass spectra were obtained on an AEI MS 9 mass spectrometer operating at 70 ev. Samples were introduced via the direct inlet technique. The n.m.r. spectra were obtained on a Varian HA-100 instrument, in the frequency-sweep mode to facilitate spin-decoupling where applicable.

[7/448 *Received, April 17th,* 1967]

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THE STRUCTURE OF OCHROMYCINONE

J. H. Bowie

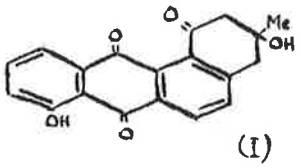
Department of Organic Chemistry,
The University of Adelaide, South Australia

A. W. Johnson

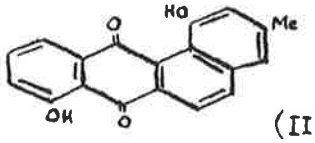
Department of Chemistry,
The University of Nottingham, England

(Received 2 February 1967)

The recent report (1) of the structures of tetrangulol (I) and tetrangomycin (II) prompts us to present a preliminary account of the structure of ochromycinone, which has been isolated together with a series of rhodomycinones and pyrromycinones (2) from several Streptomyces strains (3).



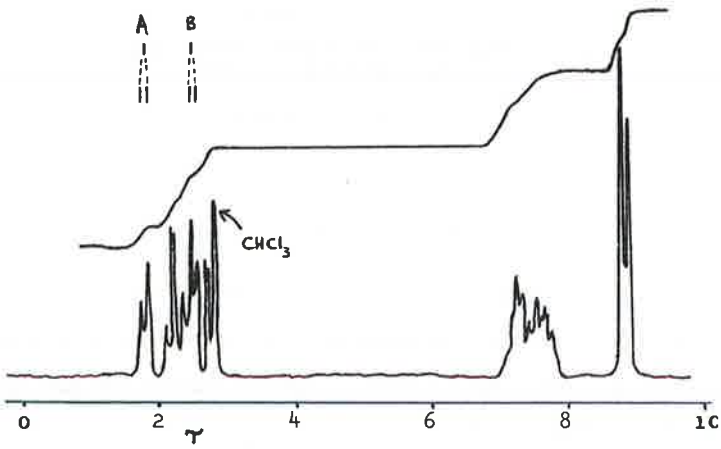
(I)



(II)

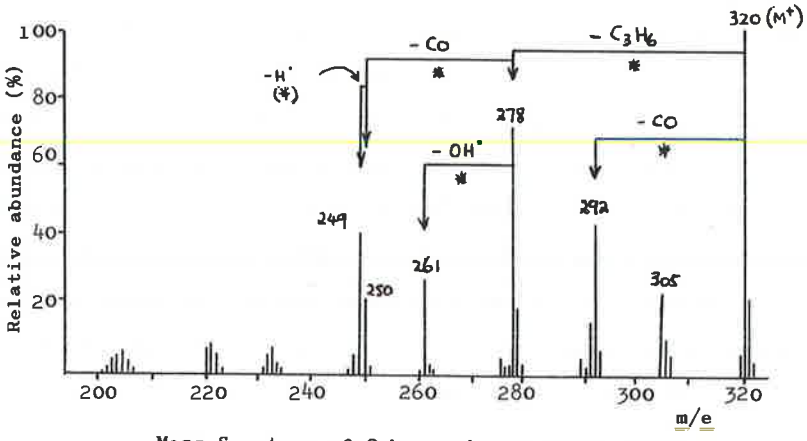
Ochromycinone, $C_{19}H_{14}O_4$, $[\alpha]_D^{25^\circ}$ 204.5° ($CHCl_3$), contains no methoxyl, ester, or non-bonded hydroxyl groups, and is stable both to acid and alkali. The ultraviolet spectrum ($\lambda_{max.}$ 265, 405 mμ; log ε 4.42, 3.55) is characteristic of a 1-hydroxy-anthraquinone (4) containing an additional auxochromic substituent. Infrared carbonyl absorptions (1703, 1668, and 1638 $cm.^{-1}$) confirm both the presence of the 1-hydroxy-anthraquinone moiety (5) and an additional conjugated carbonyl group. Aldehydic CH absorptions are absent in the infrared spectrum, and as ochromycinone forms a 2,4-dinitrophenylhydrazone under forcing conditions, the presence of a ketonic substituent on the anthraquinone is likely.

FIG. 1



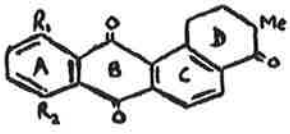
N.M.R. Spectrum (100 Mc.) of Ochromycinone in $CDCl_3$

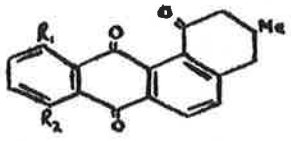
FIG. 2



Mass Spectrum of Ochromycinone methyl ether

Ochromycinone forms a monomethyl ether and a monoacetate. The ultraviolet spectra of these derivatives lend additional support to the presence of the keto-1-hydroxy-anthraquinone chromophore. The methyl ether exhibits infrared carbonyl absorptions at 1702 and 1678 $cm.^{-1}$, indicating that the phenolic group in ochromycinone is not adjacent to the α-keto group. The absence of strong absorption at 715 $cm.^{-1}$ in the infrared spectra of ochromycinone and its derivatives shows that both the terminal rings of the anthraquinone are substituted (5). Modified Kuhn-Roth oxidation of ochromycinone produces only acetic acid. Zinc dust distillation of ochromycinone yields 3-methylbenz[a]anthracene (identified by its absorption spectrum and R_F values in several solvents) (6). Assuming that methyl migration has not occurred during the zinc dust distillation, four structures (III - VI) can be written for ochromycinone.





(III) R_1 = OH, R_2 = H
(IV) R_1 = H, R_2 = OH

(V) R_1 = OH, R_2 = H
(VI) R_1 = H, R_2 = OH

The nuclear magnetic resonance spectra of ochromycinone (Figure 1) and of its derivatives shows a constant ortho AB splitting pattern (J_{AB} = 9.0 c.p.s.) due to the two protons of ring C, an unsymmetrical doublet due to the methyl protons, and a complex pattern due to the remaining protons of ring D.

The mass spectra of ochromycinone and its derivatives (see Figure 2 for the mass spectrum of ochromycinone methyl ether) are also informative structurally. These may be interpreted using a knowledge of the fragmentation modes of α-tetralones (7), as the fragmentation is only slightly complicated by the anthraquinone moiety (8). An asterisk in Figure 2 represents the presence of an appropriate metastable peak for the process indicated and exact mass measurements establish the

compositions of the major ions in the spectrum. The process $M^+ - C_3H_6 - CO - H^\bullet$ is changed to $M^+ - C_3H_4D_2 - CO - H^\bullet$ when the protons α- to the carbonyl group of ring D are exchanged with deuterium (MeOD/MeONa), thus establishing structure (V) or (VI) for ochromycinone. We prefer structure (VI) on biogenetic grounds, but hope to make the decision by syntheses of (V) and (VI) which are in progress.

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THE STRUCTURE OF THE ALKALI FUSION PRODUCT DERIVED FROM MAESOPSIN. THE EVIDENCE BASED ON MASS SPECTROMETRY AND N.M.R. SPECTROSCOPY

By J. H. Bowie* and J. W. W. Morgan†

[*Manuscript received July* 25, 1966]

Summary

Maesopsin, $C_{15}H_{12}O_6$, (obtained from the heartwood of *Maesopsis eminii*, Rhamnaceae) on fusion with alkali forms a yellow product, $C_{15}H_{10}O_5$, which on methylation forms two methyl ethers. Structures for these products are suggested from a consideration of their n.m.r. and mass spectra, which afford confirmation of the original work.

Extraction of the African timber musizi (*Maesopsis eminii*, Rhamnaceae) yields maesopsin, $C_{15}H_{12}O_6$. Maesopsin (I), when fused with a mixture of sodium and potassium hydroxides at 130°, forms a crystalline yellow product $C_{15}H_{10}O_5$, whilst on further treatment with alkali at 200° 3,5,4′-trihydroxydiphenylmethane is obtained.[1] The structure of this latter product was established by methylation and oxidation to the corresponding trimethoxybenzophenone.

The yellow fusion product on brief treatment with dimethyl sulphate–potassium carbonate yielded a monomethyl ether $C_{16}H_{12}O_5$ whereas prolonged treatment afforded a tetramethyl ether $C_{19}H_{20}O_6$. Of the alternative structures ((II), (III), and (IV)) discussed[1] for this fusion product, (IV) was favoured on the basis of infrared and n.m.r. evidence. Thus both the fusion product (ν_{max} 1820 and 1694 cm^{-1}) and its monomethyl ether (ν_{max} 1801 and 1700 cm^{-1}) exhibited carbonyl bands resembling those of coumaran-2,3-dione (ν_{max} 1807 and 1720 cm^{-1}), the 1800 band being at an unusually high frequency. Further, the methylene group had the same chemical shift (5·86 τ) in the n.m.r. spectra of the two methyl ethers as it had in that of the fusion product. It was thus concluded that the methylene group has the same environment in all three compounds, which excluded the alternatively formulated tetramethyl ether (VII) associated with fusion product structures (II) and (III).

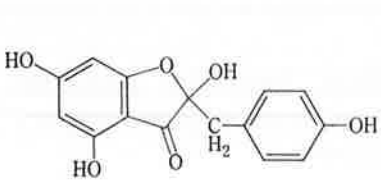
In the present work we wish to present mass spectrometric evidence in support of structure (IV) for the fusion product and (VI) for the tetramethyl ether, and which together with further n.m.r. evidence shows the monomethyl ether to be (V).

A revised analysis of the nuclear magnetic resonance spectra of these products is summarized in Table 1. As pointed out above, all the compounds show a peak due to the protons of a methylene group at 5·86 τ; this is compatible with a diphenylmethane structure,[2a] but not with a methylene group in a system of the type

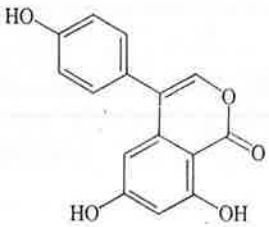
* Department of Organic Chemistry, University of Adelaide.
† Forest Products Research Laboratory, Princes Risborough, Aylesbury, Bucks., U.K.

[1] Janes, N. F., King, F. E., and Morgan, J. W. W., *J. chem. Soc.*, 1963, 1356.

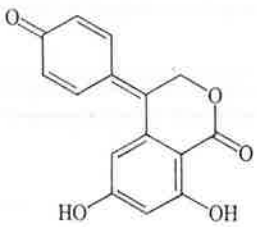
[2] "N.M.R. Spectra Catalog." Vol. 1. (*a*) Nos. 357, 661. (*b*) Nos. 51, 262, 530, 627. (Varian Associates: Palo Alto, Cal., 1962.)



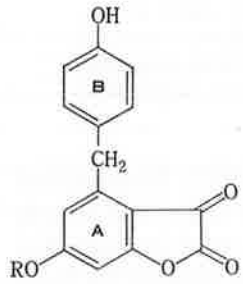
(I)



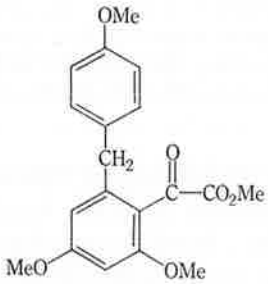
(II)



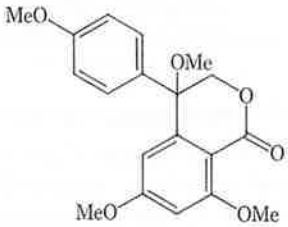
(III)



(IV) R = H (V) R = Me



(VI)



(VII)

TABLE 1

N.M.R. SPECTRA OF THE ALKALI FUSION PRODUCT AND ITS METHYL ETHERS

τ_a, chemical shift in CD_3COCD_3; τ_b, chemical shift in C_6D_6; J values in c/s; s, singlet; d, doublet

Fusion Product (IV)				Monomethyl Ether (V)					Tetramethyl Ether (VI)					Assignment
τ_a*	No.	Type	J	τ_a	τ_b‡	No.	Type	J	τ_a	τ_b	No.	Type	J	
				1·79†		1	s							–OH
2·85	1	d	8·5	2·82		2	d	8·5	2·80	2·86	2	d	8·5	§
3·24	1	d	8·5	3·22		2	d	8·5	3·14	3·22	2	d	8·5	§
3·48	2	s*		3·25		1	d	1·5	3·33	3·68	1	d	1·4	||
				3·31		1	d	1·5	3·46	3·93	1	d	1·4	||
5·86	2	s		5·86	6·03	2	s		5·86	5·71	2	s		–CH_2–
				6·04	7·06	3	s		6·10	6·56	6/3	s		–OMe
									6·10	6·69	3	s		–OMe
									6·22	6·83	3	s		–OMe
										6·85	3	s		–OMe

* On shaking solution with D_2O, no change in the signal at 3·48 is observed; however, the spectrum in the aromatic region is sharpened.

† This signal is removed when the solution is shaken with D_2O.

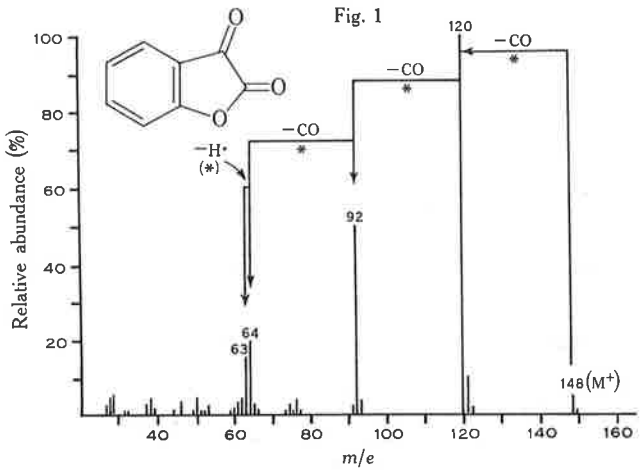
‡ Because of insolubility, the aromatic region was not visible.

§ *ortho*-Coupled AB pattern.

|| *meta*-Coupled AB pattern.

–C=C–CH_2–O–C(=O)–C=C (which generally falls between 5·0–5·3 τ).[2b] In certain other respects however the assignments differ from those previously recorded. In particular the peak at 3·48 τ in the alkali fusion product cannot be due to phenolic hydroxyl as it is not removed on treatment with D_2O. This signal is now assigned to the *meta*-protons which on treatment with t-butanol become unequivalent and exhibit *meta*-splitting. In addition, when the spectra of the monomethyl ether and

Fig. 1



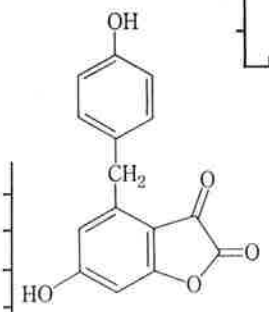
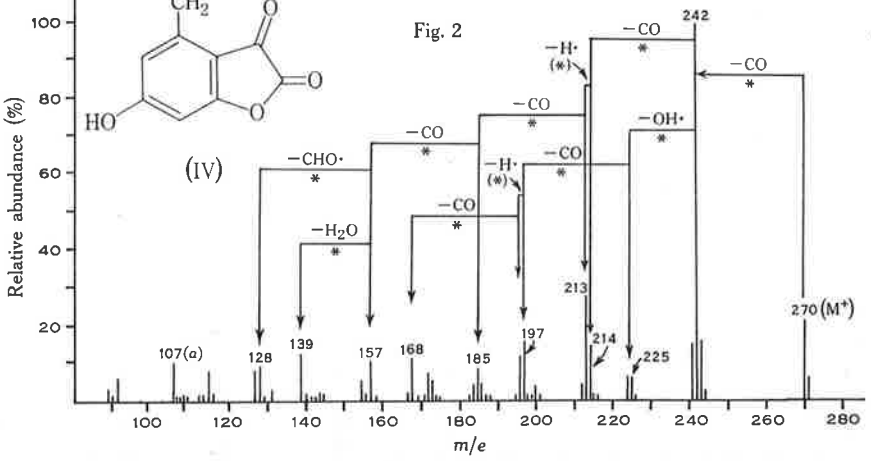


Fig. 2



the fusion product are compared, it can be clearly seen that different splitting patterns are exhibited by the *meta*-protons of ring A, together with corresponding differences in the chemical shifts of these protons. This observation demands that the methoxyl group of the monomethyl ether be situated on ring A. Confirmation of this can be seen from the large solvent shift of the methoxy group protons observed when the spectrum of the monomethyl ether is measured in benzene-d_6; viz. $\Delta(CD_3COCD_3—C_6D_6) \simeq 1$ p.p.m.; this large value can only be explained if the methoxyl group is

in proximity to a carbonyl group.[3,4] The allocation of the methoxyl group to the A ring accords with the expected ease of methylation of this hydroxyl group which is in a position analogous to the reactive 7-OH group in flavonoids.

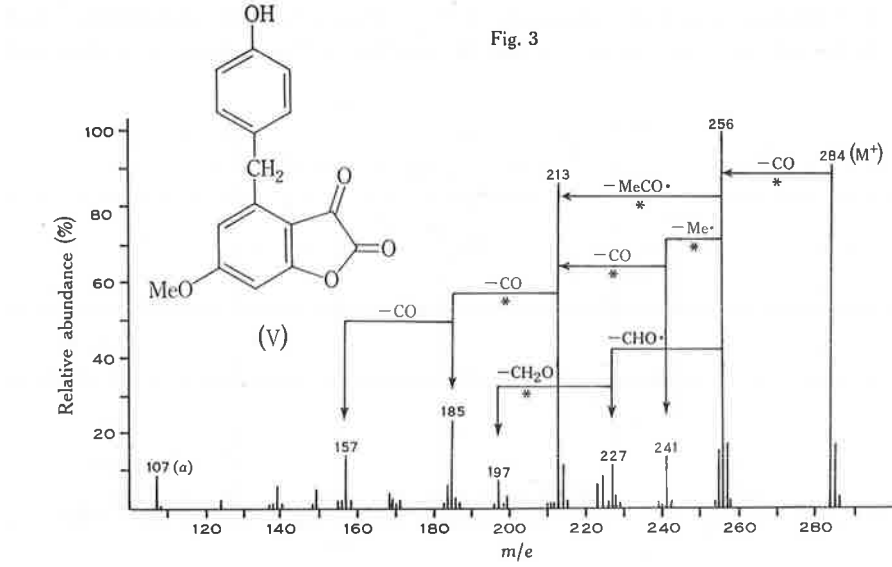


Fig. 3

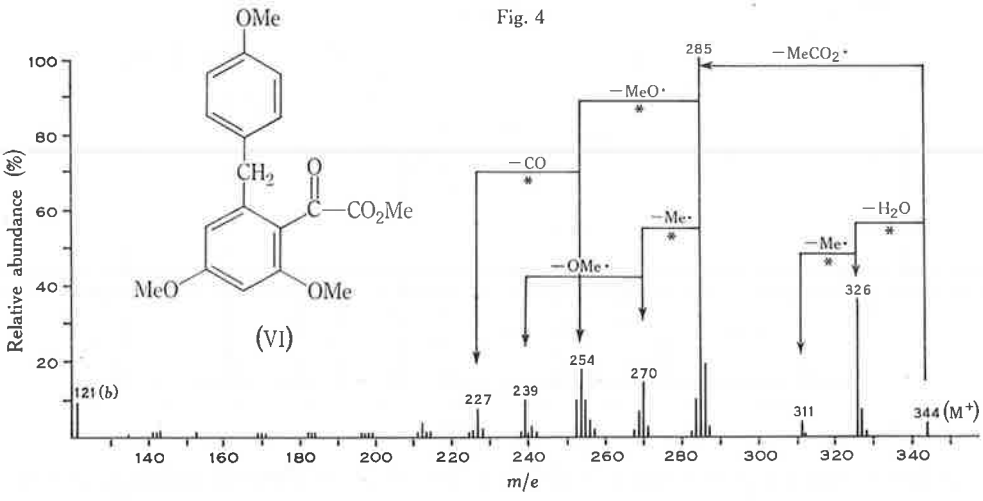


Fig. 4

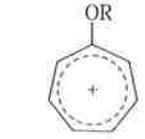
The mass spectra of (IV), (V), and (VI) together with that of coumaran-2,3-dione are reproduced in Figures 1–4. The major fragmentation schemes are indicated in Figures 1–4; an asterisk depicts the presence of an appropriate metastable ion for

[3] Bowie, J. H., Cameron, D. W., Schütz, P. E., Williams, D. H., and Bhacca, N., *Tetrahedron*, 1966, **22**, 1771.

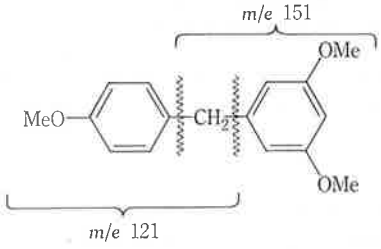
[4] Bowie, J. H., Ronaye, J., and Williams, D. H., *J. chem. Soc.* B, 1966, 785.

the transition indicated. The mass spectra are in agreement with the proposed structures.

Several salient features emerge from a study of the mass spectra of (IV)–(VI). The presence of *m/e* 107 in Figures 2 and 3 and *m/e* 121 in Figure 4 ($C_7H_7O^+$ and $C_8H_{10}O^+$ respectively by high resolution) can be attributed to the oxygenated tropylium cations *a* and *b*. These characteristic fragments show the presence of the



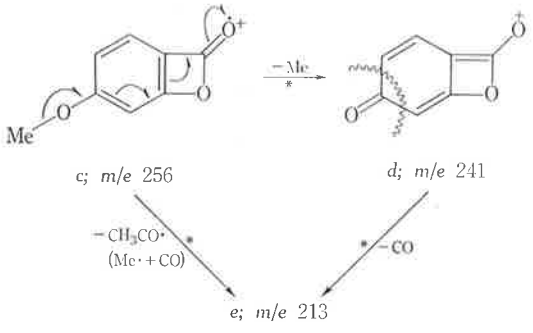
a; *m/e* 107, R = H
b; *m/e* 121, R = Me



diphenylmethane skeleton and are of comparable intensity to those observed in the spectrum of 3,5,4′-trimethoxydiphenylmethane, where *m/e* 121 and 151 represent 16 and 5% of the base peak respectively.

The spectrum of the alkali fusion product (Fig. 2) is similar to that of coumaran-2,3-dione (Fig. 1) with the exception that it may lose two molecules of carbon monoxide from the phenol substituents. Overall loss of five carbon monoxide molecules plus hydrogen would ultimately yield *m/e* 128 which is probably best represented as the naphthalene molecular ion. It should be stressed that this spectrum (Fig. 2) would equally fit the isocoumarin structure (II) if no ion at *m/e* 107 (*a*) were observed.

The mass spectrum (Fig. 3) of the monomethyl ether (V) affords further evidence for the methoxyl group being at C 5. The significant loss of a methyl radical from the M—CO ion (*m/e* 256) together with the concerted elimination of an acetyl radical from the same ion must be associated with a methoxyl group in conjugation with a carbonyl group[5] (see *c*→*d*→*e*).



Finally the mass spectrum (Fig. 4) of the tetramethyl ether establishes the presence of the Ar–CO–CO_2Me unit. The molecular ion *m/e* 344 loses $MeCO_2\cdot$ by α-carbonyl cleavage to furnish *m/e* 285 which is the base peak of the spectrum. Further fragmentations are summarized in Figure 4.

[5] Bowie, J. H., and Cameron, D. W., *Aust. J. Chem.*, 1966, **19**, 1627.

In summary, the evidence based on mass spectrometry and nuclear magnetic resonance spectroscopy when combined with the earlier reported chemical evidence[1] establish the structures of the maesopsin alkali fusion product together with those of its methyl ethers as (IV), (V), and (VI) respectively.

Experimental

N.m.r. spectra were determined with a Varian HA100 nuclear magnetic resonance spectrometer. Mass spectra were determined by the direct insertion technique with an AEI MS9 mass spectrometer operating at 70 eV and with a source temperature of *c.* 150°. Exact mass measurements were carried out at a resolution of 1 in 14,000 (10% valley definition) using heptacosafluorotributylamine to provide reference masses. All measurements were correct to within 15 p.p.m.

Acknowledgment

Part of this work was carried out while one of us (J.H.B.) was the holder of an I.C.I. Fellowship at the University Chemical Laboratories, Lensfield Road, Cambridge, England.

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MASS SPECTRA OF SPERMATHERIDINE ALKALOIDS. THE STRUCTURE OF MOSCHATOLINE*

By I. R. C. Bick,† J. H. Bowie,‡ and G. K. Douglas†§

[*Manuscript received October* 13, 1966]

Summary

The mass spectra of a series of alkaloids of the spermatheridine group, together with those of their alkoxy derivatives, are reported and discussed. The characteristic fragmentation processes, substantiated by appropriate metastable peaks, exact mass measurements, and in some cases by deuterium labelling, facilitate the location of substituents in the tetracyclic system. A structure for moschatoline is deduced from a consideration of the mass spectra of its derivatives.

The spermatheridine alkaloids are related structurally to the aporphines, whose mass spectra have been studied recently.[1] In the present work the mass spectra of spermatheridine[2–4] (I), atherospermidine[2,5,6] (II), *O*-methyl- and *O*-acetyl-moschatoline[7] (III and V), atheroline[7,8] (VI), *O*-acetyl-, *O*-methyl-, and *O*-ethyl-atheroline[6,7] (VIII, IX, and X) and the ethyl ethers[7] (XI and XII), isomeric with the latter compound, are recorded in Table 1 and Figures 1–7.

Although exact mass measurements establish the compositions of many of the fragment ions (Table 2), the structures used in this paper are nominal representations

* This paper constitutes Part IV of the series "Electron Impact Studies". For Part III see Bowie, J. H., Cooks, R. G., Dynesen, E., Lawesson, S.-O., and Schroll, G., *Ark. Kemi*, in press. This paper also forms Part III of the series: "The Alkaloids of *Atherosperma moschatum* Labill." For Part II, see Bick, I. R. C., and Douglas, G. K., *Aust. J. Chem.*, 1965, **18**, 1997.

† Department of Chemistry, University of Tasmania.

‡ University Chemical Laboratory, Cambridge, England; present address: Department of Organic Chemistry, University of Adelaide.

§ Present Address: Waite Agricultural Research Institute, Adelaide.

[1] Ohashi, M., Wilson, J. M., Budzikiewicz, H., Shamma, M., Slusarchyk, W. A., and Djerassi, C., *J. Am. chem. Soc.*, 1963, **85**, 2807.

[2] Bick, I. R. C., Clezy, P. S., and Crow, W. D., *Aust. J. Chem.*, 1956, **9**, 111.

[3] Bick, I. R. C., and Douglas, G. K., *Tetrahedron Lett.*, 1964, 1629; *Phytochemistry*, 1966, **5**, 197.

[4] Buchanan, M. A., and Dickey, E. E., *J. org. Chem.*, 1960, **25**, 1389; Taylor, W. I., *Tetrahedron*, 1961, **14**, 42; Cohen, J., Langenthal, W. von, and Taylor, W. I., *J. org. Chem.*, 1961, **26**, 4143.

[5] Bick, I. R. C., and Douglas, G. K., *Aust. J. Chem.*, 1965, **18**, 1997.

[6] Harris, W. M., and Geissman, T. A., *J. org. Chem.*, 1965, **30**, 432; Pai, B. R., and Shanmugasundaram, G., *Tetrahedron*, 1965, **21**, 2519.

[7] Bick, I. R. C., and Douglas, G. K., *Tetrahedron Lett.*, 1965, 4655.

[8] Bick, I. R. C., and Douglas, G. K., *Tetrahedron Lett.*, 1965, 2399.

TABLE 1

MASS SPECTRA OF COMPOUNDS (VII)–(IX) AND (XI)

All peaks greater than 2% of the base peak (100%) are recorded

(VII)	*m/e*	234	251	264	279	280	290	294	295	296	306	307	308	309	322
	I (%)	2	2	4	6	4	10	18	15	3	6	15	11	4	50
	m/e	323	336	337	338	339	340								
	I (%)	38	4	100	76	18	2								
															$d_0 = 61$; $d_1 = 36$; $d_2 = 3\%$
(VIII)	*m/e*	251	262	264	279	290	294	307	322	337	338	339	379(M)	380	
	I (%)	3	7	3	6	7	11	5	28	100	24	4	19	6	
(IX)	*m/e*	151	164	175·5	179	207	222	235	248	250	264	276	277	278	
	I (%)	3	4	6	3	3	6	4	3	5	4	3	6	4	
	m/e	292	293	306	308	309	320	321	322	336	337	338	350	351(M)	
	I (%)	7	5	8	17	5	14	4	5	21	11	4	14	100	
	m/e	352	353												
	I (%)	25	4												
(XI)	*m/e*	140·5	150	151	164	168·5	177	182·5	208	222	234	235	236	250	
	I (%)	6	3	5	4	4	3	4	4	6	3	3	3	4	
	m/e	251	262	263	264	265	279	280	291	292	294	306	307	308	320
	I (%)	4	7	3	6	3	5	3	3	5	10	3	6	4	8
	m/e	321	322	323	336	337	350	351	364	365(M)	366	367			
	I (%)	3	24	5	11	4	20	6	7	100	24	4			

TABLE 2

COMPOSITION OF SOME IONS IN THE SPECTRA OF COMPOUNDS (II), (X), AND (XII)

(II)		(X)			(XII)		
m/e	Composition	*m/e*	Composition		*m/e*	Composition	
262	$C_{16}H_8NO_3$	337	$C_{19}H_{15}NO_5$	(95%)	337	$C_{19}H_{15}NO_5$	
260	$C_{16}H_6NO_3$		$C_{20}H_{19}NO_4$	(5%)	336	$C_{19}H_{14}NO_5$	
234	$C_{15}H_8NO_2$	336	$C_{19}H_{14}NO_5$	(90%)	322	$C_{18}H_{12}NO_5$	
232	$C_{15}H_6NO_2$		$C_{20}H_{18}NO_4$	(10%)	308	$C_{18}H_{14}NO_4$	
206	$C_{14}H_8NO$	322	$C_{15}H_{12}NO_5$		306	$C_{18}H_{12}NO_4$	(90%)
204	$C_{14}H_6NO$	308	$C_{18}H_{14}NO_4$	(70%)		$C_{17}H_8NO_5$	(10%)
176	$C_{13}H_6N$		$C_{17}H_{10}NO_5$	(30%)	292	$C_{17}H_{10}NO_4$	
149	$C_{11}H_3N$	307	$C_{18}H_{13}NO_4$	(30%)	278	$C_{17}H_{12}NO_3$	(80%)
			$C_{17}H_9NO_5$	(70%)		$C_{16}H_8NO_4$	(20%)
		294	$C_{17}H_{12}NO_4$		164	$C_{10}H_{10}NO_3$	
		251	$C_{15}H_9NO_3$				
		250	$C_{15}H_8NO_3$				
		222	$C_{14}H_8NO_2$				

Fig. 1

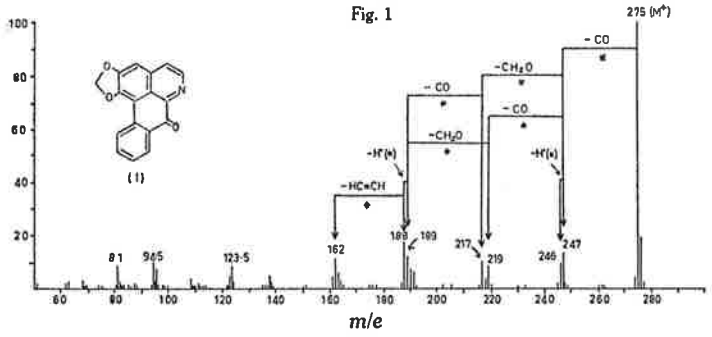
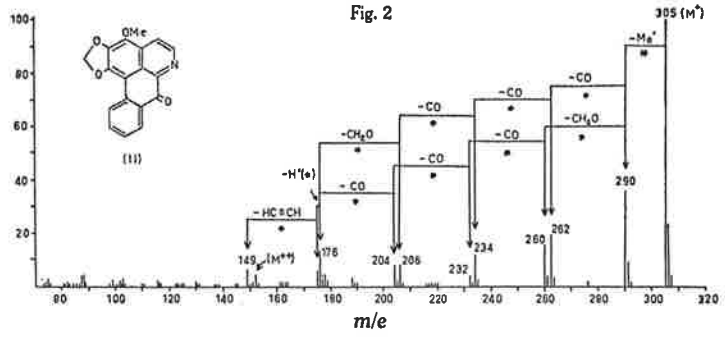


Fig. 2



Relative abundance (%)

Fig. 3

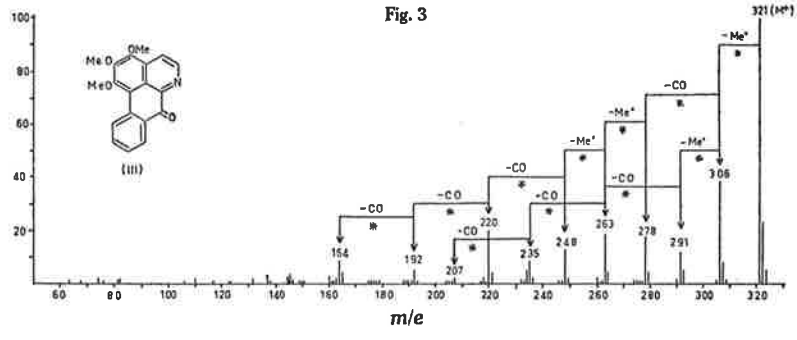
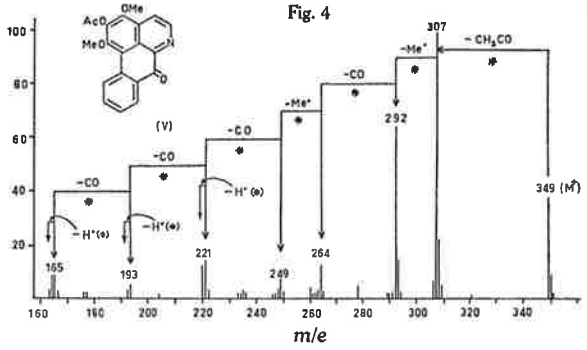
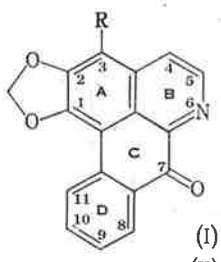


Fig. 4



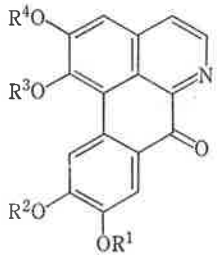
only,* but serve the important purpose of relating the fragmentation pattern to the structure of the intact molecule. An asterisk in a figure or a text depicts the presence of an appropriate metastable ion for the process indicated.

The mass spectra (Figs. 1 and 2) of spermatheridine (I) and atherospermidine (II) are remarkable for loss of all the substituents on ring A through conjugate eliminations involving the carbonyl group of ring C, resulting in complete degradation of ring A. Such fragmentations are not observed in the spectra of simple dimethoxy- and trimethoxy-benzenes, which decompose by loss of only one Me· and one CO



(I) R = H
(II) R = OMe

(III) R = Me
(IV) R = H
(V) R = Ac



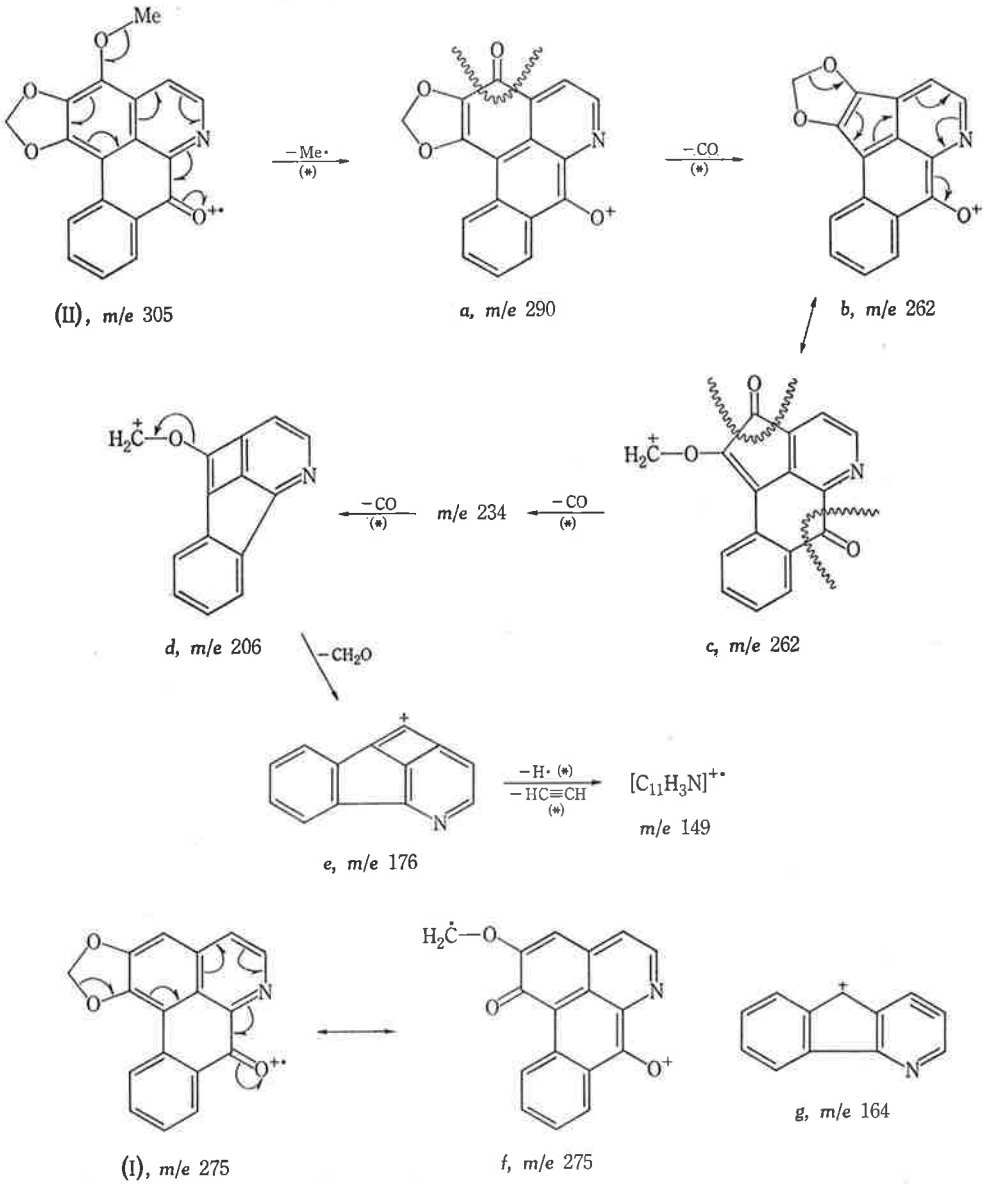
	R^1	R^2	R^3	R^4
(VI)	H	Me	Me	Me
(VII)	D	Me	Me	Me
(VIII)	Ac	Me	Me	Me
(IX)	Me	Me	Me	Me
(X)	Et	Me	Me	Me
(XI)	Me	Et	Me	Me
(XII)	Me	Me	Et	Me

molecule,[10] but are present (to a lesser extent) in the mass spectra of polymethoxyanthraquinones.[11] A fragmentation of atherospermidine (II) is summarized in Scheme 1; similar alternate fragmentations are shown in Figure 2. The compositions of the major fragment ions in the spectrum of (II) have been established by exact mass measurements (see Table 2). The initial elimination of a radical from the molecular ion may in general originate through either the C1 or C3 alkoxy group, but in the case of atherospermidine (II), loss of a Me· from the C3 methoxyl is favoured (II→*a*), followed by a series of concerted eliminations (see Scheme 1) to form ultimately a $C_{11}H_3N^+$ fragment (*m/e* 149). In contrast, the molecular ion of sper-

* It has been suggested[9] that the benzene molecular ion possesses a linear structure.

[9] Monigny, J., Brakier, L., and D'Or, L., *Bull. Acad. r. Belg. Cl. Sci.*, 1962, **48**, 1002.
[10] Barnes, C. S., and Occolowitz, J. L., *Aust. J. Chem.*, 1963, **16**, 219.
[11] Bowie, J. H., unpublished data.

matheridine (I, *m/e* 275) which lacks the 3-methoxyl substituent, plausibly rearranges (via C1) as indicated in Scheme 1 (I→*f*), and fragments as summarized in Figure 1.



Scheme 1

An even more complex series of decompositions can be seen in the mass spectrum (Fig. 3) of *O*-methylmoschatoline (III). Here, alternate concerted loss of three methyl

radicals and three carbon monoxide molecules from ring A (by similar mechanisms to those outlined in Scheme 1), starting from the C1 and/or C3 methoxy groups, followed by the C2 methoxyl, and ending with elision of carbon monoxide from the carbonyl group of ring C, results in the formation of *m/e* 164, possibly *g*.

Fig. 5

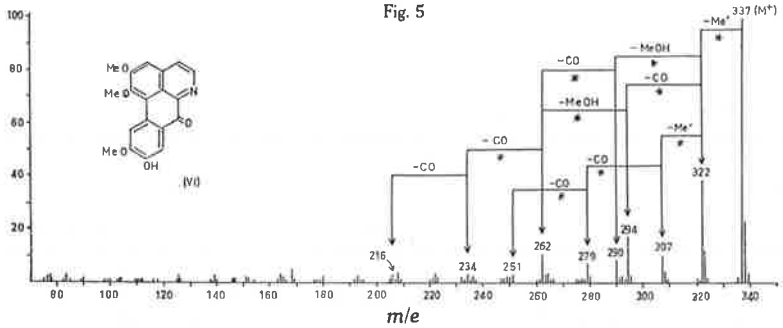


Fig. 6

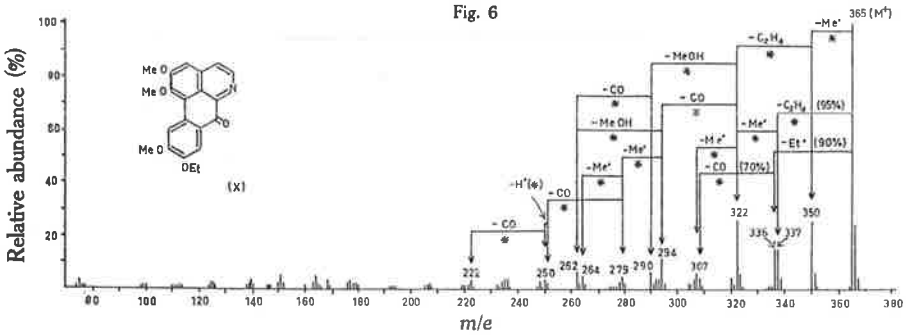
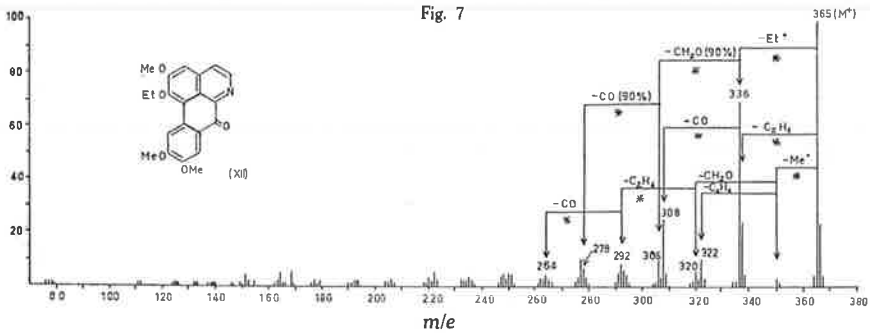


Fig. 7

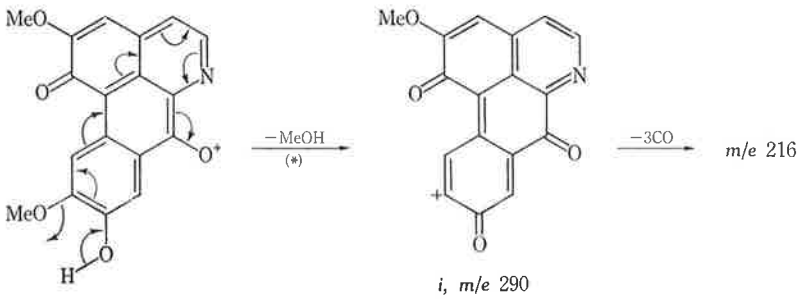


Whereas *O*-methylmoschatoline has been shown to have structure (III), the position of the hydroxyl in moschatoline has not been definitely fixed.[7] From the fragmentation schemes outlined above, it should be possible by mass spectrometry to securely differentiate between a hydroxy group at C1 (or C3) and one at C2. If the hydroxyl were at either C1 or C3, the mass spectrum should show a large contribution from a M—H· ion. Conversely, if the hydroxyl were at C2, then

the fragmentation from the molecular ion should specifically show the sequence M—Me·—CO—Me·—3CO. The corresponding *O*-acetyl compounds should give the same decomposition modes after initial loss of C_2H_2O, since phenolic acetates on electron impact have been shown to produce the molecular ion of the corresponding phenol[12,13] after elision of ketene. Figure 4 illustrates the mass spectrum of *O*-acetylmoschatoline, which in its decomposition modes clearly follows those predicted for the compound with an acetoxyl group at C 2. This strongly supports structure (V) for *O*-acetylmoschatoline and (IV) for moschatoline, as deduced tentatively from other evidence.[7]

The mass spectra of compounds containing oxygenated substituents in ring D (VI)–(XII) are more complex and less readily interpretable than those of the previous group. Although concerted eliminations of the type outlined above for alkoxy substituents on ring A might be expected also for ring D, such eliminations in practice are of lesser importance in this group of alkaloids (see Figs. 5–7); valuable structural information can nevertheless be obtained from their mass spectra, as illustrated by the following examples:

Atheroline (VI) behaves characteristically on electron impact, and the decomposition modes are shown in Figure 5. The interpretation of this spectrum was aided by a comparison with the spectrum of *O*-atheroline-d_1 (VII), prepared by introducing (VI) directly into the source with deuterium oxide.[14] The molecular ion (*m/e* 337) of atheroline (VI) loses a methyl radical (see above) to form *m/e* 322,



h, *m/e* 322 *i*, *m/e* 290

probably *h*, which then loses methanol to furnish *m/e* 290 ($C_{17}H_8NO_4^+$, high resolution). Such eliminations are not observed in the mass spectra of compounds (I)–(III), nor in the spectra of simple methoxyphenols.[10] The corresponding fragment (*m/e* 290) in the spectrum (Table 1) of *O*-atheroline-d_1 (VII) is formed by specific loss of MeOD from the M—Me· fragment, thus favouring the concerted elimination of methanol $h \rightarrow i$; *i* then loses three molecules of carbon monoxide to produce ultimately *m/e* 216. Corresponding processes are also observed in the spectra of the two ethyl ethers (XI) and (XII) (see later). *O*-Acetylatheroline (VIII) behaves unexceptionally on electron impact (Table 1), exhibiting a significant molecular ion which decomposes

[12] Bowie, J. H., Cameron, D. W., and Williams, D. H., *J. Am. chem. Soc.*, 1965, **87**, 5094.
[13] Bowie, J. H., and Cameron, D. W., *Aust. J. Chem.*, 1966, **19**, 1627.
[14] Shannon, J. S., *Aust. J. Chem.*, 1962, **15**, 265.

by loss of ketene to yield the molecular ion of atheroline (VI); further fragmentation then occurs as described previously (Fig. 5).

The derivatives (IX)–(XII) on electron impact show some interesting features. The mass spectrum (Table 1) of *O*-methylatheroline (IX) is as expected except that no loss of dimethyl ether (cf. $h \rightarrow i$) is observed. The mass spectra of the three ethyl ethers (X)–(XII) illustrate a potentially valuable means of distinguishing the type of oxy substituent at C1.

The mass spectra of *O*-ethylatheroline (X) (Fig. 6) and of (XI) (Table 1) are almost identical, and these two compounds cannot be distinguished by mass spectrometry. Extensive high resolution measurements, which are recorded in Table 2, were necessary for the interpretation of the spectra of the ethyl ethers (XI) and (XII). In compounds of this type containing both ethoxyl and methoxyl groups, it would be expected that an ethyl radical would be eliminated more readily than a methyl radical. It can be seen from Table 3 and Figure 7 that this is in fact the

TABLE 3

RELATIVE ABUNDANCES* OF M–R IONS IN THE SPECTRA OF THE ETHYL ETHERS (X)–(XII)

M–R	(X)	(XI)	(XII)
M–Me·	26	22	4
M–Et·	13	11	70

* As per cent of base peak.

case for (XII), where the ethoxyl is on C1, and the resulting fragment ion (*m/e* 336) constitutes 70% of the base peak as compared with 4% for the ion *m/e* 350 due to loss of methyl; for (X) and (XI), however, where the ethoxyl is in ring D and C1 bears a methoxyl, loss of methyl predominates. Further fragmentations of these compounds are outlined in Figures 6 and 7. This evidence lends further support to the mechanistic proposals outlined in Scheme 1, and aids structural studies in alkaloids of the atheroline family.

EXPERIMENTAL

Melting points are corrected and were measured on a Gallenkamp melting point apparatus. Microanalyses were carried out by the Australian Microanalytical Service, Melbourne. Mass spectra were measured by the direct insertion technique with an A.E.I. MS9 mass spectrometer operating at 70 eV, with the source temperature between 200 and 250°. Exact mass measurements were carried out at a resolution of 18,000 (10% valley definition) and heptacosafluorotributylamine was used to provide reference masses. All exact mass measurements were correct to within 15 p.p.m.

7-Ethoxy-6-methoxy-1-(4′,5′-dimethoxy-2′-nitrobenzoyl)isoquinoline

7-Ethoxy-3,4-dihydro-6-methoxy-1-(4′,5′-dimethoxy-2′-nitrobenzyl)isoquinoline[15] (1 g) was added to chromic oxide (1 g) in acetic acid (25 ml) and the mixture heated on the steam-bath

[15] Manske, R. H. F., Charlesworth, E. H., and Ashford, W. R., *J. Am. chem. Soc.*, 1951, **73**, 3751.

until an exothermic reaction commenced. The reaction mixture was then removed from the bath and allowed to cool, poured into water, basified (NH_3), and extracted with chloroform. The chloroform extract was washed with water, dried, and evaporated to dryness. The residue in ethanol (15 ml) was treated with a few drops of 50% aqueous sodium hydroxide and heated on a water-bath; the solution took on a deep red colour which gradually faded with the appearance of yellow prisms (200 mg), m.p. 164–166°; ν_{max} 1676s, 1520s, and 1342s (Found: C, 61·5; H, 4·9. Calc. for $C_{21}H_{20}N_2O_7$: C, 61·2; H, 4·9%).

1-Ethoxy-2,9,10-trimethoxy-7-oxodibenzo[de,g]*quinoline* (*XII*)

The above isoquinoline derivative was shaken in absolute ethanol at room temperature for 20 hr under 1 atm of hydrogen in the presence of a Raney nickel catalyst. The catalyst was removed by centrifugation, washed thoroughly with ethanol, and the washings and original supernatant liquid were combined and evaporated to dryness. The residue (140 mg) was dissolved in methanol (7 ml) and 10% sulphuric acid (7 ml) and diazotized with 1N sodium nitrite (0·6 ml); the solution was allowed to stand in the cold for 30 min, after which it was heated on the steam-bath for 30 min. The solution, which developed a deep red colour, was then cooled, basified (NH_3), and extracted with chloroform. The chloroform extract was washed with water and dried to give a yellow residue which crystallized from acetone as yellow needles (10 mg), m.p. 196–198°; λ_{max} (EtOH) (log ϵ_{max}) 244 (4·45), 272·5 (4·49), 291 (4·22), 348 (4·03), 380 (inf.) (3·96), 427 (3·70) and λ_{max} (0·05N HCl (EtOH/H_2O)) mμ (log ϵ_{max}) 257 (4·52), 285 (4·46), 385 (4·46), 385 (4·09), 500 mμ (3·33).

For exact mass measurements, see Table 2.

(4′-Ethoxy-5′-methoxy-2′-nitrobenzoyl)6,7-dimethoxyisoquinoline

This was prepared from 1-(4′-ethoxy-5′-methoxy-2′-nitrobenzyl)3,4-dihydro-6,7-dimethoxyisoquinoline[16] by a method essentially the same as that described above; m.p. 189–192° (Found: C, 61·0; H, 5·0. Calc. for $C_{21}H_{20}N_2O_7$: C, 61·2; H, 4·9%).

10-Ethoxy-1,2,9-trimethoxy-7-oxodibenzo[de,g]*quinoline* (*XI*)

Prepared as for (XII), m.p. 220–221°; λ_{max} (EtOH) (log ϵ_{max}) 244 (4·45), 272·5 (4·48), 291 (4·23), 350 (4·03), 380 (inf.) (3·96), 427 (3·70) and λ_{max} (0·05N HCl(EtOH/H_2O) (log ϵ_{max}) 257 (4·52), 285 (4·46), 385 (4·09), 500 mμ (3·33) (Found: C, 68·7; H, 5·4. Calc. for $C_{21}H_{19}NO_5$: C, 69·0; H, 5·2%).

Acknowledgments

We are grateful for the award of a Commonwealth Postgraduate Scholarship to one of us (G.K.D.), and for the provision of facilities (to I.R.C.B. and J.H.B.) in the University Chemical Laboratory, Cambridge, by Lord Todd.

[16] Barger, G., Eisenbrand, J., Eisenbrand, L., and Schlittler, E., *Ber. dt. chem. Ges.*, **1933**, **66**, 450.

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SOLVENT EFFECTS IN NMR SPECTROSCOPY—VI[1]

CHEMICAL SHIFTS INDUCED BY BENZENE IN QUINONES

J. H. BOWIE, D. W. CAMERON, P. E. SCHÜTZ and D. H. WILLIAMS
University Chemical Laboratory, Lensfield Road, Cambridge

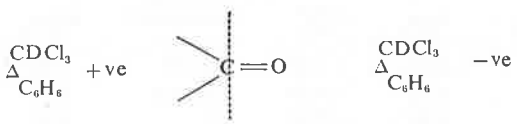
and

N. S. BHACCA
Varian Associates, Palo Alto, California

(*Received* 28 *September* 1965; *in revised form* 11 *October* 1965)

Abstract—Solvent shifts ($\Delta^{CDCl_3}_{C_6H_6} = \delta_{CDCl_3} - \delta_{C_6H_6}$ ppm) are reported for a number of methyl- and methoxy-substituted quinones. In the anthraquinones examined, a C-1 methyl group undergoes only a small upfield shift in benzene (0·06–0·17 ppm), whereas a C-2 or C-3 methyl group suffers a much larger upfield shift (0·52–0·60 ppm). These effects are only slightly modified by the presence of adjacent methyl groups. In contrast, the shifts observed for "isolated" C-1 or C-2 methoxy substituents in anthraquinones may be greatly modified in 1,2-dimethoxy or 1,3-dimethoxy-derivatives, reflecting the greater electronic interaction between the polar substituents. Solvent shifts support the previously assigned differences in stereochemistry and conformation between isoleutherin, eleutherin and a related system derived from the aphins.

IT HAS recently been shown[2–5] for a large number of ketones, that the proton chemical shifts induced by benzene relative to deuterochloroform ($\Delta^{CDCl_3}_{C_6H_6} = \delta_{CDCl_3} - \delta_{C_6H_6}$) are positive for protons behind an isolated carbonyl group and negative for protons in front of an isolated carbonyl group (see I). We wished to extend our studies to other classes of conformationally rigid compounds containing carbonyl groups and the present paper records results for a number of quinones.



I

In Table 1, the deuterochloroform and benzene solution chemical shifts of the methyl resonances in some substituted benzoquinones (II–V), naphthaquinones (VI–IX) and anthraquinones (X–XIII) are summarized, together with the $\Delta^{CDCl_3}_{C_6H_6}$ values.

Considering first the results for the anthraquinones X–XIII, it is evident that a *peri*-methyl group (at C-1) only undergoes a small upfield shift (0·06–0·17 ppm) in benzene in these compounds, whereas a C-2 or C-3 methyl group suffers a much larger upfield shift (0·52–0·60 ppm). This difference in behaviour is understandable in terms of the shifts associated with isolated carbonyl functions,[2–5] since a C-1 methyl group will be influenced by a *peri*-carbonyl group which can exert a negative

[1] Part V, D. H. Williams and D. A. Wilson, *J. Chem. Soc.* in press.
[2] J. D. Connelly and R. McCrindle, *Chem. & Ind.* 379 (1965).
[3] D. H. Williams and N. S. Bhacca, *Tetrahedron* **21**, 1641 (1965).
[4] D. H. Williams and N. S. Bhacca, *Tetrahedron* **21**, 2021 (1965).
[5] D. H. Williams, *Tetrahedron Letters* 2305 (1965).

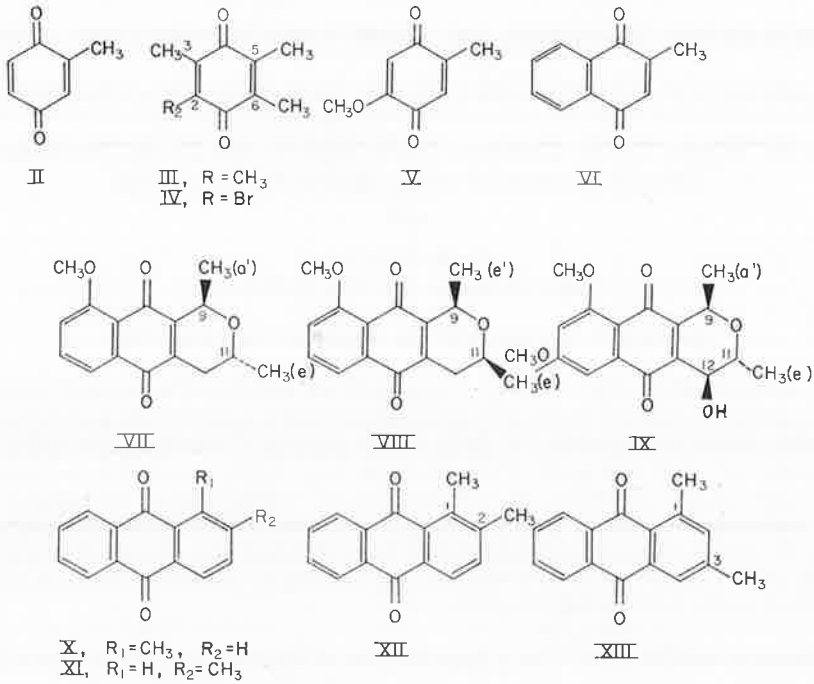


TABLE 1. CHEMICAL SHIFTS (δ_{CDCl_3}, $\delta_{C_6H_6}$) AND SOLVENT SHIFTS ($\Delta^{CDCl_3}_{C_6H_6} = \delta_{CDCl_3} - \delta_{C_6H_6}$) OF METHYL RESONANCES IN SOME SUBSTITUTED QUINONES

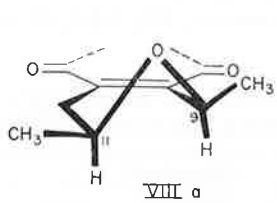
Compound (Methyl Resonance)	δ_{CDCl_3}	$\delta_{C_6H_6}$	$\Delta^{CDCl_3}_{C_6H_6}$	Compound (Methyl Resonance)	δ_{CDCl_3}	$\delta_{C_6H_6}$	$\Delta^{CDCl_3}_{C_6H_6}$
II	2·08	1·59	+0·49	IX (9)	1·58	1·50	+0·08
III	2·00	1·71	+0·29	IX (11)	1·38	1·43	−0·05
IV (3)	2·21	1·92	+0·29	X	2·83	2·70	+0·13
IV (5, 6)	2·07	1·59	+0·48	XI	2·52	1·92	+0·60
V	2·05	1·63	+0·42	XII (1)	2·75	2·58	+0·17
VI	2·19	1·68	+0·51	XII (2)	2·45	1·88	+0·57
VII (9)	1·54	1·45	+0·09	XIII (1)	2·78	2·72	+0·06
VII (11)	1·35	1·11	+0·24	XIII (3)	2·45	1·93	+0·52
VIII (9)	1·52	1·61	−0·09				
VIII (11)	1·34	1·10	+0·24				

influence on $\Delta^{CDCl_3}_{C_6H_6}$. The methyl groups in II–VI, which are directly substituted on the quinonoid ring, all have intermediate positive $\Delta^{CDCl_3}_{C_6H_6}$ values (0·29–0·51 ppm), the magnitude of which varies appreciably with the nature of additional substituents.

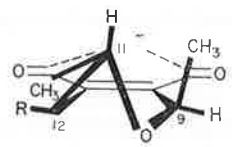
The stereochemical[6,7] and conformational[8] features of isoeleutherin (VII), eleutherin (VIII) and the naphthaquinone dimethylether (IX) are known from previous studies. The methyl resonances of VII, VIII and IX have previously been specifically

[6] H. Schmid and A. Eböthner, *Helv. Chim. Acta* **34,** 561 and 1041 (1951).
[7] W. Eisenhuth and H. Schmid, *Helv. Chim. Acta* **41,** 2021 (1958).
[8] D. W. Cameron, D. G. I. Kingston, N. Sheppard and Lord Todd, *J. Chem. Soc.* 98 (1964).

assigned to the C-9 or C-11 methyl groups in chloroform (or $CDCl_3$)[8] and the shifts in benzene solution are unambiguously available from the different coupling constants for the C-9 and C-11 methyl doublets of VII and IX. The benzene shifts for the methyl groups of VIII can be assigned since the $\Delta^{CDCl_3}_{C_6H_6}$ values for the C-11 methyl groups of VII and VIII can be predicted to be similar (the C-11 methyl groups of VII and VIII are both equatorial and in almost identical polar environments). It can be seen (Table 1) that the C-9 pseudo-axial methyl groups of VII and IX have small positive $\Delta^{CDCl_3}_{C_6H_6}$ values (+0·09 and +0·08 ppm, respectively), whereas the C-9 pseudoequatorial methyl group of VIII has a negative $\Delta^{CDCl_3}_{C_6H_6}$ value (−0·09 ppm). Dreiding models of eleutherin (see VIIIa) indicate that the pseudoequatorial C-9 methyl group is held only slightly above the plane of the *peri*-carbonyl function, whereas the corresponding models of VII and IX (see VIIa and IXa) contain the pseudo-axial C-9 methyl group much further removed from the influence of the *peri*-carbonyl function. Thus it is apparent that the solvent shifts follow the trends anticipated from the studies on compounds containing isolated keto-groups.[2–5] It should be noted that the solvent shifts of the C-11 methyl groups of VII and VIII are, as predicted, the same (0·24 ppm), but the value is changed in sign (to −0·05 ppm) by the C-12 hydroxyl group of IX.

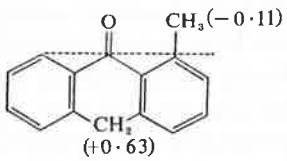


VIII a

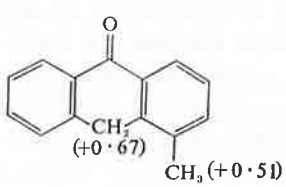


VII a, R=H
IX a, R=OH

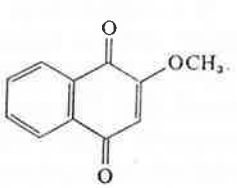
The utility of solvent shifts in determining the composition of a reduction product from an anthraquinone may be illustrated by reference to the reduction of 1-methylanthraquinone (X) by stannous chloride and concentrated hydrochloric acid.[9] The resulting mixture contained two anthrones in the ratio 4:6. The minor component gave resonances at $\delta = 4{\cdot}27$ (—CH_2—) and $\delta = 2{\cdot}83$ (—CH_3) in deuterochloroform and $\delta = 3{\cdot}64$ (—CH_2—) and $\delta = 2{\cdot}94$ (—CH_3) in benzene; the solvent shifts define this product as 1-methylanthrone (see XIV for the $\Delta^{CDCl_3}_{C_6H_6}$ values) and similarly the major component from chemical and solvent shift considerations [$\delta_{CDCl_3} = 4{\cdot}09$ (—CH_2—) and $\delta_{CDCl_3} = 2{\cdot}39$ (—CH_3); $\delta_{C_6H_6} = 3{\cdot}42$ (—CH_2—) and $\delta_{C_6H_6} = 1{\cdot}88$ (—CH_3)] is 4-methylanthrone (XV).



XIV

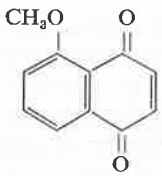


XV

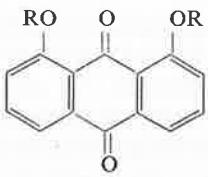


XVI

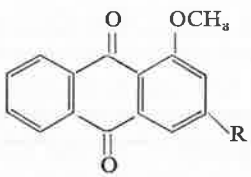
[9] D. W. Cameron, R. I. T. Cromartie, D. G. I. Kingston and G. B. V. Subramanian, *J. Chem. Soc.* 4565 (1965).



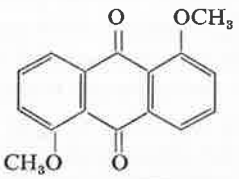
XVII



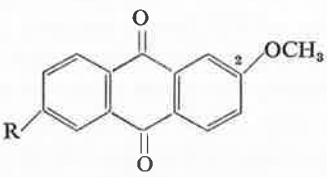
XVIII, R = CH_2CH_3
XIX, R = CH_3



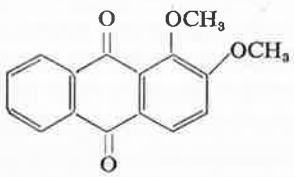
XX, R = H
XXI, R = OCH_3



XXII



XXIII, R = H
XXIV, R = OCH_3



XXV

Solvent shifts have also been determined for the methoxyl resonances of a number of methoxynaphthaquinones (XVI–XVII) and methoxyanthraquinones (XIX–XXV) and the data are summarized in Table 2, together with data for the methoxyl resonances of the previously discussed compounds V, VII, VIII, IX and the diethyl ether XVIII.

Table 2. Chemical shifts (δ_{CDCl_3}, $\delta_{C_6H_6}$) and solvent shifts ($\Delta^{CDCl_3}_{C_6H_6} = \delta_{CDCl_3} - \delta_{C_6H_6}$) of methoxyl resonances in some substituted quinones

Compound (Methoxyl Resonance)	δ_{CDCl_3}	$\delta_{C_6H_6}$	$\Delta^{CDCl_3}_{C_6H_6}$	Compound (Methoxyl Resonance)	δ_{CDCl_3}	$\delta_{C_6H_6}$	$\Delta^{CDCl_3}_{C_6H_6}$
V	3·81	2·86	+0·95	XX	4·00	3·34	+0·66
VII	3·99	3·32	+0·67	XXI (1 or 3)	4·00 and 3·95	3·33 and 3·24	+6·67, +0·71 or +0·62, +0·76
VIII	3·97	3·28	+0·69				
IX (6, 8)	3·96	3·24	+0·72				
XVI	3·92	2·88	+1·04	XXII	4·02	3·34	+0·68
XVII	4·00	3·26	+0·74	XXIII	3·97	3·16	+0·81
XVIII(—CH_2—)	4·22	3·64	+0·58	XXIV	4·00	3·20	+0·80
XVIII(—CH_3)	1·53	1·18	+0·35	XXV (1)	4·01	3·90	+0·11
XIX	4·00	3·35	+0·65	XXV (2)	4·01	3·10	+0·91

It is evident from the data in Table 2 that all the methoxyl resonances undergo upfield shifts in benzene solution and that the shifts are as large as approximately 1 ppm in V and XVI, which contain methoxyl groups directly attached to the quinonoid ring. The results are consistent with the observation[10] that aromatic methoxyl resonances usually suffer high-field shifts in benzene, irrespective of the presence of neighbouring carbonyl groups. The $\Delta^{CDCl_3}_{C_6H_6}$ values for *peri*-methoxyl groups are approximately the same (0·67, 0·69, 0·74, 0·65, 0·66, 0·68 ppm) in VII, VIII, XVII, XIX, XX and XXII, as might be expected since all those methoxyl groups have

[10] Unpublished results obtained at the University Chemical Laboratory, Cambridge.

similar steric and polar environments. Likewise, the C-2 methoxyl groups of XXIII and XXIV have very similar shifts (0·81 and 0·80 ppm respectively). However in the naphthaquinone dimethylether IX, containing *meta*-methoxyl functions, the methoxyl shifts are identical (0·72 ppm), and do not correspond with those obtained above for isolated methoxyl groups; the modified solvent shifts probably reflect the electronic interaction which can take place between the methoxyl substituents. Similarly, the methoxyl groups of 1,3-dimethoxyanthraquinone (XXI) cannot be securely differentiated. The methoxyl resonances of XXV have been specifically assigned in both solvents from the spectra of 1,2-dimethoxyanthraquinone partially deuterated in the C-1 methoxyl group; the deuterated material was prepared by methylation of 1-hydroxy-3-methoxyanthraquinone with diazomethane in the presence of deuterium oxide.[11] The difference between the solvent shifts for the C-1 and C- 2 methoxyl groups of XXV is very large (0·11 ppm vs. 0·91 ppm) and the shifts bear no relation to those induced by the isolated functions since the groups are now capable of interacting by both through-bonds and through-space mechanisms. This behaviour should be contrasted with that of adjacent methyl groups (in XII) where the mutual electronic interactions are insufficient to modify the characteristic shift values to any extent.

EXPERIMENTAL

All spectra were determined using a Perkin–Elmer 60 Mc spectrometer; tetramethylsilane was employed as an internal reference standard and the temperature of the probe was 33·3°.

Acknowledgements—The authors wish to thank I.C.I. Ltd., Dyestuffs Division for samples of 2-hydroxy-, 2,6-dihydroxy- and 1,3-dihydroxy-anthraquinones, Professor H. Schmid for samples of eleutherin and isoeleutherin, and record their gratitude to Miss Pat Grist for skilful technical assistance in obtaining some of the spectra. One of us (P. E. S.) is grateful to Ciba Ltd. for a research studentship.

[11] K. J. Van Der Merwe, P. S. Steyn and S. H. Eggers, *Tetrahedron Letters* 3923 (1964).

Solvent Shifts in Nuclear Magnetic Resonance Spectroscopy. Part VIII.* Solvent Shifts induced by Benzene and Toluene in Methoxybenzenes: a Variable-temperature N.m.r. Study

By J. H. Bowie, J. Ronayne, and D. H. Williams

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Solvent Shifts in Nuclear Magnetic Resonance Spectroscopy. Part VIII.* Solvent Shifts induced by Benzene and Toluene in Methoxybenzenes: a Variable-temperature N.m.r. Study

By J. H. Bowie, J. Ronayne, and D. H. Williams

Benzene causes upfield shifts of the methoxyl resonances (relative to carbon tetrachloride as solvent) in twenty methoxybenzenes, with the exception of the 2-methoxyl resonance of 1,2,3-trimethoxybenzene, which suffers a downfield shift. In *para*-substituted anisoles, the tendency is for an electron-withdrawing substituent to increase the upfield solvent shift of the methoxyl resonance, and for an electron-donating substituent to decrease the solvent shift (relative to anisole as reference compound). The solvent shifts do not show a particularly good correlation with the dipole moments of the molecules, but a better correlation with Hammett's σ_p values. Variable-temperature studies in toluene solution have indicated that at any given temperature, *p*-nitroanisole is complexed to a greater extent with toluene than is anisole, which in turn is complexed more than *p*-*NN*-dimethylaminoanisole. Thermodynamic parameters (ΔH, ΔG, ΔS) for complex formation of these three compounds with toluene have been calculated on the basis of an assumed 1:1 complex. It is feasible that the dependence of solvent shift of a methoxyl resonance upon the nature of other substituents in the aromatic ring may be useful in elucidating the structure of natural products.

ALTHOUGH the solvent shifts induced by benzene (as solvent) in substituted benzenes have been studied before,[1-4] the corresponding shifts induced in methoxybenzenes do not appear to have been studied. We examined these because aromatic methoxyl substituents are very common in natural products; should the magnitude of the solvent shifts be sensitive to the nature and relative orientation of additional substituents, structure elucidation might be aided by a comparison of the solvent shifts of methoxyl resonances in compounds of unknown structure and suitable model compounds.

In general, in all the methoxy-compounds studied

* Part VII, P. Laszlo and D. H. Williams, *J. Amer. Chem. Soc.*, in the press.

[1] T. Schaefer and W. G. Schneider, *J. Chem. Phys.*, 1960, **32**, 1218.

[2] R. E. Klinck and J. B. Stothers, *Canad. J. Chem.*, 1962, **40**, 1071.

[3] R. E. Klinck and J. B. Stothers, *Canad. J. Chem.*, 1962, **40**, 2329.

[4] W. G. Schneider, *J. Phys. Chem.*, 1962, **66**, 2653.

(I)—(XX), the methoxyl resonances suffer, with one exception, an upfield shift on changing the solvent from carbon tetrachloride (an inert solvent [5]) to benzene (a complexing solvent [6]). The results for the compounds (I)—(VIII) containing only methoxyl substituents are summarised in Table 1.

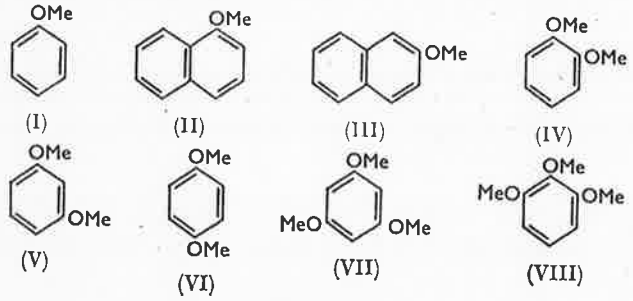

TABLE 1

Chemical shifts (δCCl_4, δC_6H_6) and solvent shifts ($\Delta = \delta CCl_4 - \delta C_6H_6$) in p.p.m. for methoxyl resonances in (I)—(VIII)

Compound	δ_{CCl_4}	$\delta_{C_6H_6}$	Δ
(I)	3·77	3·33	+0·44
(II)	3·99	3·54	+0·45
(III)	3·86	3·41	+0·45
(IV)	3·80	3·42	+0·38
(V)	3·74	3·31	+0·43
(VI)	3·72	3·35	+0·37
(VII)	3·73	3·34	+0·39
(VIII)	3·79 (1, 3)	3·41 (1, 3)	+0·38 (1, 3)
	3·71 (2)	3·82 (2)	−0·11 (2)

The results in Table 1 for (I)—(III) indicate that the solvent shifts (+0·44 to +0·45 p.p.m.) are virtually identical for a single methoxyl group located in a benzene ring or at C(1) or C(2) in a naphthalene ring. In the dimethoxybenzenes (IV)—(VI), the *meta*-isomer (V) displays a solvent shift which is very similar to that of anisole (I) itself, but the *ortho*- and *para*-isomers [(IV) and (VI)] display smaller shifts. The shift observed for 1,3,5-trimethoxybenzene (VII) is only slightly smaller than that found for (V), but the results for the trimethyl ether (VIII) of pyrogallol are startling; the central methoxyl group is deshielded in benzene relative to carbon tetrachloride, whereas the other two methoxyl groups are strongly shielded. This observation is interesting, since the occurrence of shielding and deshielding effects in the same solute molecule gives some indication of stereospecific complexing.[6] Moreover, the smaller solvent shift observed for *p*-dimethoxybenzene (VI) relative to anisole (I) suggests that it may be possible to correlate the magnitude of the shift of the methoxyl resonance with the nature of an additional *para*-substituent. This seemed worth investigating in view of the suggestion [4,7] that benzene solvent molecules can interact with solute molecules *via* a dipole–induced dipole interaction. However, the formation of a charge-transfer complex between benzene solvent molecules and *aromatic* solute molecules may account more satisfactorily for the solvent shifts in such cases.[4]

[5] P. Laszlo, *Bull. Soc. chim. France*, 1964, 2658.
[6] See, e.g., D. H. Williams, and N. S. Bhacca, *Tetrahedron*, 1965, **21**, 2021.

Relevant results were obtained by determining Δ ($\Delta = \delta_{CCl_4} - \delta_{C_6H_6}$ p.p.m.) for the methoxyl resonances of the *para*-disubstituted benzenes (IX)—(XX) (Table 2). As for the compounds (I)—(VIII) discussed previously, solution concentrations were accurately determined (since chemical shifts are known to depend markedly on concentration in some aromatic compounds [1]) and all lie in the range 0·10 ± 0·03M unless otherwise stated. Results for (I) and (VI) are included in Table 2 for comparison.

TABLE 2

Chemical shifts (δ_{CCl_4}, $\delta_{C_6H_6}$) and solvent shifts (Δ) in p.p.m. for methoxyl resonances in (IX)—(XX)

Compound	X	δ_{CCl_4}	$\delta_{C_6H_6}$	Δ
(IX)	NO_2	3·92	3·03	+0·89
(X)	CO_2H	3·86 *	3·13	+0·73
(XI)	COMe	3·83	3·20	+0·63
(XII)	CHO	3·87	3·13	+0·74
(XIII)	Br	3·74	3·12	+0·62
(XIV)	SH	3·74	3·19	+0·55
(XV)	SMe	3·74	3·24	+0·50
[(I)	H	3·77	3·33	+0·44]
(XVI)	Ph	3·80	3·36	+0·44
(XVII)	Me	3·72	3·36	+0·36
[(VI)	OMe	3·72	3·35	+0·37]
(XVIII)	OH	3·71	3·32	+0·39
(XIX)	NH_2	3·68	3·37	+0·31
(XX)	NMe_2	3·70	3·44	+0·26

* This value corresponds to a saturated solution (<0·1M) of (X) in CCl_4.

Table 2 shows that the solvent shift (Δ) of the methoxyl resonance depends strongly on the polarity of the solute molecule; the shift increases greatly with increasing polarity. There are a number of ways in which the polarisation of the *para*-disubstituted benzenes can be estimated, and the most obvious parameter to use is the dipole moment (μ). In Figure 1, solvent shift (Δ, p.p.m.) of the methoxyl resonance is plotted against the dipole moment of the compound: dipole moments have been found [8] for all compounds in Table 2 except for (X), (XIV), (XVI), and (XVIII). The correlation is not particularly good, probably owing in part to the varying molecular volumes [4] and the varying molecular geometries of the compounds. For example, it is obvious that the *p*-NMe_2 and *p*-NH_2 substituents of (XX) and (XIX) will tend to feed electrons back to the methoxyl group more than, say, a methyl group [in (XVII)] and yet, because of changing molecular geometries, the dipole moment does not allow us to express this effect [the dipole moments of (XIX) and (XX) are *larger* than the dipole moment of (XVII); see Figure 1]. The effect of each substituent X on the transannular polarisation can be better estimated in terms of Hammett σ_p values and the appropriate plot of Δ against σ_p is given in Figure 2. The ranges of σ_p in Figure 2 correspond to varying quoted values; [9] the most recent value [10] for σ_p for the formyl substituent was used. The

[7] T. L. Brown and K. Stark, *J. Phys. Chem.*, 1965, **69**, 2679.
[8] "Tables of Experimental Dipole Moments," ed. A. C. McClellan, W. H. Freeman and Co., San Francisco, 1963.
[9] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.
[10] A. A. Humffray, J. J. Ryan, J. P. Warren, and Y. H. Yung, *Chem. Comm.*, 1965, 610.

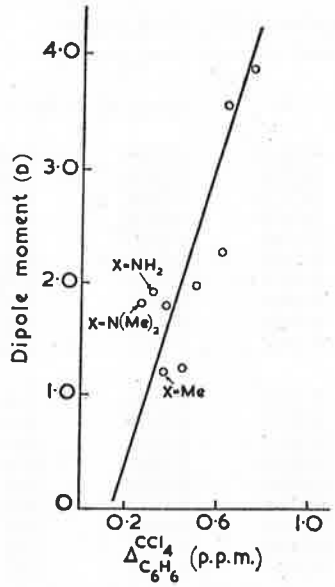

FIGURE 1 Plot of the solvent shift ($\Delta = \delta_{CCl_4} - \delta_{C_6H_6}$, p.p.m.) for the methoxyl resonances of p-X·C_6H_4·OMe [X = NO_2, COMe, CHO, Br, SMe, H, Me, OMe, NH_2, NMe_2] against dipole moment

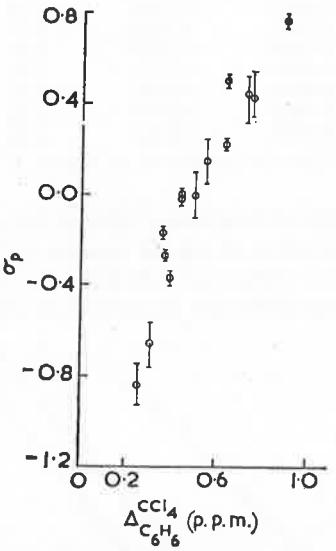

FIGURE 2 Plot of the solvent shift ($\Delta = \delta_{CCl_4} - \delta_{C_6H_6}$, p.p.m.) for the methoxyl resonances of (I), (VI), (IX—XX) against Hammett's σ_p values

solvent shift of the methoxyl resonance increases fairly regularly with increasing σ_p value of the *para*-substituent.

It appears from Table 2 that, at room temperature, the benzene–solute complex is more favourable for the highly polar solute p-nitroanisole (IX) than for the much less polar p-*NN*-dimethylaminoanisole (XX). To make a rough quantitative estimate of this effect, we studied the temperature variation of the equilibrium (1) (since benzene is obviously not suitable for low-temperature

[11] R. E. Klinck and J. B. Stothers, *Canad. J. Chem.*, 1966, **44**, 37.
[12] R. J. Abraham, *Mol. Phys.*, 1961, **4**, 369.
[13] J. V. Hatton and W. G. Schneider, *Canad. J. Chem.*, 1962, **40**, 1285.

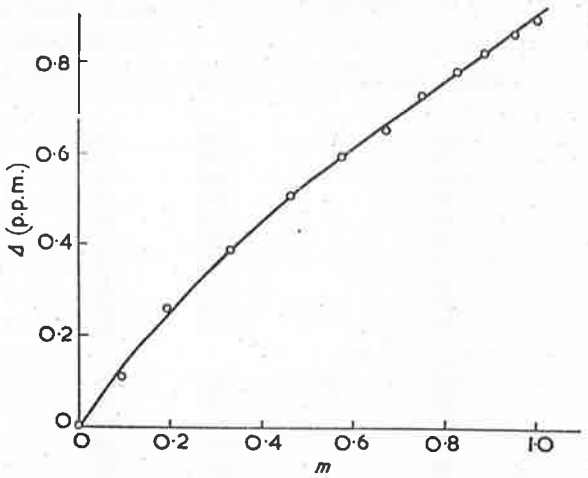

FIGURE 3 Plot of the solvent shift (Δ) for the methoxyl resonance of p-nitroanisole (IX) against the mole fraction (m) of benzene in carbon tetrachloride

work, toluene was employed, as in related work [11-14]). This treatment assumes that the complex is a 1 : 1 toluene–solute adduct, as seems a reasonable approximation by analogy with other cases.[15,16] Some evidence in favour of predominant 1 : 1 complex formation (over an alternative predominance of a 2 : 1 solvent–solute interaction) is found in a plot (Figure 3) of the solvent shift (Δ) of the methoxyl resonance of p-nitroanisole (IX) against the mole fraction (m) of benzene in carbon tetrachloride. On the assumption that the chemical shift for the pure complex does not depend upon the composition of the solvent mixture, such a plot should be linear if the stoicheiometry of the complex is 1 : 1. The line (Figure 3) is slightly curved, but the approximation to linearity is very much better than found for a plot of Δ against m^2.

$$\text{Toluene} + \text{Solute} \rightleftharpoons \text{Complex} \qquad (1)$$

It can be shown [12] that if a fraction p of the solute is complexed at a temperature T, the equilibrium constant (K) is given, for a dilute solution, by equation (2). The value of p can be obtained by application of equation (3), in which ν_t is chemical shift of a proton resonance at a temperature t and ν_c and ν_o are the chemical shifts of that proton resonance in the pure complex and in a complex free solution, respectively; [12] ν_o may be taken as the chemical shift in carbon tetrachloride solution, and ν_c obtained by extrapolation of ν_t *vs.* temperature curves for toluene solutions to absolute zero.

$$K = p/(1 - p) \qquad (2)$$

$$p = (\nu_t - \nu_o)/(\nu_c - \nu_o) \qquad (3)$$

The temperature variations of the chemical shifts of the methoxyl resonances in anisole (I), p-nitroanisole (IX), and p-*NN*-dimethylaminoanisole (XX) are given in Figure 4 and Table 3; chemical shifts are quoted in

[14] J. N. Murrell and V. M. S. Gill, *Trans. Faraday Soc.*, 1965, **61**, 402.
[15] J. E. Anderson, *Tetrahedron Letters*, 1965, 4713.
[16] P. Laszlo and D. H. Williams, *J. Amer. Chem. Soc.*, in the press.

TABLE 3

Variable-temperature n.m.r. study of anisole (I), *p*-nitroanisole (IX), and *p*-*NN*-dimethylaminoanisole (XX) in toluene

Temp. (°c)	Methoxyl resonance chemical shift (c./sec.) ν_0	ν	$\nu_t - \nu_0$	ν_c	p	K	$-\log_{10} K$	$10^3/T$ (°K)
Anisole (I)								
100	377	349	28	236 *	0·1986	0·2476	0·6059	2·68
80		346	31		0·2199	0·2819	0·5499	2·83
60		344	33		0·2340	0·3015	0·5207	3·00
40		341	36		0·2553	0·3428	0·4750	3·20
33		339	38		0·2695	0·3689	0·4331	3·27
20		337	40		0·2837	0·3961	0·4221	3·41
0		331	44		0·3121	0·4536	0·3432	3·66
−20		330	47		0·3333	0·4999	0·3011	3·95
−40		325	52		0·3688	0·5842	0·2334	4·29
−60		319	58		0·4113	0·6987	0·1557	4·69
p-*Nitroanisole* (IX)								
100	392	330	62	195 *	0·3147	0·4592	0·3380	2·68
80		326	66		0·3350	0·5038	0·2977	2·83
60		322	70		0·3553	0·5511	0·2587	3·00
40		318	74		0·3756	0·6015	0·2207	3·20
20		312	80		0·4061	0·6838	0·1651	3·41
0		308	84		0·4264	0·7438	0·1288	3·66
−20		302	90		0·4569	0·8413	0·0551	3·95
−40		296	96		0·4873	0·9505	0·0221	4·29
−60		290	102		0·5178	0·0738	−0·0310	4·69
p-NN-*Dimethylaminoanisole* (XX)								
100	370	354	16	270 *	0·1600	0·1905	0·7203	2·68
80		352	18		0·1800	0·2195	0·6586	2·83
60		351	19		0·1900	0·2346	0·6297	3·00
40		349	21		0·2100	0·2658	0·5795	3·20
33		348	22		0·2200	0·2821	0·5496	3·27
20		346·8	23·2		0·2320	0·2987	0·5248	3·41
0		343·5	26·5		0·2650	0·3605	0·4431	3·66
−20		341	29		0·2900	0·4085	0·3888	3·95
−40		337	33		0·3300	0·4925	0·3076	4·29
−60		333	37		0·3700	0·5873	0·2312	4·69

* The estimated reliability of these values for ν_c (obtained by extrapolation of the curves shown in Figure 4) is 236 ± 15, 195 ± 15, and 270 ± 20 c./sec., respectively.

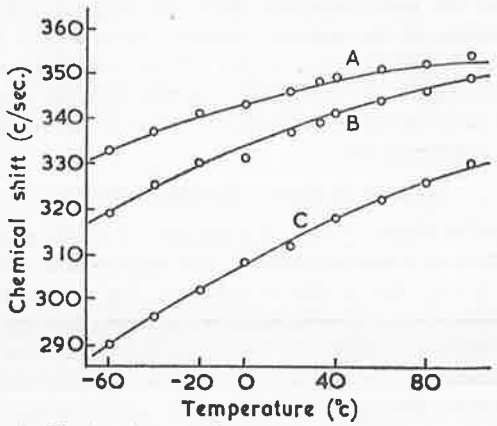

FIGURE 4 Temperature variation of the chemical shift of the methoxyl resonances of anisole (B), *p*-nitroanisole (C), and *p*-*NN*-dimethylaminoanisole (A) in toluene

c./sec. at 100 Mc./sec. and correspond to 5% w/w solutions in toluene, except for the values quoted at −60°, which correspond to a 2% w/w solution.* As expected, the temperature variation of the chemical shift is greatest for *p*-nitroanisole (IX) and least for *p*-*NN*-dimethylanisole (XX). In Table 3, the observed values of ν_0 and the calculated values of ν_c, $\nu_t - \nu_0$, p, K, and $-\log_{10}K$ are also tabulated.

Since $\log_{10}K$ is related to the enthalpy of formation (ΔH) and entropy of formation (ΔS) of the complex by equation (4), the plots of $\log_{10}K$ against $1/T$ should be linear and furnish values for ΔH from the slope of the line. These linear plots are illustrated in Figure 5 and

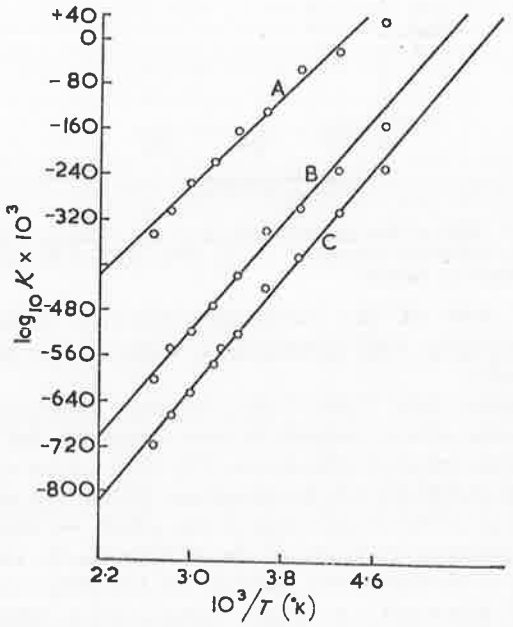

FIGURE 5 Plot of $\log_{10}K$ against $1/T$ based on results for anisole (B), *p*-*NN*-dimethylaminoanisole (C) and *p*-nitroanisole (A)

* Complete results were obtained for 2% w/w solutions, but are not reported since the values are almost identical to those obtained for 5% w/w solutions.

give the heat of formation of the complex as −1·00 kcal./mole for anisole (I), −0·89 kcal./mole for *p*-nitroanisole (IX), and −1·05 kcal./mole for *p*-*NN*-dimethylaminoanisole (XX). The interactions are obviously weak. It is emphasised that the values are considered

$$2{\cdot}303 \log_{10}K = \Delta S/R - \Delta H/RT \qquad (4)$$

to be very approximate, because of the drastic assumptions implicit in the consideration only of a 1 : 1 complex.[16]

The free energy of formation (ΔG) of the complex is also available for various temperatures from the various K values. These are in Table 4, as are ΔS values, obtained from both ΔG and ΔH. The ΔS values are satisfactorily constant over the temperature range of 160°; average values are given at the foot of the ΔS column. It is obvious from the ΔG (and p or K) values that whereas *p*-nitroanisole (IX) is complexed with toluene to the extent of about 50% at −60° C (213° K), anisole (I) and *p*-*NN*-dimethylaminoanisole (XX) are only involved in complex formation to the extent of about 41 and 37%, respectively, at this temperature.*

TABLE 4

Values of ΔG (kcal./mole) and ΔS (e.u.) for complex formation between toluene and (I), (IX), and (X)

Anisole (I)			p-*Nitroanisole* (IX)		
Temp. (°K)	ΔG	ΔS	Temp. (°K)	ΔG	ΔS
373	+1·03	−5·50	373	+0·58	−3·90
353	+0·89	−5·37	353	+0·48	−3·88
333	+0·79	−5·41	333	+0·39	−4·27
313	+0·68	−5·39	313	+0·32	−3·83
306	+0·61	−5·28	293	+0·22	−3·79
293	+0 57	−5 37	273	+0·16	−3·85
273	+0·43	−5·26	253	+0·064	−3·77
253	+0·35	−5·36	233	+0·024	−3·92
233	+0·25	−5·39	213	−0·03	−4·04
213	+0·15	−5·42			
	Average	−5·38		Average	−3·96
p-NN-*Dimethylaminoanisole* (XX)					
373	+1·23	−6·10			
353	+1·06	−5·99			
333	+0·96	−6·04			
313	+0·83	−6·01			
306	+0·77	−5·95			
293	+0·70	−5·99			
273	+0·55	−5·86			
253	+0·45	−5·93			
233	+0·33	−5·93			
213	+0·23	−5·98			
	Average	−5·98			

It is apparent that the solvent shifts of the methoxyl resonances in the methoxybenzenes in general increase with increasing electron withdrawal by the *para*-substituent. However, our results, although compatible with a dipole–induced dipole interaction,[7] do not exclude the possibility that the solvent–solute interaction increases with a simple decrease in the electron density of the aromatic ring. Indeed, our results are equally consistent with a solvent–solute interaction associated with the formation of a charge-transfer complex.[4] Additional evidence for the latter possibility is now being sought from solvent shifts in molecules having small or zero dipole moments but very low electron density in the aromatic ring (*e.g.*, 1,3,5-trinitrobenzene and related compounds).

EXPERIMENTAL

Chemical shifts obtained at one temperature (Tables 1 and 2) were measured on a Perkin-Elmer 60 Mc./sec. n.m.r. spectrometer. The variable-temperature studies were carried out on a Varian HA 100 n.m.r. spectrometer with a variable-temperature probe. Tetramethylsilane was used as internal reference in both instruments. All compounds were commercial samples whose purity was established from their n.m.r. spectra.

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CAMBRIDGE. [6/175 *Received, February 9th*, 1966]

* It is noteworthy that in a similar study of *para*-substituted benzaldehydes, complex stability did not show the same trend on variation of the *para*-substituent (ref. 11).

Solvent Effects in Nuclear Magnetic Resonance Spectroscopy. Part X.* Solvent Shifts induced by Benzene in *ortho*- and *meta*-Substituted Methoxybenzenes

By J. H. Bowie, J. Ronayne, and Dudley H. Williams, University Chemical Laboratory, Cambridge

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Solvent Effects in Nuclear Magnetic Resonance Spectroscopy. Part X.* Solvent Shifts induced by Benzene in *ortho*- and *meta*-Substituted Methoxybenzenes

By J. H. Bowie, J. Ronayne, and Dudley H. Williams, University Chemical Laboratory, Cambridge

Solvent shifts ($\Delta = \delta_{\text{carbon tetrachloride}} - \delta_{\text{benzene}}$ p.p.m.) for the methoxyl protons of *meta*-substituted anisoles correlate with σ_m of the substituent, but for *ortho*-substituted anisoles a better correlation between Δ and the dipole moment is found. The effect of introducing a methoxyl group *ortho* to a substituent in a benzene ring is to make the Δ values for protons in that substituent more negative. In the compounds examined, protons α to the benzene ring (Ar–CH<) and attached to a substituent situated between two *o*-methoxyl groups are strongly deshielded (0·4—0·6 p.p.m.) in benzene relative to carbon tetrachloride. On the basis of the observed shifts the orientating effect of an aromatic methoxyl function in a solute upon benzene solvent molecules may be surmised.

We have shown [1] for *para*-substituted anisoles that an electron-withdrawing substituent in the *para*-position increases the upfield solvent shift ($\Delta = \delta_{\text{carbon tetrachloride}} - \delta_{\text{benzene}}$, hereafter $\delta_c - \delta_b$) of the methoxyl resonance whereas an electron-donating substituent decreases the solvent shift (relative to anisole as reference compound). The solvent shifts show some correlation with the dipole moments of the molecules, but a better correlation with Hammett's σ_p values of the *para*-substituents. To investigate the mechanism by which

* Part IX, J. Ronayne, M. V. Sargent, and D. H. Williams, *J. Amer. Chem. Soc.*, 1966, **88**, 5288.

[1] J. H. Bowie, J. Ronayne, and D. H. Williams, *J. Chem. Socs (B)*, 1966, 785; for related studies on *para*-substituted toluene. and *para*-substituted *NN*-dimethylanilines see N. Nakagawa and S. Fujigawa, *Bull. Soc. Chem. Soc. Japan*, 1961, **34**, 143, and I. D. Roe and L. K. Dyall, *Austral. J. Chem.*, 1966, **19**, 835.

benzene-induced solvent shifts occur, we have now examined a variety of *meta*- and *ortho*-substituted methoxybenzenes.

The *meta*-substituted anisoles studied are given in Table 1, with the appropriate σ_m values [2,3] and the solvent

TABLE 1

Solvent shifts ($\Delta = \delta_c - \delta_b$ p.p.m.) for methoxyl resonances of the *meta*-substituted anisoles (II)—(IX) and anisole (I)

No.	R	σ_m	Δ
(II)	NO_2	+0·71	+0·87
(III)	Cl	+0·37	+0·69
(IV)	CHO	+0·36	+0·64
(V)	CO_2H	+0·36	+0·65
(VI)	SCH_3	+0·14	+0·50
(VII)	OCH_3	+0·12	+0·43
(VIII)	CH_2OH	+0·08	+0·43
(I)	H	0	+0·46 *
(IX)	CH_3	−0·07	+0·40
(X)	NH_2	−0·16	+0·34

* This value differs slightly from the Δ value (0·44) earlier reported (ref. 1) for the methoxyl resonance of anisole.

shifts (Δ) observed for the methoxyl resonances on changing the solvent from carbon tetrachloride (an " inert " solvent) to benzene (a complexing solvent).

(I; R = H) (II) — (IX)

A plot of σ_m against Δ (Figure 1) shows that there is a reasonably linear correlation between the two para-

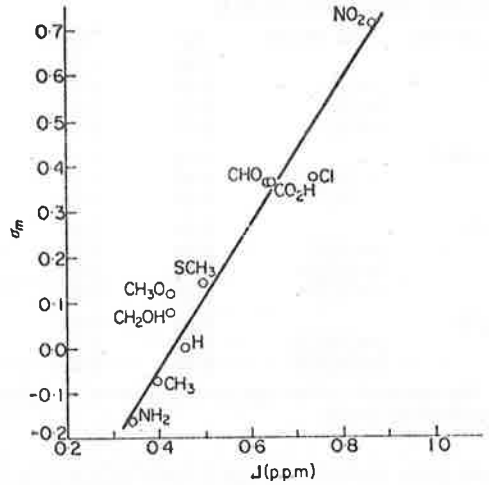


FIGURE 1 Plot of σ_m against Δ (p.p.m.) for some *meta*-substituted anisoles

meters, as found for the corresponding *para*-isomers.[1] However, dipole moments [4] of six of the compounds, plotted against Δ give a graph (Figure 2) which indicates that there is no simple relationship between μ and Δ. The possible significance of these observations will be discussed subsequently.

[2] H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191.
[3] G. B. Barlin and D. D. Perrin, *Quart. Rev.*, 1966, **20**, 80.

The corresponding solvent shifts for a number of *ortho*-substituted anisoles are summarised in Table 2,

TABLE 2

Solvent shifts ($\Delta = \delta_c - \delta_b$ p.p.m.) for methoxyl resonances of the *ortho*-substituted anisoles (XI—XX) and anisole (I)

No.	R	μ	Δ
(XI)	CO_2H	5·52	+1·01
(XII)	NO_2	4·84	+0·88
(XIII)	CHO	4·20	+0·82
(XIV)	$COCH_3$	4·02	+0·74
(XV)	CO_2CH_3	2·64	+0·56
(XVI)	Br	2·47	+0·65
(XVII)	Cl	2·44	+0·65
(XVIII)	NH_2	1·47	+0·52
(XIX)	OCH_3	1·30	+0·38
(I)	H	1·24	+0·46
(XX)	CH_3	1·00	+0·43

with the appropriate dipole moments [4] (μ) of the compounds. As expected, a plot of Δ against apparent σ_o values [3] (Figure 3) establishes that there is no simple

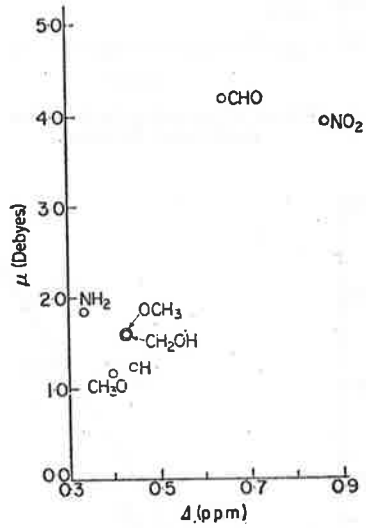
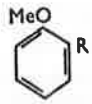


FIGURE 2 Plot of μ against Δ (p.p.m.) for some *meta*-substituted anisoles

relationship between Δ and σ_o, in contrast to the *meta*- and *para*-cases, but surprisingly the plots of μ against Δ (Figure 4) for the *ortho*-isomers shows an approximately linear correlation.



(XI — XX)

In the light of the theory developed in Part XI [5] [that the Δ value for the methoxyl resonance will largely (but not exclusively) reflect benzene solvation at the methoxyl group and that the extent of this solvation will increase with decreasing electron-density at the oxygen atom], it is not surprising that σ_p and σ_m (Figure

[4] A. L. McClellan, " Tables of Experimental Dipole Moments," W. H. Freeman and Co., San Francisco and London, 1963.
[5] J. Ronayne and D. H. Williams, following Paper.

1) give a reasonable linear correlation with Δ. This is especially true since the physical significance of σ_R seems to be best interpreted in terms of a measure of the modification in electron density at a reaction site due to the substituent R.[2] The lack of correlation between

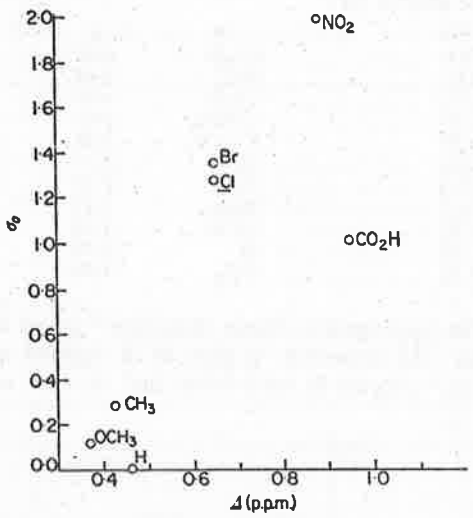


FIGURE 3 Plot of σ_o against Δ (p.p.m.) for some *ortho*-substituted anisoles

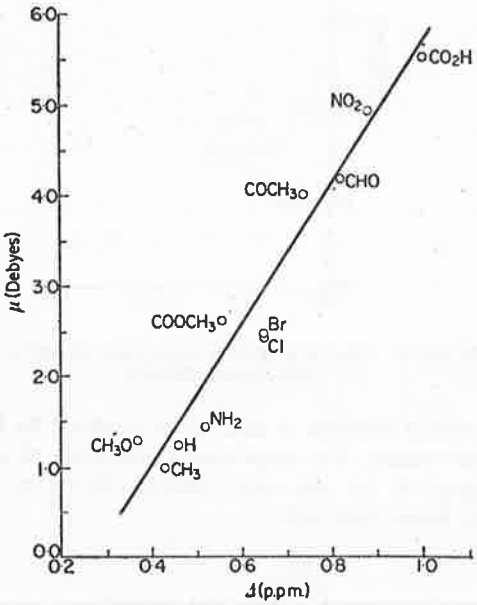
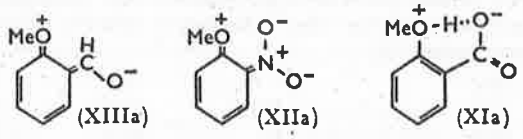


FIGURE 4 Plot of μ against Δ (p.p.m.) for some *ortho*-substituted anisoles

Δ and σ_o (Figure 3) is expected; there is no reason why the steric and polarisation factors observed for the *ortho*-R-substituted benzoic acids (upon the pK values of which the σ_o values are based) should resemble those in the *ortho*-R-substituted anisoles (XI)—(XX). The reasonably linear correlation between Δ and μ (Figure 4) for the *ortho*-isomers (XI)—(XX) is more difficult to understand and we can offer no detailed explanation for it. It can however be pointed out that the dipole moment will qualitatively reflect the electron-deficiency at the oxygen atom of the methoxyl group in contributing resonance structures such as (XIIIa) and (XIIa). The anomalously large dipole moment (and solvent shift) of *o*-anisic acid (XI) may be associated with a small contribution from the resonance form (XIa).



Having available a series of anisoles with various R substituents in the *ortho-*, *meta-*, and *para*-positions, it was of interest to examine the variation of Δ for protons in an R substituent with a change in the position of R relative to the methoxyl function. Some appropriate chemical shifts are in Table 3.

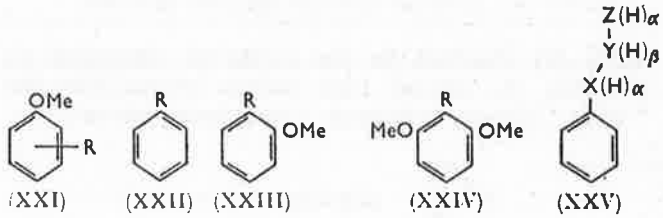


TABLE 3

Chemical shifts (p.p.m.) and Δ values for protons contained in R in various substituted anisoles (XXI) and parent compounds (XXII)

R in (XXII)	R in (XXI)	δ_a	δ_b	Δ
CH_3		2·35	2·12	+0·23
	p-CH_3	2·25	2·12	+0·13
	m-CH_3	2·31	2·12	+0·19
	o-CH_3	2·17	2·28	−0·11
CH_2OH *		4·59	4·31	+0·28
	m-CH_2OH *	4·52	4·34	+0·18
	o-CH_2OH *	4·58	4·69	−0·11
CH_3O		3·78	3·32	+0·46
	p-CH_3O	3·70	3·36	+0·34
	m-CH_3O	3·75	3·32	+0·43
	o-CH_3O	3·80	3·44	+0·36
CH_3CO		2·54	2·10	+0·44
	p-CH_3CO	2·46	2·14	+0·32
	o-CH_3CO	2·50	2·49	+0·01

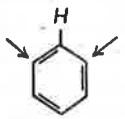
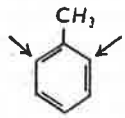
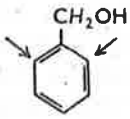
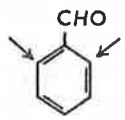
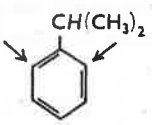
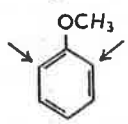
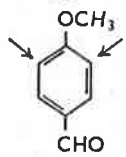
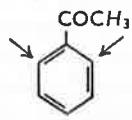
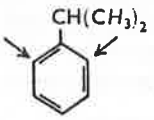
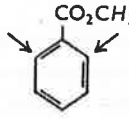
* The chemical shifts and Δ values refer to the protons of the methylene group.

There is no radical change (>0·15 p.p.m.) in Δ values for the protons of R on introduction of a *m*- or *p*-methoxy group. In contrast, there is a marked tendency or Δ values of protons in an R group *ortho* to the methoxyl function to become more negative (relative to Δ in the absence of the *o*-methoxyl function). *Thus the upfield shifts of the* CH_3- *and* CH_2-*protons of toluene and benzyl alcohol, observed on change of solvent from* CCl_4 *to* C_6H_6, *become downfield shifts in the presence of an* o-*methoxyl group*. Such specific effects have great potential in the field of structure elucidation. To evaluate this particular effect we prepared a variety of compounds of the general

structures (XXIII) and (XXIV). The Δ values for protons attached to R in (XXII)—(XXIV) then permit one to find the effect on Δ of the successive introduction of one and two methoxyl groups (Table 4). In the last

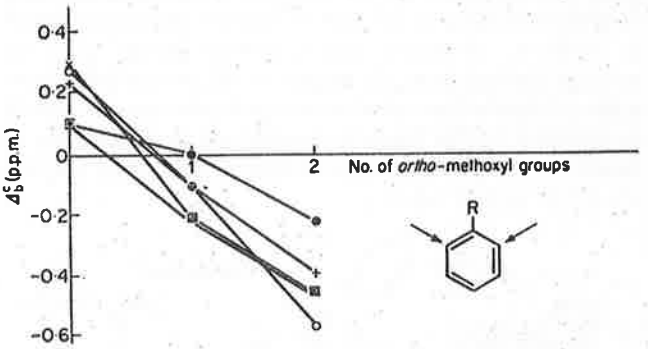
TABLE 4

Chemical shifts (p.p.m.) and Δ values for protons contained in R in various anisoles (XXIII), (XXIV) and parent compounds (XXII)

Compound	δ_o	δ_b	Δ	
XXII	7·30	7·20	+0·10	
XXIII R = H	6·83	6·83	0·00	
XXIV	6·84	6·57	−0·23	
XXII	2·35	2·12	+0·23	
XXIII R = CH_3	2·17	2·28	−0·11	
XXIV	2·02	2·42	−0·40	
XXII	4·59	4·31	+0·28	
XXIII R = CH_2OH	4·58	4·69	−0·11	
XXIV	4·60	5·17	−0·57	
XXII	10·00	9·71	+0·29	
XXIII R = CHO	10·50	10·72	−0·22	
XXIV	10·43	10·90	−0·47	
XXII	2·90	2·80	+0·10	
XXIII R = $CH(CH_3)_2$	3·38	3·59	−0·21	
XXIV	3·63	4·11	−0·48	
XXII	3·78	3·32	+0·46	
XXIII R = OCH_3	3·80	3·43	+0·37	
XXIV	3·71	3·82	−0·11	
XXII R = OCH_3	3·87	3·13	+0·74	
XXIII + *p*-CHO	3·90	3·30	+0·60	
XXIV	3·84	3·77	+0·07	
XXII	2·54	2·10	+0·44	
XXIII R = $COCH_3$	2·50	2·49	+0·01	
XXIV	2·35	2·41	−0·06	
XXII	1·27	1·16	+0·11	
XXIII R = $CH(CH_3)_2$	1·22	1·27	−0·05	
XXIV	1·26	1·57	−0·31	
XXII	3·89	3·50	+0·39	
XXIII R = CO_2CH_3	3·84	3·59	+0·25	
XXIV	3·84	3·70	+0·14	

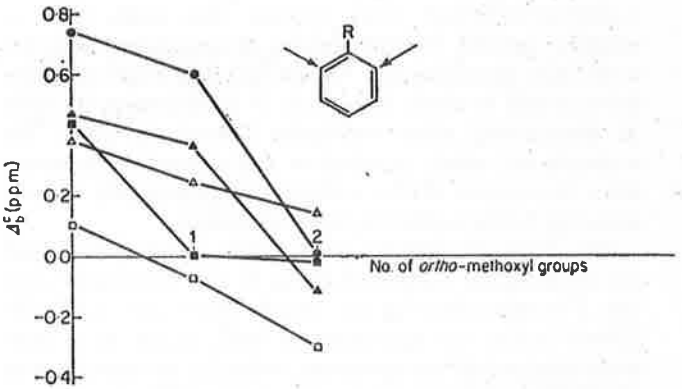
column in Table 4, the protons whose chemical shifts are being considered are in italics and the positions of introduction of methoxyl groups indicated by arrows.

The results are summarised pictorially for ring protons and for α-protons in Figure 5, and for β- and γ-protons in R [see (XXV)] in Figure 6. Marked variations in Δ values are observed, *e.g.*, the CH_2-protons of benzyl alcohol are *shielded* by 0·28 p.p.m. in benzene relative to carbon tetrachloride, but when the hydroxymethyl group is flanked by adjacent methoxyl groups in both *ortho*-positions, benzene causes *deshielding* of the CH_2-protons by 0·57 p.p.m. Without exception in the 27 compounds studied, the introduction of an *o*-methoxyl group causes a negative shift in the Δ values observed for the protons in R (Figures 5 and 6). In general,



● R = *H*, + R = CH_3, × R = *CHO*, ○ R = CH_2OH, □ R = $CH(CH_3)_2$.

FIGURE 5 Variation of solvent shifts of ring protons and α-protons (*H*) contained in R with number of *o*-methoxy groups



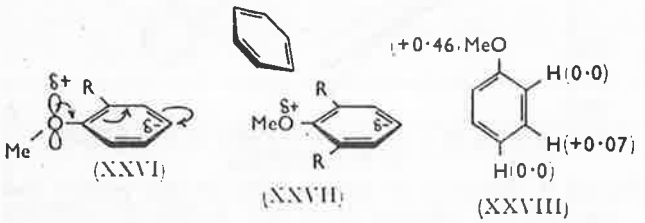
▲ R = OCH_3, ● R = OCH_3 and *p*-CHO, △ R = $COOCH_3$, ■ R = $COCH_3$, □ R = $CH(CH_3)_2$.

FIGURE 6 Variation of solvent shifts of β- and γ-protons (H) contained in R with number of *o*-methoxyl groups

protons α to the benzene ring (Ar–C*H*<) and flanked by two *o*-methoxyl groups are strongly deshielded (0·4—0·6 p.p.m.) in benzene relative to carbon tetrachloride (see Figure 5). The changes in Δ due to the introduction of the first and second methoxyl groups are not usually equal, as might be expected since the conformational preference of groups in R will in general depend on the presence of one or two *o*-methoxyl groups.

The presence of one R substituent *ortho* to a methoxyl group should not prevent the *p*-orbital overlap by which oxygen can donate electrons to the aromatic ring and become a π-electron-deficient centre. If the *O*-methyl group has a preference to reside on average as far as

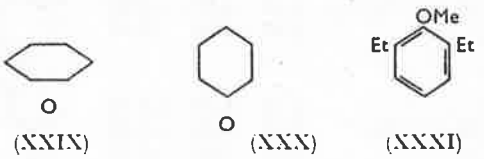
possible from R, the electron-donating *p*-orbital, perpendicular to the plane containing both C–O bonds, can interact with the π-system of the ring [see (XXVI)]. In accordance with the concepts developed in Part XI,[5] benzene should associate with an electron-donating methoxyl group at the site of partial positive charge in a non-planar complex, with the benzene ring as far as possible from the electron-rich portion of the solute. A schematic representation (XXVII) of such an association is in complete accord with the observed deshielding of *ortho*-substituents in the 18 methoxybenzenes listed in Table 4. Moreover, the *O*-methyl group, lying on average further from the negative end of the methoxyl-induced dipole than the electron-deficient oxygen should be shielded by the benzene association, again exactly as found for the 18 methoxybenzenes in Table 4 [Δ (OCH_3) = +0·41 to 0·82 p.p.m.].



It is emphasised that the oxygen atom will be π-electron-deficient, even though this atom will be roughly neutral overall (taking into account also the σ-electron distribution). It is felt that π-electron deficiency will be more important in determining the sites of association than σ-electron deficiency, since the π-clouds are more exposed to the solvent. However, some association at the σ-electron-deficient ring carbon, adjacent to the methoxyl, is not excluded.

The type of association (XXVII) which we suggest for an aromatic methoxyl group is also consistent with the Δ values observed for anisole itself (see XXVIII). (These values are approximate only, based on a first-order analysis of the spectrum, aided by the spectrum of [2,4,6-$^2H_3$]anisole.) To evaluate the effect of introducing the methoxyl group into the aromatic system, these values must be compared with Δ (+0·10 p.p.m.) for benzene itself. This shift is probably due to the tendency of disc-shaped molecules such as benzene to prefer a configuration in which the planes of the discs are parallel.[6] Hence, the association of benzene solvent induced by the methoxyl group causes deshielding of the ring protons by 0·03 to 0·10 p.p.m. We quote these figures only as supporting and not independent evidence, since the shifts involved are small (contrast those in Table 4) and becoming comparable with those which may be induced by other mechanisms.

The possibility that the negative Δ values observed for a substituent between two *ortho*-methoxyls is merely due to a shape effect has been considered and rejected. It was necessary to test this hypothesis because it is observed that the protons of methane are appreciably shielded in benzene relative to carbon tetrachloride if chloroform is used as an *external* reference.[6] The shift has been ascribed [6] to the preference of the disc-like benzene to approach the methane solute most closely in the configuration (XXIX) [as opposed to (XXX)], while the external reference of course remains unaffected. The internal reference tetramethylsilane will suffer a similar shielding in benzene, but it could be argued that benzene will less readily have access to a substituent between two methoxyl groups, thus causing an apparent "deshielding" of protons in the substituent relative to tetramethylsilane. To evaluate this possibility, 2,6-diethylanisole (XXXI) was synthesised; in this solute, the two ethyl groups have steric requirements similar to those of two methoxyl groups. It was expected that if steric effects between solute and benzene were more important than polar effects, then the Δ value for the methoxyl in (XXXI) would be similar to that (−0·11 p.p.m.) observed for the central methoxyl group of 1,2,3-trimethoxybenzene. Alternatively, if polar effects are more important, the observed Δ value should be smaller than that observed in anisole (+0·46 p.p.m.) owing to some steric hindrance of π-electron donation from the methoxyl group (and perhaps also to weak benzene–solute interactions associated with electron-donating ethyl groups), but should not be negative. The observed Δ value (+0·25 p.p.m.) for the methoxyl resonance of (XXXI) is in accord with the latter explanation.



The use of methoxyl solvent shifts in structure elucidation must be approached cautiously. The downfield shift observed in benzene for a methoxyl group situated between two others in 1,2,3-trimethoxybenzene is potentially very useful. However, Δ will change in a positive direction if there is an electron-withdrawing substituent in the *para*-position which can serve as a site for another benzene association, and also increase the partial positive charge on the *para*-oxygen atom.[5] This point is demonstrated by the introduction of a *p*-CHO substituent (Table 4 and Figure 6). A strong electron-donating substituent in the *para*-position should make the Δ value for the central methoxyl group slightly more negative.

EXPERIMENTAL

The purity of all samples was checked by n.m.r. spectroscopy, which proved ideal for the type of compound studied. Compounds whose preparation is not mentioned were commercial.

2,6-*Dimethoxybenzaldehyde*.—This was made from resorcinol dimethyl ether by Wittig's method.[7]

[6] A. D. Buckingham, T. Schaefer, and W. G. Schneider, *J. Chem. Phys.*, 1960, **32**, 1227.
[7] G. Wittig, *Angew. Chem.*, 1940, **53**, 241.

2,6-*Dimethoxybenzyl Alcohol*.—Reduction of 2,6-dimethoxybenzaldehyde with lithium aluminium hydride furnished this material, m. p. 54—56° (lit.,[8] 55·5—56°).

2,6-*Dimethoxyisopropylbenzene*.—This was made from 2,6-dimethoxyacetophenone by the method of Whalley *et al.*[9]

2,6-*Dimethoxyacetophenone*.—This was prepared from 2,6-dimethoxybenzonitrile by Mauthner's method.[10]

Methyl o-*Methoxybenzoate*.—The action of diazomethane on *o*-anisic acid provided this material. The methyl resonances were assigned by use of methyl *o*-methoxybenzoate labelled with deuterium in the ester group.

[$^2H_3$]*Methyl* o-*Methoxybenzoate*.—A solution of dideuteriomethane in dioxan, prepared by the method of Van Der Merwe *et al.*[11] was added to a solution of *o*-anisic acid in dioxan–deuterium oxide (1 : 1) and the product was extracted with ether in the usual manner.

[2,4,6-$^2H_3$]*Anisole*.—A solution of phenol (1 g.) in deuterium oxide (5 ml.) containing 200 mg. of sodium deuteroxide was heated under reflux for 12 hr. Acidification and ether extraction of the product gave [2,4,6-$^2H_3$]phenol, which was methylated with dimethyl sulphate in the usual manner.

2,6-*Diethylanisole*.—Commercial 2,6-diethylaniline was diazotised and the solution of the diazonium salt was heated to *ca.* 60° for 30 min. The resulting phenol was converted into 2,6-diethylanisole by methylation with alkaline dimethyl sulphate.

All n.m.r. spectra were obtained on a Perkin-Elmer 60 Mc./sec. and/or Varian H.A. 100 Mc./sec. instruments. The chemical shifts in carbon tetrachloride and benzene solutions were determined by use of 1—2% (w/v) solutions at normal probe temperatures.

We acknowledge an S.R.C. post-graduate award (to J. R.).

[6/1185 *Received, September 21st,* 1966]

[8] K. Hejno and Z. Arnold, *Chem. Listy*, 1953, **47**, 601.
[9] J. P. Brown, D. H. Johnson, A. Robertson, and W. Whalley, *J. Chem. Soc.*, 1951, 2019.
[10] F. Mauthner, *J. prakt. Chem.*, 1934, **139**, 290.
[11] K. J. Van Der Merwe, P. S. Steyn, and S. H. Eggers, *Tetrahedron Letters*, 1964, 3923.

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SOLVENT EFFECTS IN NMR SPECTROSCOPY

SOLVENT SHIFTS OF METHOXYL RESONANCES IN FLAVONES INDUCED BY BENZENE; AN AID TO STRUCTURE ELUCIDATION

R. G. WILSON, J. H. BOWIE[1] and DUDLEY H. WILLIAMS
University Chemical Laboratory, Cambridge, U.K.

(*Received in U.K.* 14 *June* 1967; *accepted for publication* 15 *July* 1967)

Abstract—The position and relative orientation of OMe groups in methoxyflavones can be inferred from benzene-induced solvent shifts of the OMe resonances. OMe groups at C-5, C-7, C-10 and C-12 exhibit large positive Δ values ($\Delta = \delta_{CDCl_3} - \delta_{C_6H_6} \simeq 0{\cdot}5$ to 0·8 ppm) in the absence of OMe or OH substituents *ortho* to these groups. In contrast, OMe groups at C-3, or those flanked by two *ortho*-OMe functions (or one *ortho*-OH and one *ortho*-OMe function) show small positive or negative Δ values. An OMe at C-5 suffers a drastic algebraic decrease in solvent shift upon the introduction of an OMe group at C-6. Electronic and conformational factors which may account for these differences are considered.

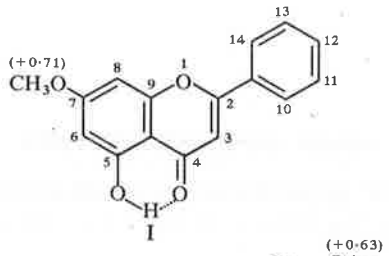
THE dependence of solvent shifts of OMe resonances induced by benzene (relative to a comparatively "inert" solvent, such as CCl_4 or $CDCl_3$) upon electronic, steric and conformational factors have been noted,[2–4] and the potential of such solvent shifts for structure elucidation in the coumarin field has been emphasized.[5] The present paper points out the utility of benzene-induced shifts in the NMR spectra of methoxyflavones.

The solvent shifts ($\Delta = \delta_{CDCl_3} - \delta_{C_6H_6}$ ppm) which are observed for the simple mono-, di-, and tri-methoxyflavones (I–IV) can be assigned without much ambiguity, and are given with the structural formulae; where ambiguities exist, alternative assignments are given in square brackets. In flavones which are more highly substituted (V–XVI), the assignments are frequently not unambiguous, and the shifts of the OMe resonances are therefore most conveniently pictured by means of line spectra of the OMe region of each compound in the two solvents. Where lines representing OMe resonances are bracketed together, unambiguous assignments are not possible even when using the criteria which are enumerated below. The numbering system of the flavone nucleus which is employed is given with structure I; conventionally the phenyl substituent ring is numbered 1′ through 6′, but to avoid possible confusion in the diagrams a continuous series of numbers is used for our present purposes.

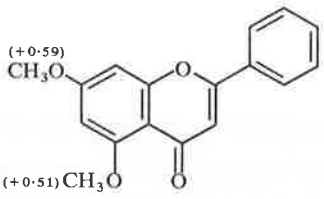
It is possible to follow the shifts of OMe resonances in multi-substituted flavones by using the following guides.

1. The data available from model compounds, e.g. the Δ value of the C-1 and C-3 OMe resonances of 1,2,3-trimethoxybenzene is +0·38 ppm, while that of the C-2 OMe resonance is −0·11 ppm.[2]

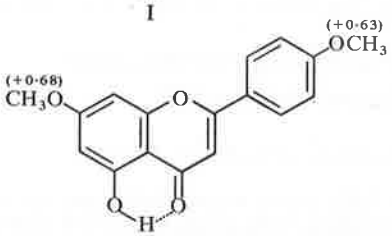
2. By making sensibly self-consistent assignments for flavones with similar structures, e.g. the OMe resonances of III are coincident at $\delta = 3{\cdot}84$ ppm in $CDCl_3$, but occur at 3·21 and 3·16 ppm in benzene. Since the corresponding figures for the



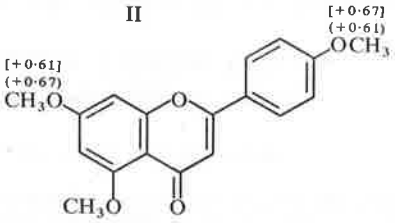
I



II



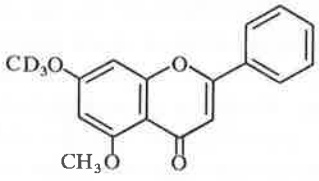
III



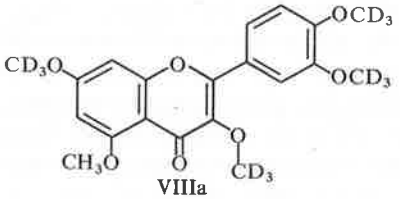
IV

7-OMe of I in the two solvents are 3·86 and 3·15 ppm (in $CDCl_3$ and C_6H_6, respectively), the larger solvent shift in III is assigned to the 7-OMe group.

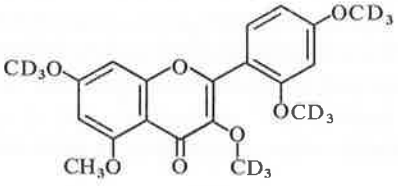
3. Specific deuteration of certain OMe groups by deuteromethylation of the corresponding phenol. For deuteromethylation, the method of Van der Merwe *et al.*[6] was employed (treatment of the phenol with diazomethane in the presence of a dioxan–deuterium oxide mixture). The following specifically deuterated flavones were prepared by this method and have been utilized in assigning the OMe resonances. In the syntheses of IIa, VIIIa and Xa, the inert nature of the hydrogen-bonded 5-OH group towards diazomethane was utilized, this group being methylated subsequently by treatment with dimethyl sulphate and alkali.



IIa

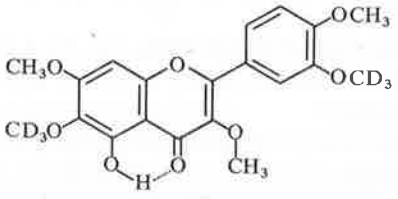


VIIIa

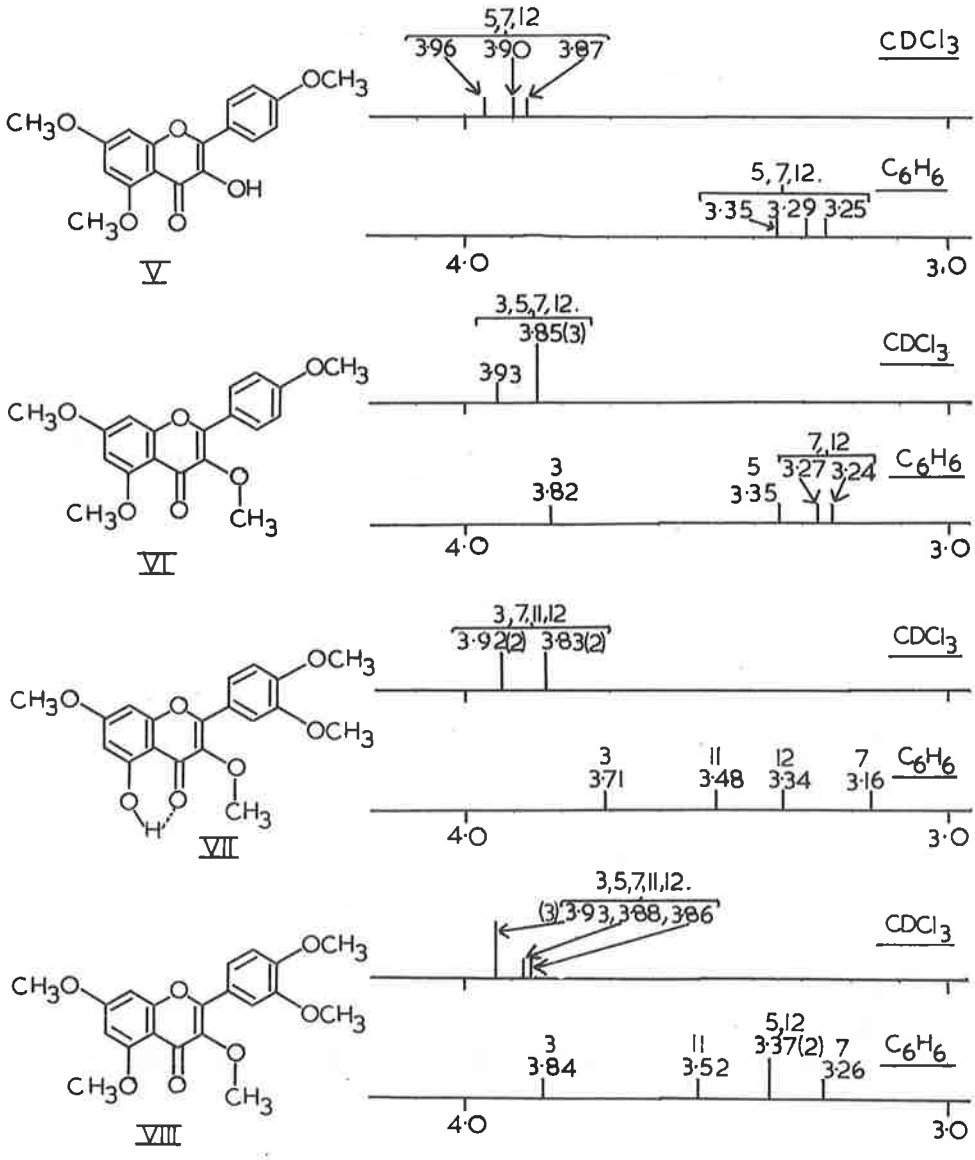


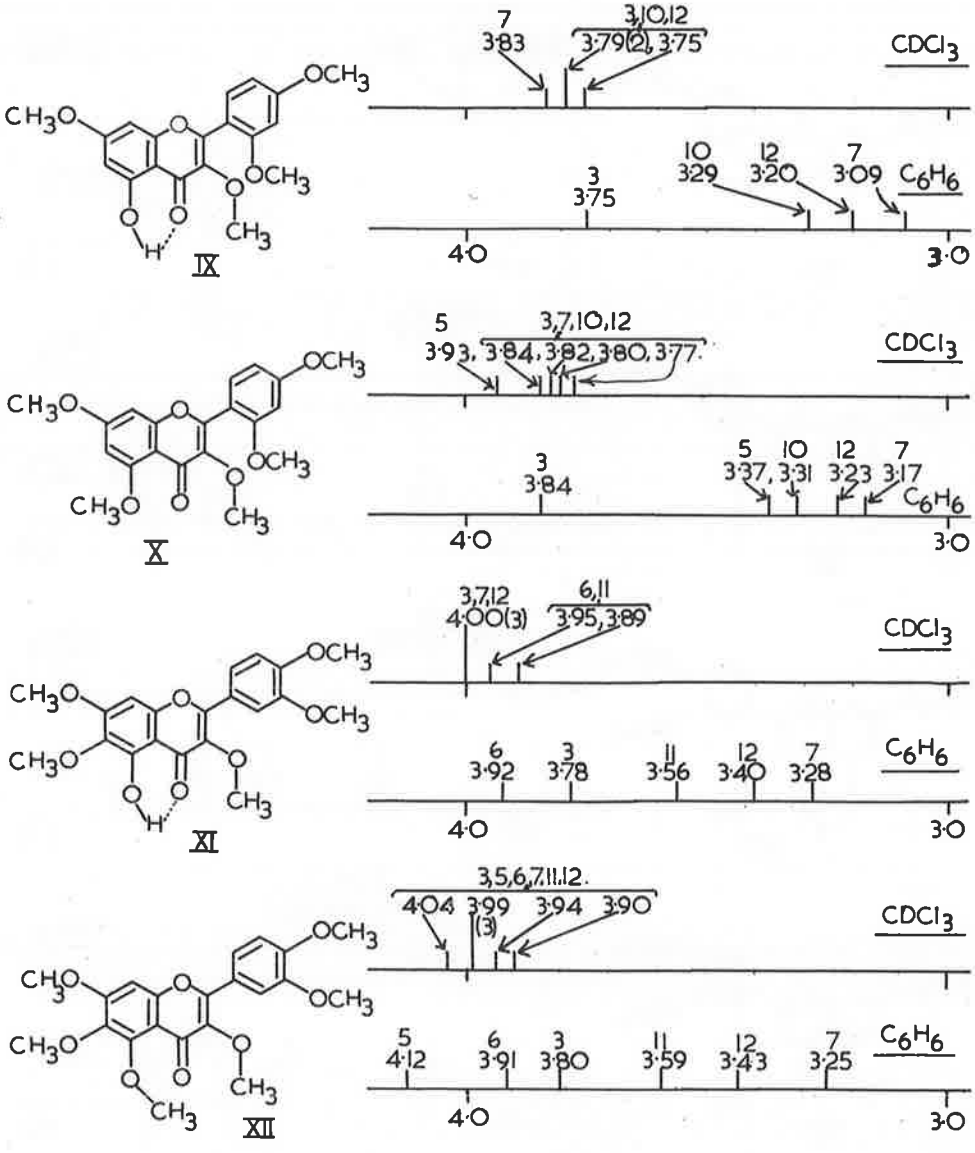
Xa

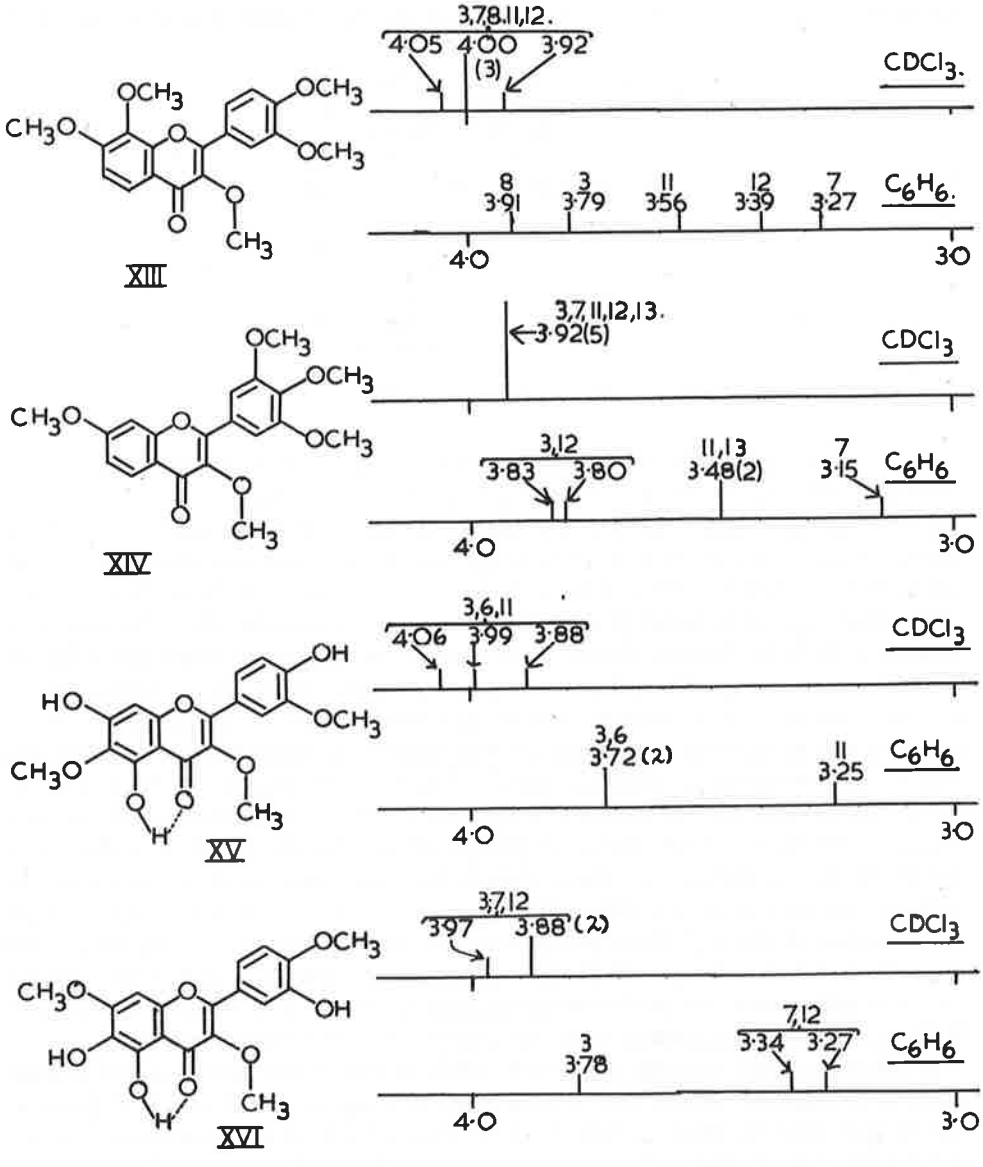
XIa



XIb


5,7,12
3·96 3·90 3·87
CDCl3
5, 7, 12.
C6H6
3·35 3·29 3·25
4·0
3·0
V
3,5,7,12.
3·85(3)
3·93
CDCl3
7,12
3
3·82
5
3·35
3·27 3·24
C6H6
4·0
3·0
VI
3,7,11,12
3·92(2) 3·83(2)
CDCl3
3
3·71
11
3·48
12
3·34
7
3·16
C6H6
4·0
3·0
VII
3,5,7,11,12.
(3) 3·93, 3·88, 3·86
CDCl3
5,12
3
3·84
11
3·52
3·37(2)
7
3·26
C6H6
4·0
3·0
VIII


7
3·83
3,10,12
3·79(2), 3·75
CDCl3
10
3·29
12
3·20
7
3·09
C6H6
3
3·75
4·0
3·0
IX
5
3·93, 3·84, 3·82, 3·80, 3·77
3,7,10,12
CDCl3
3
3·84
5
3·37, 3·31
10
12
3·23
7
3·17
C6H6
4·0
3·0
X
3,7,12
4·00(3)
6,11
3·95, 3·89
CDCl3
6
3·92
3
3·78
11
3·56
12
3·40
7
3·28
C6H6
4·0
3·0
XI
3,5,6,7,11,12
4·04
3·99
(3)
3·94
3·90
CDCl3
5
4·12
6
3·91
3
3·80
11
3·59
12
3·43
7
3·25
C6H6
4·0
3·0
XII


3,7,8,11,12.
4·05 4·00 3·92
(3)
CDCl3.
8 3 11 12 7
3·91 3·79 3·56 3·39 3·27
C6H6.
4·0
3·0
XIII
3,7,11,12,13.
3·92(5)
CDCl3
3,12
3·83 3·80
11,13
3·48(2)
7
3·15
C6H6
4·0
3·0
XIV
3,6,11
4·06 3·99 3·88
CDCl3
3,6
3·72 (2)
11
3·25
C6H6
4·0
3·0
XV
3,7,12
3·97 3·88 (2)
CDCl3
7,12
3·34 3·27
3
3·78
C6H6
4·0
3·0
XVI

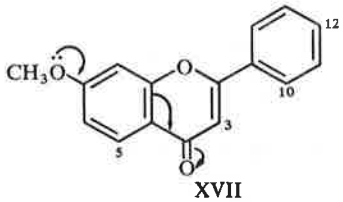
From a consideration of the results *in toto*, it is apparent that if the local environment (mainly with regard to immediately adjacent substituents) of an OMe group is defined, the solvent shifts are characteristic of that local environment, and frequently also characteristic of the position of substitution. In Table 1, the ranges of values for OMe groups at C-5, C-7, C-10 and C-12, in the absence of *o*-OMe or *o*-OH

TABLE 1. Δ VALUES ($\delta_{CDCl_3} - \delta_{C_6H_6}$ ppm) for C-3, C-5, C-7, C-10 AND C-12 OMe RESONANCES IN THE ABSENCE OF *ortho*-SUBSTITUENTS

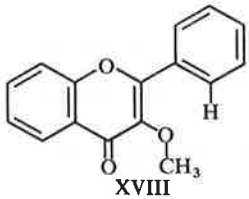
Position of OMe	Range of Δ values
C-3	−0·07 to +0·34
C-5	+0·43 to +0·58
C-7	+0·54 to +0·76
C-10	+0·46 to +0·53
C-12	+0·54 to +0·71

neighbours are given. Since the environment of the C-3 OMe group cannot be altered by substitution on an adjacent carbon atom, the range of solvent shifts for this OMe group is also included. It is apparent that OMe groups at C-5, C-7, C-10 and C-12 can in the absence of *ortho*-neighbours be differentiated from a C-3 OMe group. For "isolated" OMe groups at C-5, C-7, C-10 and C-12, the shifts are always larger than that (0·46 ppm) of the OMe resonance of anisole. This observation is consistent with the formal ability of all these OMe groups to conjugate with the electron-withdrawing carbonyl group (see, for example, XVII). This conjugation can lead to a decrease in π-electron density at oxygen atoms of the OMe groups in question, and so enhance an association with benzene at these electron-deficient sites with a resultant increased shielding effect.[2,3] The C-3 OMe resonances are in contrast deshielded or only slightly shielded in benzene (Table 1). This observation strongly suggests that the C-3 OMe group in general prefers the conformation indicated in XVIII. In this conformation, phase independent associations of benzene with the carbonyl group will have a deshielding influence on the C-3 OMe group.[7,8] Since the Δ values of the C-5 OMe group are only slightly smaller in magnitude than those for the C-7, C-10 and C-12 OMe groups, it is concluded that in the absence of a C-6 substituent, the preferred conformation for the C-5 OMe is as shown in XIX (i.e., as distant as possible from the negative end of the carbonyl dipole).

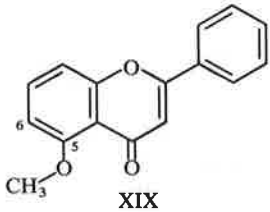
In the compounds studied, the central OMe of three OMe groups suffers a small positive or negative solvent shift (widest possible range is +0·13 to −0·12 ppm), as can be seen from the data for XII and XIV. This behaviour is analogous to the case of 1,2,3-trimethoxybenzene[2,3] which was cited earlier, and if used cautiously (i.e. by taking account of the presence of additional polar substituents) should be generally useful in indicating the presence of three adjacent OMe groups in natural products. The reason for the small positive or negative shift is probably due to some combination of (i) steric inhibition of benzene solvation of the central OMe group,[4] (ii) reduction in solvation of the central OMe (relative to the anisole case) due to the presence of two *ortho* electron-donating substituents,[2,3] and (iii) solvation of the



XVII



XVIII



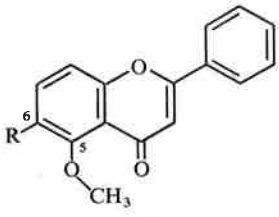
XIX

outer OMe groups, the stereochemistry of benzene association being such as to place the central OMe in a region of deshielding. It is emphasized that the steric factor cannot be the major influence, since an electron-withdrawing substituent *ortho* to an OMe function increases the upfield shift which is observed in benzene.[3]

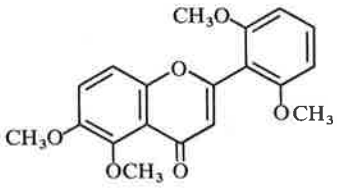
Since the heterocyclic oxygen atom attached to C-9 should have an effect similar to a hypothetical OMe substituent at the position, it might be anticipated that in 7,8-dimethoxyflavones (e.g. XIII), the C-8 OMe resonance would suffer only a small solvent shift. This supposition is confirmed by the data for XIII.

In a similar manner, an OMe group which is situated such that one neighbouring carbon atom carries an OH group and the other an OMe group, both of which can formally conjugate with the carbonyl group, has a very small positive or negative solvent shift [the C-6 OMe of XI exhibits $\Delta = +0{\cdot}03$ ppm (or $\Delta = -0{\cdot}03$ ppm as an alternative assignment); the possible assignments have been reduced with the aid of the deuterated derivatives XIa and XIb].

The solvent shift of an OMe group at C-5 suffers a drastic change in magnitude from a relatively large positive value (see Table 1) to a small or negative value (see data for XII) in the presence of an OMe at C-6. Such a change is in accord with expectations, since the introduction of an *ortho*-OMe group generally causes an algebraic decrease in Δ, and in addition a C-6 substituent should lead to a higher population of the conformer XX in which the Me of the C-5 functionality lies in close proximity to the negative end of the carbonyl dipole (which is a region of strong deshielding due to benzene association at the carbonyl group[7]). This characteristic solvent shift has proved useful in the structure elucidation of zapotin (XXI).[9]



XX



XXI

EXPERIMENTAL

NMR spectra were obtained either on a Perkin–Elmer 60 Mc instrument or a Varian Associates HA 100 Mc instrument. In all cases the concentration of the flavones in benzene or $CDCl_3$ solns was not greater than 2% w/v. The spectra were (with one exception, see below) obtained at normal probe temps (30–33°), using TMS as internal reference. Due to solubility problems, the spectra of XVI were recorded in $CDCl_3$ soln at 60° and benzene soln at 110° (sealed tube). The recorded shifts therefore differ from the values to be expected at room temp, but the trends are clear for the purposes of empirical correlation.

The preparation of specifically deuterated flavones may be exemplified by the preparation of IIa.

Chrysin 5-methyl-7-trideuteromethyl ether (IIa). Deuterium oxide (3 ml) was added to a soln of diazomethane in dry dioxan,[6] followed by slow dropwise addition of a dioxan–D_2O soln of chrysin (250 mg). After the mixture had been allowed to stand overnight, the solvents were removed and the residue recrystallized from EtOH to give chrysin 7-trideuteromethyl ether (144 mg, m.p. 160–164°; lit.[10] m.p. for chrysin 7-methyl ether is 163°). The 7-trideuteromethyl ether (100 mg) in acetone (5 ml) was treated with Me_2SO_4 (0·3 ml) and 20% NaOH aq (1·3 ml) and the reaction mixture heated on a water bath for 1 hr, after standing at room temp for 1 hr. Water (3 ml) and conc NH_4OH (3 ml) were then added to the cooled reaction mixture, and the yellow crystals which formed were isolated by filtration. Recrystallization from aqueous EtOH gave IIa (m.p. 144–146°; lit.[10] m.p. for chrysin 5,7-dimethyl ether is 143°).

Other deuterated flavones were prepared by unexceptional variations of this technique (see also Ref. 11).

Acknowledgement—The authors wish to thank Dr. J. W. W. Morgan for a generous gift of several flavone and flavanol samples.

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BENZENE-INDUCED SOLVENT SHIFTS OF PROTON RESONANCES IN THE N.M.R. SPECTRA OF α-DIKETONES*

By J. H. Bowie,† G. E. Gream,† and M. H. Laffer†

[*Manuscript received January* 24, 1968]

Summary

Solvent shifts [$\Delta^{CCl_4}_{C_6H_6} = \delta_{CCl_4} - \delta_{C_6H_6}$ p.p.m.] are recorded for a number of acyclic and cyclic α-diketones. Benzene produces upfield shifts of methyl and methylene resonances in the spectra of saturated acyclic and cyclic α-diketones. The shift of the α-methylene resonance of acyclic α-diketones may be related to the length (and bulk) of the side-chain. The formation of a 1 : 1 complex is proposed, and variable temperature studies (in toluene-d_8) have allowed calculation of thermodynamic parameters for an acyclic and a cyclic compound. The dependence of solvent shifts on the position of methyl and hydrogen substituents of aromatic α-diketones has been demonstrated.

It has been shown[1–8] for many ketones, that the proton chemical shifts induced by benzene relative to carbon tetrachloride (or deuterochloroform)

$$\Delta^{CCl_4}_{C_6H_6} = \delta_{CCl_4} - \delta_{C_6H_6}$$

conform to the pictorial representation outlined in (A). The potential use of solvent shifts for structure elucidation has been recently demonstrated for quinones,[9] coumarins,[10] flavones,[11,12] and xanthones.[13] A review on solvent-shifts is available.[14] Because of our interest in α-diketones,[15,16] we wished to determine whether "solvent-

* This paper also constitutes Part II in the series N.M.R. Studies. Part I, *Tetrahedron*, 1968, **24**, 1407.

† Department of Organic Chemistry, University of Adelaide, P.O. Box 498D, Adelaide, S.A. 5001.

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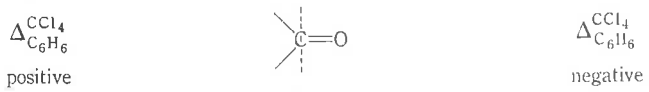
shifts" could be useful for such compounds, and this paper summarizes results for a series of acyclic, cyclic, and aromatic α-diketones.



(A)

The results obtained for the acyclic α-diketones are recorded in Table 1. Several progressions can be seen. First, the positive shift of the methyl resonance decreases markedly as its distance from the –(C=O)–(C=O)– moiety increases [e.g. (I),

TABLE 1

SOLVENT SHIFTS $\Delta^{CCl_4}_{C_6H_6} = \delta_{CCl_4} - \delta_{C_6H_6}$ OF METHYL AND METHYLENE RESONANCES IN SOME ACYCLIC α-DIKETONES

Compound	Methyl Resonance			α-Methylene (or Methine) Resonance		
	δ_{CCl_4}	$\delta_{C_6H_6}$	$\Delta^{CCl_4}_{C_6H_6}$	δ_{CCl_4}	$\delta_{C_6H_6}$	$\Delta^{CCl_4}_{C_6H_6}$
$(CH_3CO)_2$	2·26	1·80	+0·46			
$(CH_3CH_2CO)_2$	1·07	0·82	+0·25	2·71	2·37	+0·34
$(CH_3CH_2CH_2CO)_2$	0·94	0·71	+0·23	2·66	2·41	+0·25
$[CH_3(CH_2)_2CH_2CO]_2$	0·97	0·79	+0·18	2·66	2·47	+0·19
$[CH_3(CH_2)_3CH_2CO]_2$	0·94	0·84	+0·10	2·64	2·49	+0·15
$[(CH_3)_2CHCO]_2$	1·07	0·88	+0·19	3·27	3·13	+0·13
$[(CH_3)_3CCO]_2$	1·18	1·06	+0·12			

+0·46, and (V), +0·10]. This effect is unexceptional, since it is clear that the proclivity of the benzene–carbonyl complex to affect the methyl resonance will diminish as the distance between the methyl group and the complex-centre is increased. Second, and more important, the shift of the α-methylene (α to C=O) resonance in the spectra of (II–V) decreases as the length of the side-chain increases [viz. (II, ethyl) +0·34 to (V, n-pentyl) +0·15]. This decrease in solvent-shift must be due to changes in the nature of the solvent–solute complex. As the chain-length of R (in RCOCOR) increases, larger volumes are swept out in its free-rotational path, thus limiting the approach of the solvent molecule. Consequently, this reduction in solvent-shift with increasing length of the substituent is probably best explained by steric effects, although it is appreciated that the conformational free energies of alkyl substituents (on cyclohexane systems) are quite similar (e.g. ethyl = 1·97 and isopropyl = 2·38 kcal/mole).[17,18] An analogous situation is apparent from the solvent shifts of the methyl resonances of (VI) and (VII), where the positive shift also decreases as the size of the substituent increases. A combination of chemical

[17] Allinger, N. L., and Freiberg, L. A., *J. org. Chem.*, 1966, **31**, 895.
[18] Armitage, B. J., Kenner, G. W., and Robinson, M. J. T., *Tetrahedron*, 1964, **20**, 747.

shifts and solvent shifts may therefore be used empirically to indicate the size and type of side-chain in acyclic α-diketones.

$MeCOCOMe$ (I)

$Me\overset{\alpha}{C}H_2COCO\overset{\alpha}{C}H_2Me$ (II)

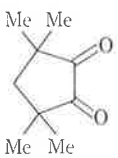
$MeCH_2CH_2COCOCH_2CH_2Me$ (III)

$Me(CH_2)_2CH_2COCOCH_2(CH_2)_2Me$ (IV)

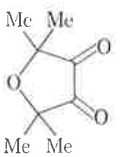
$Me(CH_2)_3CH_2COCOCH_2(CH_2)_3Me$ (V)

$(Me)_2CHCOCOCH(Me)_2$ (VI)

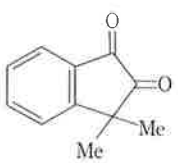
$(Me)_3CCOCOC(Me)_3$ (VII)



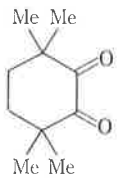
(VIII)



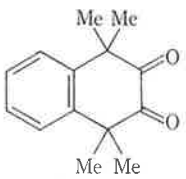
(IX)



(X)

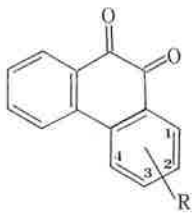


(XI)



(XII)

(XIII)



(XIV) R = 1-Me
(XV) R = 4-Me

Dilution studies have shown for ketones[19] and anisole derivatives[20] that the complex formed with benzene involves solute : benzene in a ratio 1 : 1. As two carbonyl groups are present in α-diketones, similar dilution studies were undertaken and a 1 : 1 complex is again indicated. The changes in solvent shifts of the methyl and methylene resonances in the spectra of 3,3,6,6-tetramethyl-1,2-dioxocyclohexane (XI) at different concentrations of benzene in carbon tetrachloride were measured, and the shifts plotted against concentration. A similar experiment with diacetyl (I) also indicates a 1 : 1 complex rather than an alternative 2 : 1 complex; i.e. the plots of Δ against concentration (e.g. Fig. 1) give much better approximations to linearity

[19] Laslo, P., and Williams, D. H., *J. Am. chem. Soc.*, 1966, **88**, 2799.
[20] Bowie, J. H., Ronayne, J., and Williams, D. H., *J. chem. Soc.* (*B*), 1967, 785.

than plots of Δ against concentration[2] (cf.[20]). This is only true (for the three cases considered) when the concentration of benzene is greater than 10%.

The Δ values for acyclic α-diketones (Table 1) and for cyclic α-diketones (Table 2) enable some observations to be made concerning the nature of the solute–solvent complex. As no separation of the methyl resonances of the symmetrical diketones (I)–(IX), (XI), and (XII) is observed in benzene, the benzene molecule must be placed symmetrically to the two carbonyl groups. Moreover, for (XI) and (XII), this must mean that rapid inversion of the six-membered rings is occurring even though the 1 : 1 complex has been formed. That this is the case, is shown by the considerable broadening of both the methylene and methyl resonances of (XI) when the spectrum is measured in toluene-d_8 at −60°C.

TABLE 2

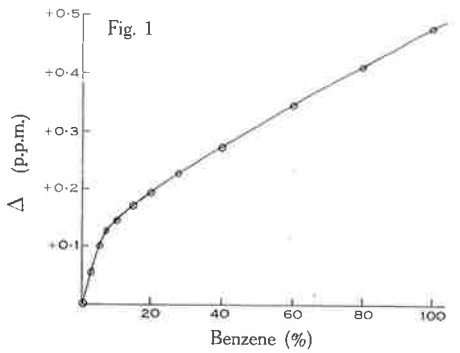
SOLVENT SHIFTS OF METHYL RESONANCES IN THE CYCLIC α-DIKETONES (VIII–XV)

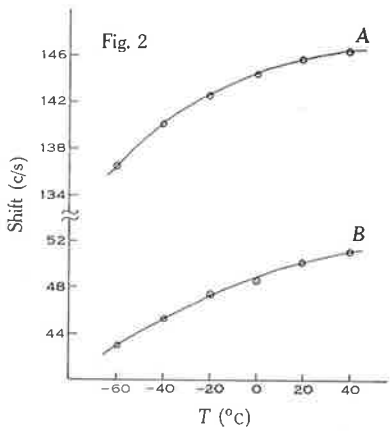
Compound	δ_{CCl_4}	$\delta_{C_6H_6}$	$\Delta^{CCl_4}_{C_6H_6}$
(VIII)	1·21	0·83	+0·38
(XI)	1·34	0·97	+0·37
(X)	1·42	0·93	+0·49
(XI)	1·13	0·85	+0·28
(XII)	1·47	1·19	+0·28
(XIII)	0·92	0·36	+0·56 (b)
	1·02	0·44	+0·58 (c)
	1·05	0·78	+0·27 (a)
(XIV)	2·68	2·54	+0·14
(XV)	2·75	2·15	+0·60

The Δ values for the methyl resonances of (VIII) and (IX) and (XI) and (XII) are very similar. Consequently, the introduction of the heteroatom of (IX) has no effect on the solvent shift when related to (VIII), and the introduction of the aromatic system of (XII) has no effect when compared with that of (XI). This implies, *in these particular cases*, that the nature of the benzene : solute complex is not altered by the additional influences of these groups. This observation, together with the symmetry considerations outlined above, shows that the complexing solvent molecule cannot be juxtaposed parallel to the carbonyl–carbonyl plane of the solute molecule. (as in (B)). The formation of this type of complex would also be vitiated by the steric requirements of the *gem*-dimethyl groups. Whatever the nature of the complex, it seems unlikely that it can be represented by the simple dipole–dipole interaction (or charge-transfer complex) between the positive end of the carbonyl and the π-system of benzene which is thought to occur in simple ketones.[2]

Variable temperature studies (in toluene-d_8) were used to determine the change in chemical shifts of the methyl resonance of (XI) and the α-methylene resonance of (III) in order to measure the heats of formation of the two complexes. The variations of chemical shift with change in temperature are shown in Figure 2. Assuming a 1 : 1 complex (see above) for the equilibrium: solvent + solute ⇌ complex, then the plot of $\log_{10}K$ against $1/T$ gives ΔH directly from the slope of the straight line

(see Fig. 3). Both the theoretical treatment and a discussion of the large errors inherent in this calculation can be found in previous publications.[19,20] The calculated heats of formation are (III) : toluene, −1·22 kcal/mole, and (XI) : toluene, −1·25 kcal/mole. Even though these are very small values, they are larger than those of the complexes formed between substituted anisoles and toluene (−0·9 to −1·05 kcal/mole),[20] and between 5α-androstan-11-one and toluene (−0·65 kcal/mole).[19] It is surprising that both the above complexes have such similar heats of





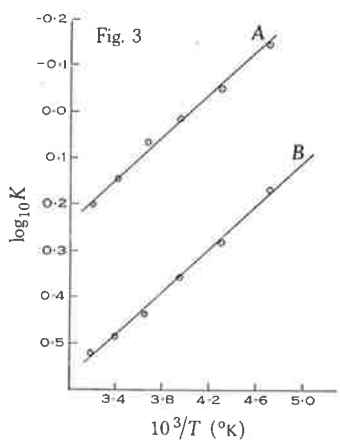


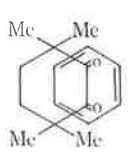
Fig. 1.—Plot of $\Delta^{CCl_4}_{C_6H_6}$ for the methyl resonance of diacetyl against the concentration of benzene in carbon tetrachloride.
Fig. 2.—Plots of chemical shift (c/s in toluene-d_8) against temperature (°C) for
(*A*) the α-methylene resonance of (III);
(*B*) the methyl resonance of (XI).
Fig. 3.—Plots of $\log_{10}K$ against 1/temperature (T) for
(*A*) the methyl resonance of (XI);
(*B*) the α-methylene resonance of (III).

formation, as the two complexes should be different, viz. the (III)–toluene complex may be the "normal" dipole–dipole (or charge-transfer) type (cf. (B)), while the other complex should not be of this type (see above). Alternatively, the similar heats of formation may indicate that the two complexes do have the same type of structure. Further work is being undertaken to attempt to clarify this apparent anomaly.

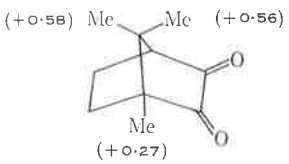
The solvent-shifts obtained for (VIII–XII) (Table 2) may be used to assign Δ values to the methyl resonances of camphorquinone (XIII). The chemical shifts of the methyl protons of (XIII) in carbon tetrachloride have been assigned[21] by

[21] Yonezawa, T., Morishima, I., and Takeuchi, K., *Bull. chem. Soc. Japan*, 1967, **40**, 1812.

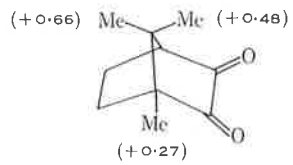
comparison with the spectrum of camphor.[1] The recent report of Karabatsos *et al.*[22] indicates that the methyl group above the carbonyl groups may be deshielded rather than shielded, and so labelling studies would be necessary to authenticate the assignments for camphor. Suggested Δ values are listed in Table 2 and indicated in (C). The alternate assignments of Yonezawa *et al.*[21] (see(D)) are also possible, and labelling studies would be necessary to differentiate between the two.*



(B)

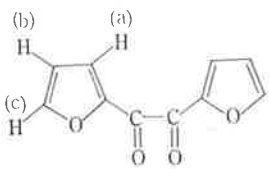


(C)

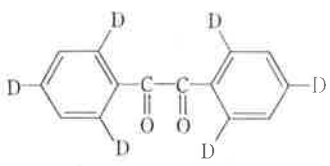


(D)

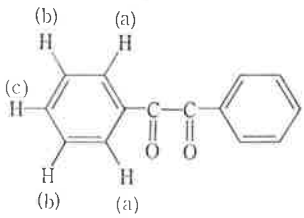
It was of interest to ascertain whether negative Δ values (see (A)) could be obtained for methyl resonances in favourable cases where the "normal" dipole–dipole (or charge-transfer) complexes may be formed. The most readily available model was 1-methylphenanthraquinone (XIV) and the Δ value for its methyl resonance is +0·14 (Table 2). This is the same as the Δ value for the methyl resonance of 1-methylanthraquinone,[9] and it seems unlikely that negative Δ values will be observed for methyl substituents attached to the aromatic system of a quinone. The analogous shift for 4-methylphenanthraquinone is +0·60 p.p.m.



(XVI)



(XVII)



(XVIII)

The application of solvent-shifts to the assignment of aromatic protons is demonstrated by the Δ values for α-furil (XVI) and benzil (XVIII). These values are summarized in Table 3. The spectrum of α-furil is similar to that of the aromatic protons of furan-2-aldehyde.[23] Deuterobenzene causes an upfield shift of +0·34 p.p.m. for the protons at the 3-positions [(a) in (XVI)] while the other four protons are shifted by +0·87 p.p.m. A comparison of the n.m.r. spectra of benzil-d_6 (XVII) and benzil (XVIII) allows the assignment of Δ values for the protons of (XVIII). The

* Since this paper went to press, Professor W. L. Meyer has kindly informed us that the n.m.r. spectrum of camphorquinone-9,9,9-d_3 supports the assignments of the chemical shifts in CCl_4 (Table 2) (see A. P. Lobo, Ph.D. Thesis, Indiana University 1966). A recent report (K. M. Baker and B. R. Davis, *Tetrahedron*, 1968, **24**, 1663) of the solvent-shifts of camphorquinone-9-d_1 substantiates the assignments of Yonezawa *et al.*[21] (see D).

[22] Karabatsos, G. J., Sonnichsen, G. C., Hsi, N., and Fenoglio, J., *J. Am. chem. Soc.*, 1967, **89**, 5067.

[23] "N.M.R. Spectra Catalog." No. 95. (Varian Associates: Palo Alto, Cal. 1962.)

ortho-protons (a) must be almost in front (see (A)) of the carbonyl group (of the complex) as the shift is only +0·01 p.p.m. The other protons have the same shift (+0·50) and cannot be distinguished by this method.

TABLE 3

Δ VALUES FOR PROTON RESONANCES IN (XVI)–(XVIII)
m, multiplet; s, singlet

Compound	δ_{CCl_4}	$\delta_{C_6D_6}$	$\Delta^{CCl_4}_{C_6H_6}$
(XVI)	7·74 m	6·87	+0·87 (c)
	7·62 m	7·29	+0·33 (a)
	6·60 m	5·73	+0·87 (b)
(XVII)	7·46 s	6·96	+0·50
(XVIII)	7·98–7·82 m	7·97–7·81	+0·01 (a)
	7·61–7·24 m	7·11–6·74	+0·50 (b and c)

EXPERIMENTAL

All spectra were measured as 0·1M solutions (except 1- and 4-methylphenanthraquinone which were measured as saturated solutions) with a Varian DP60 spectrometer operating at 60 Mc/s and 25°, using tetramethylsilane as an internal standard.

The variable temperature experiments were performed in toluene-d_8 with a Varian A60A spectrometer.

The syntheses of compounds (I–XI), (XIII), (XVII), and (XVIII) have been reported previously.[16] Other compounds were prepared by reported procedures: (XII),[24] (XIII),[25] and (XIV).[25]

ACKNOWLEDGMENTS

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Rearrangement Reactions of some Simple Ketones and Esters upon Electron Impact

By J. H. BOWIE, R. GRIGG, and D. H. WILLIAMS
(*University Chemical Laboratory, Cambridge, England*)
and S.-O. LAWESSON and G. SCHROLL
(*Department of Organic Chemistry, Aarhus University, Denmark*)

ATTENTION has recently been drawn[1,2] to the relative rarity of alkyl migrations which have been established to occur in the mass spectrometer. We now report the occurrences, in the spectra of some simple ketones and esters, of fragment ions which necessitate the formation of C–C or C–O bonds upon electron impact.

The compounds in which the examples of C–C and/or C–O bond formation have been established are listed in the Table. In every case the composition of the rearrangement ion has been substantiated by exact mass measurements. Elimination of the ketone carbonyl group in the fragmentation of the β-keto-esters (IV) and (V) is proved by ^{18}O-labelling of the ketone moiety.[3]

The relative abundances quoted in the Table give some indication of the prevalence of the rearrangement ions as they appear in conventionally represented spectra. The importance of the rearrangement processes is indicated in some cases by additional high-resolution measurements. For example, ions at *m/e* 191, 205 (21 and 31% of the base peak) and at *m/e* 165, 178, 179 (11, 13, and 26% of the base peak) in the spectra of (II) and (III) respectively are due to $C_{15}H_{11}^+$, $C_{16}H_{13}^+$ and $C_{13}H_9^+$, $C_{14}H_{10}^+$, $C_{14}H_{11}^+$, all skeletal rearrangement fragments. Further details of these spectra will be reported subsequently.

TABLE

Rearrangement Ions in the Spectra of Some Simple Ketones and Esters

Compound		Rearrangement ion	Migrating group	R.A.*
$MeCO{\cdot}CH_2{\cdot}COMe$ .. (I)		$M^+ - CO$	CH_3	10
$(PhCH{=}CH)_2CO$ .. (II)		$M^+ - CO$	$C_6H_5CH{=}CH$	17
$PhCH{=}CH{\cdot}COPh$ .. (III)		$M^+ - CO$	C_6H_5	10
$MeCO{\cdot}CH_2{\cdot}CO_2Me$ .. (IV)		$M^+ - CO$	CH_3	6
$MeCO{\cdot}CH_2{\cdot}CO_2Et$ .. (V)		$M^+ - CO$	CH_3	4
$MeCO{\cdot}CH_2{\cdot}COPh$ .. (VI)		$C_7H_7^+$	C_6H_5	14
$(Me_2C{=}CH)_2CO$ .. (VII)		$M^+ - C_2H_3O$	—	13
$MeCO_2{\cdot}C{\equiv}C{\cdot}CO_2Me$ .. (VIII)		$M^+ - CO_2$	CH_3	40
$Ph{\cdot}R{\cdot}C(CO_2Et)_2$				
(IX; R = H) ..		$M^+ - CO_2$	C_2H_5	18
(X; R = Et) ..		$M^+ - CO_2$	C_2H_5	7
$PhCH{\cdot}CN{\cdot}CO_2Et$ ..	(XI)	$M^+ - CO_2$	C_2H_5	8
$Pr^iCH{\cdot}CN{\cdot}CO_2Et$ ..	(XII)	$M^+ - CO_2H$	C_2H_4 or C_2H_5	7

* R.A. = Relative Abundance as % of the base peak.

(*Received, August 5th, 1965; Com. 489.*)

[1] F. Komitsky, J. E. Gurst, and C. Djerassi, *J. Amer. Chem. Soc.*, 1965, **87**, 1399.
[2] P. Brown, C. Djerassi, G. Schroll, H. J. Jakobsen, and S.-O. Lawesson, *J. Amer. Chem. Soc.*, in press.
[3] W. J. Richter, M. Senn, and A. R. Burlingame, *Tetrahedron Letters*, 1965, 1235.

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SKELETAL REARRANGEMENT REACTIONS IN SULPHIDES, DISULPHIDES, SULPHOXIDES AND SULPHONES UPON ELECTRON IMPACT

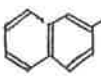
J. Ø. Madsen, C. Nolde, S.-O. Lawesson and G. Schroll
Department of Organic Chemistry, Aarhus University, Denmark.
J. H. Bowie and D. H. Williams
University Chemical Laboratory, Cambridge, England.

(Received 6 October 1965)

In order to facilitate structure elucidation by mass spectrometry, it is necessary that skeletal rearrangement processes which occur on electron impact be well documented. Recently, such rearrangement processes have been demonstrated to occur in some ketones (1,2), esters (2-5), thioesters (6) and carbamates (7). We now report the occurrence of some skeletal rearrangement reactions in sulphides, disulphides, sulphoxides and sulphones upon electron impact.

The rearrangement reactions which occur in the sulphides (I-V), the disulphides (VI, VII), the sulphoxide (VIII) and the sulphone (IX) are summarised in the table. The compositions of all rearrangement ions have been established by exact mass measurements.

Rearrangement Ions in the Mass Spectra of Some Sulphides, Disulphides, Sulphoxides and Sulphones

Compound	Rearrangement Ion	R.A.‡
$C_6H_5SCH_3$ (I)	M-HS (*)	26
 (II)	M-HS (*)	13
$C_6H_5SC_6H_5$ (III)	M-S	4
	M-HS	6
	M-H_2S	9
$C_6H_5CH_2SC_6H_5$ (IV)	M-H_3S	4
$C_6H_5CH_2SCH_2C_6H_5$ (V)	M-S	2
$C_6H_5SSC_6H_5$ (VI)	M-S (*)	16
	M-HS (*)	15
	M-2S	11
$C_6H_5CH_2SSCH_2C_6H_5$ (VII)	M-S	19
	M-2S	12
	M-CH_2S	10
$C_6H_5CH_2\overset{\overset{O}{\|}}{S}CH_2C_6H_5$ (VIII)	M-SO	30
$C_6H_5-\overset{\overset{O\ O}{\|\|}}{S}-C_6H_5$ (IX)	M-SO_2	5

‡ R.A. = Relative Abundance as % of the base peak.

Those cases in which the rearrangement fragment is formed in a one-step process from the molecular ion, as indicated by an appropriate metastable peak, are indicated in the table by an asterisk (*). Generally speaking, the sulphides or disulphides may eliminate a sulphur atom (with or without additional hydrogen atoms) and the terminal groups then combine. The sulphoxide (VIII) and the sulphone (IX) behave analogously.

Additional exact mass measurements establish that rearrangement fragments occur at lower masses, and these may be decomposition products of the primary rearrangement ions, e.g., m/e 152 (8%, $C_{12}H_8^+$) and m/e 153 (7%, $C_{12}H_9^+$) from IX.

Although some sulphones are known to rearrange thermally with elimination of sulphur dioxide at relatively high temperatures,[8] the possibility of thermal rearrangement has been excluded in the case of IX by obtaining the spectrum by the direct inlet procedure at approximately 60°C.

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4. W. H. McFadden, K. L. Stevens, S. Meyerson, G. J. Karabatsos and C. E. Orzech, J. Phys Chem., 69, 1742 (1965).

5. F. Weiss, A. Isard and G. Bonnard, Bull. Soc. Chim. Fr., 2332 (1965).

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Studies in Mass Spectrometry. I. Mass Spectra of Substituted Naphthoquinones

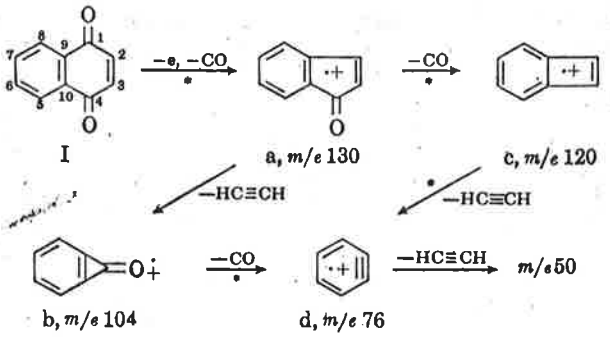
J. H. Bowie, D. W. Cameron, and D. H. Williams

Contribution from the University Chemical Laboratory, Cambridge University, Cambridge, England. *Received May 28, 1965*

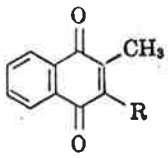
The mass spectra of 21 substituted naphthoquinones are reported and discussed. The characteristic fragmentation and rearrangement processes, substantiated in most cases by appropriate metastable peaks and/or deuterium labeling, greatly facilitate the location of substituents in the bicyclic system.

Naphthoquinone (I) breaks down in a well-defined manner upon electron impact,[1] and plausible structures can be assigned to the most abundant fragment ions (see Scheme I and also Table I). The mass spectra of 21 substituted naphthoquinones (II–XXII), reported by us in this paper, indicate that the essential features of the breakdown of I are preserved in the spectra of the substituted derivatives. Details of the spectra are summarized in Figures 1 and 2 and Table I; in the table all ions having an abundance greater than 5% of that of the base peak (arbitrarily taken as 100%) are recorded.

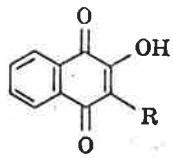
Scheme I[a]



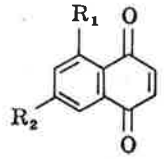
[a] Transitions indicated by an asterisk are supported by the presence of an appropriate metastable peak.



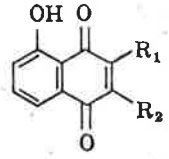
II, R = H
III, R = CH_3
IV, R = OH
IVa, R = OD
V, R = $NHCH_3$
Va, R = $NDCH_3$



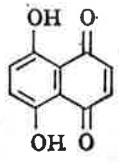
VI, R = H
VIa, R = D (OD instead of OH)
VII, R = Cl



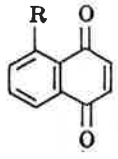
VIII, R_1 = OH; R_2 = H
VIIIa, R_1 = OD; R_2 = H
IX, R_1 = H; R_2 = OH
X, R_1 = R_2 = OH



XI, R_1 = H; R_2 = OH
XII, R_1 = H; R_2 = CH_3
XIII, R_1 = H; R_2 = Cl
XIV, R_1 = OH; R_2 = H
XIVa, R_1 = OD; R_2 = H
XV, R_1 = R_2 = Cl



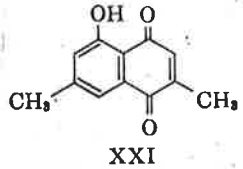
XVI



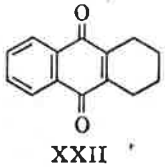
XVII, R = OCH_3

XVIII R = $OCCH_3$ (O)

XIX, R = OCH_3
XX, R = N



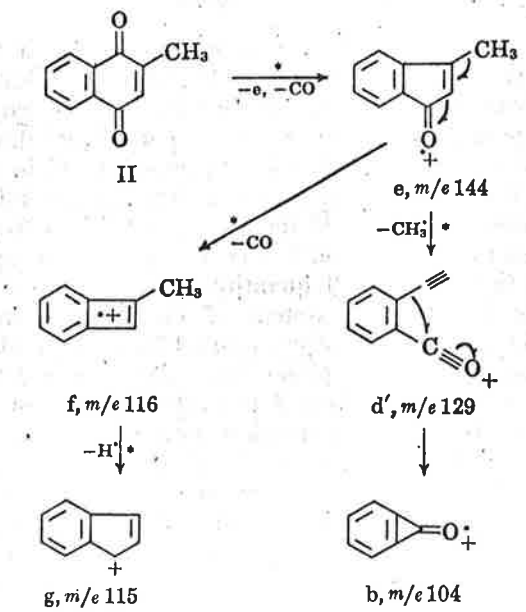
XXI
XXIa (OD instead of OH)



XXII

The mass spectra of 2-methylnaphthoquinone (II) and 2,3-dimethylnaphthoquinone (III) are much as expected. In the case of the 2-methyl derivative (II), the loss of a methyl radical is more pronounced from the M − CO fragment (e, *m/e* 144) than from the molecular ion, and may be represented by e → d′ (*m/e* 129).[2] Most important, the presence of the abundant *m/e* 104 ion (b), and its decomposition products *m/e* 76 (d) and *m/e* 50, substantiates the location of the methyl group at C-2 rather than on the benzene ring. An abundant species f (*m/e* 116) is formed by elision of two carbon monoxide molecules from the molecular ion. As expected, the odd-electron species f decomposes by loss of a hydrogen radical to afford *m/e* 115, most plausibly represented as the benzocyclopentadienyl cation g formed by ring expansion (Scheme II).

Scheme II



In the spectrum of the 2,3-dimethyl compound (III), in addition to the loss of a methyl radical both from the M − CO ion (h, *m/e* 158) and directly from the molecular ion, to furnish *m/e* 143 and *m/e* 171, respectively, there is appreciable expulsion of a hydrogen

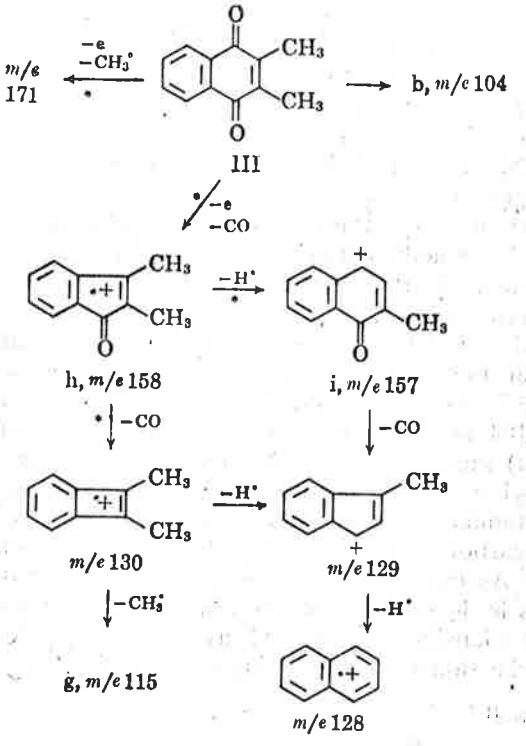
(1) J. H. Beynon and A. E. Williams, *Appl. Spectry.*, 14, 156 (1960).

(2) In the plausible fragmentation sequences given for asymmetric quinones, the choice of CO group which is expelled is purely arbitrary.

[Reprinted from the Journal of the American Chemical Society, 87, 5094 (1965).]

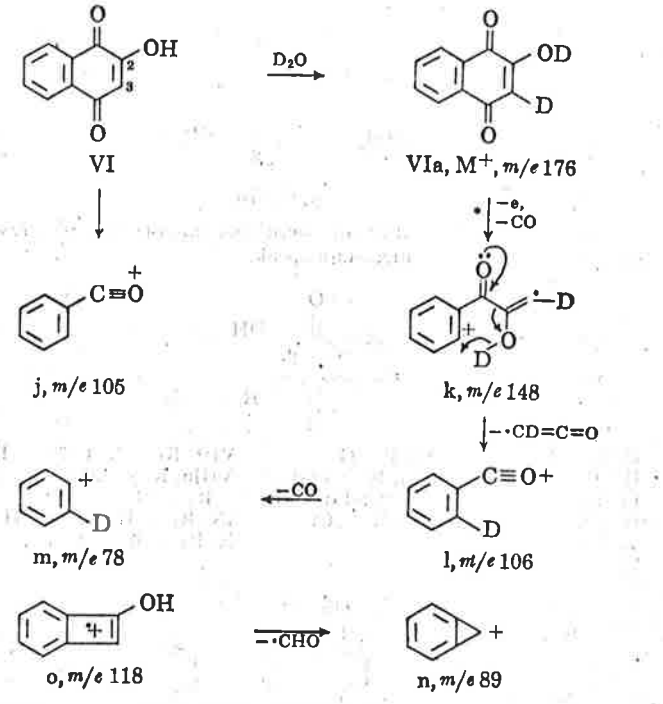
radical from h to afford *m/e* 157. This last process obviously reflects the presence of two methyl groups in h from which a hydrogen radical may be lost to give an even-electron ion (*e.g.*, i). Some of the decomposition processes, many of which are supported by the presence of metastable peaks, are summarized in Scheme III; exact mass measurements substantiate the composition of all these fragment ions. Once more the appearance of an abundant *m/e* 104 ion (b) and its characteristic decomposition products establishes the absence of 5-, 6-, 7-, or 8-substituents.

Scheme III



The spectra of naphthoquinones containing a C-2 or C-3 hydroxyl substituent (*e.g.*, IV, VI, VII, and XIV) are noteworthy for a highly characteristic hydrogen rearrangement which results in a partial or almost total shift of the *m/e* 104 ion b, encountered in the spectra hitherto discussed, to *m/e* 105, corresponding to the benzoyl ion j. If the spectrum of 2-hydroxynaphthoquinone (lawsone, VI) is determined after introduction of a small quantity of deuterium oxide into the heated inlet system of the spectrometer,[3] the molecular ion then occurs at *m/e* 176, corresponding to the predominant d_2-species VIa. Evidently the C-3 hydrogen atom is activated towards replacement by deuterium through equilibration with the tautomeric trione. As may be anticipated, *m/e* 105 shifts to *m/e* 106 in the spectrum of VIa, but this compound cannot be utilized to distinguish between hydrogen rearrangement from the C-2 hydroxyl group and rearrangement of the C-3 hydrogen, even though the former seems *a priori* more likely. However, in the spectrum of O-d_1-2-hydroxy-3-methylnaphthoquinone (O-d_1-phthiocol, IVa), obtained by introducing IV into the inlet system with deuterium oxide, the *m/e* 105 ion of IV is shifted almost quantitatively to *m/e* 106, establishing the hydroxyl group as the principal source of the rearranged hydrogen. We conclude therefore that the benzoyl ion (j, *m/e* 105) may in general be formed by rearrangement of the hydroxyl hydrogen in the spectra of various 2-hydroxy- or 3-hydroxynaphthoquinones. A number of appropriate metastable ions indicate that the hydrogen rearrangement occurs in the M − CO ion; a plausible mechanism involving a six-membered cyclic transition state (k → l) is indicated for d_2-lawsone (VIa) in Scheme IV. The structures proposed for j and l are strongly supported by their decomposition to the phenyl cation (*m/e* 77) and d_1-phenyl cation (m, *m/e* 78), respectively. In other respects, the decomposition of lawsone (VI) is analogous to that of naphthoquinone (I), except for the formation of a $C_7H_5^+$ ion (*m/e* 89), which may be formulated as the benzocyclopropenyl cation (n) arising *via* the elimination of a formyl radical from the M − 2CO ion (o, *m/e* 118). Finally, before leaving our discussion of the rearrangement typified by k → l, it should be noted that the increasing ratio of *m/e* 105 to *m/e* 104 on progressive substitution of C-2 and C-3 by a methyl group (see spectra of II and III in Table I) is evidence that an analogous but less preponderant rearrangement of a methyl hydrogen may operate in these cases.

Scheme IV[a]



[a] The composition of all fragment ions which are considered have been established by exact mass measurements.

The isomeric compounds 2-hydroxy-3-methylnaphthoquinone (phthiocol, IV) and 2-methyl-5-hydroxynaphthoquinone (plumbagin, XII) may of course be readily differentiated by the presence of the abundant *m/e* 105 ion present only in the spectrum of the former. The far more abundant M − CH_3 ion (*m/e* 173) derived from XII relative to IV (22% and <1% of molecular ion base peak, respectively) also serves to differentiate these isomers, although the cause of this difference in behavior is not readily apparent. In general, the presence of a hydroxyl group in the benzenoid ring of XII, VIII, IX, XI, XIII, XIV, and XV is indicated by the presence of a prominent *m/e* 120 ion (p) in their spectra which breaks down to the hydroxybenzyne

(3) J. S. Shannon, *Australian J. Chem.*, 15, 265 (1962).

Table I. Mass Spectra of Naphthoquinone (I) and Substituted Naphthoquinones (II–XXII)[a]

Compd.																				
I	*m/e*	50	51	66	74	75	76	77	102	104	105	130	131	158 (M)	159					
	I, %	23	12	6	12	14	40	6	39	46	7	40	6	100	11					
II	*m/e*	39	50	51	63	74	75	76	77	104	105	115	116	129	144	145				
	I, %	15	21	8	7	13	15	48	12	60	16	41	40	6	54	6				
		172 (M)		173																
		100		14																
III	*m/e*	50	51	75	76	77	104	105	115	128	129	130	143	157	158	171				
	I, %	8	6	5	20	7	27	12	12	9	13	8	6	13	20	5				
		186 (M)		187																
		100		16																
IV	*m/e*	50	51	55	76	77	78	103	104	105	115	131	132	133	159	160				
	I, %	11	8	7	13	15	6	6	10	18	6	20	18	8	6	16				
		161	188 (M)		189															
		6	100		23															
IVa	*m/e*	76	77	78	103	104	105	106	131	132	133	134	160	161	188					
	I, %	18	16	14	6	14	18	21	8	28	21	6	9	15	34					
		189	190	(d_0 = 25, d_1 = 73, d_2 = 2%)																
		100	15																	
V	*m/e*	50	51	52	74	75	76	77	90	103	104	105	115	116	128	130				
	I, %	10	7	6	6	8	24	20	7	9	13	13	29	14	6	8				
		131	132	143	144	145	158	159	160	161	172	186	199	200	201 (M)					
		11	13	8	30	10	13	11	35	6	21	8	13	21	100					
		202																		
		24																		
Va[b]	*m/e*	50	51	76	77	78	104	105	115	116	131	132	133	144	145	160				
	I, %	6	5	9	7	5	8	10	8	11	7	11	6	6	28	20				
		161	173	187	200	201	202 (M)		203											
		6	15	9	8	22	100		19											
VI	*m/e*	50	51	59	63	69	73	74	75	76	77	89	90	104	105	106	118			
	I, %	18	8	8	6	11	7	10	10	20	27	18	12	11	82	11	11			
		146	174 (M)		175															
		21	100		13															
VIa	*m/e*	50	51	52	60	63	64	70	74	75	76	77	78	90	91	104	105			
	I, %	8	8	8	6	6	6	8	10	8	29	14	22	8	7	11	37			
		106	107	147	148	174	175	176	177	(d_0 = 7, d_1 = 38, d_2 = 55%)										
		80	13	12	17	12	62	100	13											
VII	*m/e*	76	77	104	105	145	173	180	181	182	208 (M)		209	210	211					
	I, %	21	13	16	12	24	30	41	11	19	100		21	40	10					
VIII	*m/e*	37	38	39	45	50	51	53	54	59	61	62	63	64	65	74	75	77		
	I, %	12	16	21	14	20	19	22	8	13	19	34	66	31	8	14	10	10		
		83	85	89	90	91	92	102	118	119	120	121	146	147	173	174 (M)				
		18	13	33	25	10	67	7	89	15	60	7	37	7	35	100				
		175	176																	
		30	11																	
VIIIa	*m/e*	62	63	64	65	89	90	91	92	93	118	119	120	121	122	146	147			
	I, %	14	25	18	7	8	9	8	26	18	32	21	34	28	6	14	10			
		148	173	174	175	176	177	178	179	(d_0 = 52, d_1 = 28, d_2 = 10, d_3 = 7; d_4 = 3%)										
		8	27	100	66	27	17	10	6											
IX	*m/e*	50	51	63	64	91	92	118	120	146	174 (M)		175	176						
	I, %	7	6	13	11	7	19	24	30	18	100		17	17						
X	*m/e*	50	51	53	61	62	63	69	77	78	79	105	108	134	135	136	161			
	I, %	12	31	12	7	12	13	36	11	10	7	9	34	52	6	44	6			
		162	189	190 (M)		191														
		36	7	100		13														
XI	*m/e*	92	105	106	120	121	122	134	162	188	190 (M)		191	192						
	I, %	8	24	8	14	42	11	12	18	10	100		29	6						
XII	*m/e*	39	51	63	64	77	92	120	121	131	132	145	160	173	174	188 (M)				
	I,	8	6	10	6	8	14	18	14	18	13	6	18	22	6	100				
		189																		
		28																		
XIII	*m/e*	53	62	63	74	89	92	95	145	146	152	173	174	180	208 (M)					
	I, %	12	12	18	8	17	17	11	58	6	14	48	39	22	100					
		209	210	211																
		14	48	9																
XIV	*m/e*	39	43	51	53	57	60	62	63	64	65	69	73	78	87	92	93	105		
	I, %	8	8	9	7	7	9	10	14	9	9	13	8	7	7	18	14	14		
		106	120	121	134	162	163	190 (M)		191										
		6	40	65	15	29	6	100		33										
XIVa	*m/e*	60	61	62	63	64	65	66	67	68	69	70	71	73	74	75	76	77		
	I, %	19	21	17	22	21	16	10	21	12	34	18	27	22	27	15	22	52		
		78	79	80	81	82	83	84	85	87	89	91	92	93	94	95	96	97		
		22	16	10	20	13	22	11	16	11	11	21	18	26	18	15	10	12		
		98	104	105	106	107	120	121	122	123	135	136	137	163	164					
		11	10	66	28	11	31	54	69	64	10	14	11	18	23					
		165	190	191	192	193	194	195	196	(d_0 = 7, d_1 = 25, d_2 = 36, d_3 23, d_4 = 5, d_5 = 3%)										
		18	20	61	100	69	21	11	7											

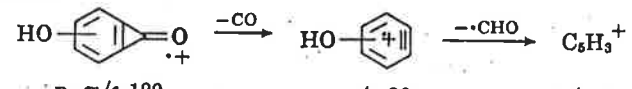
Table I (*Continued*)

Compd.																	
XV	*m/e*	36	40	53	54	61	62	63	73	74	87	92	97	116	120	123	125
	I, %	19	16	9	9	15	18	24	7	14	15	14	8	9	8	18	6
		179	180	181	207	208	209	242 (M)		243	244	245	246				
		45	10	15	100	13	34	100		15	60	9	10				
XVI	*m/e*	108	134	136	189	190 (M)		191									
	I, %	11	8	6	34	100		12									
XVII	*m/e*	39	44	50	51	62	63	74	75	76	77	89	91	102	103		
	I, %	9	6	9	6	12	16	9	19	38	7	7	8	37	9		
		104	105	114	130	131	132	133	142	159	160	170	171				
		35	9	16	27	20	8	7	7	19	9	11	7				
		188 (M)		189	190												
		100		16	7												
XVIII	*m/e*	42	43	44	63	92	118	120	146	173	174	175	216 (M)				
	I, %	12	14	18	6	7	12	10	7	15	100	13	6				
XIX	*m/e*	50	51	63	69	74	75	76	77	89	101	102	104	105	130	131	
	I, %	15	7	7	15	8	10	22	7	46	7	38	10	6	9	7	
		158	159	173	188 (M)		189	190									
		36	20	39	100		15	7									
XX	*m/e*	41	42	50	51	52	53	54	55	56	57	63	67	68	69	74	75	76
	I, %	15	8	20	18	10	8	6	16	10	6	6	6	7	6	14	20	40
		77	78	79	80	82	83	84	85	89	101	102	103	104	105	115	128	
		16	14	8	6	7	10	34	6	12	19	44	9	36	15	10	6	
		129	130	131	146	156	157	158	159	172	184	185	186	198	200			
		11	16	8	8	6	8	28	6	11	14	12	13	10	6			
		212	224	236	239	240	241 (M)		242									
		16	6	8	17	26	100		21									
XXI	*m/e*	50	51	52	63	77	105	106	131	134	135	145	146	159	174			
	I, %	6	8	6	6	12	6	12	10	14	12	12	10	5	24			
		187	202 (M)		203													
		23	100		15													
XXIa	*m/e*	50	51	52	69	77	78	79	106	107	132	134	135	136	145	146		
	I, %	6	9	7	6	9	11	6	9	10	9	10	24	14	7	12		
		147	174	175	176	187	188	189	202	203	204	205	206					
		11	11	20	6	11	24	10	53	100	44	19	7					
		(d_0 = 24, d_1 = 48, d_2 = 17, d_3 = 8, d_4 = 3%)																
XXII	*m/e*	50	51	76	77	104	105	115	128	133	141	152	165	180	183	194		
	I, %	6	6	12	11	8	17	6	6	6	5	9	9	8	8	7		
		195	197	208	211	212 (M)		213										
		9	32	11	14	100		17										

[a] All ions having an abundance greater than 5% of that of the base peak (arbitrarily taken as 100%) are recorded. [b] This spectrum corresponds to the N-d_1 derivative; the spectrum of unlabeled material has been removed by subtraction.

ion radical (q, *m/e* 92, Scheme V). The latter fragment appears to decompose consistently by expulsion of a formyl radical to give the $C_5H_3^+$ cation (*m/e* 63). Except for the formation of *m/e* 63, 5-hydroxynaphthoquinone (juglone, VIII) and 6-hydroxynaphthoquinone (IX) fragment analogously to naphthoquinone (I) itself.

Scheme V



p, *m/e* 120 q, *m/e* 92 *m/e* 63

Of the isomeric dihydroxynaphthoquinones X, XI, XIV, and XVI, naphthazarin (XVI) is unusual, its spectrum exhibiting an abundant molecular ion and very little fragmentation (Table I); this behavior reflects the stabilization of the naphthazarin system by hydrogen bonding and resonance. However, the fragmentation which does occur is of the expected type leading to the dihydroxybenzyne ion r (*m/e* 108). The qualitatively similar, but quantitatively much more pronounced decomposition of 5,7-dihydroxynaphthoquinone (X) is illustrated in Figure 1. Comparison of this spectrum with that (Figure 2) of 2,5-dihydroxynaphthoquinone (XI) clearly illustrates the useful generalization that a "doublet" at M − 54 and M − 56 is characteristic of a 2,3-unsubstituted naphthoquinone; in these cases, the nature and number of substituents on the benzene ring can readily be inferred from the M − 82 peak (M − 2CO—HC≡CH) and its decomposition products. It is noteworthy that although the M −

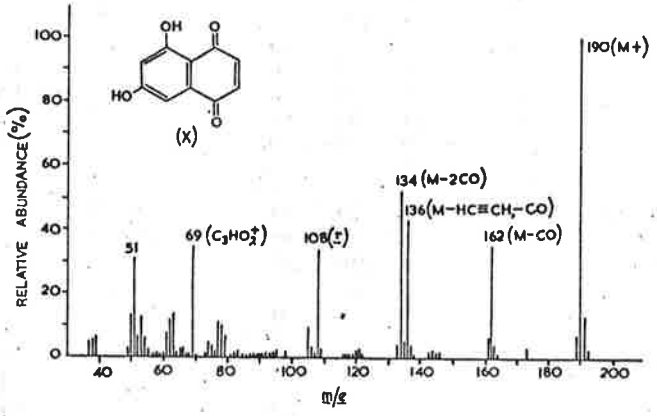


Figure 1. Mass spectrum of 5,7-dihydroxynaphthoquinone (X).

CO and M − 2CO peaks in the spectra of naphthoquinones containing phenolic hydroxyl groups could in principle arise in part *via* expulsion of a carbon monox-

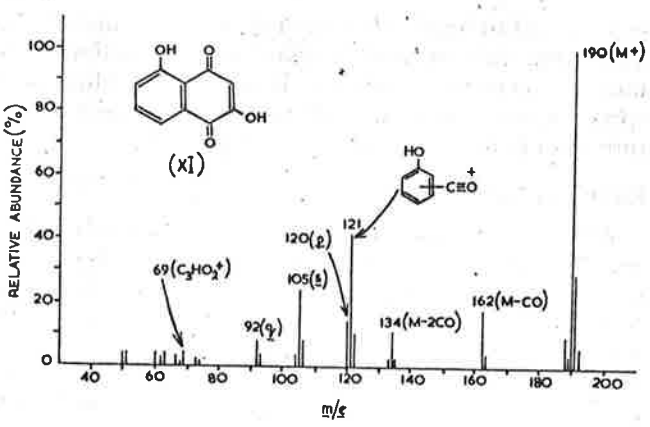
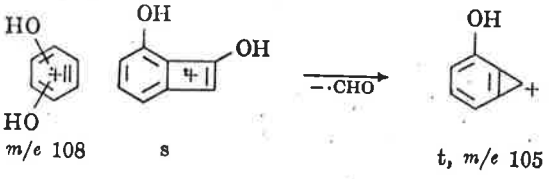


Figure 2. Mass spectrum of 2,5-dihydroxynaphthoquinone (XI).

ide molecule from the phenolic ring,[4] such processes do not appear important. For example, the *m/e* 134 ion in the spectrum (Figure 2) of XI is preferably formulated as s, since it decomposes to t (*m/e* 105) in a manner analogous to the fragmentation of its deoxy analog (see o → n). The formulation of *m/e* 105 as t rather than as the isobaric benzoyl ion j seems secure in the absence of an *m/e* 77 ion (phenyl cation) in the spectrum (Figure 2) of XI.

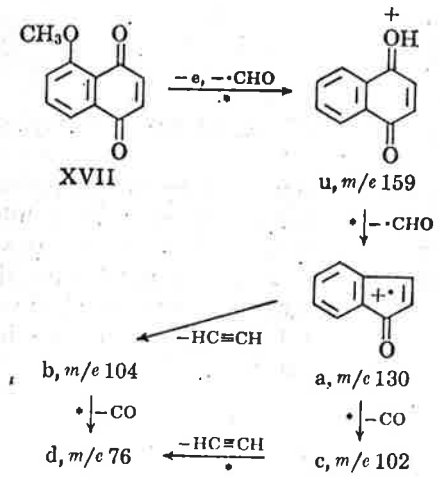


The spectra of the three chloronaphthoquinones (VII, XIII, and XV) are particularly amenable to analysis due to the characteristic abundances of the two chlorine isotopes ($^{35}Cl:^{37}Cl \simeq 3:1$). In all cases loss of a chlorine radical from the molecular ion or the M − CO ion is pronounced (see Table I). Conversely a carbon monoxide molecule may be expelled from the molecular ion or the M − Cl species, but ions corresponding to M − 2CO − Cl are negligible in all three chloro compounds. M − 2CO species are not detectable except in the spectrum of 2-chloro-5-hydroxynaphthoquinone (XIII) in which this species constitutes 14% of the base peak [*m/e* 152 ion (see Table I) corresponding to ^{35}Cl isotope]. All these processes are confirmed by appropriate metastable ions.

5-Methoxynaphthoquinone (XVII) was prepared by methylation of the hydroxy compound (VIII) with methyl iodide and silver oxide. The product contained traces of a dihydrojuglone methyl ether (as evidenced by peaks at *m/e* 190 and *m/e* 175 in its mass spectrum) which could be removed by column chromatography under nitrogen in the dark and crystallization of the purest fraction from carbon tetrachloride. In the mass spectrum of XVII, the expulsion of a formyl radical from the molecular ion is observed to afford *m/e* 159, represented as the protonated naphthoquinone u (Scheme VI). Elimination of a second formyl radical furnishes *m/e* 130, the representation of which as a is consistent with its usual breakdown to *m/e* 104 (b), *m/e* 102 (c), and *m/e* 76 (d).

(4) *Cf.* behavior of simple phenols: H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day Inc., San Francisco, Calif., 1964, pp. 167, 168.

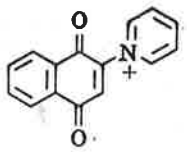
Scheme VI



The isomeric 2-methoxynaphthoquinone (XIX) behaves very differently. The spectrum contains abundant M − CH_3 (*m/e* 173) and M − CH_2O (*m/e* 158) ions. The latter decomposition occurs in part with formation of the naphthoquinone molecular ion as evidenced by the characteristic a → b → d and a → c → d sequences which are apparent in the spectrum of XIX and supported by appropriate metastable ions. Thus in the methyl ethers XVII and XIX, the initial fragmentation involves the methoxyl groups and the naphthoquinone skeleton is only broken subsequently. An additional noteworthy feature of the spectrum of XIX is the presence of an *m/e* 69 ion ($C_3HO_2^+$), which appears in the spectra of all the naphthoquinones (VI, X, XI, XIV, and XIX) containing the (O—C—C—C—O) unit. A plausible structure for this fragment is $O{=}C{=}CH{-}C{\equiv}O^+$.

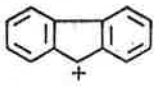
The spectra of the aminonaphthoquinones which have been examined show some interesting features. The relatively abundant M − 5 species (6% of base peak) in the spectrum of 2-piperidinonaphthoquinone (XX) corresponds to the pyridinium ion v; similar behavior is exhibited by a number of simpler pyrrolidine and piperidine enamines.[5] The M − 29 (*m/e* 212) and M − 43 (*m/e* 198) fragments are associated with the well-studied breakdown[6] of the piperidine ring system upon electron impact. Elimination of the C-2 substituent occurs with concomitant hydrogen rearrangement to the quinone ring and the naphthoquinone molecular ion so formed breaks down as usual. The *m/e* 84 ion is due to the immonium ion w. Interpretation of the spectrum of 2-methyl-3-methylaminonaphthoquinone (V) has been aided by the spectrum of the N-d_1 derivative Va. The M − CHO ion (*m/e* 172), whose composition has been determined by high resolution measurements, retains deuterium in the spectrum of Va and therefore the hydrogen atom lost in this process is almost certainly one of those from the methyl groups. The M − C_2H_3N ion (*m/e* 160) in the spectrum of V does not retain the deuterium atom in the spectrum of Va. The cleavage must involve therefore a hydrogen transfer from the N-methyl group to the ring system, but the process must be rather complex.

(5) J. T. B. Marshall and D. H. Williams, unpublished work.
(6) A. M. Duffield, H. Budzikiewicz, D. H. Williams, and C. Djerassi, *J. Am. Chem. Soc.*, 87, 810 (1965).



v, *m/e* 236 (M − 5)

w, *m/e* 84



x, *m/e* 165

The one acetate examined, 5-hydroxynaphthoquinone acetate (XVIII) behaves unexceptionally, exhibiting the anticipated loss of ketene (M − 42) in its spectrum, subsequent cleavages being identical with those observed for 5-hydroxynaphthoquinone (juglone, VIII). The most interesting feature of the tetrahydroanthraquinone (XXII) spectrum is the appearance of an *m/e* 165 ion, corresponding to x which must be formed by extensive rearrangement.

In summary, mass spectrometry is of considerable utility in locating a naphthoquinone substituent in the benzenoid or quinonoid ring. Moreover, the O—C=CH—C—O unit is indicated by the presence of an appreciable $C_3HO_2^+$ ion (*m/e* 69); quinonoid hydroxyl groups lead to highly characteristic rearrangement ions. Therefore, this method, applied in conjunction with nuclear magnetic resonance, infrared, and ultraviolet spectroscopic techniques, should greatly assist structure elucidation in this class of compounds.

Experimental Section

All spectra were determined using an A.E.I. MS 9 mass spectrometer operating at 70 e.v. With the exception of 5,7-dihydroxynaphthoquinone (X) and 5,8-dihydroxynaphthoquinone (XVI), samples were introduced through a heated inlet system at a temperature of approximately 200°. The direct insertion technique was employed to obtain the spectra of X and XVI.

Acknowledgments. We wish to thank Professor R. H. Thomson for a sample of 5,7-dihydroxynaphthoquinone (X) and Dr. G. M. Blackburn for a sample of 2,7-dimethyl-5-hydroxynaphthoquinone (XXI). Our sincere thanks are expressed to Mr. Eric Liddell for skillful assistance in obtaining some of the spectra.

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Studies in Mass Spectroscopy. III.[1] Mass Spectra of β-Keto Esters

J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams

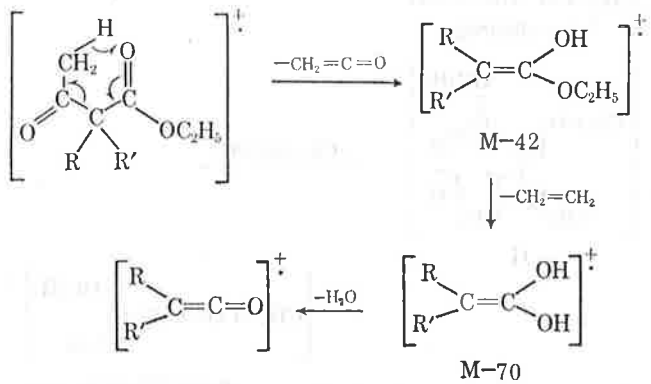
Contribution from the University Chemical Laboratory, Cambridge, England, and the Department of Organic Chemistry, Aarhus University, Aarhus C, Denmark. *Received August 9, 1965*

The spectra of 16 β-keto esters are reported and discussed. Ethyl acetoacetate and its derivatives, in which one of the active methylene hydrogens has been replaced by a substituent, break down in a well-defined manner upon electron impact. The spectra of some substituted ethyl benzoylacetates are noteworthy for the probable occurrence of an intramolecular acylation of the aromatic ring which takes place in an acylium ion fragment.

In view of the importance of β-keto esters and their derivatives as synthetic intermediates, it was thought desirable that the mass spectra of representative members of this class should be determined and interpreted. Prior to the present study, the only mass spectrum of a member of this series which has been discussed appears to be that of methyl 3-oxooctadecanoate.[2]

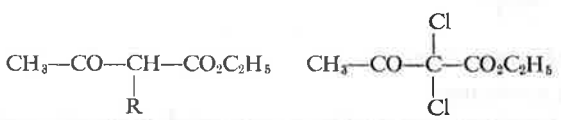
The mass spectra of ethyl acetoacetate (I) and seven derivatives (II–VIII) are recorded in Table I and Figures 1 and 2. The parent compound I and all the derivatives II–VI break down to a large extent by the general sequence which is outlined in Scheme I. The formation of enolic fragment ions (see M − 42), from processes involving hydrogen rearrangement in the mass spectrometer, has previously been demonstrated.[3a] Moreover, the elimination of ethylene from the M − 42 ion closely parallels the loss of an olefin from vinyl ethers[3a] and acetals.[3b]

Scheme I[a]

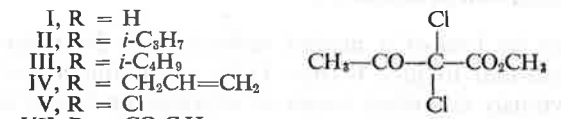


[a] Throughout this paper, specific structures have been drawn for fragment ions primarily to give a self-consistent rationale for the interpretation of the spectra. Although exact mass measurements confirm the composition of the fragment ions in many instances, some structures are nominal only.

The sequence indicated in Scheme I is supported by a number of appropriate metastable peaks in many of the spectra. It is noteworthy that the M − 42, M − 70, and M − 88 ions are all odd electron fragments and therefore, depending on the nature of R and R′, a



VI



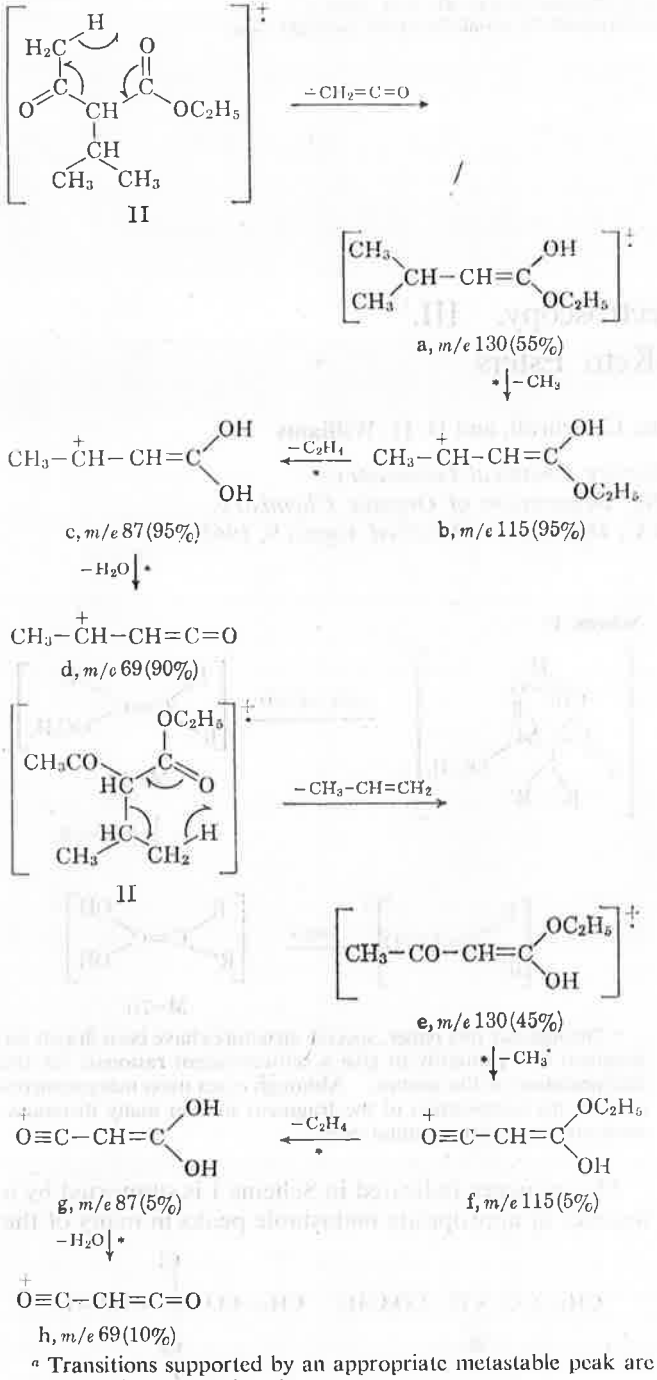
IX

I, R = H
II, R = *i*-C_3H_7
III, R = *i*-C_4H_9
IV, R = $CH_2CH{=}CH_2$
V, R = Cl
VII, R = $CO_2C_2H_5$
VIII, R = OCOPh

(1) Part II: R. Grigg, M. V. Sargent, J. Knight, and D. H. Williams, *Tetrahedron*, in press.
(2) R. Ryhage and E. Stenhagen, *Arkiv Kemi*, **15**, 545 (1960).
(3) (a) S. Meyerson and J. D. McCollum, *Advan. Anal. Chem. Instr.*, 2, 179 (1963); (b) R. A. Friedel and A. G. Sharkey, *Anal. Chem.*, **28**, 940 (1956).

radical may be expelled from one of these substituents at some stage in the sequence. This behavior may be illustrated by reference to the spectrum (Figure 1) of ethyl 2-isopropyl-3-oxobutyrate (II). The abundant *m/e* 130 ion is associated in part (55%, as established by high-resolution measurements) with the loss of ketene to afford a (Scheme II). This ion then decom-

Scheme II[a]



[a] Transitions supported by an appropriate metastable peak are indicated with an asterisk (*).

poses by loss of a methyl radical from the isopropyl substituent to give b (*m/e* 115), which undergoes the previously described losses of ethylene and then water to yield *m/e* 87 (c) and *m/e* 69 (d). High-resolution measurements on *m/e* 130, 115, 87, and 69 establish that all these peaks are doublets whose compositions are indicated in Scheme II. The alternative decomposition path e → f → g → h accounts for the lower mass

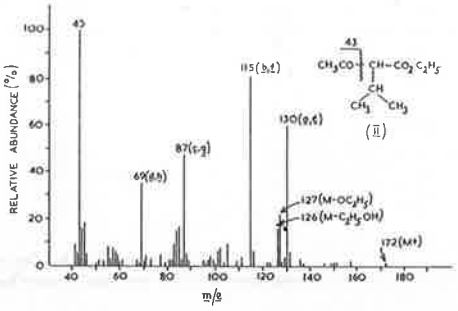


Figure 1. Mass spectrum of ethyl 2-isopropyl-3-oxobutyrate (II).

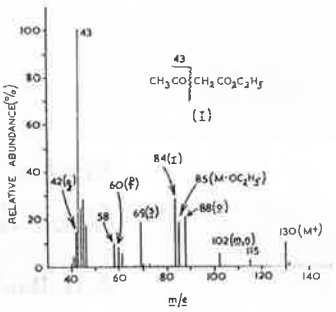


Figure 2. Mass spectrum of ethyl acetoacetate (I).

portions of all these doublets, and indeed is identical in form with the first sequence with the exception that the first step involves elimination of propylene instead of the isobaric ketene fragment. Evidence for the participation of ester–enols in these fragmentation sequences is available in the decomposition of *m/e* 87 (c or g) to *m/e* 69 (d or h) by loss of water; if the *m/e* 87 species were simply the $CH_2COOC_2H_5$ ion, formed by elimination of the isopropyl and acetyl groups from the molecular ion with a hydrogen rearrangement to carbon, then this certainly would not fragment specifically by loss of water. Moreover, the very pronounced loss of a methyl group from $C_7H_{14}O_2^+$ (a, *m/e* 130) to afford b (*m/e* 115) is consistent with the presence of two allylic methyl groups in the enol a.

The self-consistent behavior of these compounds is illustrated by the spectrum (Table I) of the isobutyl derivative III. The M − CH_2=C=O ion (i, *m/e* 144) should now eliminate an isopropyl radical to give j (*m/e* 101) which is anticipated to decompose by successive losses of ethylene (to k, *m/e* 73) and water (to l,

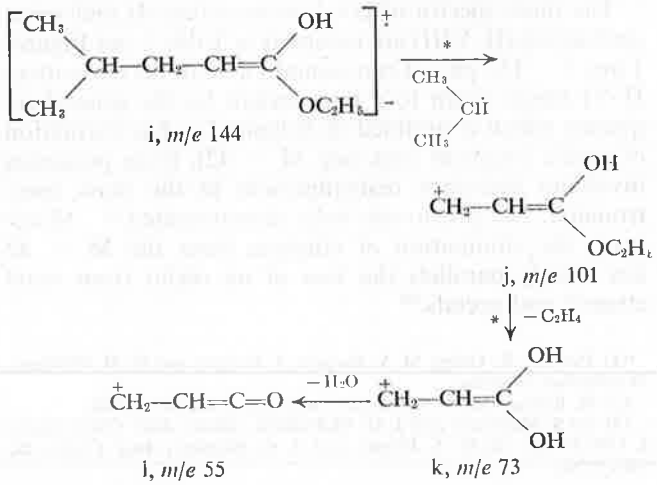


Table I[a]

III	*m/e*	41	42	43	44	45	46	55	56	57	58	69
	I (%)	15	6	87	15	13	7	32	4	10	11	9
		70	71	73	83	84	85	87	97	98	99	101
		10	7	40	5	10	10	5	22	6	8	100
		102	115	125	130	131	140	141	143	144	157	171
		9	9	9	35	4	8	11	17	31	9	4
		186(M)										
		3										
IV	*m/e*	39	41	43	45	53	54	55	56	58	69	81
	I (%)	9	11	100	10	11	11	22	6	4	3	22
		82	83	95	96	97	99	100	101	106	109	124
		14	16	4	7	14	20	21	5	4	6	6
		125	127	128	152	155	170(M)					
		5	51	29	2	2	2					
V	*m/e*	42	43	44	45	69	76	78	92	94	96	118
	I (%)	4	100	11	12	3	7	3	20	6	6	6
		119	120	122	124	136	138	164(M)	166(M)			
		4	3	23	8	3	1	3		1		
VI	*m/e*	42	43	44	45	62	73	76	94	110	112	114
	I (%)	4	100	7	4	2	2	3	3	5	3	1
		122	124	126	128	130	132	155	156	158	160	
		4	2	4	21	14	2	2	18	10	2	
VII	*m/e*	41	42	43	44	46	55	56	58	69	84	85
	I (%)	9	5	39	15	19	5	3	10	34	58	100
		86	87	88	102	103	113	115	130	143	157	
		11	35	8	34	3	16	25	34	7	18	
VIII	*m/e*	43	51	77	105	106	122	205	208	209	250(M)	
	I (%)	10	4	16	100	9	2	3	21	3	3	
IX	*m/e*	42	43	44	45	47	49	59	61	63	76	
	I (%)	4	100	8	3	3	4	7	4	4	3	
		77	79	83	85	110	112	114	127	129	131	141
		7	3	5	3	5	3	1	5	2	1	3
		142	144	146								
		10	6	2								
X	*m/e*	43	44	45	46	50	51	77	78	105	106	120
	I (%)	6	9	9	5	3	9	26	3	100	8	7
		146	147	192(M)	193							
		12	5	9		2						
XI	*m/e*	41	44	45	51	77	78	105	106	120	145	146
	I (%)	3	3	4	6	24	3	100	9	7	3	6
		192	193	201	202	248(M)						
		17	3	3	7	1						
XII	*m/e*	42	51	69	77	105	106	120	145	146	192	193
	I (%)	7	6	3	25	100	9	5	3	4	14	3
XIV	*m/e*	42	51	57	77	78	105	106	117	218	368(M)	
	I (%)	2	4	2	25	2	100	9	2	4	4	
XV	*m/e*	39	40	41	42	43	44	45	46	50	51	52
	I (%)	24	14	43	27	32	100	88	43	5	9	5
		53	54	55	56	57	58	67	68	69	70	71
		10	10	93	39	24	5	16	16	22	24	6
		77	79	81	82	83	84	85	94	95	96	97
		5	5	9	10	33	25	5	10	13	9	12
	m/e	98	101	105	109	110	111	112	113	125	127	128
	I (%)	5	6	4	7	12	6	44	7	9	3	4
		129	134	138	139	142	156	184(M)	185			
		5	6	47	24	4	8	10	3			

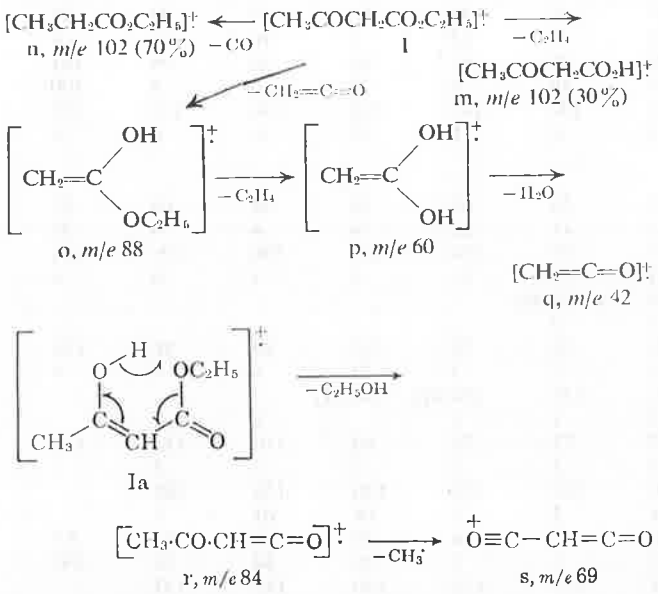
[a] All ions having an abundance greater than 2% of the base peak are recorded; molecular ions (and fragment ions of diagnostic value) of lesser abundance are included in the table.

m/e 55). In fact this sequence describes the main breakdown path of III (*m/e* 101 is the base peak). It can be seen that the difference of 14 mass units between the ions b, c, d, and j, k, l reflects the α-branching (methyl group) of the C-alkyl chain in II.

Additional evidence that the $C_6H_{10}O_3$ ion should be formulated as e rather than as the ethyl acetoacetate molecular ion is provided by the mass spectrum (Figure 2) of ethyl acetoacetate (I) itself, which indicates that the molecular ion of I fragments to a prominent *m/e* 88 ion, almost absent in the spectrum (Figure 1) of the isopropyl derivative II. The formation of most of the fragment ions in the ethyl acetoacetate spectrum is summarized in Scheme III. Particularly important are the M − C_2H_5O (*m/e* 85) and M − C_2H_5OH (*m/e* 84) ions; the former is present in the spectra of all the ethyl acetoacetate derivatives examined, whereas the formation of the latter is dependent on the presence of an active methylene hydrogen, *i.e.*, no M − C_2H_5OH ion occurs in the spectrum of the dichloro derivative VI. These observations are consistent with the formation of *m/e* 84 *via* a six-membered transition state involving the enol form Ia. The spectrum (Figure 2) is remarkable for the appearance of an M − 28 ion (*m/e* 102) which corresponds to only a small extent (*ca.* 30%) to loss of ethylene (I → m), and mainly (*ca.* 70%) to the elision of carbon monoxide from the keto group as established by ^{18}O labeling[4] and high-

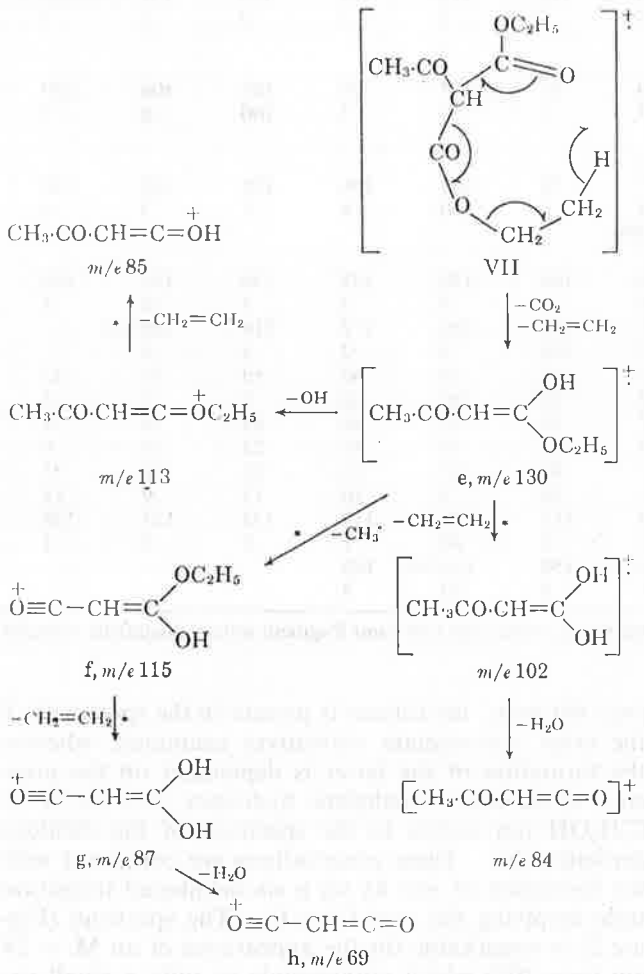
(4) W. J. Richter, M. Senn, and A. L. Burlingame, *Tetrahedron Letters*, 1235 (1965).

Scheme III



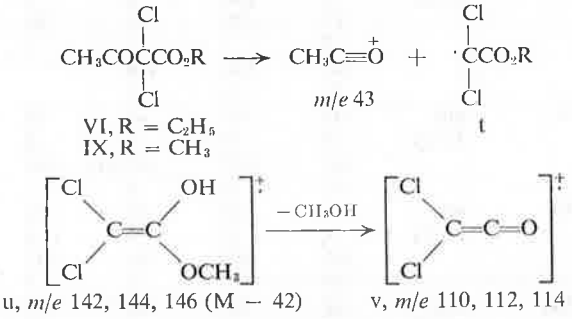
resolution measurements. This latter process (perhaps I → n) requires an alkyl migration, examples of which are relatively few in mass spectroscopy.[5]

Scheme IV

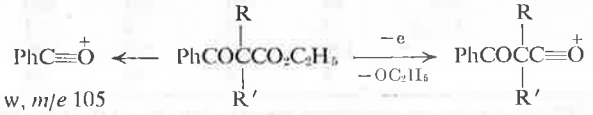


M − 72 ions, corresponding to the elimination of $CO_2C_2H_4$ fragments, occur in the spectra of ethyl acetoacetate (I), the chloro analogs V and VI, and diethyl acetylmalonate (VII), but are absent in the spectra of the alkyl derivatives (II, III, IV) and the benzoyloxy compound VIII. The absence of any M − $CO_2C_2H_4$ ion in the spectrum of the one methyl ester examined (IX) points to the participation of the β-hydrogen of the ethyl group in this rearrangement. In the instance of diethyl acetylmalonate (VII), there is evidence which indicates that the rearrangement takes place to oxygen with formation of the ester–enol e (*m/e* 130). Thus, *m/e* 130 decomposes as outlined previously in Scheme II to *m/e* 115 (f), *m/e* 87 (g), and *m/e* 69 (h) and additionally as indicated in Scheme IV. The compositions of all pertinent ions have been checked by high-resolution measurements and the majority of transitions indicated are supported by appropriate metastable peaks.

The dichloro compounds VI and IX do not exhibit molecular ions in their spectra, presumably because of the extremely facile cleavage which affords the acetyl ion (*m/e* 43, base peak) and the tertiary radical t. The M − 42 ion (u) formed from methyl 2,2-dichloro-3-oxobutyrate (IX), unable to eliminate ethylene like its ethyl analog (see Scheme I), decomposes directly to v (*m/e* 110, 112, 114) by loss of methanol.



The base peak in the spectra of ethyl benzoylacetate (X) and its derivatives (XI–XIV) is due to the benzoyl ion w (*m/e* 105), which decomposes in the established manner[6] to the phenyl cation (*m/e* 77) and $C_4H_3^+$ (*m/e* 51). M − 45 ions (x), arising from the loss of an ethoxyl radical, are present in the spectra of X, XI, and XIII.



X, R = R′ = H
XI, R = H; R′ = *n*-C_4H_9
XII, R = H; R′ = *i*-C_4H_9
XIII, R = H; R′ = $CO_2C_2H_5$
XIV, R = OCOPh; R′ = *i*-C_4H_9

M − C_2H_5OH (M − 46) peaks are evident in the spectra of X, XI, and XIII. In the cases of XI and XIII, appropriate metastable ions indicate that the M − 46 ion is formed, at least in part, by the loss of a hydrogen radical from the M − OC_2H_5 species. Moreover, in the spectrum (Figure 3) of XIII, the M − C_2H_5OH ion decomposes by the loss of a second molecule of ethanol to *m/e* 172, as indicated by an appropriate metastable ion. This latter observation de-

(5) (a) A. S. Newton and P. O. Strom, *J. Phys. Chem.*, **62**, 24 (1958); (b) F. Komitsky, Jr., J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 1399 (1965); (c) P. Brown, C. Djerassi, G. Schroll, H. J. Jakobsen, and S.-O. Lawesson, *ibid.*, **87**, 4559 (1965).

(6) See, for example: (a) T. Aczel and H. E. Lumpkin, *Anal. Chem.*, **33**, 386 (1961); (b) S. Meyerson and P. Rylander, *J. Am. Chem. Soc.*, **79**, 1058 (1957).

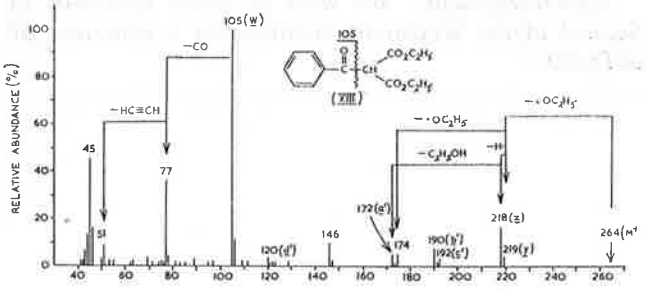


Figure 3. Mass spectrum of diethyl benzoylmalonate (XIII).

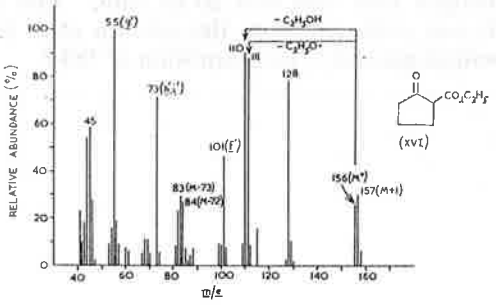
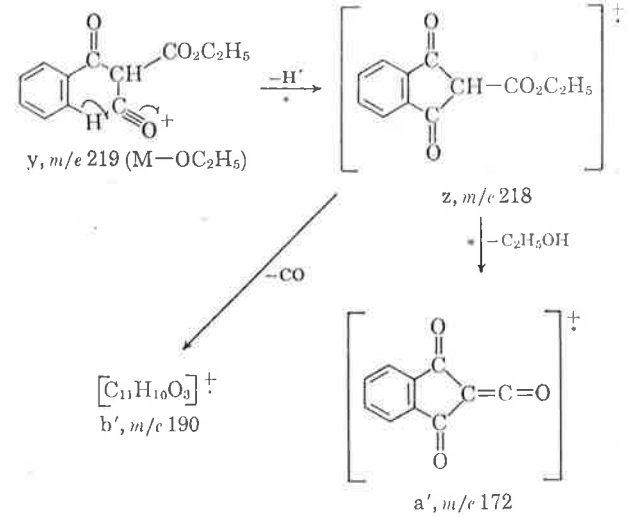


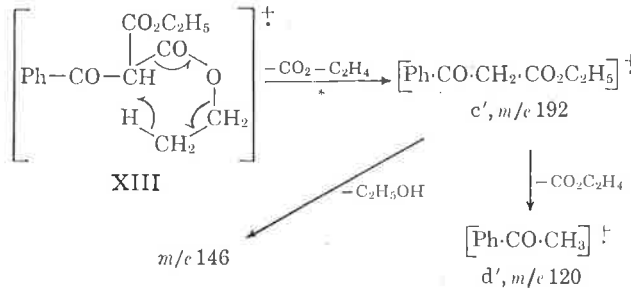
Figure 4. Mass spectrum of ethyl cyclopentanone-2-carboxylate (XVI).

mands that the *m/e* 172 ion has lost a hydrogen from the phenyl ring, as confirmed by high-resolution measurements. Thus, it appears that in the spectra of XI and XIII, the M − OC_2H_5 acylium ion (*e.g.*, y) is eliminating a hydrogen radical from the aromatic ring to give what is probably a bicyclic ion–radical (*e.g.*, z). This process obviously bears some analogy to a Friedel–Crafts acylation, except that a hydrogen radical is lost instead of a proton.

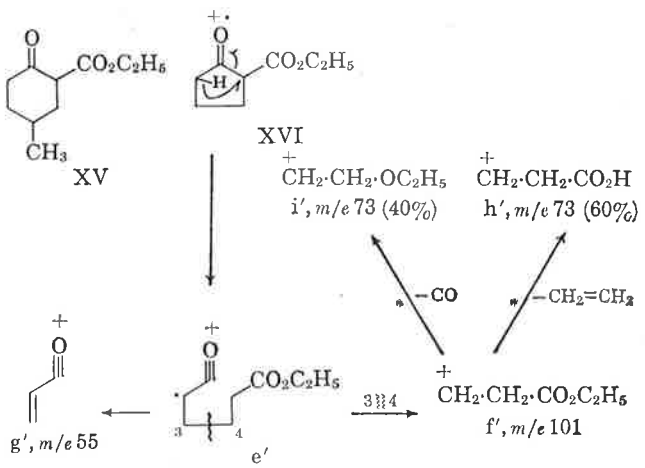


M − 72 ions (M − $CO_2CH_2CH_2$), corresponding to loss of the ethyl ester substituent with hydrogen rearrangement, are also present in the spectra of X, XI, and XIII. In these cases the hydrogen rearrangement may well be taking place to carbon, since the M − 72 ion (*m/e* 192) in the spectrum (Figure 3) of XIII decomposes in the same manner as the ethyl benzoylacetate molecular ion; these and other fragmentation modes of XIII are summarized in Scheme V and Figure 3. The alkyl derivatives XI and XII also of course yield *m/e* 192 ions from elimination of the alkyl group with hydrogen rearrangement.

Scheme V



In the spectra of the cyclic β-keto esters XV and XVI, peaks due to the loss of an ethoxyl radical (M − 45) and ethanol (M − 46) are important features of the high mass regions. Ethyl cyclopentanone-2-carboxylate (XVI, see Figure 4) affords an M − 28 ion which is associated with elimination of carbon monoxide (80%) and ethylene (20%). In analogy to the behavior of cyclopentanone itself,[7] the *m/e* 101 ion ($C_5H_9O_2^+$) can be formed by the process of α-cleavage and hydrogen transfer (XVI → e′), followed by heterolysis of the 3–4 bond to give f′; homolysis of the same linkage affords g′ (*m/e* 55, base peak). The *m/e* 73 peak is a doublet ($C_3H_3O_2^+$, 60%; $C_4H_9O^+$, 40%); the latter fragment can only reasonably be formed by an ethoxyl migration, and, since a metastable ion indicates the transition *m/e* 101 → *m/e* 73, it appears that f′ decomposes by loss of both ethylene and carbon monoxide to give h′ and i′, respectively.



Experimental Section

All spectra were determined using an A.E.I. MS 9 mass spectrometer operating at 70 e.v. and with the heated inlet system and source at a temperature of approximately 150°.

Ethyl 3,3-d$_2$*-2-*^{18}*O-Oxobutyrate* (*Ib*). Ethyl acetoacetate (100 mg.) and $D_2{}^{18}O$ (400 mg., 82% ^{18}O) were applied[4] to a tandem g.l.p.c. column (two-coiled stainless steel 0.25 in. × 5 ft. columns packed with (a) Celite (60–80) coated with 5% phosphoric acid and (b) Apiezon L on Celite (60–80) (1:4)), contained in an Autoprep Model A700 (Wilkins Instruments, Walnut Creek, Calif.). The column temperature was 60°, and

(7) P. Natalis, *Bull. soc. chim. Belges.*, **67**, 599 (1958).

the hydrogen flow rate was 50 cc./min. The labeled ester Ib was collected from the column after 16 min. This method gave 66% incorporation of ^{18}O.[4]

Acknowledgment. We wish to thank Professor D. Samuel of the Weizmann Institute for a generous gift of $D_2{}^{18}O$.

Studies in Mass Spectrometry. Part V.[1] Mass Spectra of Benzoquinones

By J. H. Bowie, D. W. Cameron, R. G. F. Giles, and D. H. Williams

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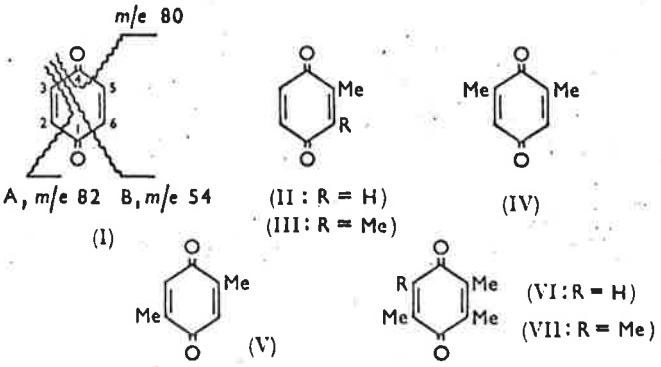
Studies in Mass Spectrometry. Part V.[1] Mass Spectra of Benzoquinones

By J. H. Bowie, D. W. Cameron, R. G. F. Giles, and D. H. Williams

The mass spectra of fifteen benzoquinones, variously substituted with methyl, hydroxyl, and methoxyl groups, are reported and discussed. The fragmentation patterns, which have been investigated in a number of cases by exact mass measurements and deuterium labelling, can be usefully correlated with the type of substituent and the nature of the substitution pattern.

ALTHOUGH the mass spectrum of 1,4-benzoquinone (I) is available,[2] a detailed investigation of members of this class has not been reported. In this Paper, the mass spectra of 15 substituted benzoquinones (II—XVI) are reported (in Figures 1—5 and the Table; an asterisk



(*) in the figures or in a degradation sequence indicates a process supported by the presence of an appropriate metastable ion).

The mass spectra of the benzoquinones (II—VII), carrying only methyl groups as substituents, retain a number of features of the spectrum of benzoquinone (I) itself. All contain pronounced molecular ions and M — CO fragments. Ions corresponding to the m/e 82 species from benzoquinone [see fragmentation A in (I)] are also evident, but in those quinones (II), (III), and (VI), which are asymmetrically substituted, the preferentially eliminated fragment always corresponds to the most substituted acetylene. For example, 2,3-dimethylbenzoquinone (III) (Figure 1) and 2,3,5-trimethylbenzoquinone (VI) give m/e 82 (90% $C_4H_2O_2^+$) and m/e 96 ions, respectively (M — CH_3–C≡C–CH_3), but do not afford ions arising from the elimination of acetylene and methylacetylene, respectively. The tetramethyl compound (VII) gives only a very low abundance ion (m/e 110, see Figure 3) due to the formal loss of dimethylacetylene.

Similarly, fragmentation B (see I) is evident from the spectra of (II—VII), and in the asymmetrically substituted quinones (II), (III), and (VI) again the most substituted neutral fragment is preferentially eliminated. This feature may be seen in the relative abundances of

[1] Part IV, R. Grigg, H. J. Jakobsen, S.-O. Lawesson, M. V. Sargent, G. Schroll, and D. H. Williams, preceding Paper.

[2] J. H. Beynon and A. E. Williams, *Appl. Spectroscopy*, 1960, **14**, 156.

m/e 82 (10% $C_5H_6O^+$) and *m/e* 54 in the spectrum (Figure 1) of 2,3-dimethylbenzoquinone. Appropriate metastable ions (see, for example, Figures 1 and 2) indicate that fragmentation B is in many cases, at least in part, a two-step process, the elimination of an acetylene being followed by elision of carbon monoxide. A comparison of the spectra (Figures 1 and 2) of the isomeric compounds (III) and (V) clearly indicates how the above-described behaviour can aid the structure elucidation of this type of compound.

An additional feature of the spectra of compounds (I—VII) is the appearance of ions corresponding to the loss of two molecules of carbon monoxide (Figures 1—3) from the molecular ion, definitely established by high resolution (h.r.) measurements in the instances of (I), (II), and (VII). The genesis of such $M - 2CO$ fragments necessitates the formation of at least one carbon–carbon bond, and it is interesting that they are most simply represented as ionised cyclobutadienes. This representation is employed in Scheme 1, which gives plausible structures for some of the fragments derived from the tetramethylbenzoquinone (VII); the compositions of all ions in this Scheme have been established by high resolution measurements and their relative abundances are indicated in Figure 3. The rearranged methylhydroxytropylium structure (*c*) for *m/e* 121 is speculative, but supported by two pieces of evidence. Firstly, the decomposition of the $M - CO$ ion from the monomethylbenzoquinone (II) by loss of H· or CH_3· is negligible, but $M - CO$ ions from dimethyl-derivatives (III—V) lose H· (*m/e* 108 ⟶ *m/e* 107 in Figures 1 and 2) but not CH_3·, whereas the trimethyl- and tetramethyl-derivatives (VI) and (VII) exhibit a pronounced loss of both radicals from their $M - CO$ ions. Evidently, the presence of two methyl substituents is necessary to permit an $M - CO$ ion to decompose by elimination of a radical to give a relatively stable carbonium ion; the most favourable incipient radical remaining [namely H· in (III—V) and CH_3· in (VI) and (VII)] is preferentially eliminated. This relatively stable carbonium ion is formulated as (*c*) (*m/e* 121) from (VII), or the hydroxytropylium ion itself (*f*; *m/e* 107) from (III—VI), since two methyl groups are in fact the anticipated requirement for an $M - CO$ ion to ring expand to a favourable

Principal peaks in the mass spectra of substituted 1,4-benzoquinones. Peaks are listed in ascending order of *m/e* ratio, with intensities expressed as percentages of the base peak. All ions having an abundance greater than 5% of that of the base peak are recorded

Compound									
(I)	*m/e*	39	49	50	51	52	53	54	55
	I (%)	7	8	15	10	31	32	100	6
	m/e	61	62	80	82	108(*M*)		109	
	I (%)	6	6	22	37	100		8	
(II)	*m/e*	38	39	40	42	43	44	53	54
	I (%)	15	38	40	8	52	34	15	94
	m/e	55	58	65	66	67	68	82	94
	I (%)	12	26	15	32	10	34	18	56
	m/e	95	96	122(*M*)		123			
	I (%)	6	6	100		16			
(IV)	*m/e*	38	39	40	44	67	68	69	77
	I (%)	7	30	37	14	6	66	6	6
	m/e	79	80	91	96	107	108	136(*M*)	
	I (%)	21	11	6	20	11	28	100	
	m/e	137							
	I (%)	18							
(VI)	*m/e*	39	40	41	43	44	51	53	54
	I (%)	27	12	6	6	6	8	11	14
	m/e	68	77	79	82	94	96	107	121
	I (%)	28	8	28	6	6	14	35	14
	m/e	122	150(*M*)		151				
	I (%)	29	100		14				
(VIII)	*m/e*	38	39	40	41	43	50	51	52
	I (%)	27	93	9	8	8	22	39	21
	m/e	53	54	62	63	65	66	67	68
	I (%)	43	23	7	15	18	14	100	8
	m/e	74	77	78	91	92	93	94	117
	I (%)	7	48	14	40	9	79	8	8
	m/e	118	119	121	122	149	150	173	185
	I (%)	9	8	89	11	36	7	6	7
	m/e	187	199	200	210	202	203	213	215
	I (%)	7	6	73	9	67	8	6	6
	m/e	228	230(*M*)		231				
	I (%)	48	53		6				

Compound									
(IXa)	*m/e*	37	38	39	40	41	42	43	44
	I (%)	13	25	72	43	23	20	39	24
	m/e	51	52	53	54	55	56	57	64
	I (%)	8	11	8	10	14	14	8	8
	m/e	65	66	67	68	69	70	71	72
	I (%)	6	8	11	24	65	66	52	27
	m/e	82	83	84	95	96	97	110	111
	I (%)	23	33	18	7	14	8	7	13
	m/e	112	138	139	140	141	142		
	I (%)	9	44	100	74	18	9		

($d_0 = 19$; $d_1 = 44$; $d_2 = 30$; $d_3 = 5$; $d_4 = 2\%$) *

(X)	*m/e*	37	38	39	41	42	43	44	53
	I (%)	7	15	9	28	74	22	9	27
	m/e	54	55	66	67	69	70	71	72
	I (%)	6	13	24	7	73	38	53	10
	m/e	84	85	94	95	112	113	140(*M*)	
	I (%)	29	9	13	9	19	7	100	
	m/e	141							
	I (%)	28							
(Xa)	*m/e*	36	37	38	39	40	41	42	43
	I (%)	8	15	20	15	15	29	67	74
	m/e	44	45	46	53	54	55	56	57
	I (%)	68	19	8	32	29	9	19	15
	m/e	66	67	68	69	70	71	72	73
	I (%)	19	29	17	74	93	57	68	44
	m/e	74	84	85	86	87	88	94	95
	I (%)	15	8	23	32	23	7	10	15
	m/e	96	97	98	112	113	114	115	140
	I (%)	15	7	6	6	15	18	13	18
	m/e	141	142	143	144				
	I (%)	67	100	66	23				

($d_0 = 7$; $d_1 = 25$; $d_2 = 38$; $d_3 = 23$; $d_4 = 7\%$) *

TABLE (*Continued*)

Compound									
(XI)	*m/e*	39	40	41	42	43	44	45	51
	I (%)	39	10	15	8	23	40	8	9
	m/e	52	53	54	55	56	57	65	66
	I (%)	8	28	17	69	32	7	14	57
	m/e	67	69	77	78	83	84	85	94
	I (%)	27	14	8	7	37	9	37	37
	m/e	95	97	111	112	122	139	140	
	I (%)	9	21	46	21	8	37	40	
	m/e	168(*M*)		169					
	I (%)	100		11					
(XIa)	*m/e*	37	38	39	40	41	43	44	51
	I (%)	8	10	28	10	10	16	10	8
	m/e	53	54	55	56	57	65	66	67
	I (%)	23	11	49	30	14	14	63	26
	m/e	83	84	85	86	87	94	95	97
	I (%)	33	10	23	19	6	36	14	13
	m/e	98	111	112	113	114	122	139	140
	I (%)	13	26	36	21	7	6	20	46
	m/e	141	142	168	169	170	171		
	I (%)	38	14	82	100	39	7		
	($d_0 = 39$; $d_1 = 45$; $d_2 = 15$; $d_3 = 1\%$) *								
(XII)	*m/e*	38	39	40	41	53	66	68	69
	I (%)	11	32	15	9	23	24	14	100
	m/e	84	109	122	123	124	137	152(*M*)	
	I (%)	9	10	14	6	14	10	33	
(XIII)	*m/e*	38	39	40	41	44	50	51	53
	I (%)	9	9	8	11	16	10	11	28
	m/e	54	55	57	59	66	69	70	77
	I (%)	7	7	10	18	6	100	8	11
	m/e	95	110	111	122	123	125	127	138
	I (%)	33	8	8	8	8	12	7	7
	m/e	139	153	168(*M*)					
	I (%)	28	25	10					

Compound									
(XIV)	*m/e*	38	39	40	41	43	44	50	51
	I (%)	16	64	54	14	24	16	10	16
	m/e	52	55	56	66	67	68	69	77
	I (%)	16	8	6	8	14	40	29	7
	m/e	79	80	81	83	84	96	109	111
	I (%)	6	6	10	92	9	20	9	30
	m/e	121	122	123	125	126	136	137	138
	I (%)	9	8	7	8	10	10	100	10
	m/e	139	153	167	182(*M*)		183		
	I (%)	27	6	20	57		6		
(XVI)	*m/e*	36	39	40	41	43	47	49	52
	I (%)	14	10	8	6	12	14	42	17
	m/e	52	53	59	63	67	68	69	71
	I (%)	14	9	14	6	7	16	13	25
	m/e	72	73	75	77	83	85	87	88
	I (%)	10	12	30	9	26	6	94	6
	m/e	89	90	93	94	99	100	102	103
	I (%)	33	12	7	8	7	10	6	87
	m/e	104	105	106	107	108	109	111	115
	I (%)	6	33	13	10	7	8	8	8
	m/e	118	119	121	129	130	137	138	139
	I (%)	14	14	10	8	6	100	7	67
	m/e	141	143	144	145	146	149	151	157
	I (%)	10	13	11	14	6	9	9	6
	m/e	163	164	165	166	167	170	171	172
	I (%)	56	7	72	6	33	8	7	8
	m/e	173	175	177	178	179	180	181	182
	I (%)	19	6	8	8	11	15	6	8
	m/e	190	193	195	201	206	207	208	209
	I (%)	7	16	13	13	16	44	18	32
	m/e	210	211	236	238	240(*M*)			
	I (%)	8	6	17	16	7			

* Isotopic purity.

tropylium species.[3] Secondly, the decomposition of *m/e* 107 (*f*) by successive losses of carbon monoxide and hydrogen to *m/e* 79 and 77 (Figures 1 and 2), or of *m/e* 121 (*c*) to *m/e* 93 (*d*) and *m/e* 91 (*e*) (Figure 3), exactly parallels the breakdown of the hydroxytropylium ion in the spectrum [4] of benzyl alcohol.

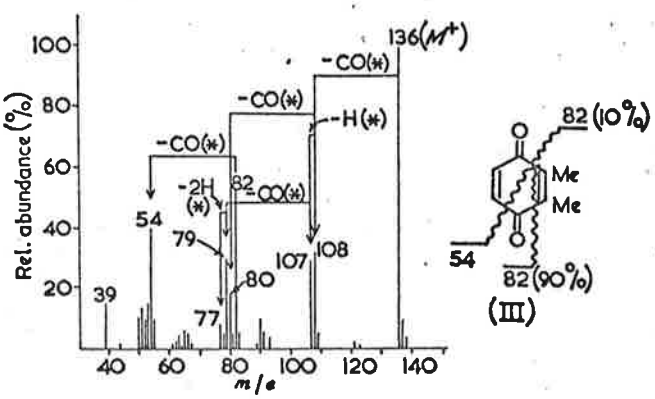


FIGURE 1 Mass spectrum of 2,3-dimethylbenzoquinone

In the light of the above generalisations, the M — CO ion from 2-bromo-3,5,6-trimethylbenzoquinone (VIII) should lose a bromine radical to afford *m/e* 121 (*c*) and then *m/e* 93 (*d*) and (*e*) (*m/e* 91), as observed and supported by appropriate metastable ions and high resolution measurements on *m/e* 91 ($C_7H_7^+$). The rearrangement of

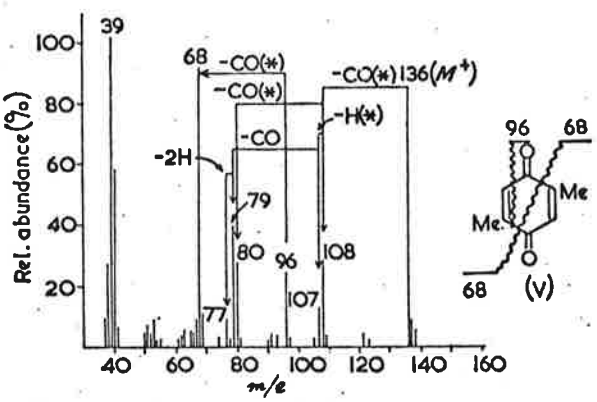


FIGURE 2 Mass spectra of 2,5-dimethylbenzoquinone

(VIII) to give benzenoid fragment ions upon electron impact is also suggested by the presence in its spectrum of an abundant *m/e* 77 ion ($C_6H_5^+$, h.r.), which is very

[3] H. M. Grubb and S. Meyerson in "Mass Spectrometry of Organic Ions," ed. F. W. McLafferty, Academic Press, New York, 1963, ch. 10.

[4] J. S. Shannon, *Austral. J. Chem.*, 1962, **15**, 265.

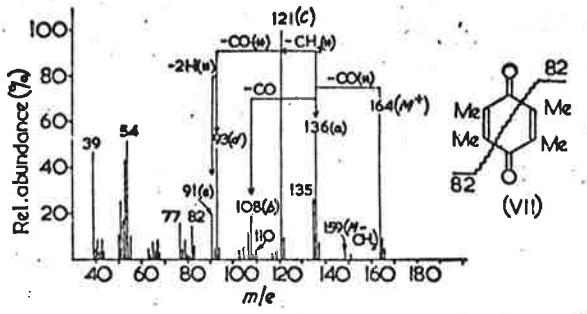
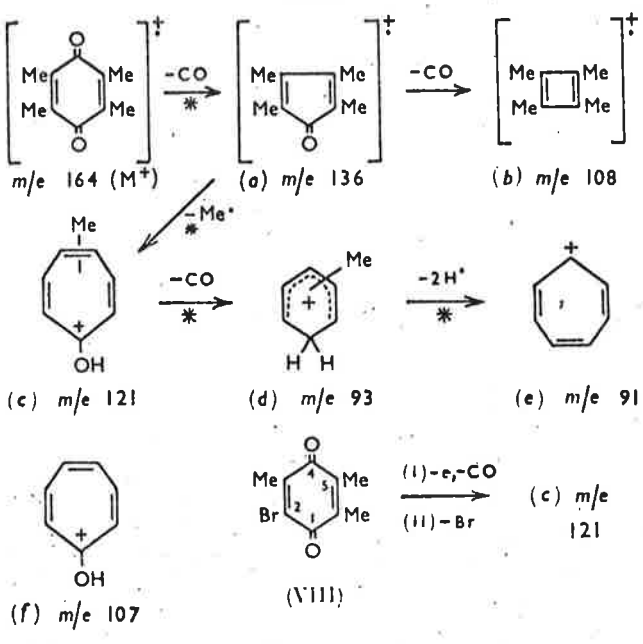


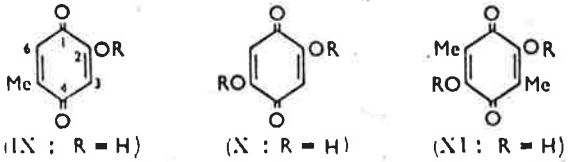
FIGURE 3 Mass spectrum of 2,3,5,6-tetramethylbenzoquinone

probably the phenyl cation. The most abundant ion from (VIII) is at *m/e* 67 ($C_4H_3O^+$), which can arise through cleavage of the 1,2- and 4,5-bonds and loss of a bromine radical from the charge-retaining fragment.

Scheme 1



The mass spectra of the hydroxybenzoquinones which have been investigated (IX—XI) all contain the molecular ion as the base peak, and M — CO and M — 2CO ions of moderate abundance. The most interesting



(IX : R = H) (X : R = H) (XI : R = H)
(IXa: R = D) (Xa: R = D) (XIa: R = D)

feature of their spectra is that cleavage of the 1,2- and 4,5-bonds (or 3,4- and 1,6-bonds; these processes cannot be distinguished) now occurs with hydrogen rearrangement. The spectra of monodeuterated-(IX), dideuterated-(X), and monodeuterated-(XI) [(IXa), (Xa), and (XIa), respectively †] were obtained by admitting the unlabelled compounds into the heated inlet system of the spectrometer with deuterium oxide,[4] and indicate that the hydroxyl group is the predominant source of the rearranged hydrogen. For example, the portion (60%) of *m/e* 69 which corresponds to $C_4H_5O^+$

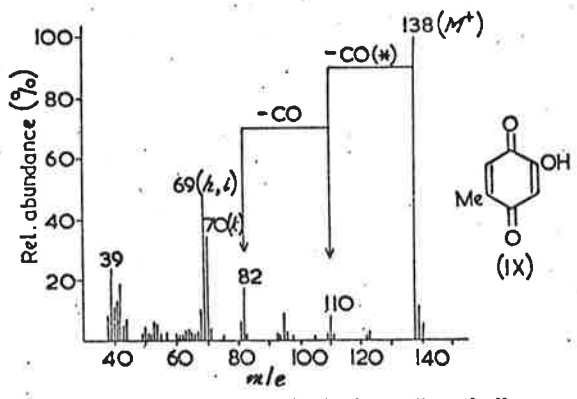


FIGURE 4 Mass spectrum of 2-hydroxy-5-methylbenzoquinone

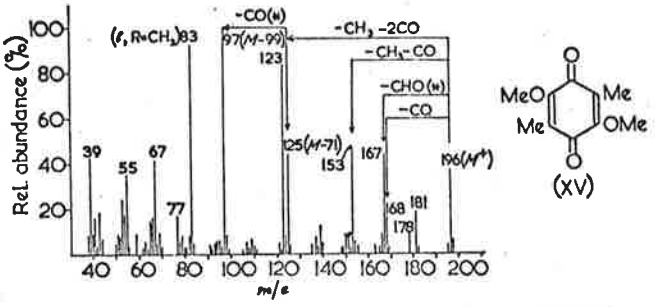


FIGURE 5 Mass spectrum of 2,5-dimethoxy-3,6-dimethyl benzoquinone

in the spectrum (Figure 4) of 2-hydroxy-5-methylbenzoquinone (IX) shifts mainly to *m/e* 70 in the spectrum of (IXa) and therefore, by analogy with the behaviour of 2-hydroxynaphthaquinones,[5] may arise *via* a hydrogen transfer in the M — CO ion (*g*) to give (*h*) (*m/e* 69, Scheme 2). The remaining part (40%) of *m/e* 69 is due to $C_3HO_2^+$(i), which is a common fragment in the spectra of compounds containing the $-O-\overset{|}{C}=CH-\overset{|}{C}=O$ system ;[6] by analogy, (XI) gives an ion (*j*) (*m/e* 83), which is the methyl homologue of (*i*). The *m/e* 70 ion present in Figure 4 is associated with a $C_4H_6O^+$ species (h.r.), necessitating a double hydrogen transfer (substantiated by deuterium labelling) to give an ion for which (*k*) is a plausible representation.

The spectra of the methoxybenzoquinones (XII—XVI) are somewhat more complicated than those discussed so far, and lend themselves less to generalisations and to predictions of the behaviour of related compounds. The most general feature of their spectra is associated with the appearance of an ion (*l*), formed by the cleavage

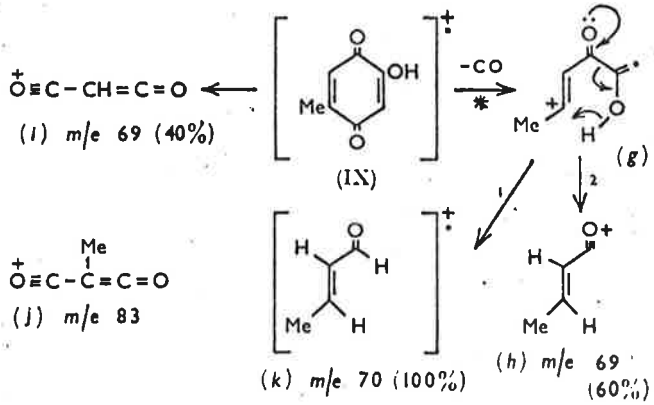
† These substances are not isotopically pure, since some deuterium is introduced at C-3 in (IX) and C-3 and C-6 in (X) *via* the tautomeric triones. The isotopic purities are given in the Table.

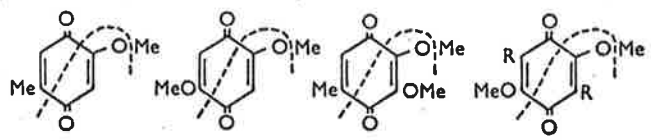
[5] J. H. Bowie, D. W. Cameron, and D. H. Williams, *J. Amer. Chem. Soc.*, 1965, **87**, 5094.

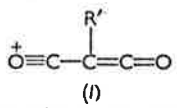
[6] J. H. Bowie and D. H. Williams, unpublished work.

indicated by dotted lines in (XII—XVI); (*l*) is the analogue of (*i*) and (*j*) derived from hydroxybenzoquinones. The composition of each of these ions has been established by exact mass measurements; when the peak is a doublet (spectra of XII—XIV), the

Scheme 2



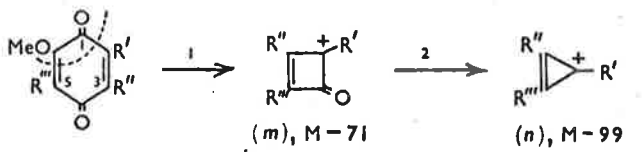




m/e 69 (90%) from (XII) (R′=H); base peak.
m/e 69 (85%) from (XIII) (R′=H); base peak.
m/e 69 (70%) from (XIV) (R′=H); 30% of base peak.
m/e 83 (100%) from (XV) (R′=CH_3); 93% of base peak (Figure 5).
m/e 103/105 (100%) from (XVI) (R′=Cl); 87% of base peak.

$C_4H_5O^+$ ion makes up the complement. No shift is observed for ion (*l*) when R′ is expected to correspond to the CH_3O-function of the parent compound (XIV), apparently because the methyl ether group is eliminated as formaldehyde during the cleavage reaction.

The mass spectra of (XIV—XVI) exhibit pronounced M − 71 ions (see Figure 5), shown in all cases to correspond to the formal loss of two molecules of carbon monoxide and a methyl group from the molecular ion. These *M* − 71 fragments then decompose by loss of carbon monoxide, as established by metastable peaks in the spectra of (XIV) and (XV) (Figure 5). This observation strongly suggests that the *M* − 71 fragments contain an intact carbonyl group and arise through cleavage of the 1,2- and 5,6-bonds to give a fragment which may be represented as (*m*): elision of carbon monoxide then affords a favourable cyclopropenyl cation (*n*) (*M* − 99). These and other decomposition modes of (XV) are summarised in Figure 5; all the proposed decomposition paths have been established by exact mass measurements.



(XIV: R′=H, R″=Me, R‴=OMe)
(XV: R′=R‴=Me, R″=OMe)
(XVI: R′=R‴=Cl, R″=OMe)

(XIV: *m/e* 111)
XV: *m/e* [125 (Figure 5)]
(XVI: *m/e* 165/167/169)

(XIV: *m/e* 83)
[XV: *m/e* 97 (Figure 5)]
(XVI: *m/e* 137/139/141)

1, —O=C=Ċ—OMe; 2, —CO.

EXPERIMENTAL

All spectra were determined using an A.E.I. MS 9 mass spectrometer operating at 70 ev. Samples were introduced throuth a heated inlet system at a temperature of approximately 200°.

We thank Professor W. Flaig for a sample of 2,5-dihydroxybenzoquinone.

UNIVERSITY CHEMICAL LABORATORY,
CAMBRIDGE.

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Studies in Mass Spectroscopy. VI.[1a] Mass Spectra of Substituted Diethyl Malonates

J. H. Bowie, D. H. Williams,[1b]

University Chemical Laboratory, Cambridge, United Kingdom

S.-O. Lawesson, and G. Schroll

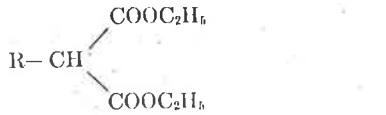
Department of Chemistry, Aarhus University, Aarhus C, Denmark

Received November 18, 1965

The mass spectra of representative mono- and dialkyl diethyl malonates have been investigated. These molecules break down mainly by loss of an alkyl substituent with hydrogen rearrangement (McLafferty rearrangement). The enolic nature of the resulting fragment is suggested by its subsequent decompositions. Enolic fragments are also apparently formed upon elimination of $COOC_2H_4$ (loss of ester group with hydrogen rearrangement) in the spectra of monoalkyl diethyl malonates.

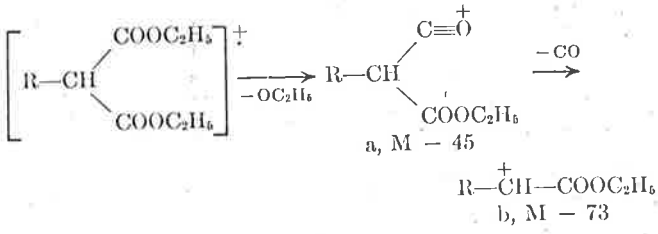
Although the mass spectra of a number of malonic acids have been determined,[2] a detailed study of the synthetically important malonate esters has not been reported. This paper deals with the interpretation of the mass spectra (Table 1 and Figures 1–6) of diethyl malonate and a number of the more important alkyl and aryl derivatives. The most important reactions occurring upon electron impact in many of these compounds appear to lead to enolic fragment ions (as deduced from the further decomposition of these fragment ions). The evidence upon which specific structures for such fragment ions are based comes from allylic cleavage reactions (which occur in a predictable manner); the specific structures aid interpretation of the spectra in a general and self-consistent manner. However, it is emphasized that this is the only evidence available for assigning fragment ion structures, which therefore must be regarded as speculative throughout this paper.

In the spectra of diethyl malonate (I) and the monosubstituted derivatives II–XI, a molecular ion is generally observed only for those cases in which the substituent does not carry a suitable hydrogen atom to participate in the McLafferty rearrangement[3] with a carbonyl group of the ester. Thus, diethyl malonate (I) and the methyl, allyl, phenyl, and benzyl derivatives (II, IV, X, and XI) exhibit molecular ions in their spectra.



I, R = H
II, R = CH_3
III, R = C_2H_5
IV, R = $CH_2CH{=}CH_2$
V, R = *n*-C_3H_7
VI, R = *i*-C_3H_7
VII, R = *n*-C_4H_9
VIII, R = *i*-C_4H_9
IX, R = *t*-C_4H_9
X, R = C_6H_5
XI, R = $C_6H_5CH_2$

In general, three important types of fragmentation are evident from the spectra (Table I and Figures 1–4) of these compounds. First, all the spectra contain pronounced (13–100% relative to the base peak) M − C_2H_5O ions (a) which correspond to the base peak when R = H (I) or when R is a small alkyl group [R = CH_3 (II) or C_2H_5 (III)]. Frequently ion a decomposes by elimination of carbon monoxide to an M − $COOC_2H_5$ species, b, as evidenced by appropriate metastable ions in the spectra of III, IV, and VI.



a, M − 45

b, M − 73

Second, loss of one ester group occurs with hydrogen rearrangement to give an M − $COOC_2H_4$ ion (M − 72), whose relative abundance decreases with increasing size of the alkyl substituent as indicated in Table II. The decrease in the relative abundance of the M − 72 fragment is due to the increasing importance of the McLafferty rearrangement as R becomes larger and also the additional tendency for the M − 72 ion to fragment further when R is larger. The further fragmentation of the M − 72 species strongly supports its representation as the enolic form c, perhaps formed *via* a cyclic transition state (see XII → c). Thus, if the alkyl substituent R is large enough to permit loss of an alkyl radical through allylic cleavage in c, then abundant fragment ions corresponding to the formation of d

(1) (a) Part V: J. H. Bowie, D. W. Cameron, R. G. F. Giles, and D. H. Williams, *J. Chem. Soc.*, in press. (b) To whom inquiries should be addressed.

(2) R. I. Reed and W. K. Reid, *ibid.*, 5933 (1963).

(3) F. W. McLafferty in "Determination of Organic Structure by Physical Methods," Vol. 2, Academic Press, Inc., New York, N. Y., 1962, pp 129–149.

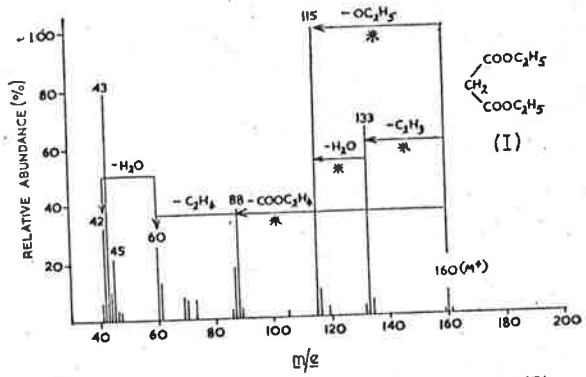


Figure 1.—Mass spectrum of diethyl malonate (I).

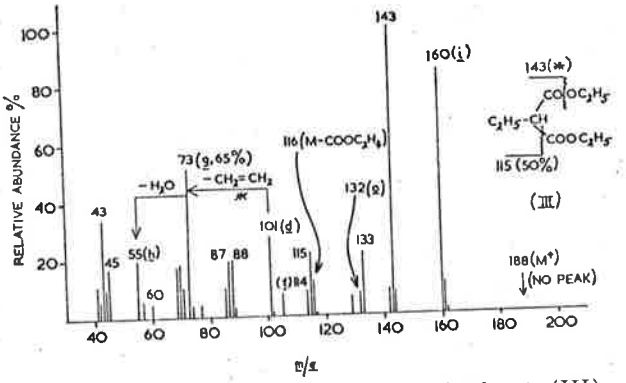
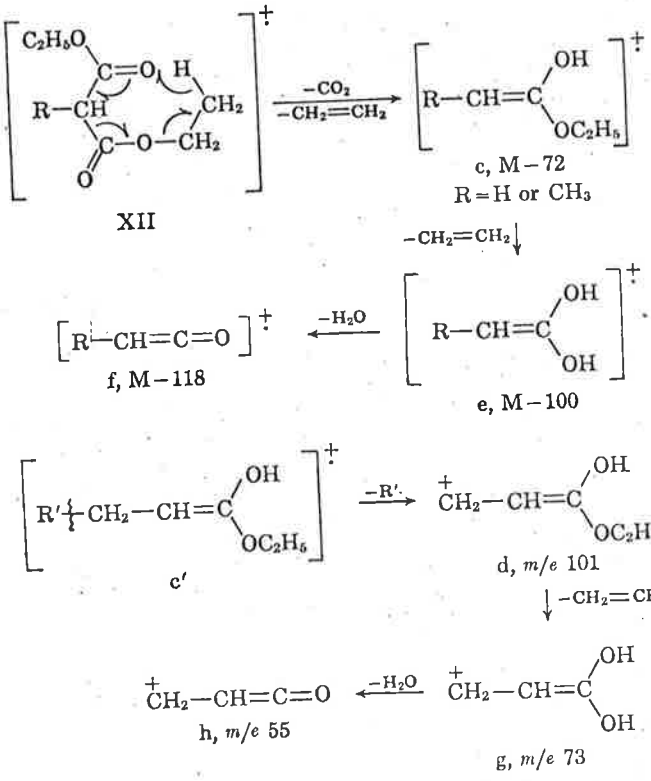


Figure 2.—Mass spectrum of diethyl ethylmalonate (III).



from c′ appear in the spectrum. Alternatively, if R is H or CH_3, then c can decompose by successive eliminations of ethylene and water to ions plausibly represented as e and f, respectively; analogous processes may afford g and h from d.

Third, when the McLafferty rearrangement can operate (in III and V–IX), the base peak in the spectrum corresponds to a fragment i (*m/e* 160) in all cases except

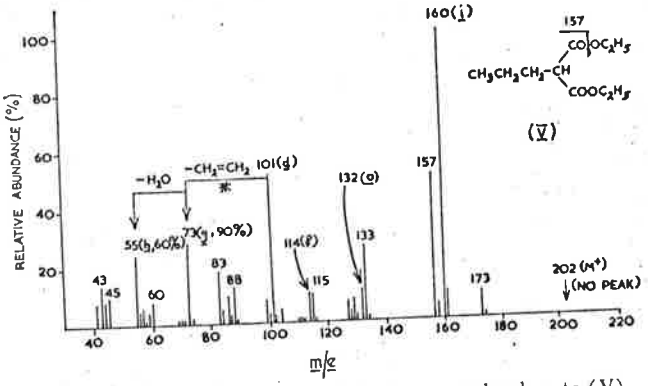


Figure 3.—Mass spectrum of diethyl *n*-propylmalonate (V).

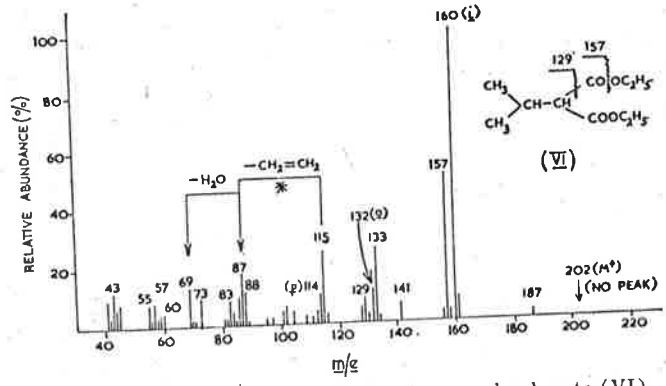
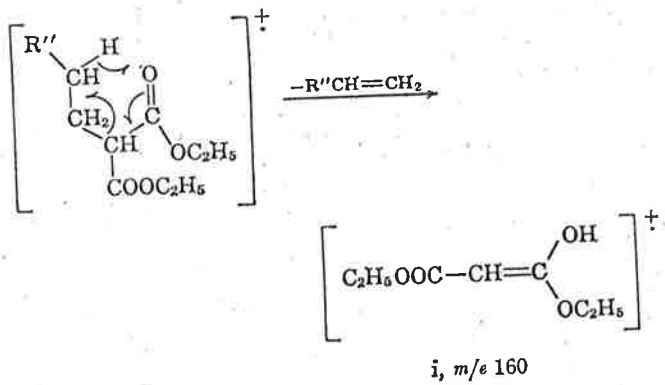


Figure 4.—Mass spectrum of diethyl isopropylmalonate (VI).

that of the ethyl derivative III, when the M − OC_2H_5 ion (*m/e* 143, Figure 2) is slightly more abundant.



The evidence which supports the generalizations outlined above may be illustrated by reference to the spectra of diethyl malonate (I) and its ethyl (III), propyl (V), and isopropyl (VI) derivatives (Figures 1, 2, 3, and 4, respectively).[4] The compositions of the ions which give rise to *m/e* 42, 43, 60, 88, and 115 in the spectrum (Figure 1) of I have been established by exact mass measurements. An M − C_2H_3 ion (*m/e* 133 in Figure 1) is also abundant in the spectrum of the methyl derivative II and corresponds to the oxonium ion j.[5] A comparison of Figure 1 with Figures 2–4 clearly indicates that the *m/e* 160 ion in Figures 2–4 has much less tendency to fragment than the diethyl malonate molecular ion. This observation is consistent with its

(4) Transitions marked by an asterisk, both in these figures and subsequently in the text, indicate a process supported by the presence of an appropriate metastable peak.

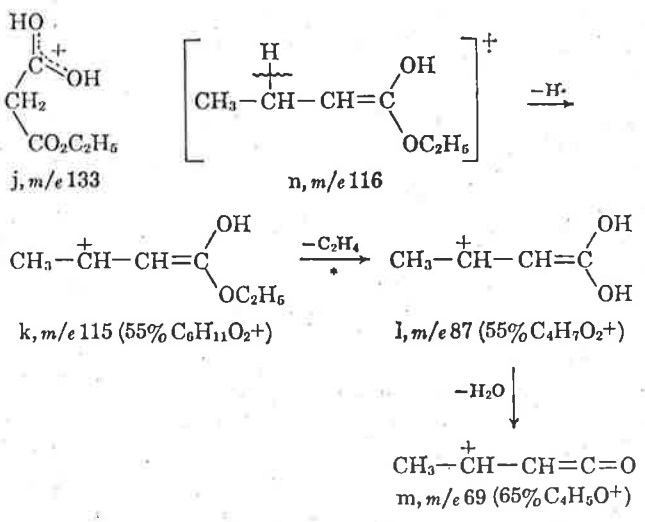
(5) F. W. McLafferty and R. S. Gohlke, *Anal. Chem.*, **31**, 2076 (1959); see also A. G. Harrison and E. G. Jones, *Can. J. Chem.*, **43**, 960 (1965).

TABLE I[a]

	m/e	41	43	44	45	55	56	57	73	74	75	87	88	101	102	115	116	128	129	130	147
	I, %	9	12	10	16	9	30	28	22	76	8	4	10	12	35	10	6	13	100	11	19
	m/e	174 (M)																			
	I, %	11																			
IV	*m/e*	41	42	43	44	45	53	54	55	57	60	67	69	70	71	72	81	82	87	88	97	98
	I, %	30	10	30	22	21	20	18	38	20	7	10	14	12	11	6	59	33	10	15	18	88
	m/e	99	100	108	109	110	115	126	127	128	133	153	154	155	160	199	200 (M)					
	I, %	46	11	58	100	8	38	55	93	16	24	16	28	32	9	4	8					
VII	*m/e*	41	42	43	44	45	55	60	69	70	86	88	91	97	98	99	101	102	104	114	115	116
	I, %	10	5	9	9	9	18	4	20	3	10	14	3	19	4	4	20	3	6	14	18	3
	m/e	132	133	142	143	144	160	161	171	172	173											
	I, %	12	25	5	8	3	100	9	44	6	14											
VIII	*m/e*	41	43	45	55	56	57	60	69	73	74	86	87	88	97	99	101	104	114	115	127	132
	I, %	11	10	8	18	5	5	4	12	26	3	8	4	10	14	6	24	5	14	13	14	10
	m/e	133	142	143	160	161	171	172	173	201												
	I, %	23	3	5	100	9	23	3	14	3												
IX	*m/e*	41	43	45	55	57	59	60	69	73	82	83	86	87	88	99	100	101	104	105	114	115
	I, %	10	10	7	10	31	4	5	5	6	5	10	13	14	16	23	6	8	9	5	16	64
	m/e	116	127	132	133	134	155	157	160	161	171	201	216 (M)									
	I, %	3	17	16	35	4	11	10	100	9	15	5	4									
X	*m/e*	41	43	44	45	46	51	55	57	62	63	64	65	69	73	77	78	79	80	81	83	89
	I, %	5	7	24	17	6	8	7	4	4	11	5	5	5	6	19	6	38	3	3	4	34
	m/e	90	91	92	95	97	105	107	108	117	118	119	120	135	136	137	146	163	164	165	190	191
	I, %	45	86	9	5	5	16	48	5	11	88	29	3	56	76	6	9	100	97	10	27	14
	m/e	192	236 (M)		237																	
	I, %	14	17	57	8																	
XI	*m/e*	43	44	45	55	65	87	88	89	91	92	102	103	104	105	107	130	131	132	147	148	149
	I, %	4	7	5	5	8	14	10	6	61	8	5	19	18	8	7	8	100	17	16	29	15
	m/e	158	159	160	175	176	177	167	204	205	250 (M)		251									
	I, %	7	55	8	8	93	47	8	6	14	63		11									
XIV	*m/e*	38	39	41	42	43	44	45	53	55	57	59	69	70	71	73	83	86	87	88	97	98
	I, %	8	11	26	5	24	7	30	5	22	12	8	39	5	10	38	14	8	17	4	19	14
	m/e	99	101	102	113	114	115	116	118	127	129	130	141	142	143	144	145	155	157	160	170	171
	I, %	20	46	3	7	17	54	17	3	10	44	4	15	34	64	24	3	3	8	13	6	48
	m/e	172	173	174	187	188	189															
	I, %	6	33	5	7	100	12															
XVII	*m/e*	39	41	43	44	45	51	57	73	74	77	78	79	89	91	92	102	103	104	105	107	115
	I, %	4	8	3	7	9	5	8	58	4	12	4	4	3	68	5	3	18	3	15	23	15
	m/e	116	117	118	119	120	131	135	136	145	146	147	149	163	164	174	177	190	191	192	193	218
	I, %	6	48	13	48	6	6	100	17	6	32	11	7	6	7	6	8	7	64	72	9	3
	m/e	219	220	236	264 (M)		265															
	I, %	3	8	3	28		4															

[a] All ions having an abundance greater than 2% of the base peak (arbitrarily taken as 100%) are recorded.

formulation as the enolate i, which can still decompose to a small extent to *m/e* 133 ($-C_2H_3$), 115 ($-OC_2H_5$), and 88 ($-COOC_2H_4$) as indicated by all the necessary metastable peaks in the spectra of V, VI, VIII, and IX.[6] Most importantly, whereas the *n*-alkyl derivatives III and V exhibit fairly abundant ions at *m/e* 101 (d), 73 (g), and 55 (h) (Figures 2 and 3), the corresponding species in the spectrum (Figure 4) of the isopropyl derivative (VI) appear at *m/e* 115 (k), 87 (l), and 69 (m), the increments of 14 mass units being associated with the α branching of the substituent in VI.[7] As expected *m/e* 115 is a doublet [$C_5H_7O_3^+$ by loss of C_2H_5O from i (*m/e* 160) and $C_6H_{11}O_2^+$ (k)] in the spectra of III and VI, since the M $-$ $COOC_2H_4$ ion (n) from III can lose an allylic hydrogen atom to furnish k. However, a $C_6H_{11}O_2^+$ ion cannot arise from the M $-$ CO-OC_2H_5 ion of V by an allylic cleavage, and therefore



m/e 115 is a singlet in this spectrum; this observation supports the postulated decomposition mechanism above.

Extensive exact mass measurements on the spectra of III, V, and VI suggest an additional decomposition mode (Scheme I) of i (*m/e* 160) and lend further support to the enol formulation.

(6) The possibility that a small proportion of the *m/e* 160 ion in the spectra of diethyl alkylmalonates has the same structure as the diethyl malonate molecular ion cannot be excluded. Moreover, although it is possible that the enolate i is intrinsically less prone to decompose than the diethyl malonate molecular ion, the difference in their behavior could also arise owing to the smaller internal energy of i, which is already the product of an energy-dissipating reaction.

(7) Percentages quoted in the figures indicate the proportion having the required composition, as established by high resolution (hr) measurements.

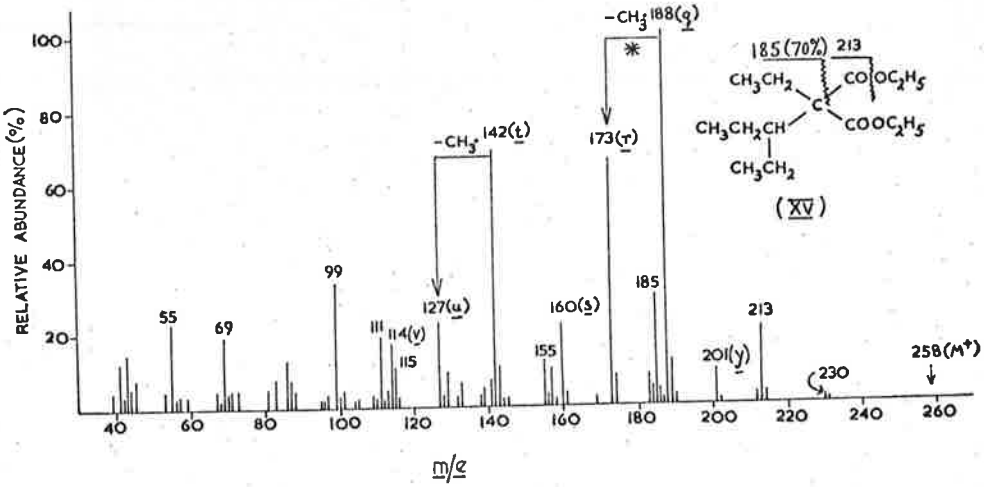


Figure 5.—Mass spectrum of diethyl ethyl(1-ethyl-*n*-propyl)malonate (XV).

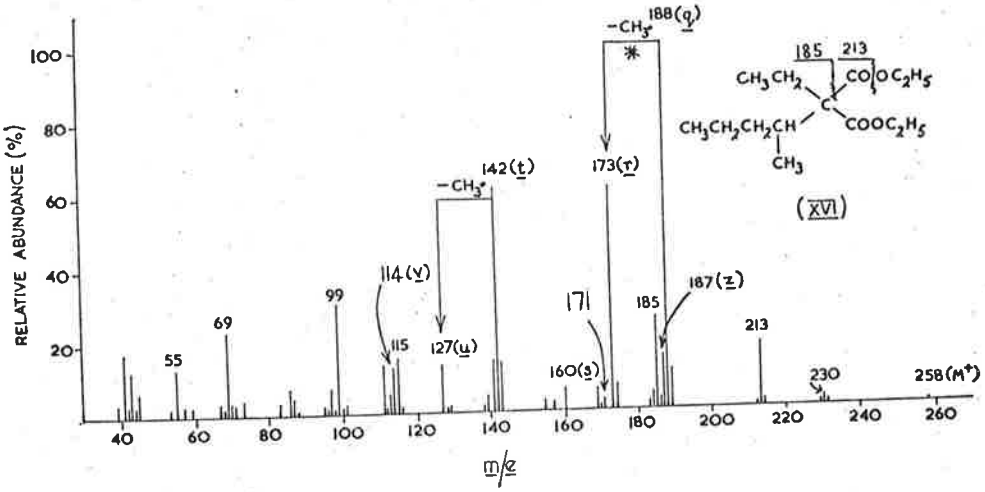


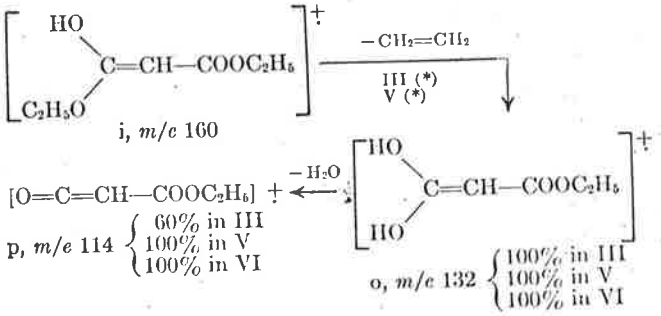
Figure 6.—Mass spectrum of diethyl ethyl(1-methyl-*n*-butyl)malonate (XVI).

TABLE II

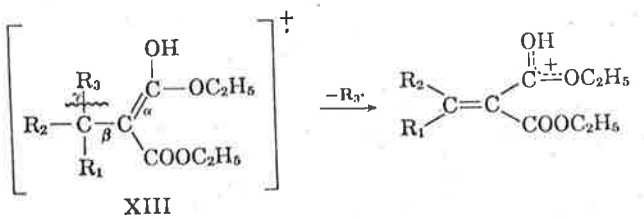
RELATIVE ABUNDANCE OF M − 72 IONS IN THE SPECTRA OF SOME MONOSUBSTITUTED DIETHYL MALONATES

Substituent (R)	H	CH_3	C_2H_5	n-C_3H_7	i-C_3H_7	n-C_4H_9	i-C_4H_9	t-C_4H_9
Relative abundance of M − 72 ion	38	35	12	2	2	2	1	0

SCHEME I



The spectra of several of the alkyl derivatives establish that a C–C bond of the alkyl group which formally is γ with respect to a carbonyl group (see XIII)



XIII

is prone to cleavage. The γ bond which is broken is the one which can lead to elision of the largest alkyl radical (Table III). The fragmentation is consistent with the existence of some enol form in the molecular ion of these compounds.

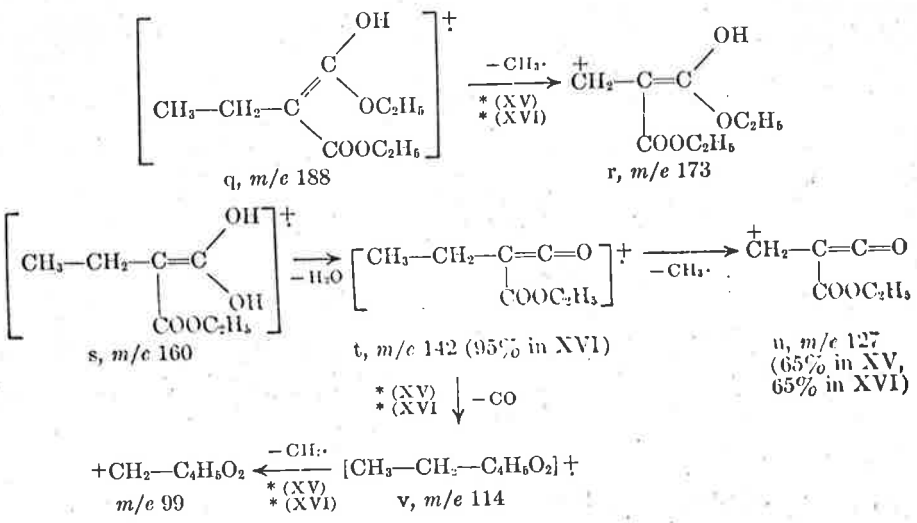
TABLE III

M − R_3 IONS IN THE SPECTRA OF DIETHYL ALKYLMALONATES

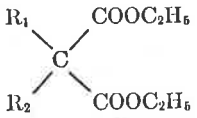
Alkyl substituent	R_3	m/e value (rel abundance, %)
n-C_3H_7 (V)	C_2H_5	173 (9)
i-C_3H_7 (VI)	CH_3	187 (3)
n-C_4H_9 (VII)	n-C_3H_7	173 (14)
i-C_4H_9 (VIII)	i-C_3H_7	173 (14)
t-C_4H_9 (IX)	CH_3	201 (5)

The behavior of the diethyl dialkylmalonates XIV–XVII upon electron impact (the spectra are summarized in Table I) is similar to that of the monosubstituted derivatives and may be illustrated by reference to the spectra (Figures 5 and 6) of the isomeric diethyl ethyl(1-ethyl-*n*-propyl)malonate (XV) and diethyl ethyl(1-methyl-*n*-butyl)malonate (XVI). The two spectra are very similar over-all and in each case the base peak

SCHEME II

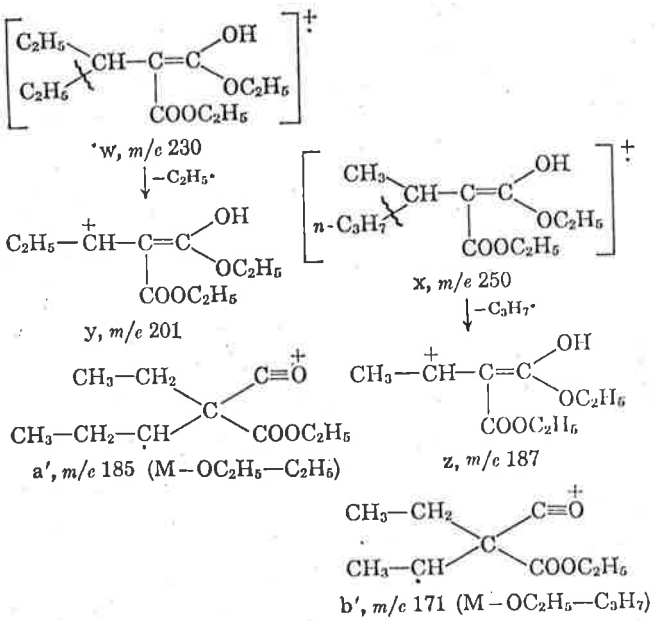


(*m/e* 188, M − C_5H_{10}) arises from participation of the largest alkyl group in the McLafferty rearrangement. The resulting enolate ion q (*m/e* 188) decomposes exactly as anticipated, probably to r, s, t, and u and additionally to *m/e* 114 (v) and 99 (see Figures 5 and 6 and Scheme II above).

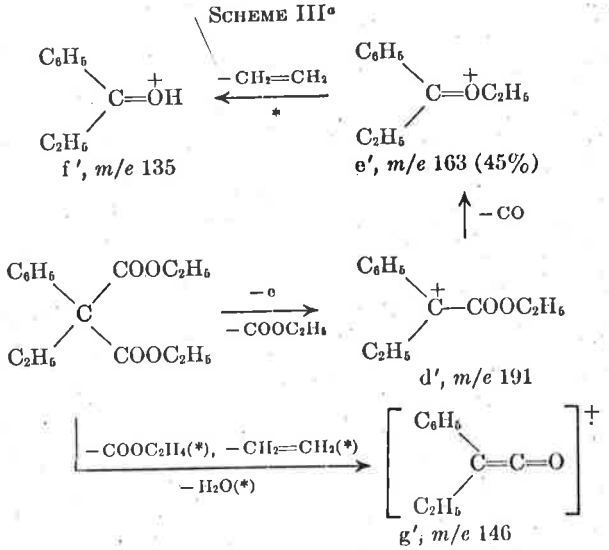


XIV, $R_1 = R_2 = C_2H_5$
XV, $R_1 = C_2H_5$; $R_2 = CH(C_2H_5)_2$
XVI, $R_1 = C_2H_5$; $R_2 = CH(CH_3)$-*n*-C_3H_7
XVII, $R_1 = C_2H_5$; $R_2 = C_6H_5$

Alternatively, the McLafferty rearrangement may involve the ethyl substituent in both XV and XVI, but as expected this process occurs to a much smaller extent, to give *m/e* 230 ions which are structurally different from XV and XVI (w and x, respectively). The enolic ions w and x should decompose by elimination of an ethyl radical and a propyl radical, respectively, to



SCHEME III[a]



[a] The compositions of all fragments represented in this scheme have been established by exact mass measurements.

afford *m/e* 201 (y) and 187 (z). In fact the presence of *m/e* 201 and the virtual absence of *m/e* 187 in Figure 5, and *vice versa* in Figure 6, constitutes the main difference between the two spectra, as predicted.

An additional difference between the behavior of XV and XVI, which is uncovered by high-resolution measurements, is that *m/e* 185 is a doublet [$C_{10}H_{17}O_3^+$ (30%) and $C_{11}H_{21}O_2^+$ (70%)] in the spectrum of XV, but a singlet ($C_{11}H_{21}O_2^+$) in the spectrum of XVI. The $C_{10}H_{17}O_3^+$ species from XV corresponds to a′ and consequently an *m/e* 171 ion (b′) is the corresponding fragment from XVI; a small *m/e* 171 ion is in fact present in Figure 6 and absent in Figure 5.

If one of the substituents which replaces the active methylene hydrogens is a phenyl group, as in diethyl phenylethylmalonate (XVII), then the fragmentation pattern follows a somewhat different course. The McLafferty rearrangement in the spectrum of XVII is not an important process, but instead a large proportion of the decomposition takes place by complete loss of an ester group, perhaps because the resulting carbonium ion d′ (*m/e* 191, see Scheme III) is relatively favorable. Appropriate metastable peaks and exact mass measure-

ments indicate that m/e 191 decomposes further by successive losses of carbon monoxide and ethylene to m/e 163 (45% of $C_{11}H_{15}O^+$) and 135 (100% of $C_9H_{11}O^+$ and the base peak of the spectrum). Both of these ions must be skeletal rearrangement fragments,[8] most plausibly arising as indicated in Scheme III, although either ethyl group could in principle be eliminated in passing from e′ to f′. The usual sequence of loss of an ester group (with hydrogen rearrangement), ethylene, and then water is operative and terminates in the formation of a $C_{10}H_{10}O^+$ fragment (m/e 146, represented as g′).

Finally, it should be noted that both XVII and diethyl phenylmalonate (X) lose carbon dioxide (hr) from their molecular ions to form m/e 220 and 192 (8 and 17% or the base peaks, respectively), thus necessitating ethyl migrations in both cases.[8]

(8) For numerous examples of skeletal rearrangement processes occurring in ketones and esters upon electron impact, see J. H. Bowie, R. Grigg, D. H. Williams, S.-O. Lawesson and G. Schroll, *Chem. Commun.*, (London), 403 (1965); W. H. McFadden, K. L. Stevens, S. Meyerson, G. J. Karabatsos, and C. E. Orzech, *J. Phys. Chem.*, **69**, 1742 (1965); P. Natalis and J. L. Franklin, *ibid.*, **69**, 2943 (1965).

Experimental Section

This investigation was carried out using an A.E.I. MS9 double-focussing mass spectrometer. Spectra were obtained with an ionizing energy of 70 ev at a source pressure between 0.1×10^{-6} and 1.0×10^{-6} mm. Samples were introduced into the ionization chamber *via* a heated inlet system operating at a temperature of approximately 150°.

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Studies in Mass Spectrometry. IX.[1] Mass Spectra of β-Diketones

J. H. Bowie, D. H. Williams,

University Chemical Laboratory, Cambridge, England

S.-O. Lawesson, and G. Schroll

Department of Chemistry, Aarhus University, Aarhus C, Denmark

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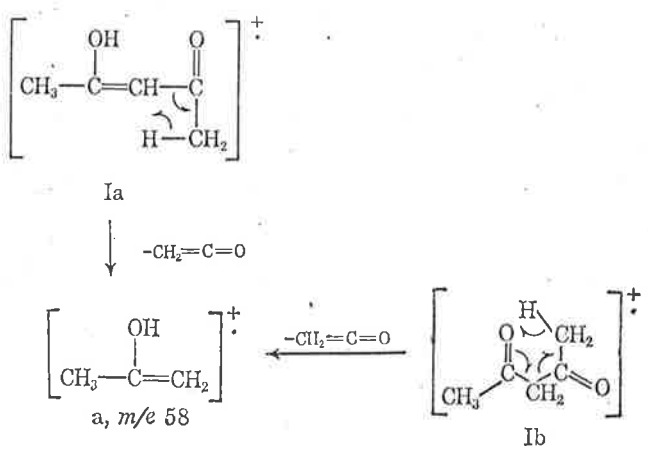
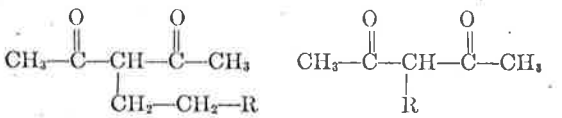
β-Diketones break down in a well-defined manner upon electron impact. The spectra have uncovered examples of methyl and phenyl migrations, but are most noteworthy for the elimination of ketene from the acetyl group of a β-diketone with the formation of a charged enolate, the further composition of which is dependent upon the nature of any alkyl substituents in the molecule.

The only mass spectra of β-diketones which appear to have been discussed are those of dimedone and ethyl dimedone.[2] In view of the importance of β-diketones as synthetic intermediates, we have undertaken, in addition to our examination of β-keto esters[3] and diethyl malonates,[4] a study of the mass spectra of representative members (I–XV) of this class of compounds; the results are summarized in Table I and Figures 1–5.

The mass spectrum (Figure 1) of the parent compound, acetylacetone (I), is noteworthy for the presence of an *m/e* 72 ion, which arises from the loss of carbon monoxide from the molecular ion [as established by high-resolution measurements and the spectrum (see Table I) of 3,3-d_2-pentane-2,4-dione (Ic)]. This process necessitates a methyl migration, substantiated examples of which are very few in mass spectrometry.[5] Other fragmentations are summarized in Figure 1. It will be seen subsequently that fragments formed by elimination of ketene from the molecular ion of β-diketones are best represented as the enol (a, *m/e* 58, in the present instance). Such an enol may be formed either by hydrogen rearrangement to carbon in the enol form (Ia → a) or hydrogen rearrangement to oxygen in the diketo form (Ib → a). By analogy to the McLafferty rearrangement,[6] the latter representation seems more plausible and is employed throughout the following discussion.



All the simple C-alkylacetylacetones examined (II–VI) afford low abundance M − CH_3, M − H_2O, and



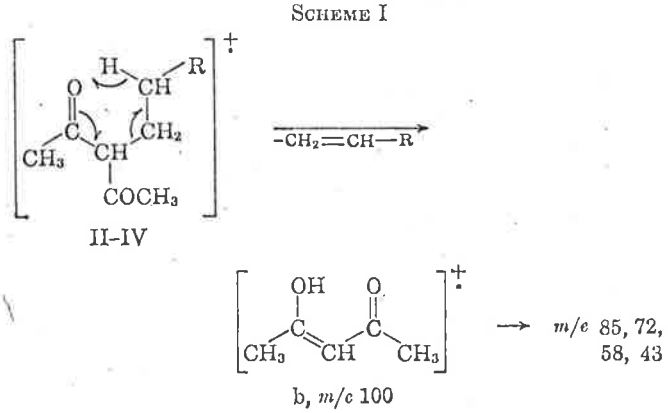
II, R = H
III, R = CH_2CH_3
IV, R = $CH(CH_3)_2$

V, R = CH_2–CH=CH_2
VI, R = CH_2–C_6H_5
VIa, R = CD_2–C_6H_5

M − CH_3 − H_2O ions in the high mass regions of their spectra and abundant acetyl ions at *m/e* 43. In those cases where the alkyl substituent is a saturated hydrocarbon chain of two or more carbon atoms (II–IV), the two main decomposition sequences summarized in Scheme I and Scheme II provide a self-consistent rationale for the formation of most of the abundant ions in the spectra.

The behavior summarized in Schemes I and II may be illustrated by reference to the spectrum (Figure 2) of 3-*n*-butylpentane-2,4-dione (III). Elimination of the *n*-butyl substituent, most plausibly as but-1-ene, through the McLafferty rearrangement,[6] can afford b (*m/e* 100); b is the enol form of the acetylacetone molecular ion and may accordingly decompose to *m/e* 85 (25% $C_4H_5O_2^+$), *m/e* 72, *m/e* 58, and *m/e* 43 (90% $CH_3C{\equiv}O^+$) as indicated in Figure 1. Alternatively, loss of ketene from the molecular ion gives an M − 42 species formulated as c [R = C_2H_5, *m/e* 114, 90% $C_7H_{14}O^+$ by high resolution (HR)]. Cleavage of the

Scheme I



(1) Part VIII: J. Harley-Mason, T. P. Toube, and D. H. Williams, *J. Chem. Soc.*, in press.

(2) T. Goto, A. Tatematsu, Y. Nakajima, and H. Tsuyama, *Tetrahedron Letters*, 757 (1965).

(3) J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams, *J. Am. Chem. Soc.*, **87**, 5742 (1965).

(4) J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams, *J. Org. Chem.*, in press.

(5) A. S. Newton and P. O. Strom, *J. Phys. Chem.*, **62**, 24 (1958); F. Komitsky, Jr., J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 1399 (1965); for related rearrangements, see also J. H. Bowie, R. Grigg, S.-O. Lawesson, G. Schroll, and D. H. Williams, *Chem. Commun.* (London), 403 (1965); D. R. Black, W. H. McFadden, and J. W. Corse, *J. Phys. Chem.*, **68**, 1237 (1964); W. H. McFadden, K. L. Stevens, S. Meyerson, G. J. Karabatsos, and C. E. Orzech, *J. Phys. Chem.*, **69**, 1742 (1965).

(6) F. W. McLafferty, "Determination of Organic Structures by Physical Methods," Vol. 2, Academic Press Inc., New York, N. Y., 1962, pp 129–149; S. Meyerson and J. D. McCollum, *Advan. Anal. Chem. Instr.*, **2**, 179 (1963).

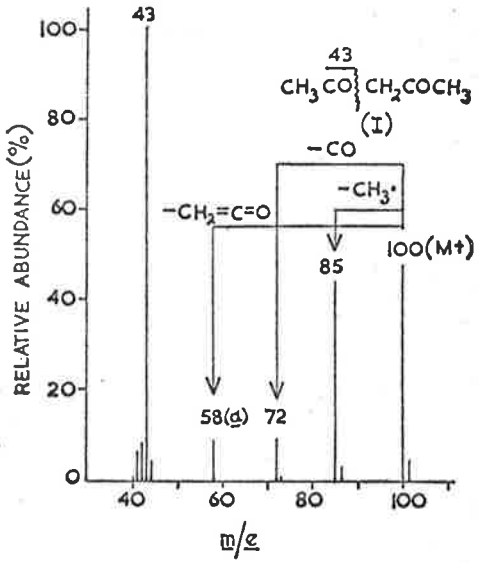


Figure 1.

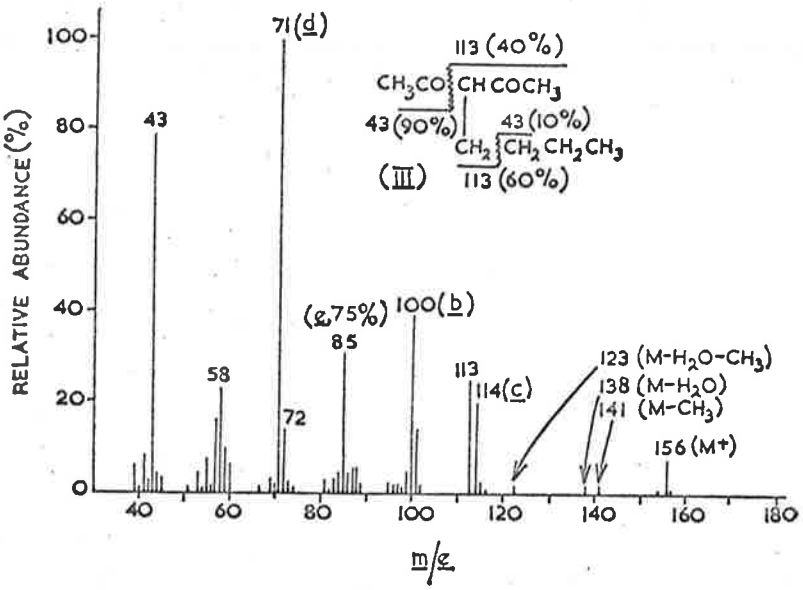
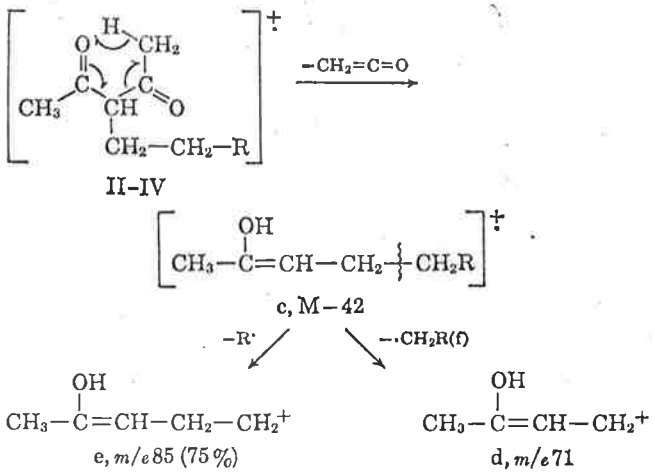


Figure 2.

SCHEME II



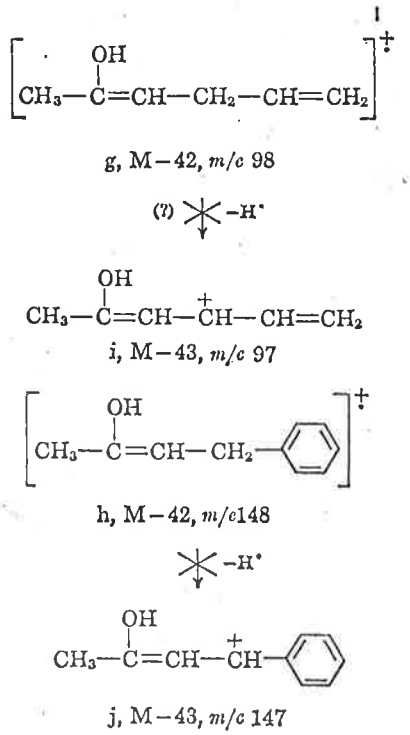
allylic bond in the enol c can then lead to the ion d (*m/e* 71, $C_4H_7O^+$ by HR) *via* elimination of the radical f (R = C_2H_5), although some homoallylic cleavage to give *m/e* 85, e, also occurs.

If the substituent is one which precludes the decomposition path indicated in Scheme I, as in the allyl derivative V and the benzyl derivative VI,[7] then the elimination of ketene to give an analog of c (Scheme II) is an important primary process. However, the M − 42 ions g and h (from V and VI, respectively) do not decompose by elimination of a vinyl radical, since either of these processes would necessitate the unfavorable cleavage of a vinylic bond. In principle, g and h (Scheme III) could each decompose by elision of a hydrogen radical to give stable M − 43 carbonium ions i and j (or its tropylium equivalent), respectively. However, the spectrum of the d_2-benzyl derivative VIa establishes that the abundant M − 43 ion in the spectrum of VI arises completely by simple loss of an intact acetyl group and not by the sequence $M^+ \rightarrow h \rightarrow j$.

(7) The inhibition of γ-hydrogen rearrangement in the spectrum of the allyl derivative V is consistent with the observation of a similar effect in the spectrum of 4-methylhept-6-en-3-one [L. Ahlquist, R. Ryhage, E. Stenhagen, and E. von Sydow, *Arkiv Kemi*, **14**, 211 (1959)]. The effect has been discussed by S. Meyerson and L. C. Leitch in a paper presented at the A.S.T.M. Committee E-14 Annual Conference on Mass Spectrometry, St. Louis, Mo., May, 1965.

Evidently, the relatively large amount of energy required to eliminate a hydrogen radical is not completely offset by the favorable nature of the hypothetical carbonium ion j. By analogy, the M − 43 ion from the allyl derivative V is probably also derived by direct loss of an acetyl radical and not *via* the sequence $V \rightarrow g \rightarrow i$. Both the M − 43 ions from V and VI decompose further by elimination of water to *m/e* 79 and *m/e* 129, respectively, as evidenced by appropriate metastable peaks.

SCHEME III



The spectra of the benzoyloxyacetylacetones examined (VII–IX) (Scheme IV) all contain pronounced M − CH_2=C=O ions (k, M − 42).[8] The formulation of k as an enol is consistent with, but not proved by,

(8) Processes supported by the presence of an appropriate metastable peak are indicated by an asterisk (*).

TABLE I

MASS SPECTRA OF SOME β-DIKETONES[a]

	Compd													
m/e	Ic[b]	II	IV	V	VI	VIa	VII	VIII	IX	X	Xa[c]	XI	XII	XVa[d]
39	12	6	8	5		3				11	6			5
40	9	8				4				4				
41	8	6	14	6	3	3			2	5	4			7
42	21	100	4							10				
43	100	16	100	100	56	100	13	13	9	57	23	22	12	7
44	37			2		7				5	11			15
45	5													
50						4	3	3		19	6	4	3	6
51						7	8	8	3	48	19	14	8	17
52						6				6	4			5
53		4	4	3		4								
55	4	5	10	4	3					5		6		5
56	4		3									4		4
57	4	4	3			4								6
58	9	8	13											
59	14		3											
60	6													
62					3									
63						5				7				
64						4				9				
65					4	4				4				
66						5				11				
67		6				7				4				
68			3							4				
69	3	5	15											
70	3		14							75	18			18
71		69	60	2						4	27			18
72	7	6	6											
73	15													
74	7													
75										8	6			
76										8	6			
77				2						8	6	4		5
78					6	6	22	22	20	83	47	50	28	48
79				3		10	3	3	3	19	13	8	3	11
80						6				5	5			5
81			3			5								
83				9									3	
85	39	8	22											
86	74	42	4							21	4			
87	38	3	3								6			
88	3		3								6			
89														
90										6				
91					28	5				4				
92					3	9				14	3		4	
93						24					5			4
94						5					4			
95		5	13			4								
97				20	4									
98			3	10		5								
99			3			5								
100	28	11	31											
101	58		15											
102	32													
103	3				5					5				
104					3	5				5				
105						8	100	100	100	100	100	100	100	100
106						6	9	11	9	9	11	17	9	12
107				2		22								
108						5								
109						4								
110			26			8								
111		3	4											
113		12	16											
115					3									
120										5		3		
121										7	5			
											6			4

Table I (*Continued*)

	Compd												
m/e	Ic[b]	II	IV	V	VI	VIa	VII	VIII	IX	X	Xa[c]	XI	XII	XVa[d]
122							3	3			7			4
125				2										
128		13(M)	11		3	3								
129					13	5								
130					3	10								
131					3	11								
132					5									
133						4						26		
134												24		
135						8								
136							3							
138				2										
140				3(M)										
144												6		
145												5		
146					3									
147					100					65	11			19
148					13	3	3			8	28			33
149						83					23	7		17
150						17					5	3		
151						3								
154									3					
155			3											
159													16	
160													7	
161										34	7	3		
162										74(M)	22			
163								5		9	41			
164											34			
165											13			
166											4			
170			5(M)											
172					3	2								
173						3								
175					4							5		
176												8(M)		
177						3								
178							13		2					
190					7(M)									
191									2					
192						6(M)								
201													3	
202													10(M)	
206								27						
207								3						3
208														3
209														3
220							3(M)							
223														27
224														76
225														75
226														33
227														6
234									18					
235									2					
248								2(M)						
276									2(M)					

[a] All ions having an abundance of 2% or greater relative to the base peak (100%) are recorded in the table. [b] $d_0 = 25$; $d_1 = 50$; $d_2 = 25\%$. [c] $d_0 = 17$; $d_1 = 45$; $d_2 = 35$; $d_3 = 3\%$. [d] $d_0 = 28$; $d_1 = 47$; $d_2 = 25\%$.

the facile cleavage of the allylic C–O bond in k to give *m/e* 105 (1, base peak for VII–IX) as evidenced by appropriate metastable peaks in the spectra of VIII and IX. Fragmentation sequences arising from the McLafferty rearrangement involving the alkyl chains of VIII and IX are not observed.

The spectra of benzoylacetone (X) and its alkyl derivatives XI–XIV, and of dibenzoylmethane (XV) (Figure 3), show several interesting features. First, those compounds (X, XV) which do not contain an alkyl substituent, or those (XI,XII) containing an alkyl substituent which cannot promote any facile

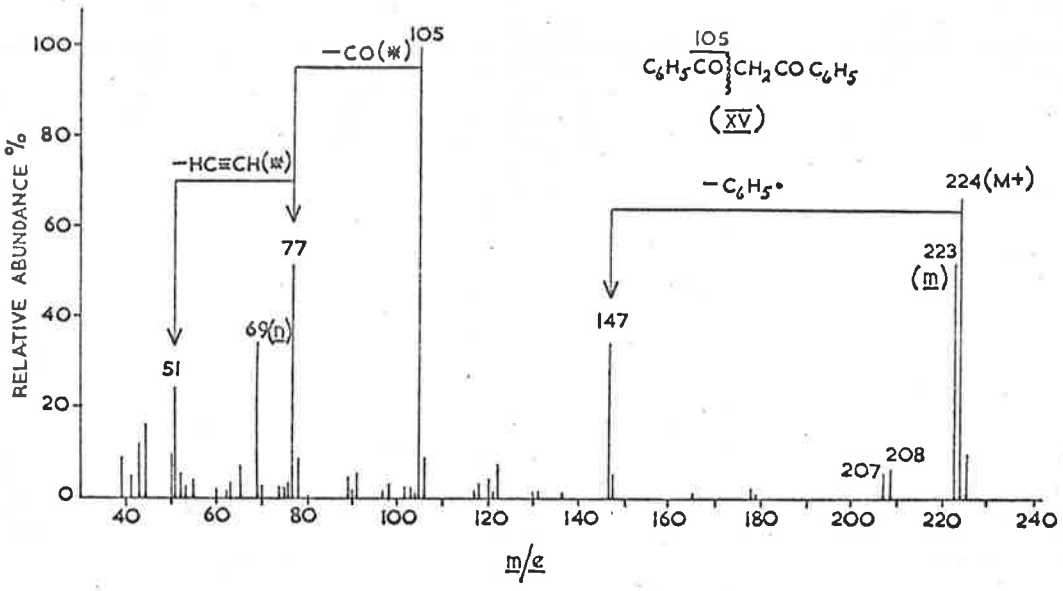


Figure 3.

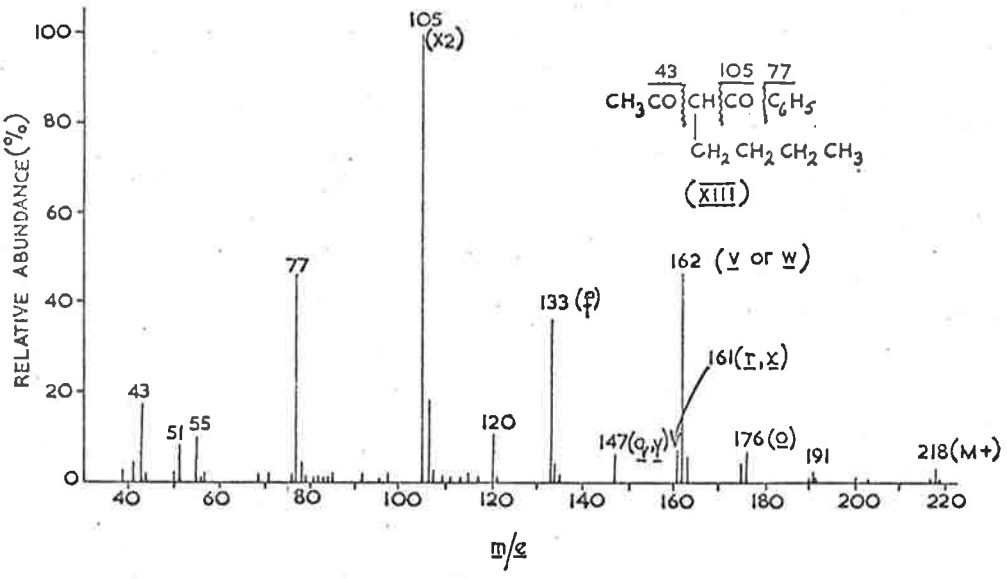
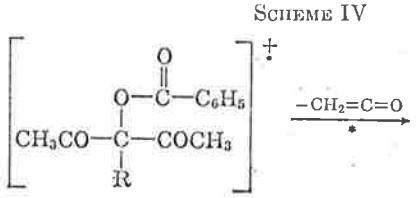
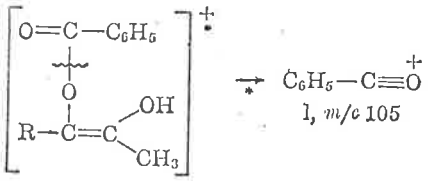


Figure 4.

SCHEME IV



VII, R = H
VIII, R = C_2H_5
IX, R = n-C_4H_9



k, M-42

cleavage processes, all afford mass spectra exhibiting pronounced M − 1 ions (see Figure 3). Corresponding abundant M − 1 ions are not observed in the spectra of acetylacetone and its derivatives; therefore, this phenomenon has been investigated with the aid of the spectra of d_2-benzoylacetone (Xa) and d_2-dibenzoylmethane (XVa). The spectrum of XVa establishes that the M − 1 peak is formed by loss of a hydrogen atom from one of the aromatic rings, whereas that of Xa establishes that the M − 1 peak does not involve loss of a hydrogen atom from the active methylene group. These observations are compatible with the correspondence of the M − 1 ion to a favorable oxonium species which may be formed by aromatic substitution (*e.g.*, m from XV). The remaining fragmentations of dibenzoylmethane (XV), summarized in Figure 3, are unexceptional apart from the formation of M − O (*m/e* 208) and M − OH (*m/e* 207) ions and a $C_3HO_2^+$ species (n, *m/e* 69).[9]

(9) The presence of M − O and M − OH ions in the spectrum (Figure 3) of XV is somewhat surprising. However, identical ions are quite abundant in the spectrum of the derived piperidine enamine [Ph-C(NC5H10)=C-CO-Ph] (which is obviously structurally related to the enol form of XV) and also in the spectra of other enamines derived from β-diketones (H. J. Jakobsen, S.-O. Lawesson, J. T. B. Marshall, G. Schroll, and D. H. Williams, *J. Chem. Soc.*, submitted for publication).

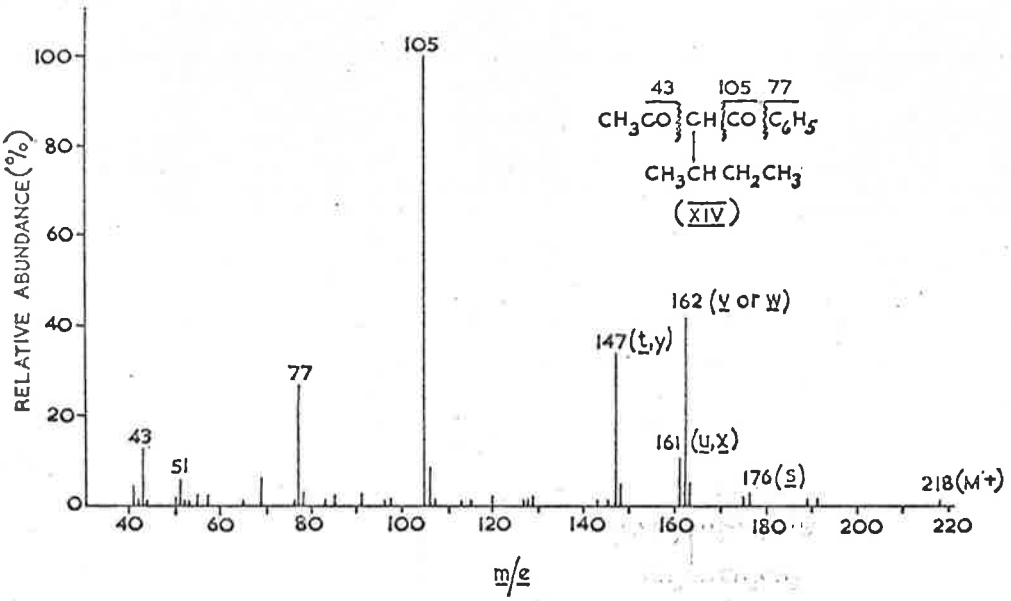


Figure 5.

The spectrum of benzoylacetone (X), in contrast with that of acetylacetone (I) (Figure 1) does not contain an M − CO ion which would establish the occurrence of a methyl or a phenyl migration. However, the presence of an *m/e* 91 ion (shifted to *m/e* 93 in the spectrum of Xa and due to the tropylium ion) in the spectrum of X proves that some phenyl migration to the active methylene group is taking place upon electron impact (see Scheme V).

SCHEME V

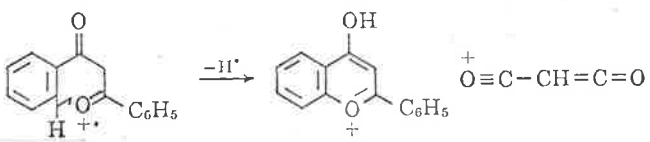
$C_6H_5-CO-CH_2-CO-CH_3$ (X)

$C_6H_5-CO-CH(R)-CO-CH_3$

XI, R = CH_3
XII, R = $CH_2-CH=CH_2$
XIII, R = $CH_2-CH_2-CH_2-CH_3$
XIV, R = $CH(CH_3)-CH_2-CH_3$

$C_6H_5-CO-CH_2-CO-C_6H_5$ (XV) $C_6H_5-CO-CD_2-CO-CH_3$ (Xa)

$C_6H_5-CO-CD_2-CO-C_6H_5$ (XVa)



m, M-1, *m/e* 223 n, *m/e* 69

Generally speaking, the spectra of benzoylacetone X and its substituted derivatives XI–XIV contain the benzoyl ion 1 (*m/e* 105) as base peak and M − CH_2=C=O (M − 42) peaks of variable intensity in the high-mass region. The pronounced fragmentation, by allylic cleavage, of the enolic M − 42 ions derived from alkylated β-diketones requires that the breakdown pattern should be dependent on the nature of α branching in the alkyl substituent. This can readily be seen to be the case on comparison of the spectra of the isomeric *n*-butyl and *sec*-butyl derivatives XIII (Figure 4) and XIV (Figure 5). The enolate ion o (*m/e* 176), which is produced by elimination of ketene from XIII, decomposes almost completely by loss of a propyl radical to p (*m/e* 133) and only to a very small extent by loss of an ethyl radical to q (25% of *m/e* 147) or by loss of a methyl radical to r (5% of *m/e* 161) as indicated in Scheme VI. In sharp contrast, *m/e* 133 is completely absent in the spectrum (Figure 5) of XIV, since the enolate ion s (*m/e* 176) can only eliminate an ethyl radical to give t (65% of *m/e* 147) or a methyl radical to furnish u (15% of *m/e* 161); the elimination of the larger alkyl group is of course greatly preponderant[10] (Scheme VII). The loss of the alkyl substituent from either XIII or XIV as a neutral olefin may occur with hydrogen rearrangement to the carbonyl group of the acetyl moiety or the benzoyl moiety. The resulting enolates v and w (*m/e* 162) can lose a hydrogen radical and a methyl radical (most plausibly, respectively) to account for the doublet nature of *m/e* 161 and *m/e* 147 in both spectra (see Scheme VIII). The compositions of all the ions discussed above have been established by high-resolution measurements.

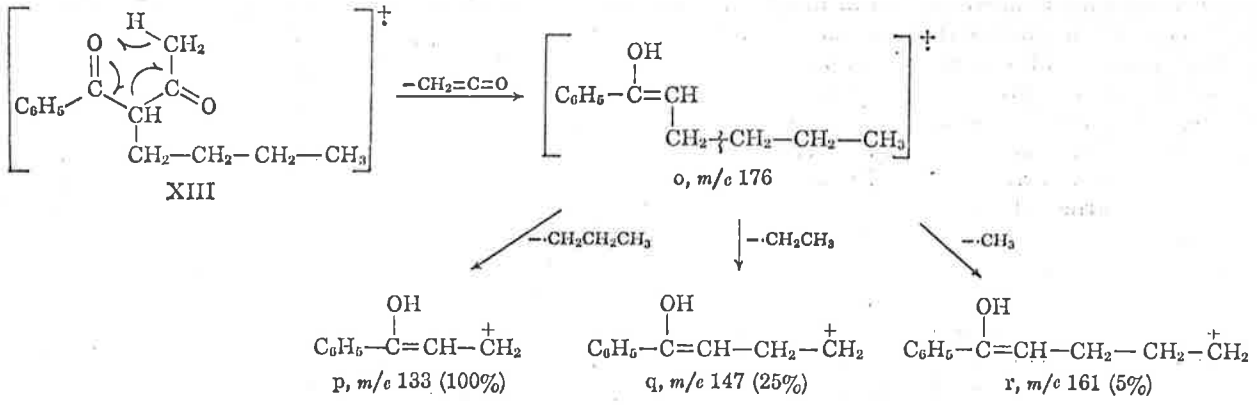
Experimental Section

All mass spectra were determined using an AEI MS 9 mass spectrometer operating at 70 ev. Samples were introduced through a heated inlet system at a temperature of *ca.* 150°. The spectra of d_2-benzoylacetone (Xa) and d_2-dibenzoylmethane (XVa) were obtained by introducing the parent diketones into the inlet system of the spectrometer with deuterium oxide.[11] d_2-Benzyl alcohol, which was required as an intermediate in the preparation of d_2-benzylacetylacetone (VIa), was prepared by

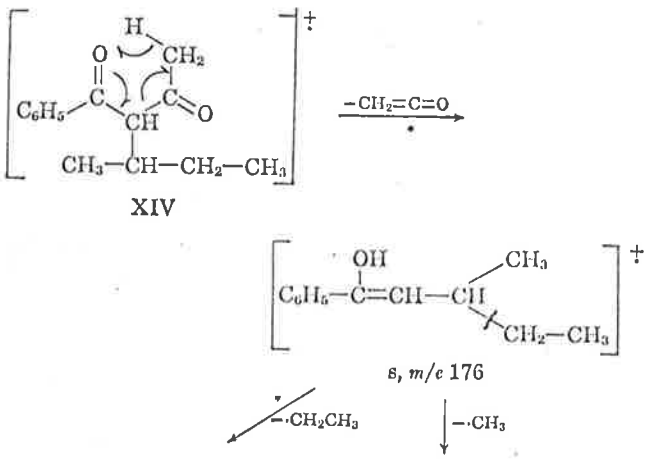
(10) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, p 29.

(11) J. S. Shannon, *Australian J. Chem.*, **15**, 265 (1962).

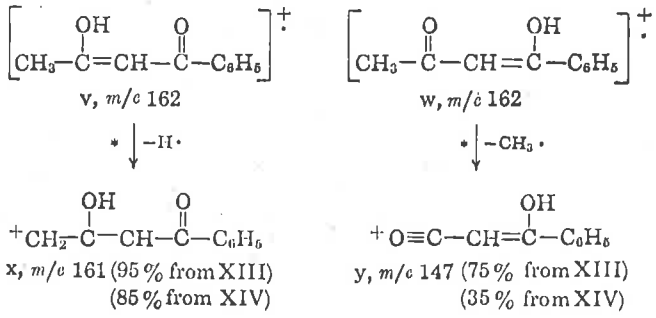
SCHEME VI



SCHEME VII



SCHEME VIII



reduction of ethyl benzoate with lithium aluminium deuteride.[12]

Acknowledgments.—One of us (J. H. B.) is grateful for the award of an Imperial Chemical Industries Post Doctoral Fellowship. Thanks are also expressed to Lucidol Division, Wallace and Tiernan, Inc., Buffalo, New York, for a grant which supported this work.

(12) R. L. Letsinger and D. F. Pollart, *J. Am. Chem. Soc.*, **78**, 6079 (1956).

Studies in Mass Spectrometry. X.[1] High-Resolution Mass Spectra of Cyanoacetates. Alkyl Migrations upon Electron Impact

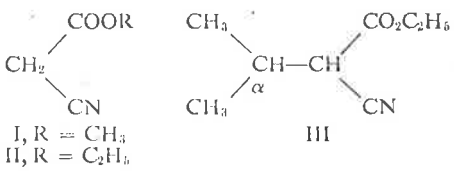
J. H. Bowie,[2] R. Grigg,[2] S.-O. Lawesson,[3] P. Madsen,[3] G. Schroll,[3] and D. H. Williams[2]

Contribution from the University Chemical Laboratory, Cambridge University, Cambridge, England, and the Department of Organic Chemistry, Aarhus University, Aarhus C, Denmark. *Received November 8, 1965*

Abstract: The mass spectra of a number of methyl and ethyl cyanoacetates have been determined and interpreted by means of high-resolution measurements and deuterium labeling. Important fragmentation paths upon electron impact occur by elimination of the elements of CO_2 from the ester group with an associated methyl or ethyl migration.

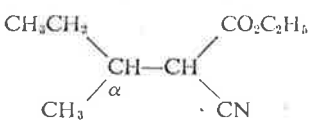
The fragmentation reactions of aliphatic cyanides upon electron impact are relatively complicated.[4-6] A study of cyanoacetates has now been undertaken to see if these compounds behave in a simple manner analogous to other active methylene compounds (β-keto esters,[7] diethyl malonates,[8] and β-diketones[9]), or if the complex behavior of aliphatic cyanides is exhibited.

The mass spectra of methyl cyanoacetate (I), ethyl cyanoacetate (II), and the alkyl derivatives III–VII have been determined and are illustrated in Figures 1–7. Generally speaking, these spectra contain low-abundance molecular ions and frequently appreciable M + 2 peaks, in contrast to alkyl cyanides, which exhibit M − 1 and M + 1 peaks in their mass spectra.[4-6]

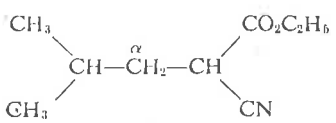


I, R = CH_3
II, R = C_2H_5

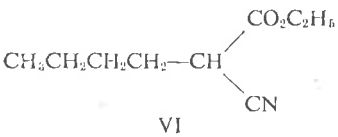
III



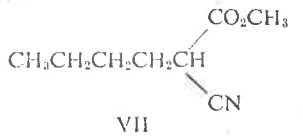
IV



V

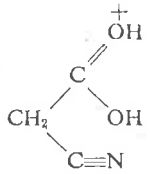


VI

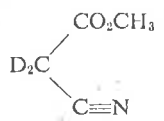


VII

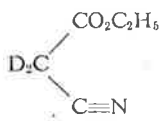
Conventional fragmentation processes which are evident in the mass spectra (Figures 1 and 2) of methyl cyanoacetate (I) and ethyl cyanoacetate (II) are summarised in the figures;[10] the elimination of C_2H_3 from the ethyl group of II can occur with the formation of the protonated acid ion a.[11] However, high-resolution measurements uncover two very unusual features in these spectra, namely, that I can decompose by loss of CO_2 to *m/e* 55 ($C_3H_5N^+$) (and hence by loss of a hydrogen radical to *m/e* 54 ($C_3H_4N^+$)), while II can eliminate HCO_2 to afford *m/e* 68 ($C_4H_6N^+$ (10% of the base peak intensity), the remaining 90% of this peak arising *via* elimination of the ethoxyl group to give $C_3H_2NO^+$). These processes necessitate interesting alkyl migrations of a methyl group and an ethyl group (or ethylene or its equivalent), respectively, upon electron impact. All the fragmentation reactions proposed for I and II are supported by the spectra of the partially deuterated derivatives Ia and IIa, which were obtained by introduction of the esters into the inlet system of the spectrometer with deuterium oxide.[12]



a, *m/e* 86



Ia, d_0 = 43%
d_1 = 36%
d_2 = 21%



IIa, d_0 = 20%
d_1 = 41%
d_2 = 39%

Fragmentation processes which necessitate the elimination of CO_2 with an associated alkyl migration[13] are extremely important in the spectra of ethyl isopropylcyanoacetate (III, Figure 3a), the isomeric butyl derivatives IV, V, and VI (Figures 4, 5, and 6), and of methyl *n*-butylcyanoacetate (VII, Figure 7). The compositions of the fragment ions associated with many of the intense peaks in these spectra have been determined by exact mass measurements and are summarized in Table I. A list of relevant metastable ions occurring in the spectra of III–VII is given in Table II, which gives both observed and calculated values.

(1) Part IX: see ref 9.
(2) University Chemical Laboratory, Cambridge, England.
(3) Department of Organic Chemistry, Aarhus University, Aarhus, Denmark.
(4) F. W. McLafferty, *Anal. Chem.*, 34, 26 (1962).
(5) R. Beugelmans, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, 86, 1386 (1964).
(6) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964.
(7) J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams, *J. Am. Chem. Soc.*, 87, 5742 (1965).
(8) J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams, *J. Org. Chem.*, in press.
(9) J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams, *ibid.*, in press.
(10) Throughout this paper, transitions supported by an appropriate metastable peak are indicated by an asterisk (*).
(11) See, for example, A. G. Harrison and E. G. Jones, *Can. J. Chem.*, 43, 960 (1965).
(12) J. S. Shannon, *Australian J. Chem.*, 15, 265 (1962).
(13) For additional examples of the decomposition of esters by elimination of CO_2 upon electron impact, see J. H. Bowie, R. Grigg, D. H. Williams, S.-O. Lawesson, and G. Schroll, *Chem. Commun.* (London), 403 (1965), and P. Natalis and J. L. Franklin, *J. Phys. Chem.*, 69, 2943 (1965).

[Reprinted from the Journal of the American Chemical Society, 88, 1699 (1966).]

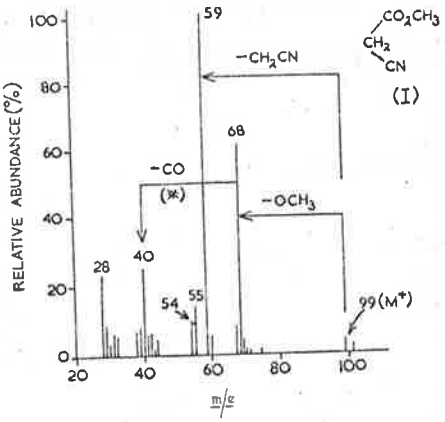


Figure 1. Mass spectrum of methyl cyanoacetate (I).

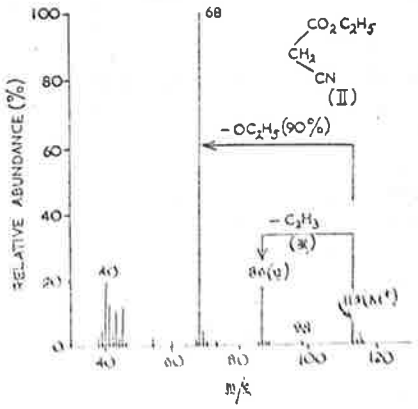


Figure 2. Mass spectrum of ethyl cyanoacetate (II).

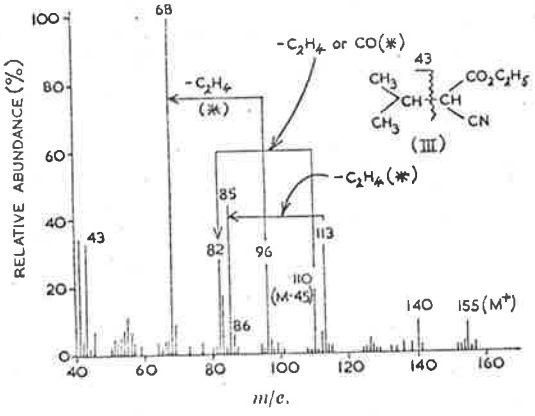


Figure 3a. Mass spectrum of ethyl isopropylcyanoacetate (III).

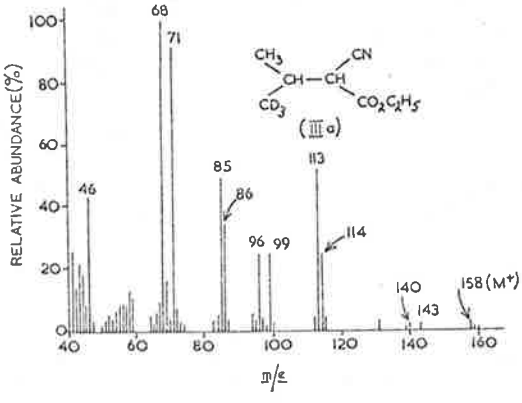


Figure 3b. Mass spectrum of ethyl d_a-isopropylcyanoacetate (IIIa).

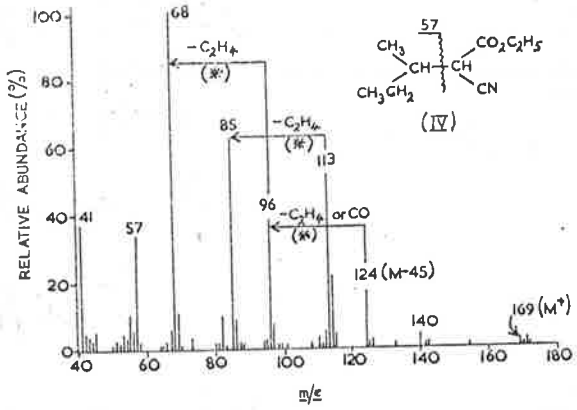


Figure 4. Mass spectrum of ethyl *sec*-butylcyanoacetate (IV).

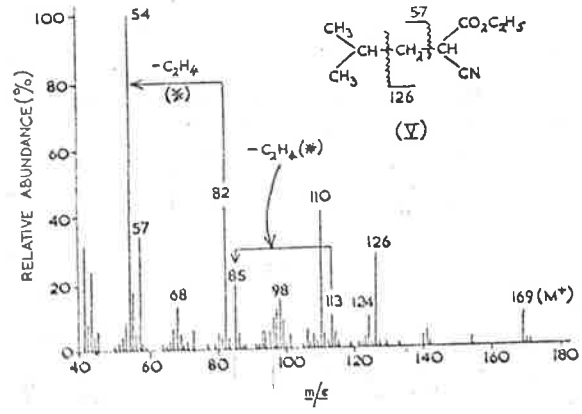


Figure 5. Mass spectrum of ethyl isobutylcyanoacetate (V).

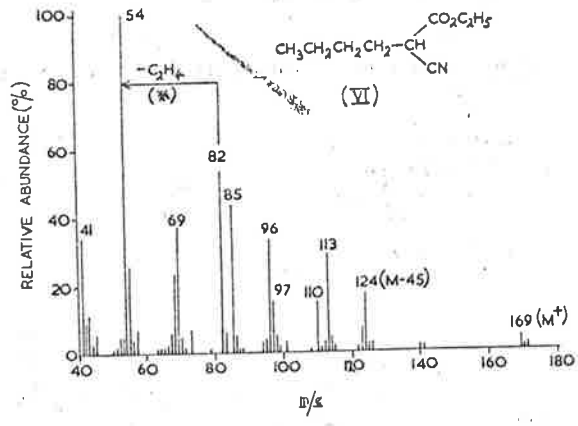


Figure 6. Mass spectrum of ethyl *n*-butylcyanoacetate (VI).

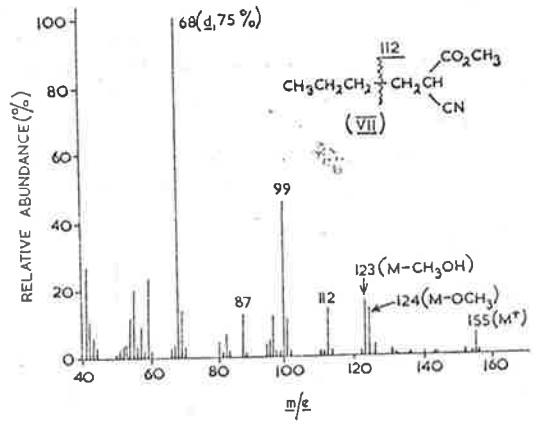


Figure 7. Mass spectrum of methyl *n*-butylcyanoacetate (VII).

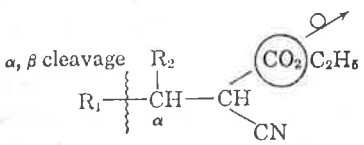
Table I. Compositions of Some of the Major Fragment Ions in the Mass Spectra of the Cyanoacetates III–VII

m/e values	Compound, % III	IV	V	VI	VII
54			C_3H_4N	C_3H_4N	
57		C_4H_9	C_4H_9		
68	C_4H_6N, 80 C_3H_2NO, 20	C_4H_6N	C_3H_2NO, 65 C_4H_6N, 35	C_4H_6N, 65 C_3H_2NO, 35	C_4H_6N, 75 C_3H_2NO, 25
69				C_4H_7N, 60 C_5H_9, 40	
82	C_6H_8N		C_5H_8N	C_5H_8N	
85	$C_3H_3NO_2$	$C_3H_3NO_2$	$C_3H_3NO_2$	$C_3H_3NO_2$	
87					$C_4H_7O_2$
96	$C_6H_{10}N$	$C_6H_{10}N$	$C_6H_{10}N$	$C_6H_{10}N$	
97			$C_6H_{11}N$, 80 C_6H_9O, 20		
98			$C_4H_4NO_2$		
99					$C_4H_5NO_2$
110	C_6H_8NO, 65 $C_7H_{12}N$, 35		$C_7H_{12}N$	$C_7H_{12}N$	
112					$C_6H_6NO_2$
113	$C_6H_7NO_2$	$C_6H_7NO_2$			
123					C_7H_9NO
124		$C_7H_{10}NO$, 80 $C_8H_{14}N$, 20		$C_7H_{10}NO$, 83 $C_8H_{14}N$, 17	

Table II. Some Metastable Ions (Calculated and Observed Values) Found in the Spectra of III–VII

Compd	Obsd	Calcd	Transition
III	64.0	63.9	113 → 85
	61.2	61.1	110 → 82
	48.1	48.2	96 → 68
IV	74.5	74.5	124 → 96
	64.0	63.9	113 → 85
	48.1	48.2	96 → 68
V	76.1	76.2	126 → 98
	64.0	63.9	113 → 85
	35.5	35.6	82 → 54
VI	35.5	35.6	82 → 54
VII	73.5	73.4	123 → 95

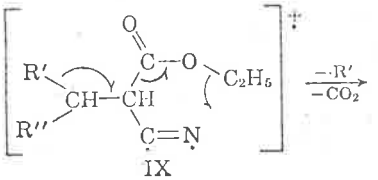
The most outstanding difference between the spectra (Figures 3–6) of the substituted ethyl cyanoacetates (III–VI) is that V and VI, which have no α branching in the alkyl substituent, give rise to base peaks at *m/e* 54 ($C_3H_4N^+$), while III and IV, which are α branched (with a methyl substituent at the branched α position), afford base peaks at *m/e* 68 ($C_4H_6N^+$ (80%) and $C_4H_6N^+$ (100%) from III and IV, respectively). Metastable peaks at 35.5 in the spectra of V and VI indicate that the $C_3H_4N^+$ ions (*m/e* 54) are formed by elimination of ethylene from a $C_5H_8N^+$ species (*m/e* 82), whereas metastable peaks at 48.1 in the spectra of III and IV likewise establish the formation of the $C_4H_6N^+$ ions (*m/e* 68) from $C_6H_{10}N^+$ ions (*m/e* 96), again by elimination of ethylene (see Figures 3–6). Evidently, the most pronounced decomposition pathway of V and VI upon electron impact is *via* the over-all elimination of C_3H_7 and CO_2 to *m/e* 82 ($C_5H_8N^+$) (and hence by loss of ethylene to *m/e* 54), whereas III and IV prefer to eliminate (CH_3 + CO_2) and (C_2H_5 + CO_2), respectively, to give *m/e* 96 ($C_6H_{10}N^+$) and subsequently *m/e* 68 by loss of ethylene. Hence, it may be seen that the spectra can only be interpreted in a self-consistent manner if the major fragmentation mainly involves the loss of CO_2 from the ester group (with an accompanying ethyl migration) and associated cleavage of the C(α)–C(β) bond in the alkyl substituent to eliminate the larger available radical (see VIII).



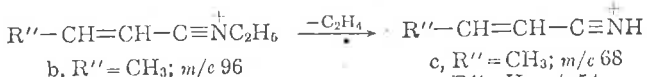
VIII

III, $R_1 = R_2 = CH_3$
IV, $R_1 = C_2H_5$; $R_2 = CH_3$
V, $R_1 = i\text{-}C_3H_7$; $R_2 = H$
VI, $R_1 = n\text{-}C_3H_7$; $R_2 = H$

The apparent occurrence of such remarkable rearrangement processes requires supporting evidence. It should be pointed out that the formation of a $C_6H_{10}N^+$ ion (*m/e* 96, M − CH_3CO_2) in the spectrum (Figure 3a) of III demands some kind of alkyl migration from the ethyl group of the ester. The spectrum (Figure 3b) of the trideuterio derivative of III (IIIa) establishes that the intact ethyl group migrates and that a terminal methyl group is lost from the isopropyl substituent. The observation that the *m/e* 68 and *m/e* 96 peaks of Figure 3a are both split into *m/e* 68/71 and *m/e* 96/99 doublets in Figure 3b indicates that in the transition *m/e* 96 → *m/e* 68 ethylene is expelled from the ethyl group which was originally part of the ester. While any mechanistic proposals concerning these migrations must be regarded as speculative, it seems very reasonable to implicate the cyano group in the rearrangement step, since such processes have not been noted in the spectra of simple esters. One possibility is that the energy of the electron bombardment is sufficient to uncouple a pair of π electrons of the cyano group, and then the elimination of an alkyl radical R′ and CO_2



IX



b, R″ = CH_3; *m/e* 96
R″ = H; *m/e* 82

c, R″ = CH_3; *m/e* 68
R″ = H; *m/e* 54

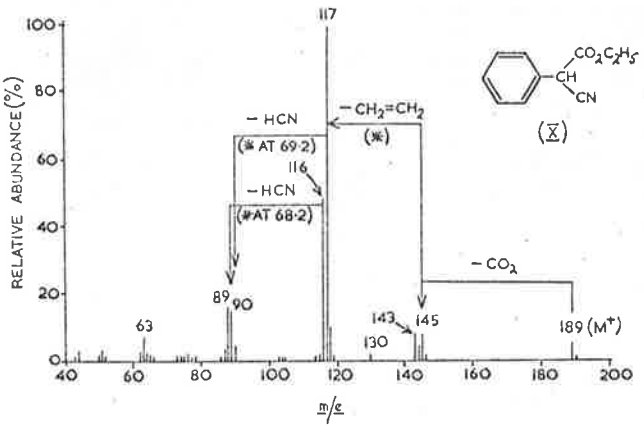
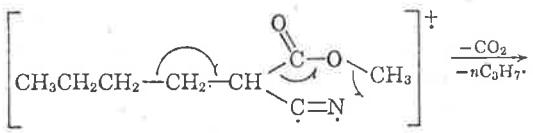


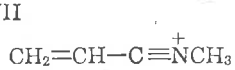
Figure 8. Mass spectrum of ethyl phenylcyanoacetate (X).

can occur with associated ethyl migration to nitrogen (IX → b); subsequent loss of ethylene may then afford c. Hence *m/e* 96 and *m/e* 68 will result when R'' = CH_3 (from III and IV), and *m/e* 82 and *m/e* 54 when R'' = H (from V and VI).

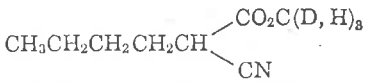
Additional evidence for this type of rearrangement has been sought in the mass spectrum (Figure 7) of methyl *n*-butylcyanoacetate (VII). On the basis of the spectrum (Figure 6) of the corresponding ethyl ester (VI), the base peak in the spectrum of VII should be anticipated at *m/e* 68 ($C_4H_6N^+$) perhaps corresponding to structure d. It should be noted that d is not, of course, able to eliminate ethylene and, in addition, no loss of methylene from d is anticipated since this is known to be an energetically unfavorable process.[14] In fact, *m/e* 68 is the base peak of Figure 7 and has been shown by exact mass measurements to correspond to the extent of 75% to $C_4H_6N^+$ (see Table I). Moreover, in the spectrum of the partially deuterated ester VIIa, prepared by esterification of the acid with diazomethane in the presence of deuterium oxide,[15] the $C_4H_6N^+$ ion retains the isotopic label, thus unequivocally establishing the methyl migration.



VII

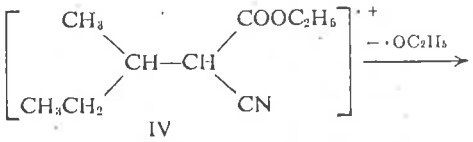


d, *m/e* 68

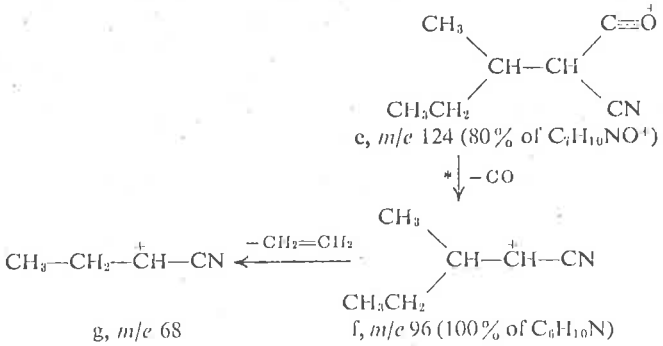


VIIa, $d_0 = 38\%$; $d_1 = 38\%$; $d_2 = 20\%$; $d_3 = 4\%$

However, there is no definite evidence that the formation of the ions represented by b and d occurs in a one-step process. Indeed, in the spectrum (Figure 4) of IV there is some evidence that ions corresponding to b *in composition* cannot arise completely *via* a one-step process. In this case (Figure 4), a metastable peak indicates that *m/e* 96 ($C_6H_{10}N^+$) can arise, at least in part, by elision of ethylene from $C_8H_{14}N^+$ (20% of *m/e* 124, M − CO_2H) or loss of carbon monoxide from $C_7H_{13}NO^{+\cdot}$ (80% of *m/e* 124, M − OC_2H_5). It is therefore possible that in the spectrum of IV some portion of the *m/e* 68 ion is formed by the more conventional sequence IV → e → f → g.



IV



e, *m/e* 124 (80% of $C_7H_{10}NO^+$)

g, *m/e* 68

f, *m/e* 96 (100% of $C_6H_{10}N$)

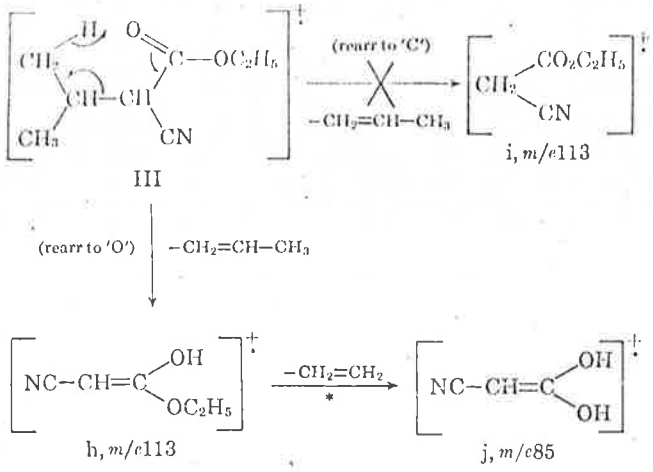
In the spectra (Figures 3a, 4, and 5) of III, IV, and V the M − 45 ions were of sufficient abundance to warrant investigation by exact mass measurements. The results (Table I) establish that in all three spectra extremely unusual M − HCO_2 ions accompany the anticipated M − OC_2H_5 fragments; the formation of the former group again requires an ethyl (or ethylene) migration from the ester, perhaps in a manner similar to that discussed previously. Finally the *m/e* 110 ions ($C_7H_{12}N^+$; M − CH_3CO_2) furnished by V and VI are presumably formed by related rearrangement processes (perhaps loss of carbon dioxide and a terminal methyl group in each case).

More conventional fragmentation processes which are evident from the spectra of these cyanoacetates merit brief comment. The spectra of all the substituted ethyl esters (III–VI) contain fairly abundant *m/e* 113 ions, shown by representative exact mass measurements (Table I) to arise through the elimination of the alkyl substituent (presumably as the olefin) with hydrogen rearrangement. The hydrogen atom involved in the rearrangement originates from the β-carbon atom of the alkyl group in the spectrum (Figure 3a) of III, as may be seen on examination of Figure 3b.[16] Probably a McLafferty rearrangement is operative (see III → h), although hydrogen rearrangement to nitrogen cannot be excluded. However, hydrogen rearrangement to carbon (see III → i) to give the ethyl cyanoacetate molecular ion is untenable, because the *m/e* 113 ions decompose by explusion of ethylene to an *m/e* 85 species ($C_3H_3NO_2^+$, see Table I and Figures 3a, 4, and 5), in contrast to the behavior of the ethyl cyanoacetate molecular ion which eliminates C_2H_3 to afford *m/e* 86 (see Figure 2). A plausible representation for the *m/e* 85 ions is j, although it should be noted that they do not show any marked tendency to eliminate water (contrast the decomposition of analogous ions from β-keto esters[7] and diethyl malonates[8]).

(14) For a summary of the isolated examples of loss of CH_2 from the parent ion of a hydrocarbon, see S. Meyerson, *J. Am. Chem. Soc.*, 85, 3340 (1963).

(15) K. J. van der Merwe, P. S. Steyn and S. H. Eggers, *Tetrahedron Letters*, 3923 (1964).

(16) The shifts which can be discerned on comparison of Figures 3a and 3b are *m/e* 110 → *m/e* 113 and *m/e* 113 → *m/e* 114 (~50%), while approximately 50% of *m/e* 113 is not shifted, because either a CH_3 or CD_3 group may participate in the rearrangement process.



The mass spectrum (Figure 8) of ethyl phenylcyanoacetate (X) has been briefly mentioned in an earlier communication.[17] The *m/e* 145 ion is formed by elimination of CO_2 from the molecular ion and can then lose a methyl radical or ethylene (from the ethyl group at its new site of attachment) to give *m/e* 130 and *m/e* 117, respectively. However, there is no evidence for additional rearrangement ions in this spectrum, the *m/e* 143 and *m/e* 144 ions arising by simple loss of ethanol and an ethoxyl radical, respectively. It is of course possible for the *m/e* 117 ion ($M - CO_2C_2H_4$) to arise in part other than *via* a skeletal rearrangement pathway, but, regardless of its mode of formation, a portion of this $C_8H_7N^+$ ion does have the structure of the benzyl cyanide molecular ion, as evidenced by the very similar spectra of the two compounds below *m/e* 117 and identical metastable peaks at *m/e* 88.5, *m/e* 69.2, and *m/e* 68.2.

(17) See the first reference quoted in footnote 13.

Experimental Section

All mass spectra were obtained on an AEI MS 9 mass spectrometer operating at 70 ev. Samples were introduced into the ion chamber through a heated inlet system operating at approximately 150°.

Exact mass measurements were performed either against reference masses in the spectrum of heptacosafluorotributylamine or against ions of previously established composition in the spectrum of the cyanoacetate itself. The measurements were performed at a resolving power of approximately 15,000 (10% valley definition) and calculated and observed values were always in agreement within 15 ppm, thus rigorously excluding alternative compositions.

Methyl cyanoacetate (I) and ethyl cyanoacetate (II) were commercial samples. Known procedures were employed for the preparation of ethyl propylcyanoacetate (III),[18] ethyl *sec*-butylcyanoacetate (IV),[19] ethyl isobutylcyanoacetate (V),[20] ethyl *n*-butylcyanoacetate (VI),[20] and ethyl phenylcyanoacetate (X).[21] Ethyl (3-trideuteriomethyl)ethylcyanoacetate (IIIa, bp 95.5–96.5° (12 mm), $n^{25}D$ 1.4215) was prepared by a Grignard reaction, using the addition of trideuteriomethylmagnesium iodide to ethyl ethylidenecyanoacetate.

Methyl *n*-butylcyanoacetate (VII, bp 111° (11 mm), $n^{20}D$ 1.4281) was available by alkylation of methyl cyanoacetate in methanol. *Anal.* Calcd for $C_8H_{13}NO_2$: C, 61.95; H, 8.44; N, 9.03. Found: C, 61.74; H, 8.55; N, 8.98.

All compounds were distilled at least twice and their purities were checked by nuclear magnetic resonance, infrared, and mass spectroscopy, and also by vapor phase chromatography. The analysis was performed by Alfred Bernhardt, Mülheim (Ruhr), Germany.

Acknowledgment. One of us (J. H. B.) is grateful for the award of an ICI Postdoctoral Fellowship.

(18) E. Fischer and E. Flatau, *Chem. Ber.*, **42**, 2981 (1909).
(19) P. E. Gagnow, U. Savard, R. Gaudry, and E. M. Richardson, *Can. J. Res.*, **25**, 30 (1947).
(20) J. C. Hessler and W. F. Henderson, *J. Am. Chem. Soc.*, **43**, 672 (1921).
(21) S. Widequist, *Arkiv Kemi Mineral Geol.*, **24B**(14) (1947).

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Studies in Mass Spectroscopy

Part XI.* Mass Spectra of 1,4-Dicarbonyl Compounds

S.-O. LAWESSON, J. Ø. MADSEN, G. SCHROLL

Department of Organic Chemistry, Aarhus University, Aarhus C, Denmark

J. H. BOWIE, R. GRIGG and D. H. WILLIAMS

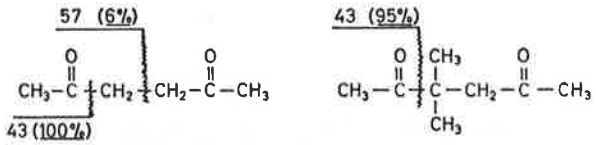
University Chemical Laboratory, Cambridge, England

The mass spectra of a series of γ-diketones and γ-ketoesters have been determined and interpreted with the aid of high resolution measurements. The spectra all contain molecular ions and are virtually free of skeletal rearrangement fragments. The fragmentation patterns are greatly dependent on the nature and location of substituents and hence mass spectrometry can be a great aid to structure determination in this class of synthetically important compounds.

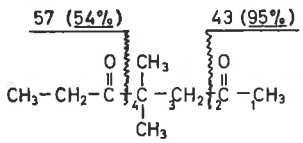
1,4-Dicarbonyl compounds are substances of considerable synthetic importance, especially as precursors in the synthesis of furans, thiophenes, pyrroles, and γ-lactones. In the light of this synthetic importance, we have undertaken a study of the mass spectra of some γ-diketones and γ-ketoesters in the hope that mass spectrometry will serve as a useful method to characterise such compounds. Some details of the spectra (see Tables 1 and 2 and Figs. 1—6) of representative γ-diketones (I—IV), and γ-ketoesters (V—XIII) are discussed in this paper.

Generally speaking, all the compounds studied give molecular ions which are easily recognised. Moreover, exact mass measurements on a number of ions in many of the spectra have uncovered only a single composition which requires a skeletal rearrangement upon electron impact. Hence, the spectra of these diketones and ketoesters can be interpreted by reference to the more abundant ions, without the complications introduced by the skeletal rearrangements recently observed to occur in some compounds.[1–6]

* Part X: Bowie, J. H., Grigg, R., Lawesson, S.-O., Madsen, P., Schroll, G. and Williams, D. H. *J. Am. Chem. Soc.* **88** (1966) 1699.



I II



III

Details of the mass spectra on the γ-diketones I—III are summarised in Table 1 and in the formulae (I—III); in those cases where the composition of the ion has been established by exact mass measurements, the relative abundance are underlined.

It should be pointed out that the base peak *m/e* 43 ions from II and III are doublets, the complements to $CH_3C{\equiv}O^+$ being associated with $C_3H_7^+$ ions (5 % in both cases); this observation is understandable since II and III (in contrast to I) contain intact C-3 units carrying sufficient hydrogen atoms to afford a $C_3H_7^+$ species by two bond cleavages and a hydrogen rearrangement. Similarly, *m/e* 57 from III has a small hydrocarbon ($C_4H_9^+$) contribution (which brings the total abundance of this ion to 62 %) that can arise in a similar manner.

In these compounds (I—III) cleavage of the centre carbon-carbon bond between the carbonyl groups does not seem to be a favourable process unless a substituted carbonium ion can be formed by such a cleavage. Thus, I gives only a low abundance ion (*m/e* 57) due to rupture of the centre C—C bond; this behaviour is probably associated with the unfavourable nature [7] of a primary carbonium ion adjacent to a carbonyl group (as in the $^+CH_2COR$

Table 1. Details of the mass spectra of some γ-diketones (I—III)

Compound	Relative abundances (%) of ions*							
	M+	M−CH_3	M−H_2O	M−C_2H_5	M−CH_2CO	M−CH_3CO	M−C_3H_4O	M−C_3H_5O
I	6	22	—	—	—	12	—	6
II	5	2	1	—	11	6	—	*29*
III	6	2	2	14	—	—	6	13

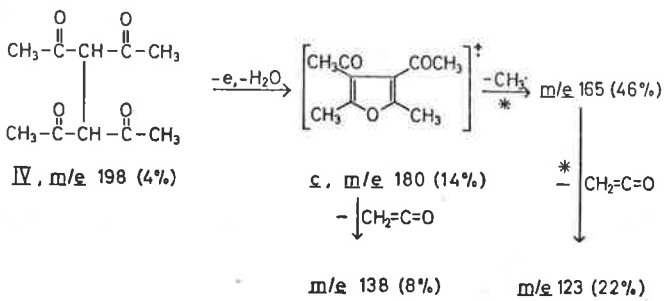
* Related to the base peak arbitrarily taken as 100 %.

a, m/e 85 (29%) b, m/e 57 (4%)

fragment). Moreover, II furnishes a prominent ion due to *a* (M — C_3H_5O, see Table 1) but a low abundance ion associated with *b*. Hence the major portion of the *m/e* 57 ion ($C_3H_5O^+$) from III can fairly confidently be ascribed to the cleavage indicated in III, rather than to rupture of the 3,4-bond.

The influence of a tertiary centre on the breakdown pattern is also evident from the finding that whereas II gives prominent M — CH_2CO and M — CH_3CO ions, III undergoes no such losses but gives only ions associated with the expulsion of an additional CH_2-group. Hence the M — CH_2CO and M — CH_3CO ions from II can be associated with the loss of the CH_3CO-group attached to the tertiary centre (with and without hydrogen rearrangement, respectively).

The majority of the fragmentation in the high mass region of the spectrum of 3,4-diacetylhexan-2,5-dione (IV) occurs from an M — H_2O ion (*m/e* 180) as established by appropriate metastable peaks. The importance of the M — H_2O ion in determining the fragmentation pattern suggests, but does not prove, that this ion may have an especially favoured structure. A plausible structure for the *m/e* 180 ion is the furan molecular ion *c*.* Regardless of the structure assigned to *m/e* 180, it decomposes by loss of the fragments indicated, as established by appropriate metastable peaks [indicated by an asterisk (*)]; the *m/e* values indicated in the scheme account for all ions of abundance greater than 6 % (relative to the *m/e* 43 base peak) above *m/e* 115.



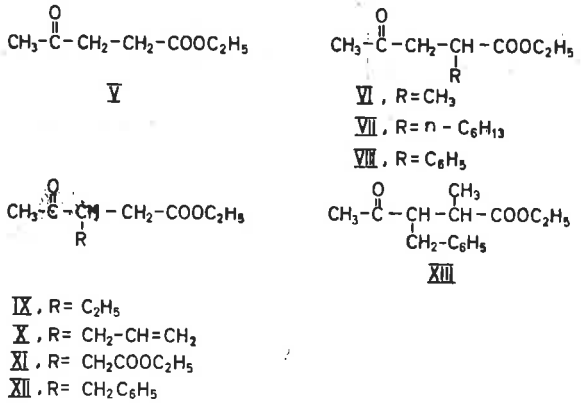
IV, m/e 198 (4%) c, m/e 180 (14%) m/e 165 (46%) m/e 138 (8%) m/e 123 (22%)

We now turn to a discussion of the spectra of ethyl laevulinate (V) and related compounds containing substituents α to the ester group (VI—VIII) or β to the ester group (IX—XII); one α,β-disubstituted ethyl laevulinate (XIII) has been studied. The composition of ions in Figs. 1—6 which have

* Molecular ions of furans do not necessarily have the structures of the furans in the ground state.[8] Some of the structures used in this paper are nominal only, but serve the important purpose of relating the fragmentation pattern to the structure of the intact molecule.

Table 2. Compositions of some ions in the spectra of V, VI, VIII, IX, XII, and XIII (Figs. 1—6), established by exact mass measurements.

Compound							
V	*m/e*	55	56	71	73	74	
	Comp.	C_3H_3O (90 %) C_4H_7 (10 %)	C_3H_4O	C_4H_7O	$C_3H_5O_2$	$C_3H_6O_2$	
VI	*m/e*	69	71	73	87	88	101
	Comp.	C_4H_5O	C_4H_7O	$C_3H_5O_2$ (80 %) C_4H_9O (20 %)	$C_4H_7O_2$	$C_4H_8O_2$	$C_5H_9O_2$
VII	*m/e*	171	183				
	Comp.	$C_{10}H_{19}O_2$	$C_{11}H_{19}O_2$				
IX	*m/e*	43	55	56	73	83	85
	Comp.	C_2H_3O	C_4H_7 (80 %) C_3H_3O (20 %)	C_4H_8	$C_3H_5O_2$ (85 %) C_4H_9O (15 %)	C_5H_7O	C_5H_9O
	m/e	101	115	126	127	130	144
	Comp.	$C_5H_9O_2$	$C_6H_{11}O_2$	$C_7H_{10}O_2$	$C_7H_{11}O_2$	$C_7H_{14}O_2$	$C_7H_{12}O_3$
XII	*m/e*	117	145	146	147	188	189
	Comp.	C_9H_9	$C_{10}H_9O$	$C_{10}H_{10}O$	$C_{10}H_{11}O$	$C_{12}H_{12}O_2$	$C_{12}H_{13}O_2$
XIII	*m/e*	43	131	147	148	159	173
	Comp.	C_2H_3O (85 %) C_3H_7 (15 %)	C_9H_7O (35 %) $C_{10}H_{11}$ (65 %)	$C_{10}H_{11}O$	$C_{10}H_{12}O$	$C_{11}H_{11}O$	$C_{12}H_{13}O$ (60 %) $C_{11}H_9O_2$ (40 %)
	m/e	174	177	178	202	203	
	Comp.	$C_{12}H_{14}O$ (60 %) $C_{11}H_{10}O_2$ (40 %)	$C_{12}H_{17}O$	$C_{12}H_{18}O$	$C_{13}H_{14}O_2$	$C_{13}H_{15}O_2$	



been substantiated by exact mass measurements are summarised in Table 2. Only the formation of $C_4H_9O^+$ (*m/e* 73), a minor fragment from (VI) and (IX), requires a skeletal rearrangement for its formation.

Some of the important fragmentations suffered by ethyl laevulinate (V) upon electron impact are summarised in Fig. 1. The elimination of ketene from the molecular ion gives rise to an ion at *m/e* 102 (Fig. 1) and it is of

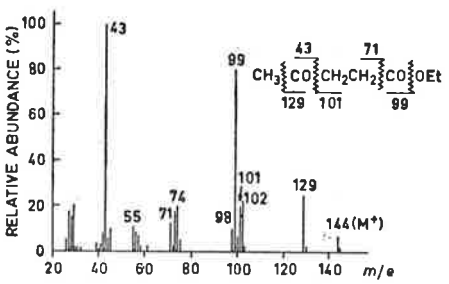
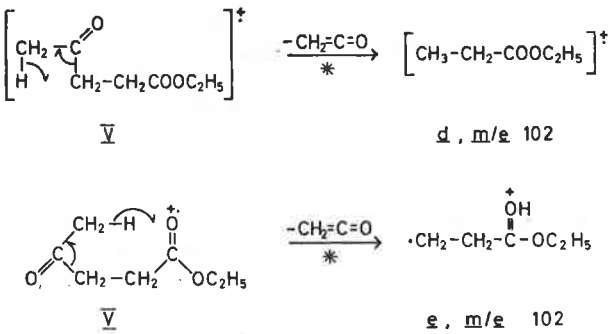


Fig. 1.

interest to try to determine whether the migrating hydrogen becomes bonded to carbon (V → *d*) or to oxygen (V → *e*) * when such fragmentations occur in γ-dicarbonyl compounds.

If the hydrogen migration occurred to carbon with the formation of the ethyl propionate molecular ion (*d*), then *m/e* 102 might be expected to decompose as does ethyl propionate in its mass spectrum [9] [*i.e.*, by loss of an ethoxyl radical to give *m/e* 57 (100 %, base peak) from the molecular ion (*m/e* 102, 16 %]. Far from being an abundant ion, *m/e* 57 is a very minor fragment in Fig. 1. Hydrogen rearrangement to oxygen (V → *e*) is therefore a plausible alternative. This latter mode has been shown to operate in the loss of ketene from derivatives of ethyl acetoacetate,[10] but it should be noted that in such

* A similar migration to the oxygen of the ethoxyl group is also feasible.



V d, m/e 102

V e, m/e 102

cases, the elimination can occur in a concerted manner *via* a six-membered cyclic transition state.

There is some evidence to support partial operation of the type of mechanism exemplified by V → *e* in the spectrum (Fig. 2a) of the ethyl derivative IX (all the major ions in this spectrum have been analyzed by exact mass measurements as indicated in Table 2). In this spectrum (Fig. 2a), the M — CH_2-CO ion (*m/e* 130) decomposes by loss of an ethyl group (metastable peak at 78.5) to give *m/e* 101. This behaviour is understandable if the ketene elimination is accompanied by a 1,2-hydrogen shift to generate the ionised enol *f* (*m/e* 130), which can then lose an ethyl group by allylic cleavage to give *g* (*m/e* 101). It is emphasised that the molecular ion of ethyl pentanoate (which would be generated by hydrogen migration to carbon) decomposes to some extent by loss of an ethyl radical, but mainly eliminates propylene (to give *m/e* 88) and an ethoxyl radical (to give *m/e* 85) as indicated in Fig. 2b; *m/e* 85 and *m/e* 88 are of relatively low abundance in Fig. 2a. McLafferty rearrangements [11] involving the ketone and ester carbonyl groups of IX (and a hydrogen atom from the methyl and methylene groups, respectively, of the ethyl substituent) may lead to the ions at *m/e* 144 (M — C_2H_4) and *m/e* 88 (M — CH_3CO — $CH{=}CH{-}CH_3$), but these processes do not dominate the fragmentation.

The important effect [9] of substituents on the prevalence of cleavage of the central C—C bond between the two carbonyl groups may be seen from a comparison of Figs. 3—6. The ion at *m/e* 101 in Fig. 3, which corresponds to

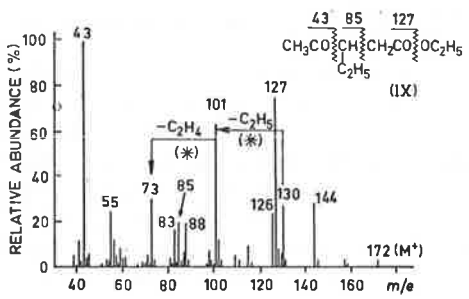


Fig. 2a.

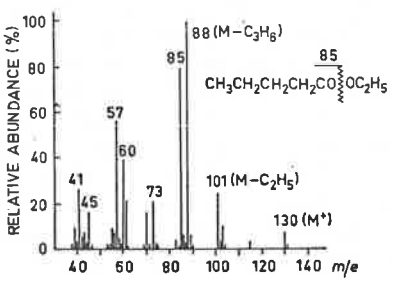
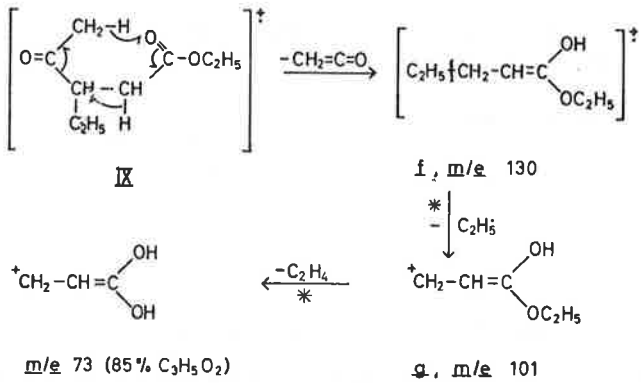


Fig. 2b.



a secondary carbonium ion, is much more abundant than *m/e* 57 (which would arise from a $CH_3COCH_2^+$ fragment). However, a *large* alkyl group has a much more profound influence than a simple methyl substituent, as may be seen from the base peak at *m/e* 171 from VII (Fig. 4), corresponding again to the forma-

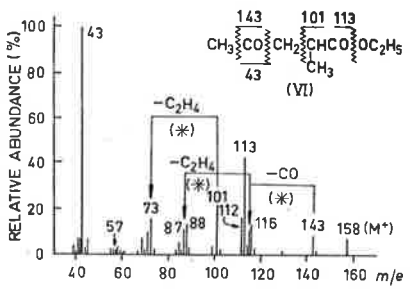


Fig. 3.

tion of a secondary carbonium ion. Similarly, the large benzyl substituents of XII and XIII promote the formation of *m/e* 147 ions as base peaks in the spectra (Figs. 5 and 6) of these compounds. The corresponding cleavage in

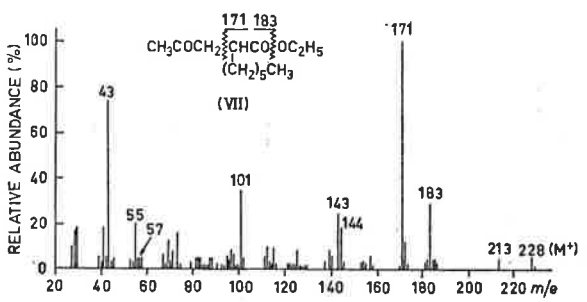
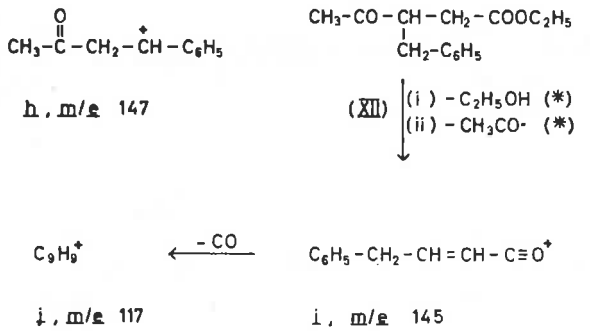


Fig. 4.



IX to give *m/e* 85 (see Fig. 2a) is not very pronounced, as it must be remembered that in the case of a benzyl group there is not only the possibility of group size causing secondary carbonium ion stabilisation, but also one of a 1,2-hydrogen shift accompanying the C—C bond fragmentation, so that *m/e* 147 may be stabilised as the benzylic cation *h* (or as a related tropylium ion).

The formation of the very abundant ion at *m/e* 145 in the spectrum (Fig. 5)

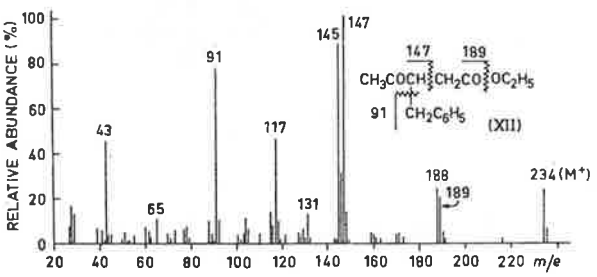


Fig. 5.

of XII is of some interest. Although exact measurements establish that loss of two hydrogen atoms from *m/e* 147 would give a fragment of the required composition, the shift of this ion to *m/e* 159 in the spectrum (Fig. 6) of XIII

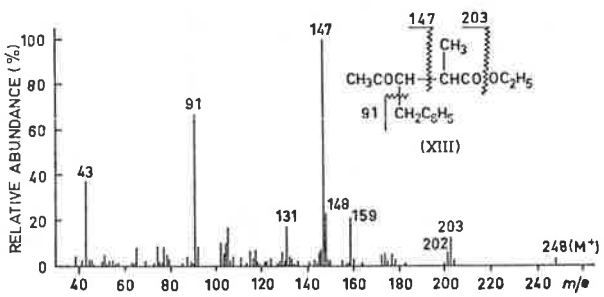
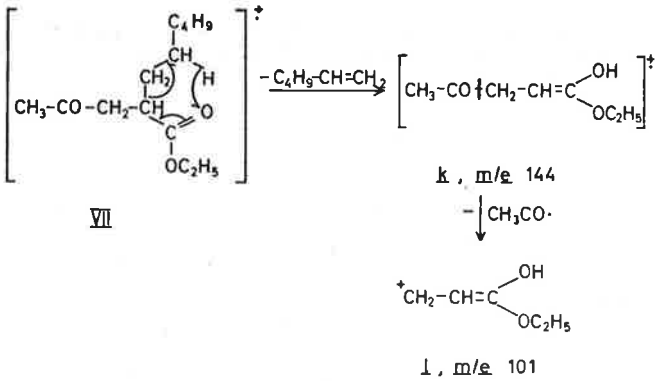


Fig. 6.



VII

necessitates the retention of the carbon atom adjacent to the ester function in this fragment. Metastable peaks at *m/e* 151.0 and *m/e* 111.8 establish that it arises, at least in part, by the sequential loss of ethanol and an acetyl radical from the molecular ion. Hence, it may correspond to *i*, $C_{10}H_9O^+$, (high resolution), which can decompose by loss of carbon monoxide to *j* (*m/e* 117, $C_9H_9^+$, high resolution).

In the compounds studied, the McLafferty rearrangement [11] only gives rise to a diagnostically obvious decomposition path when the alkyl group is large (in VII, see Fig. 4). Elimination of a neutral olefin affords *m/e* 144 (*k*), whose enolic structure is suggested by the appearance of an ion at *m/e* 101 (see Fig. 4), corresponding to *l* which can be formed by allylic cleavage in *k*.

The spectra of the allyl and carboethoxymethyl derivatives (X and XI) are largely unexceptional and do not merit separate discussion in this context, although the decomposition of the phenyl derivative VIII occurs quite specifically by loss of ethanol to *m/e* 174. The phenyl substituent must make this process particularly favourable in VIII, although M — C_2H_5OH ions are a consistent feature in the spectra of this series of compounds (see, for example, *m/e* 98 in Fig. 1, *m/e* 126 in Fig. 2a, *m/e* 112 in Fig. 3, *m/e* 188 in Fig. 5, and *m/e* 202 in Fig. 6).

The spectra of several γ-ketoacids of this series have been determined, but the spectra of the esters are more amenable to interpretation for structural purposes. β-Benzoylpropionic acid behaves somewhat exceptionally, affording a skeletal rearrangement ion at *m/e* 122 (3 % of the abundance of the benzoyl cation base peak) corresponding in composition to ionised benzoic acid (high resolution).

In summary, the γ-diketones and γ-ketoesters studied give relatively simple spectra containing moderately abundant molecular ions. The fragmentation patterns are greatly dependent on the nature and location of substituents, while skeletal rearrangement processes are of negligible importance. Mass spectrometry should therefore prove to be a valuable analytical tool for the analysis of this important class of synthetic compounds.

EXPERIMENTAL

Mass spectra were determined in an A.E.I. MS 9 double focussing mass spectrometer at 70 eV and a source pressure in the range $(0.1-2.0) \times 10^{-6}$ mm Hg. Samples were

introduced through a heated inlet system at a temperature of approximately 150°. High resolution measurements were carried out with a resolving power of approximately 12 000 (10 % valley definition).

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Studies in Mass Spectrometry. Part XIII.* Mass Spectra of Disulphides; Skeletal Rearrangements upon Electron Impact

By J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, C. Nolde, G. Schroll, and D. H. Williams

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Studies in Mass Spectrometry. Part XIII.* Mass Spectra of Disulphides; Skeletal Rearrangements upon Electron Impact

By J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, C. Nolde, G. Schroll, and D. H. Williams

The mass spectra of a number of disulphides have been determined. In general, the saturated aliphatic disulphides, with the exception of dimethyl disulphide, fragment without the formation of abundant skeletal rearrangement ions. However, disulphides examined which contain sites of unsaturation (*e.g.*, diallyl disulphide and aromatic disulphides) decompose to a large extent with skeletal rearrangement; the loss of one or two sulphur atoms (with or without additional hydrogen atoms) is a common fragmentation process.

MUCH attention has been focused on skeletal rearrangements which occur on electron impact.[1] Sulphur compounds were obviously of interest, since thio-esters undergo an important skeletal rearrangement upon electron impact.[2] We have reported some results for sulphides, disulphides, sulphoxides, and sulphones,[3] and now present our work on aliphatic and aromatic disulphides.

The only discussion of the mass spectra of aliphatic disulphides of which we are aware concerns appearance potential results deduced from the spectra of dimethyl disulphide (I), diethyl disulphide (II), and dipropyl disulphide (VIIa).[4a] However, the mass spectra of the

* Part XII, H. J. Jakobsen, S.-O. Lawesson, J. T. B. Marshall, G. Schroll, and D. H. Williams, preceding Paper.

[1] For a review of some skeletal rearrangement processes see P. Natalis, *Ind. chim. Belgé*, 1964, **29**, 471; see also P. Brown and C. Djerassi, *Angew. Chem.*, in the press.

[2] W. H. McFadden, R. M. Seifert, and J. Wasserman, *Analyt. Chem.*, 1965, **37**, 560.

[3] J. Ø. Madsen, C. Nolde, S.-O. Lawesson, G. Schroll, J. H. Bowie, and D. H. Williams, *Tetrahedron Letters*, 1965, 4377.

[4] (*a*) B. G. Gowenlock, J. Kay, and J. R. Majer, *Trans. Faraday Soc.*, 1963, **59**, 2463; (*b*) "Catalogue of Mass Spectral Data," American Petroleum Institute Research Project 44, Carnegie Institute of Technology, Pittsburg, Pa.

aliphatic disulphides (I)—(VIII) have been reported in the A.P.I. catalogue;[4b] some spectra reported there are devoid of metastable ions and no high-resolution data are available. We have therefore independently prepared and/or determined the spectra of (I), (II), (VIIb), and (X) and additionally examined di-t-butyl disulphide (IX). The observed and calculated positions of some metastable ions in the spectra of (I), (II), (VIIb), (IX), and (X) are given in Table 1. High-resolution results for (I), (II), (VIIb), and (X) are given in Table 2. The spectra of dimethyl disulphide (I), diethyl disulphide

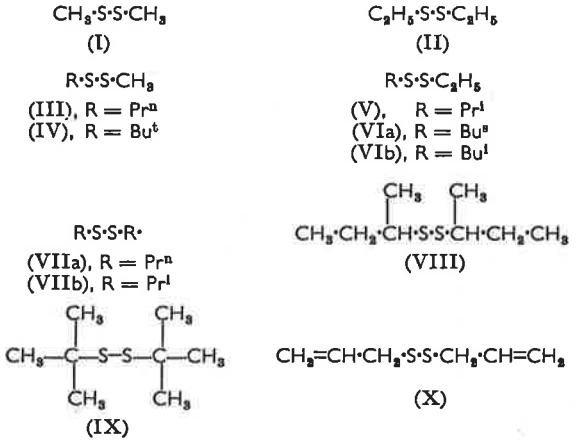
$CH_3{\cdot}S{\cdot}S{\cdot}CH_3$ (I)

$C_2H_5{\cdot}S{\cdot}S{\cdot}C_2H_5$ (II)

$R{\cdot}S{\cdot}S{\cdot}CH_3$
(III), R = Pr^n
(IV), R = Bu^t

$R{\cdot}S{\cdot}S{\cdot}C_2H_5$
(V), R = Pr^i
(VIa), R = Bu^s
(VIb), R = Bu^i

$R{\cdot}S{\cdot}S{\cdot}R{\cdot}$
(VIIa), R = Pr^n
(VIIb), R = Pr^i



(IX)

$CH_2{=}CH{\cdot}CH_2{\cdot}S{\cdot}S{\cdot}CH_2{\cdot}CH{=}CH_2$ (X)

TABLE 1

Some metastable peaks observed in the mass spectra of aliphatic disulphides (I), (II), (VIIb), (IX), and (X)

Compound	Obs.	Calc.	Transition
(I)	66·4	66·4	94 → 79(−CH_3·)
	43·0	43·1	47 → 45(−H_2)
	39·6	39·6	94 → 61(−SH·)
	25·6	25·6	79 → 45(−H_2S)
(II)	72·4	72·4	122 → 94(−C_2H_4)
	58·2	58·3	107 → 79(−C_2H_4)
	46·3	46·3	94 → 66(−C_2H_4)
	25·2	25·1	29 → 27(−H_2)
(VIIb)	77·7	77·7	150 → 108(−C_3H_6)
	40·3	40·3	108 → 66(−C_3H_6)
	39·2	39·1	43 → 41(−H_2)
	37·2	37·1	41 → 39(−H_2)
(IX)	83·6	83·5	178 → 122(−C_4H_8)
	37·1	37·1	41 → 39(−H_2)
(X)	87·5	87·5	146 → 113(−SH·)
	86·0	86·0	114 → 99(−CH_3·)
	37·2	37·1	41 → 39(−H_2)

TABLE 2

High-resolution results for ions in the spectra of (I), (II), (VIIb), and (X) *

Compound						
(I)	Peak (*m/e* value)	76	64	61(R)		
	Composition	CS_2	S_2	C_2H_5S		
(II)	Peak (*m/e* value)	94	76	66	61	60	59
	Composition	$C_2H_6S_2$	CS_2	H_2S_2	C_2H_5S	C_2H_4S	C_2H_3S
(VIIb)	Peak (*m/e* value)	108	93	76		66	
	Composition	$C_3H_8S_2$	$C_3H_5S_2$	CS_2 (55%) C_3H_6S (45%)		H_2S_2	
(X)	Peak (*m/e* value)	114(R)	113(R)	105	99(R)		
	Composition	$C_6H_{10}S$	C_6H_9S	$C_3H_5S_2$	C_5H_7S		
(X) (cont.)	Peak (*m/e* value)	81(R)	73	67(R)	54(R)		
	Composition	C_6H_9	C_3H_5S	C_5H_7	C_4H_6		

* In those cases where the fragment ion arise *via* a skeletal rearrangement the *m/e* value is followed by "R" in parentheses.

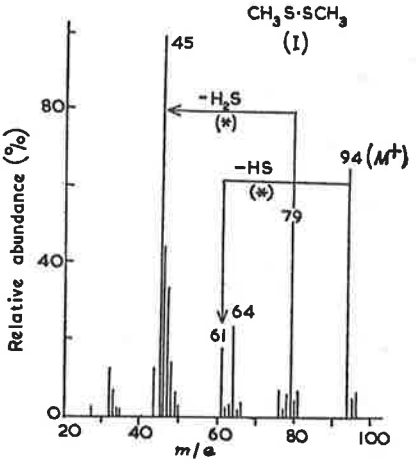


FIGURE 1

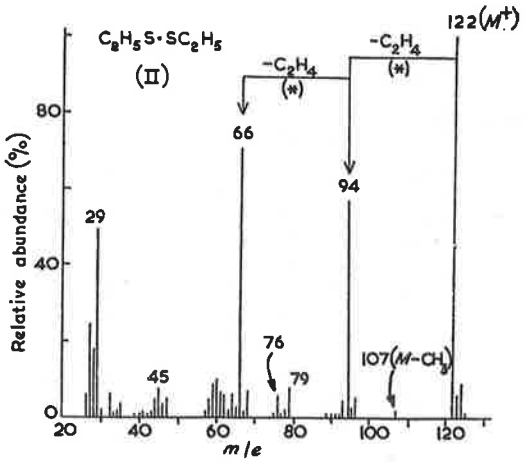


FIGURE 2

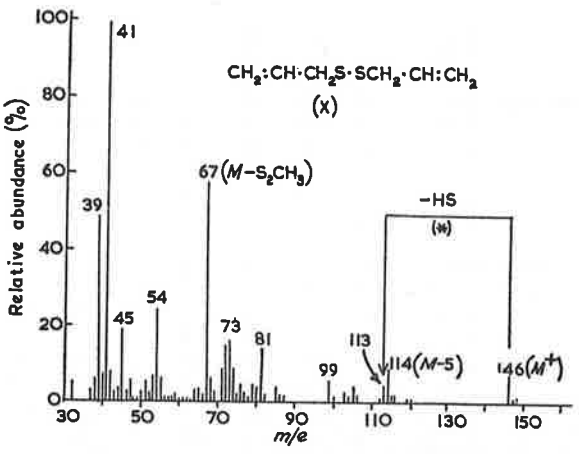


FIGURE 3

TABLE 3

Mass spectra of disulphides (IX), (XIII), and (XV)—(XIX *

(IX)	*m/e*	37	38	39	40	41	42	44	45
	I (%)	6	9	58	14	100	6	3	4
	m/e	49	50	51	53	55	56	57	58
	I (%)	4	9	8	9	15	26	45	4
	m/e	59	122	178(*M*)					
	I (%)	4	7	7					
(XIII)	*m/e*	39	41	44	45	50	51	52	53
	I (%)	10	5	5	29	4	6	5	6
	m/e	55	57	63	64	65	66	67	69
	I (%)	3	6	7	4	27	5	5	12
	m/e	70	71	77	78	93	95	96	97
	I (%)	8	4	16	6	13	11	10	21
	m/e	108	109	110	111	112	115	121	123
	I (%)	6	32	6	26	4	5	4	4
	m/e	125	126	137	138	139	140	141	142
	I (%)	39	6	14	21	22	71	12	5
	m/e	153	154	160	200	214	230	232	246
	I (%)	3	6	4	5	4	5	4	8
	m/e	278(*M*)		279	280	281			
	I (%)	100		19	12	3			
(XV)	*m/e*	50	51	74	75	76	77	78	105
	I (%)	16	28	5	5	5	44	8	100
	m/e	106	198	226					
	I (%)	100	13	6					
(XVI)	*m/e*	39	41	42	44	45	46	47	48
	I (%)	9	52	12	100	20	6	5	7
	m/e	54	55	56	57	58	59	60	61
	I (%)	4	26	9	8	14	18	9	4
	m/e	64	69	70	71	72	73	74	76
	I (%)	19	13	4	34	7	12	16	12
	m/e	84	85	86	87	88	100	111	114
	I (%)	16	6	14	9	9	4	6	8
	m/e	116	117	118	119	120	133	134	
	I (%)	36	4	81	7	6	16	8	
(XVII)	*m/e*	39	40	41	42	43	44	50	51
	I (%)	12	4	23	22	15	22	4	7
	m/e	52	53	54	55	56	57	64	67
	I (%)	12	7	14	54	17	10	4	7
	m/e	68	69	70	71	79	80	81	82
	I (%)	6	4	10	4	13	7	14	14
	m/e	83	84	85	86				
	I (%)	44	100	56	6				
(XVIII)	*m/e*	39	41	44	45	46	47	53	54
	I (%)	9	9	5	10	7	5	5	4
	m/e	55	56	59	60	64	73	78	79
	I (%)	100	8	5	10	10	5	5	5
	m/e	84	86	87	120(*M*)				
	I (%)	4	8	8	75				
(XIX)	*m/e*	39	41	42	44	45	46	47	55
	I (%)	20	30	4	50	50	10	8	8
	m/e	57	58	59	60	61	64	68	69
	I (%)	4	8	14	12	12	14	7	18
	m/e	71	72	73	76	78	85	86	87
	I (%)	29	34	16	14	11	10	16	7
	m/e	102	103	104	105	106	107	111	116
	I (%)	4	12	9	100	9	11	4	6
	m/e	117	118	132	134	150(*M*)		151	152
	I (%)	4	7	6	4	74		7	9

* All ions having a relative abundance greater than 2% of the base peak (arbitrarily taken as 100%) are included in the Table.

(II), and diallyl disulphide (X) are given in Figures 1, 2, and 3,[5] respectively, whereas the spectrum of di-t-butyl disulphide (IX) is summarised in Table 3 (with other spectra to be discussed subsequently in the Paper); the spectra of (I) and (II) (Figures 1 and 2), obtained in the present work, are qualitatively very similar to those previously reported,[4b] but quantitative differences are observed, presumably because different instruments and temperatures were used for the determinations.

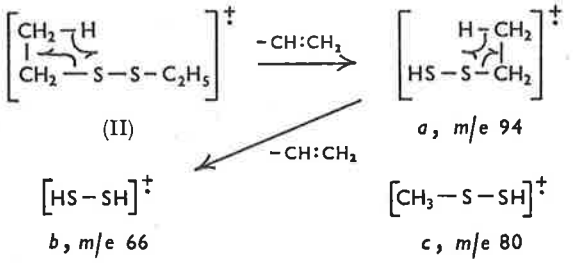
Tables 1—3 and Figures 1—3 show that among aliphatic disulphides abundant (>10% in relative abundance) skeletal rearrangement ions are only observed in the spectra of dimethyl disulphide (I) and diallyl disulphide (X). Spectra of the remaining disulphides (A.P.I. catalogue [4b]) suggest that this observation includes these compounds also, but high-resolution data are not available in these cases. The observed behaviour is plausible for two reasons. First, saturated aliphatic disulphides containing an alkyl residue larger than methyl decompose by elimination of a neutral olefin upon electron impact (see Figure 2). Dimethyl disulphide is unable to undergo the relatively easy olefin elimination and therefore some of the energy gained upon electron impact may be used to reorganise the skeleton of the molecular ion. Secondly, the unsaturated disulphide (X) has a much greater opportunity to rearrange, because not only is olefin elimination unfavourable, but electron-deficient centres may be generated in the molecular ion of (X) (by removal of, for example, a π-electron from an allyl group), which can then facilitate formation of a carbon–carbon bond between the allyl groups.

The importance of olefin elimination from the disulphides containing saturated alkyl groups larger than methyl can be illustrated by reference to the spectrum (Figure 2) of diethyl disulphide (II). The successive eliminations of ethylene are established by appropriate metastable peaks (Table 1), and are most reasonably represented by the sequence (II) ⟶ *a* ⟶ *b*. If *both* alkyl groups of the disulphide are larger than methyl, then usually an abundant ion corresponding to H_2S_2 (see *b*, *m/e* 66) will appear in the spectrum (di-t-butyl disulphide is an exception to this generalisation; Table 3). Alternatively, if one of the alkyl groups is methyl [and the other ethyl or larger; see (III) and (IV)], then an abundant ion at *m/e* 80 (represented as *c*) appears in the spectra of the compounds examined.

Two features of the spectrum (Figure 1) of dimethyl disulphide (I) are remarkable. One is the elimination of HS from the molecular ion, and the other is the loss of H_2S (not necessarily as neutral hydrogen sulphide) from the $M - CH_3$ ion (*m/e* 79) in a one-step process to give the base peak at *m/e* 45 (CHS^+). Hence the molecular ion must at least partially rearrange (to eliminate

[5] Transitions marked with an asterisk (*), both in the text and in the Figures, are substantiated by appropriate metastable peaks.

HS) and moreover, the structure of the $M - CH_3$ ion seems unlikely to be simply CH_3–S–S$^+$. Whatever



rearrangement occurs in the molecular ion (either before, or associated with fragmentation), it must involve formation of either a C–C or a C–S bond, and the latter

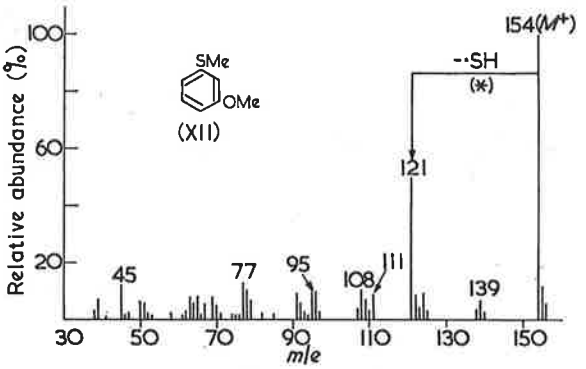
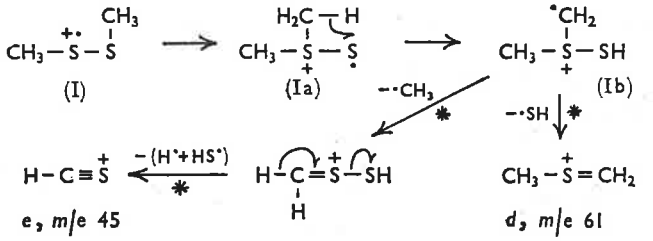


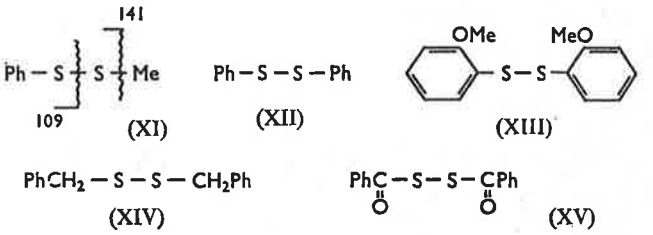
FIGURE 4

seems more probable. While mechanistic suggestions are tentative, the possibility of methyl migration to sulphur in the molecular ion [to give (Ia)], followed by transfer of a hydrogen radical from carbon to sulphur [(Ia) ⟶ (Ib)], can account for the formation of both *m/e* 61 (*d*) and *m/e* 45 (*e*).

The spectrum (Figure 3) of diallyl disulphide (X) is remarkable, since the majority of abundant fragment ions above *m/e* 50 are skeletal rearrangement fragments (see Table 2 and Figure 3). In the light of the important rearrangement processes in the spectrum of the diallyl derivative (X), we examined some aromatic disulphide to see if the unsaturated centres of the aromatic rings might promote related reactions. As a result, (XII)—(XV) were synthesised and their spectra determined. Purified commercial methyl phenyl disulphide (XI) was examined, but as purification was only partial, its spectrum is not reported in detail: small peaks corresponding to the molecular ions of diphenyl disulphide



[(XII), M^+, *m/e* 218] and its fragment ions were observed [see Figure 4 for the spectrum of (XII)], and, in addition, peaks occur which are probably due to traces of dimethyl



disulphide. This observation is hardly surprising since (XI) disproportionates into a mixture of (I) and (XII) on standing.[6] However, since (I) and (XII) were only minor impurities present in methyl phenyl disulphide (XI), and since the spectra of both (I) and (XII) have been measured, we can state that (XI) gives an abundant molecular ion at *m/e* 156 (99%) and fragments mainly without rearrangement to *m/e* 141 [71%, $M - CH_3$, see (XI] and *m/e* 109 [100%, $M - SCH_3$, see (XI)]. Rearrangement ions are, however, observed at *m/e* 124 (M — S, 5%), *m/e* 123 (M — SH, 5%), and *m/e* 91 ($C_7H_7^+$, 10%); a metastable peak at *m/e* 66·8 supports the transition *m/e* 124 ⟶ 91 by elimination of HS.

The skeletal rearrangement behaviour of diphenyl disulphide (XII) (Figure 4) and the dimethoxy-derivative

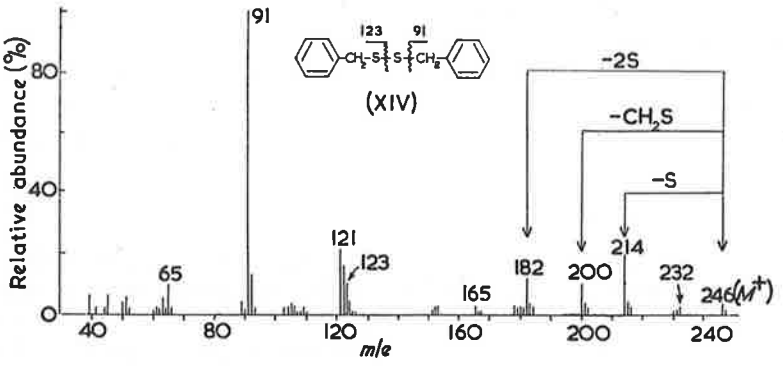


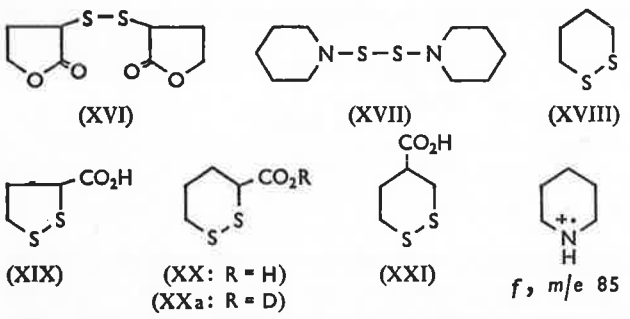
FIGURE 5

[6] E. E. Reid, "Organic Chemistry of Bivalent Sulphur," Vol. III, Chemical Publishing Co., New York, 1950, ch. 7.

(XIII, Table 3) are similar inasmuch as both spectra contain pronounced $M - S$ and $M - 2S$ fragment ions. Diphenyl disulphide (XII) additionally gives ions at *m/e* 185 ($C_{12}H_9S^+$) and *m/e* 184 ($C_{12}H_8S^+_{\cdot}$). All these results have been substantiated by high-resolution measurements. It should be noted that pyrolysis of aryl disulphides (usually at above 400°) has been used to couple aromatic rings by elimination of S_2 groups,[7] but the processes at present under discussion are definitely induced by electron impact, since they are substantiated by appropriate metastable peaks (Figure 4).

The spectrum (Figure 5) of dibenzyl disulphide (XIV) is noteworthy for the presence of $M - CH_2S$ (*m/e* 200, $C_{13}H_{12}S^+_{\cdot}$ by high resolution) and $M - CH_2$ (*m/e* 232) peaks, which accompany abundant $M - S$ and $M - 2S$ ions. Since $M - CH_2$ ions are very uncommon in mass spectra [8] the purity of (XIV) has been rigorously established by vapour-phase chromatography. Dibenzoyl disulphide (XV) does not afford a molecular ion in its mass spectrum (Table 3), but decomposes by loss of SO (not necessarily in one step) to *m/e* 226 ($C_{14}H_{10}SO^+_{\cdot}$, H.R.); this skeletal-rearrangement fragment then decomposes further by elimination of CO to $C_{13}H_{10}S^+_{\cdot}$ (*m/e* 198), as established by high-resolution measurements and an appropriate metastable peak at *m/e* 173·5 (calc., *m/e* 173·5). The base peak of this spectrum is associated with the benzoyl cation (*m/e* 105).

Other compounds examined include the linear disulphides (XVI) and (XVII) and cyclic disulphides [(XVIII)—(XXI)]. The spectra (Table 3) of (XVI) and (XVII) do not contain molecular ions, but that of the former is noteworthy for skeletal rearrangement ions at *m/e* 133 ($C_8H_5O_2^+$) and *m/e* 134 ($C_8H_6O_2^+_{\cdot}$); *m/e* 134 corresponds to complete loss of the sulphur bridge and, in addition, two molecules of water ($M - 2S - 2H_2O$). The spectrum of (XVII) contains no abundant ions above *m/e* 85, which presumably corresponds to the piperidine ion-radical *f*.



The base peak in the spectrum (Table 3) of (XVIII) occurs at *m/e* 55 ($C_4H_7^+$, $M - HS_2$), but in the case of a cyclic disulphide, its formation does not of course necessitate skeletal rearrangement. The isomeric carboxylic acids (XX) and (XXI) can readily be differentiated from their mass spectra (Figures 6 and 7, respectively). Both compounds give $M - S$ (*m/e* 132) and $M - SH$ (*m/e* 131) ions, but only (XX) gives an abundant ion at *m/e* 119 ($M - CO_2H$, H.R.), since in this case the carboxylic acid group can be lost with associated formation of a sulphonium ion *g* (*m/e* 119). The base peak (*m/e* 87, $C_4H_7S^+$) in the spectrum (Figure 6) of (XX) can formally arise *via* elimination of a sulphur atom from *g*, or by loss of the carboxylic acid residue from the $M - S$ ion (perhaps *h*, *m/e* 132). The cyclic structure *i*

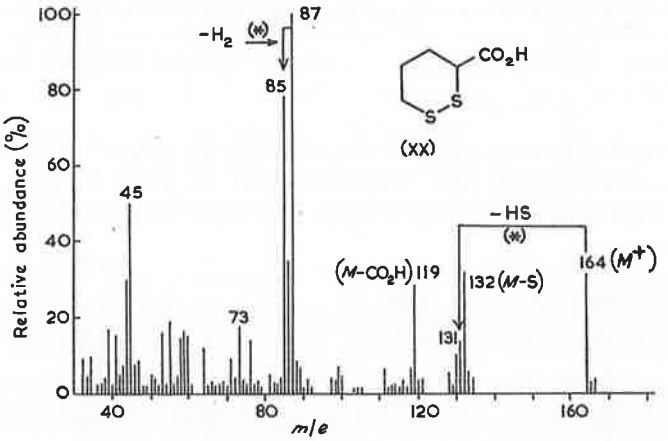


FIGURE 6

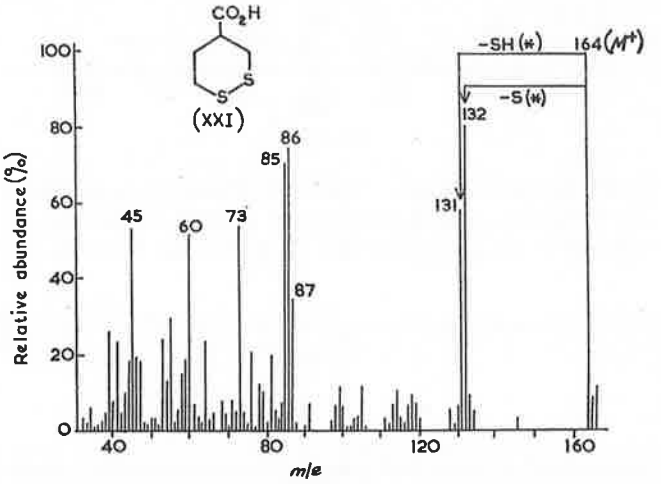


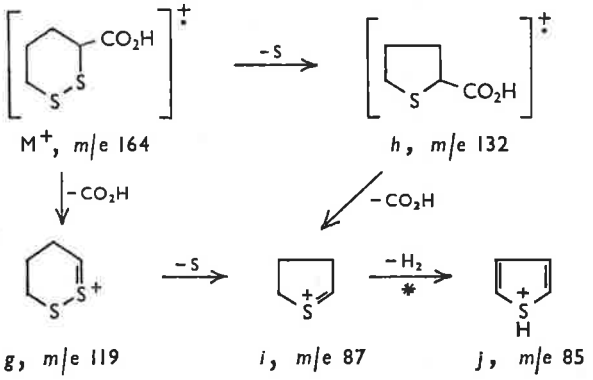
FIGURE 7

for *m/e* 87 is consistent with its decomposition by loss of H_2 (metastable peak at *m/e* 83·0, calc. *m/e* 83·0) to *m/e* 85 ($C_4H_5S^+$, H.R.), which probably corresponds to the protonated thiophen *j*. The loss of the carboxylic acid proton in the formation of *m/e* 119 (*g*) is established by the spectrum of the [*hydroxy*-$^2H_1$]carboxylic acid [(XXa)], obtained by introduction of (XX) into the inlet system of the spectrometer with deuterium oxide; [9] in this spectrum, *m/e* 119 is not shifted. The base peak (*m/e* 105) in the spectrum (Table 3) of the five-membered ring analogue (XIX) corresponds to an $M - CO_2H$ ion ($C_3H_5S_2^+$, H.R.).

In summary, the mass spectra of disulphides are obviously useful for analysis but extreme caution must be

[7] W. Z. Heldt, *J. Org. Chem.*, 1965, **30**, 3897.
[8] S. Meyerson, *J. Amer. Chem. Soc.*, 1963, **85**, 3340.
[9] J. S. Shannon, *Austral. J. Chem.*, 1962, **15**, 265.

exercised in the light of the extensive rearrangements. In the unsaturated compounds examined some re-



organisation of the skeleton upon electron impact seems to be the rule.

EXPERIMENTAL

Mass spectra were determined on an A.E.I. MS 9 double-focusing mass spectrometer operating at 70 ev. Samples were introduced through a heated inlet system in the range 100—200°. The source pressure was maintained in the range $1{\cdot}0 \times 10^{-6}$ to $1{\cdot}0 \times 10^{-7}$ mm./Hg.

(I) and (XI) were purified commercial samples. All other disulphides were synthesised by previously published procedures: (II),[10] (VIIb),[11] (IX),[12] (X),[13] (XII),[14] (XIII),[15] (XIV),[16] (XV),[17] (XVI),[18] (XVII),[19] (XVIII),[20] (XIX),[21] (XX),[22] and (XXI).[23] All samples were purified by careful distillation and purity checked by nuclear magnetic resonance, infrared, and mass spectral analysis.

We thank Dr. G. Claeson for samples of (XVI) and the cyclic disulphides (XVII)—(XXI), and Dr. A. F. Thomas of Firmenich et Cie, Geneva, for establishing the purity of dibenzyl disulphide (XIV). One of us (J. H. B.) is grateful for the award of an I.C.I. Fellowship.

(J. H. B. and D. H. W.) University Chemical Laboratory, Cambridge.
(S.-O. L., J. Ø. M., C. N., G. S.) Department of Chemistry, Aarhus University, Aarhus C, Denmark. [6/112 *Received, January 28th*, 1966]

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Studies in Mass Spectrometry. Part XIV.* Mass Spectra of Aromatic Thioethers. The Effect of Structural Variations on the Relative Abundance of Skeletal Rearrangement Ions

By J. H. Bowie, S.-O. Lawesson, J. Ø. Madson, G. Schroll, and D. H. Williams

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By J. H. Bowie, S.-O. Lawesson, J. Ø. Madson, G. Schroll, and D. H. Williams

The mass spectra of a number of compounds of the general formula $C_6H_5{\cdot}SR$ and $XC_6H_4{\cdot}S{\cdot}CH_3$ are discussed. In the first group of compounds ($C_6H_5{\cdot}SR$), skeletal rearrangement ions are more abundant when R = CH_3 or when R contains double bonds (R = allyl, C_6H_5) than when R is a larger, saturated alkyl group (R = C_2H_5, n-C_5H_{11}). In the second group ($XC_6H_4{\cdot}S{\cdot}CH_3$), M − SH ions are a common feature of the spectra, but the abundance of such ions is in some cases greatly dependent upon the relative orientation of X and SCH_3 groups. For example, when X = CH_3 or OCH_3, the abundance of the M − SH skeletal rearrangement ions is by far the greatest in the *meta*-isomers.

Our interest in the behaviour of aromatic thioethers upon electron impact was aroused by the observation [1-3] that thioanisole (I) contains in its mass spectrum a prominent peak (25% relative abundance; see Figure 1) at *m/e* 91 ($C_7H_7^+$, M − SH). A similar rearrangement ion is present in the spectrum of 2-methylthionaphthalene.[3] We have therefore determined the mass spectra of a number of phenyl thioethers with a view to evaluating the effect of structural variations on the relative abundance of skeletal rearrangement ions. This study also serves to record for phenyl thioethers data similar to those already available for various anisoles.[4,5]

The mechanism of the formation of the *m/e* 91 ion ($C_7H_7^+$) in the spectrum (Figure 1)† of thioanisole (I)

* Part XIII, J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, C. Nolde, G. Schroll, and D. H. Williams, preceding Paper.

† A transition indicated by an asterisk (either in the Figures or the text) is supported by the presence of an appropriate metastable peak.

[1] Catalog of Mass Spectral Data, American Petroleum Institute Research Project 44, Carnegie Institute of Technology, Pittsburgh, spectrum no. 969.

[2] B. G. Gowenlock, J. Kay, and J. R. Majer, *Trans. Faraday Soc.*, 1963, **59**, 2463.

[3] J. Ø. Madsen, C. Nolde, S.-O. Lawesson, G. Schroll, J. H. Bowie, and D. H. Williams, *Tetrahedron Letters*, 1965, 4377.

[4] C. S. Barnes and J. L. Occolowitz, *Austral. J. Chem.*, 1963, **16**, 219.

[5] Z. Pelah, J. M. Wilson, M. Ohashi, H. Budzikiewicz, and C. Djerassi, *Tetrahedron*, 1963, **19**, 2233.

has been investigated by a comparison with the spectrum (Figure 2) of trideuteromethyl–thioanisole (Ia). In this spectrum (Figure 2), $C_7H_5D_2^+$ (M — SD, *m/e* 93) and $C_7H_4D_3$ (M — SH, *m/e* 94) ions are observed in the approximate ratio of 2 : 1. Metastable peaks at *m/e* 68·2 and 69·7 corresponding to the transitions 127 ⟶ 93 and 127 ⟶ 94 are observed in approximately the same abundance ratio (~2 : 1) and have the same peak profile. The elimination of SH and SD perhaps therefore occurs from a common, rearranged molecular ion.[6]

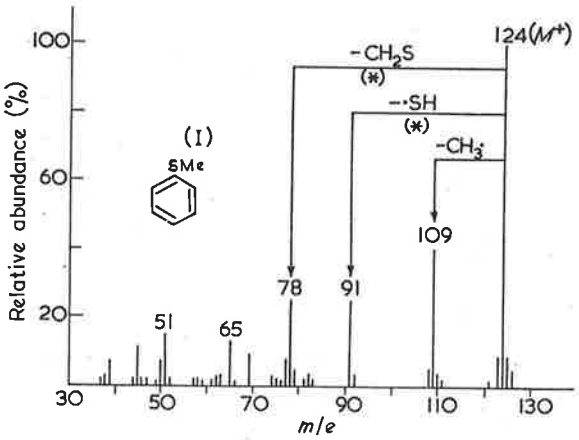


FIGURE 1

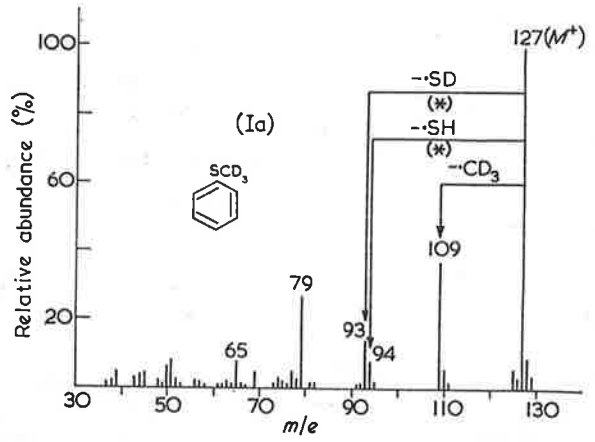
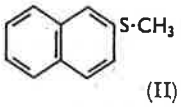


FIGURE 2

It has been pointed out [2] that the appearance potential (12·1 ev) of $C_6H_5S^+$ (*m/e* 109) in the mass spectrum of (I) is relatively high and leads to a high value of $D(C_6H_5S\text{–}CH_3)$. The possibility that the high value was due to a rearrangement process has been considered,[2] but our results exclude any rearrangement which would involve reciprocal hydrogen transfers between the methyl group and the aromatic nucleus.

If the methyl group of (I) is replaced by the ethyl group of (III), then the abundance of rearrangement ions at *m/e* 91 ($C_7H_7^+$) and *m/e* 105 (M — SH; high resolution) is very low (see Figure 3). In the spectrum (Figure 4) of phenyl n-pentyl sulphide (IV), a small peak is again evident at *m/e* 91 ($C_7H_7^+$), but no *M* — SH species (*m/e* 147) appears in the spectrum. This pattern of behaviour

(I : R = CH_3)
(Ia: R = CD_3)
(III: R = C_2H_5)
(IV : R = n-C_5H_{11})
(V : R = $CH_2{\cdot}CH{:}CH_2$)
(VI : R = $C_6H_5{\cdot}CH_2$)
(VII: R = C_6H_5)



(II)

is similar to that of dialkyl disulphides,[7] *i.e.*, the extent of skeletal rearrangement is greatest when the saturated alkyl group attached to sulphur is methyl. Ethyl and

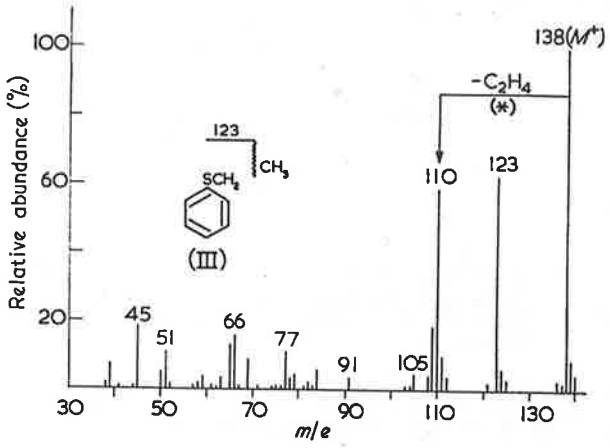


FIGURE 3

larger groups are readily eliminated, with associated hydrogen rearrangement to the charged fragment, to afford *m/e* 110 ($C_6H_6S^+$, see Figures 3 and 4); in this manner much of the energy of the molecular ion can

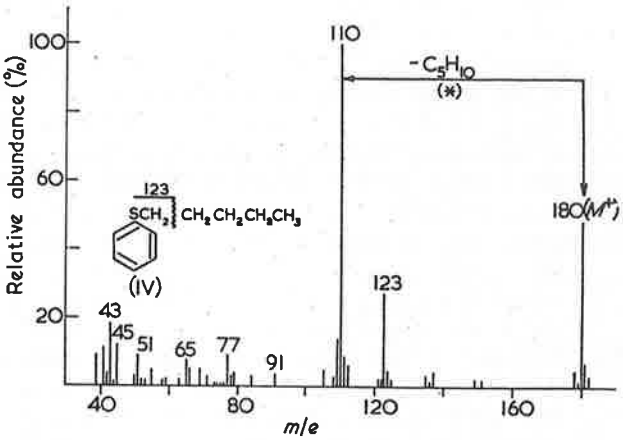


FIGURE 4

be dissipated, and hence it is not available to promote complex rearrangements.

However, if the group attached to sulphur (in addition

[6] J. H. Beynon, B. E. Job, and A. E. Williams, *Z. Naturforsch.*, 1965, **20***a*, 883.

[7] J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, C. Nolde, G. Schroll, and D. H. Williams, preceding Paper.

to phenyl) contains unsaturated linkages [allyl (V) or phenyl (VII) [3,8]], then, in the compounds studied, rearrangement ions once more become prominent in the spectra. Some of these rearrangement ions are listed in the Table. Apparently the removal of π-electrons from double bonds upon electron impact may generate electron-deficient centres, which can then be utilised to promote C–C or C–S bond formation in reactions of the type $[ABC]^+ \longrightarrow [AC]^+$. Rearrangement ions are not prominent in the spectrum of benzyl phenyl sulphide (VI), presumably because tropylium ion formation (*m/e* 91, $C_7H_7^+$) occurs so readily.

Some rearrangement ions in the spectra of (V)—(VII)*

Compound	R	*m/e*	Composition	Relative abundance (%)
(V)	$CH_2{\cdot}CH{:}CH_2$	117	$M - HS$	39
		105	$C_8H_9^+$	10
		91	$C_7H_7^+$	12
(VI)	$C_6H_5CH_2$	165	$M - H_2S$	4
(VII)	C_6H_5	154	$C_{12}H_{10}$	4
		153	$C_{12}H_9$	6
		152	$C_{12}H_8$	10
		142	$C_{11}H_{10}$	3
		141	$C_{11}H_9$	4
		139	$C_{11}H_7$	2

* The spectra of those compounds which are not reported in full detail in this Paper have been placed on record with Professor E. Stenhagen, Institutionen för Medicinsk Biokemi, Göteborgs Universitet, Medicinaregatan 9, Göteborg SV, Sweden.

Having evaluated the effect of structural variation in R on the relative abundance of skeletal rearrangement ions in compounds of the general formula $C_6H_5{\cdot}SR$, we then examined the effect of substituents (*ortho*, *meta*, and *para*) in the aromatic ring. The results for 2- (VIII), 3- (IX), and 4-methylthioanisole (X) are recorded in Figures 5—7, respectively. The relative abundances of the $M - CH_3$ ions for the three isomers are in the order *ortho* > *para* > *meta* and are very similar to those of the $M - CH_3$ ions in the spectra of the corresponding methyl anisoles.[4,5] Other similarities to the spectra of the methyl anisoles are very striking, *e.g.*, the abundance of the $M - 1$ ion is greatest for the *para*-isomers of both series, whereas the abundance of the *m/e* 92 ion ($M - CH_2S$ or $M - CH_2O$) is greatest for the *meta*-isomers of both series. However, the spectra of the two series are different in two important ways. First, the spectra of the methyl-thioanisoles (VIII)—(X) contain fairly abundant (6—10%) $M - 17$ ions (*m/e* 121) which are not evident in the spectra of the methyl-anisoles. A high-resolution measurement confirms their only reasonable composition ($M - CH_5$). The $C_7H_5S^+$ (*m/e* 121) fragment must have enhanced stability because it has been observed by us in a large number of sulphur compounds containing the $CH_2{\cdot}C_6H_4{\cdot}S-$ and $C_6H_5{\cdot}CH_2{\cdot}S-$ units. Secondly $M - SH$ (*m/e* 105) ions are present in the spectra of the methyl-thioanisoles (VIII)—(X), and the relative abundance of these skeletal rearrangement ions follows the reverse order (*meta* > *para* > *ortho*) of the relative abundances of the $M - CH_3$ ions; analogous rearrangements do not occur in the methylanisoles.[4,5] Evidently, the skeletal rearrangement becomes more prominent when simple reactions (*e.g.*, the formation of $M - CH_3$ fragments) are not especially favourable. Hence, the *m/e* 105 ($M - SH$) ion is very small when loss of the *S*-methyl group can be facilitated

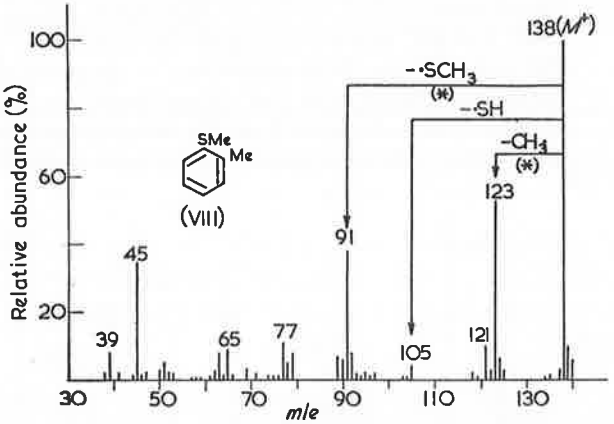


FIGURE 5

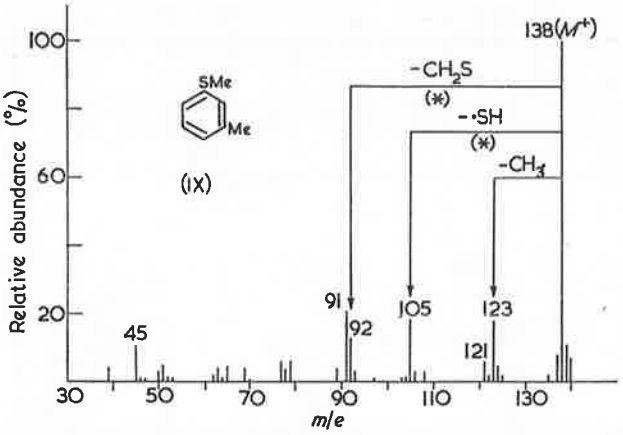


FIGURE 6

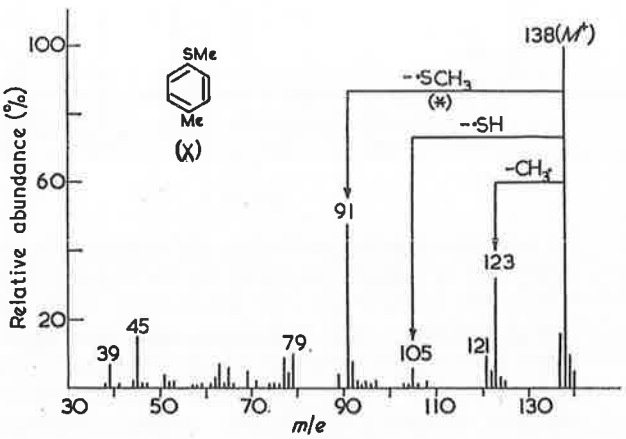


FIGURE 7

* Ref. 1, spectrum no. 637.

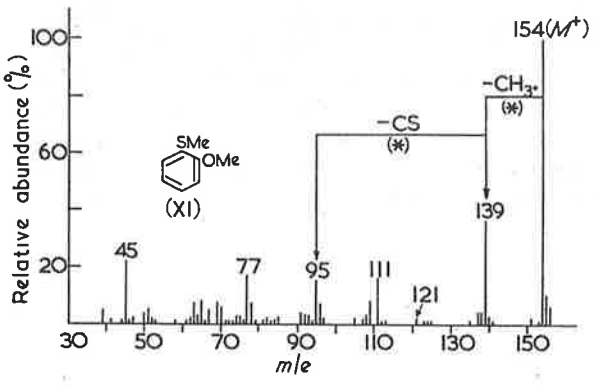
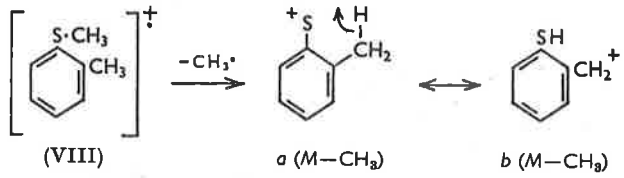


FIGURE 8

by hydrogen transfer to furnish a benzyl (or tropylium [10]) cation [5,9] [see (VIII) ⟶ *a* ⟷ *b*].



The effect of substituent orientation on the abundance of the rearrangement (M — SH) ions may again be seen on comparison of the spectra (Figures 8—10) of 2- (XI), 3- (XII), and 4-methoxythioanisole (XIII). The $M - CH_3$ ion (*m/e* 139) is very abundant from the *para*-isomer (Figure 10), of medium abundance from the *ortho*-isomer (Figure 8), but of very low abundance from the *meta*-isomer (Figure 9); this pattern parallels that observed for the corresponding dimethoxybenzenes,[4,9] and probably the relatively favourable expulsion of a methyl radical from the *ortho*- and *para*-isomers reflects their ability to form quinoid oxonium ions such as *c* (*m/e* 139). When the elimination of a methyl radical from the molecular ion is a relatively facile process, then the *M* — HS rearrangement ions are of very small abundance (2 and 1% in Figures 8 and 10, respectively), but the *M* — SH peak (*m/e* 121) is very large in the spectrum (Figure 9) of the *meta*-isomer (XII).*

To determine the relative proportions of the *m/e* 139 ions in Figures 8—10 which are formed by loss of an *S*-methyl or *O*-methyl group, we prepared the *S*-trideuteromethyl derivatives (XIV), (XV), and (XVI). The spectra of these compounds indicate that the *ortho*-isomer (XI) loses the *O*-methyl to the extent of about 80% and the *S*-methyl to the extent of about 20%, whereas the corresponding figures for the *para*-isomer (XIII) are 57 and 43%, and for the *meta*-isomer 25 and 75%, *i.e.*, where a quinoid oxonium ion can be formed the loss of *O*-methyl predominates, but the *S*-methyl group is mainly eliminated in the absence of this conjugative effect. A metastable peak at *m/e* 64·9 in the spectrum (Figure 8) of the *ortho*-isomer (XI) establishes that the M — CH_3 ion (*m/e* 139) decomposes by elimination of CS to *m/e* 95; in the spectrum of the trideutero-derivative (XIV), the *m/e* 95 ion of (XI) is partially shifted (~65%) to *m/e* 98, and a metastable peak at *m/e* 67·7 establishes the transition *m/e* 142 ⟶ *m/e* 98, also by elimination of CS. Therefore, loss of the *O*-methyl group may precede the expulsion of CS. This

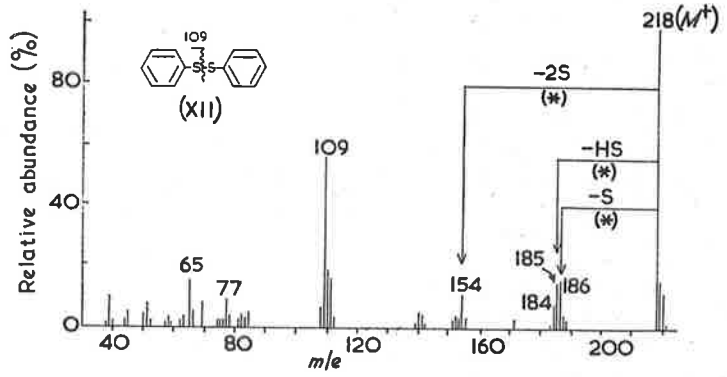


FIGURE 9

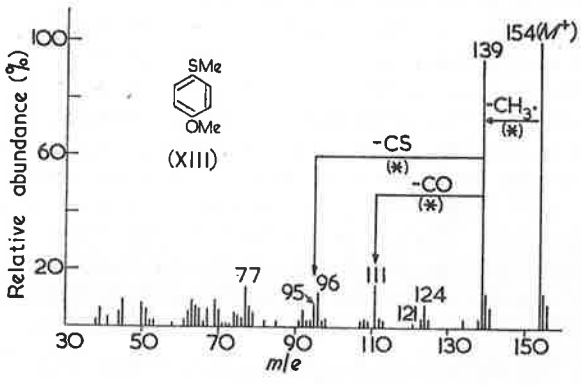


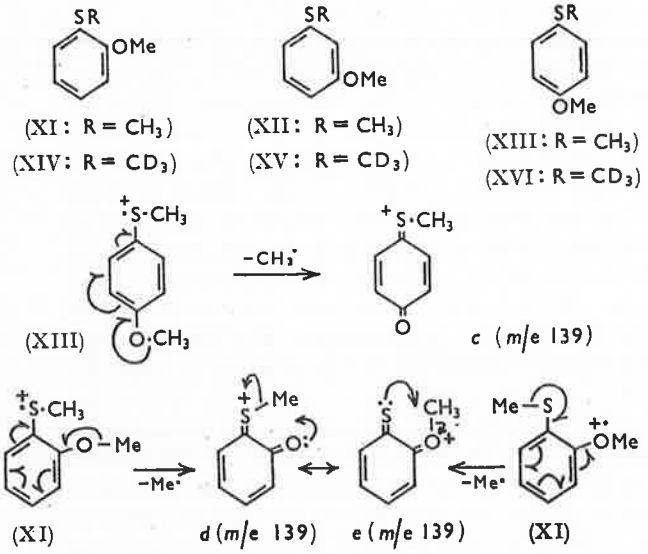
FIGURE 10

* The greater relative abundance of the *M* — SH ions in the spectra of the *meta*-isomers may additionally, of course, be due to active promotion of the skeletal rearrangement by an electron-donating substituent in the *meta*-position.

[9] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of the Mass Spectra of Organic Compounds," Holden-Day, San Francisco, 1964, pp. 175—181.

[10] H. M. Grubb and S. Meyerson, in "Mass Spectrometry of Organic Ions," ed. F. W. McLafferty, Academic Press, New York, 1963, ch. 10.

is not the case when the functional groups are not adjacent, since the *m/e* 95 ions ($C_6H_7O^+$, high resolution) from the *meta*- and *para*-isomers (XII) and (XIII) are not shifted in the spectra of the labelled derivatives. Hence, in the *ortho*-isomer only, the *S*-methyl group must largely



migrate in the formation of the *m/e* 95 ion. It is plausible that, in the quinoid $M - CH_3$ ion *d* (*m/e* 139), the methyl group migrates to oxygen to furnish *e* (*m/e* 139), which may then eliminate CS to give *m/e* 95. The transition between *d* and *e* is probably reversible. This follows since *m/e* 111 ($M - CH_3{\cdot}CO$) from (XI) (see Figure 8) is shifted to *m/e* 114 (2 parts) and unshifted (1 part) in the spectrum of the trideuteromethyl derivative (XIV), and a metastable peak at *m/e* 88·5 establishes the transition *m/e* 139 ⟶ *m/e* 111 by loss of CO, *i.e.*, a minor portion of *m/e* 111 arises by loss of the *S*-methyl group which precedes the elimination of carbon monoxide. Finally, it is noteworthy that the labelled *meta*-isomer (XV) eliminates SH and SD in the ratio 60 : 40, *i.e.*, in the formation of M — SH ions a smaller proportion of the eliminated hydrogen originates from the *S*-methyl group in the *m*-methoxy-derivative (XI) than in the parent compound (I).

The effect of the orientation of an electron-withdrawing substituent upon the relative abundance of M — SH ions is less clear, no large variations in the abundance of the *m/e* 135 ions (M — SH) in the spectra (Figures 11—13) of the isomeric carboxylic acids (XVII)—(XIX) being evident. The *ortho*-isomer (XVII) undergoes degradation by loss of water to *m/e* 150 ($C_8H_6SO^+$, high resolution) and thence by loss of CO to *m/e* 122 ($C_7H_6S^+$, high resolution and metastable peak at *m/e* 99·2), a sequence which does not occur in the spectra of the other isomers. Evidently, the second hydrogen atom which is required for the elimination of water from the carboxylic acid group is available from the *ortho*-

[11] F. W. McLafferty and R. S. Gohlke, *Analyt. Chem.*, 1959, **31**, 2076.

S-methyl group (an "*ortho*-effect").[11] Surprisingly, however, the $M - CH_3$ (*m/e* 153), M — OH (*m/e* 151), and $M - H_2O$ (*m/e* 150) ions from (XVII) appear as $M - CH_3$ (~50%), $M - CH_2D$ (~50%), M — OH (~70%), and $M - H_2O$ (~70%) species in the spectrum of the deuterated acid(*f*). These observations suggest that the deuterium of *f* is not retained solely in the

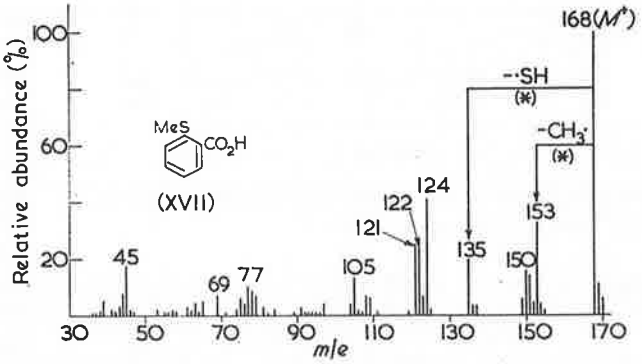


FIGURE 11

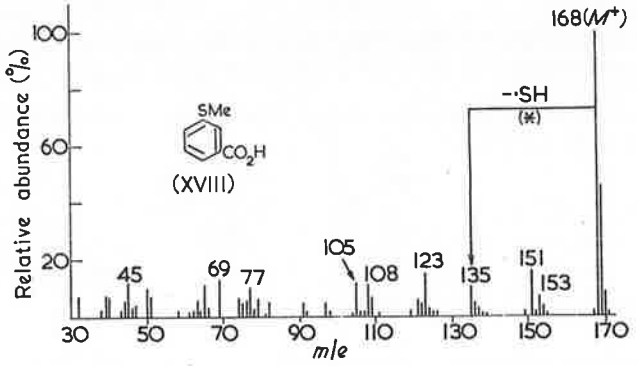


FIGURE 12

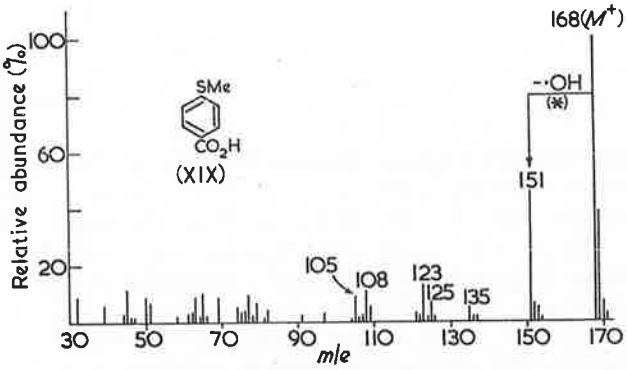
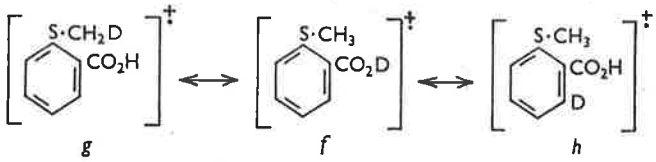


FIGURE 13

carboxyl group after ionisation; it appears to be partially scattered in the *S*-methyl group (see *f* ⟶ *g*) as evidenced by the appearance of the $M - CH_2D$ peak. Even a mixture of *f* and *g* would not decompose so specifically (~70%) by loss of H_2O (rather than HDO) in an "*ortho*-effect," and therefore scattering of the deuterium into the vacant *ortho* position of the aromatic ring (see *f* ⟶ *h*) is probably also operative, as has been

shown [6] to occur in the case of *O*-deuterated benzoic acid.



g *f* *h*

EXPERIMENTAL

All mass spectra were determined on an A.E.I. MS9 mass spectrometer, operating at 70 ev. Samples were introduced through a heated inlet system at 100—200°, and at a source pressure of 2—8 × 10^{-7} mm. The spectrum of methylthiobenzoic [^{2}H]acid (see *f*) was obtained by introduction of the unlabelled acid into the source with deuterium oxide.[12]

The following published procedures were employed for the preparation of the thioethers: (I),[13] (II),[14] (III),[15] (IV),[16] (V),[17] (VI),[18] (VII),[19] (VIII),[20] (IX),[21] (X),[22] (XI),[23] (XII),[24] (XIII),[25] (XVII)—(XIX).[26] The trideuteromethyl derivatives (Ia) and (XIV)—(XVI) were prepared by alkylation of the free thiols with aqueous sodium hydroxide and di(trideuteromethyl) sulphate; these derivatives had an isotopic purity of at least 98%. The purity of all compounds was checked by infrared, n.m.r., and mass spectra. If any ambiguity as to purity remained after application of these physical methods, the purity was checked by vapour-phase chromatography.

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(J. H. B. and D. H. W.) University Chemical Laboratory, Cambridge.
(S.-O. L., J. Ø. M., G. S.) Department of Chemistry, Aarhus University, Aarhus C, Denmark. [6/341 *Received, March 16th*, 1966]

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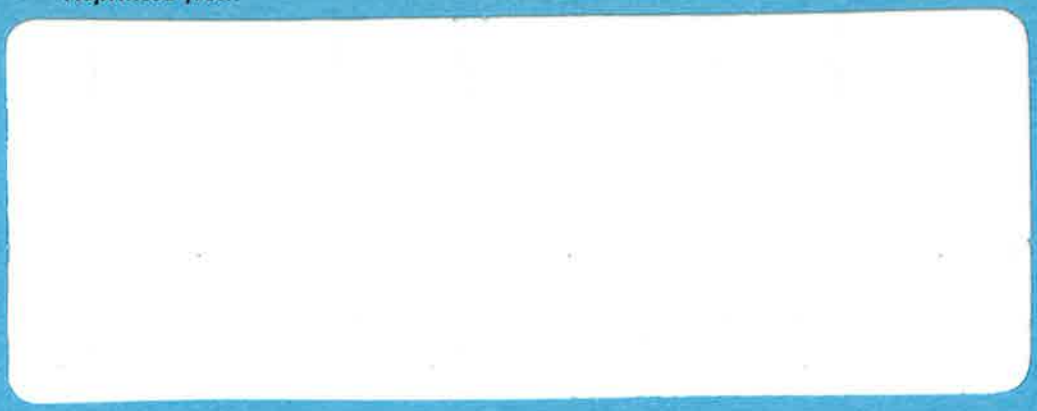

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Tetrahedron, 1966, Vol. 22, pp. 3515 to 3525. Pergamon Press Ltd. Printed in Northern Ireland

STUDIES IN MASS SPECTROMETRY—XV[1]

MASS SPECTRA OF SULPHOXIDES AND SULPHONES. THE FORMATION OF C—C AND C—O BONDS UPON ELECTRON IMPACT

J. H. BOWIE and D. H. WILLIAMS
University Chemical Laboratory, Lensfield Road, Cambridge, U.K.
and
S.-O. LAWESSON, J. Ø. MADSEN, C. NOLDE and G. SCHROLL
Department of Organic Chemistry, Aarhus University, Denmark

(*Received* 8 *April* 1966)

Abstract—Although dialkyl sulphoxides and sulphones behave relatively simply upon electron impact, aromatic sulphoxides and sulphones show a pronounced tendency to undergo C—O bond formation, as evidence by a number of decomposition pathways which involve the elimination of carbon monoxide. For example, dibenzothiophene dioxide (XV) decomposes from its molecular ion by successive eliminations of carbon monoxide.

DETAILS of the behaviour of sulphoxides upon electron impact have not been reported, except for our preliminary communication[2] which noted the loss of SO from dibenzyl sulphoxide (V). With respect to sulphones, the spectra of methyl vinyl sulphone and methyl ethyl sulphone have been reported by Quayle,[3] and those of isopropyl and cyclopropyl phenyl sulphones discussed by Meyerson and McCollum.[4] The only detailed study deals with diphenyl sulphone and a number of derivatives alkylated in the phenyl rings.[5] Molecular weight determinations by mass spectrometry have recently been recorded for two bridged naphthalene sulphones,[6] while interesting rearrangements occur in some sulphonylhydrazones[7] upon electron impact. The present paper gives details of the spectra of a variety of sulphoxides and sulphones, including a number of reactions of the type ABC → AC + B and examples of C—O bond formation occurring to an important extent upon electron impact.

The mass spectra of the aliphatic sulphoxides I–IV which have been determined are relatively simple. In the spectrum (Fig. 1) of dimethyl sulphoxide (I), the base peak (*m/e* 63) arises from the loss of a methyl group, but the formation of *m/e* 61 by the elimination of OH from the molecular ion in a one-step process is somewhat unexpected.[8] The decomposition of the M—CH_3 ion by loss of water in a one-step

[1] Part XIV, J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, G. Schroll and D. H. Williams, *J. Chem. Soc.* in press.
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[8] Transitions indicated by an asterisk (*) either in the figures or in the text are supported by the presence of an appropriate metastable peak.

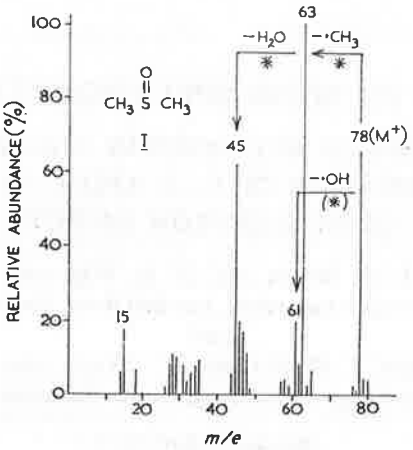
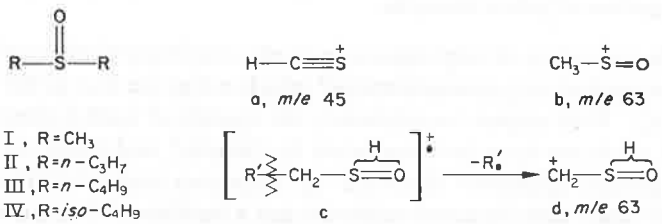


FIG. 1

process to *m/e* 45 (probably the thioformyl cation *a*) does not favour its representation solely as the simple cation *b*.



In general, the spectra of the sulphoxides II–IV containing larger alkyl groups contain prominent peaks due to loss of R with an associated hydrogen rearrangement to the charged fragment. Formally, this process corresponds to the elimination of a neutral olefin, e.g., to the elimination of propylene from dipropyl sulphoxide (II) to give *m/e* 92 (see Fig. 2). No metastable peaks are present in the spectra to confirm that

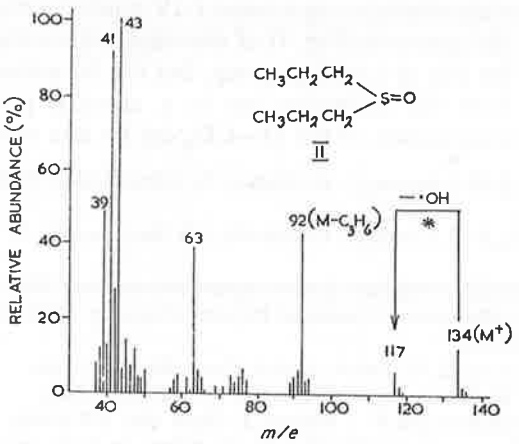


FIG. 2

the olefin elimination is induced by electron impact, and indeed the reaction is almost certainly in part thermally induced since dialkyl sulphoxides can undergo olefin elimination at 250° in the injection port of a GLC instrument,[9] or upon refluxing in dimethyl sulphoxide solution.[10] However, we believe the olefin elimination to be largely an electron impact phenomenon, since the spectrum (Fig. 2) of II is very similar whether obtained by introduction of the sample through a heated inlet system (at approximately 150°) or obtained by the direct inlet procedure at a source temperature of approximately 60°. Another feature common to the spectra of II–IV is the occurrence of prominent peaks at *m/e* 63 (CH_3SO^+, high resolution, see Fig. 2). Ions

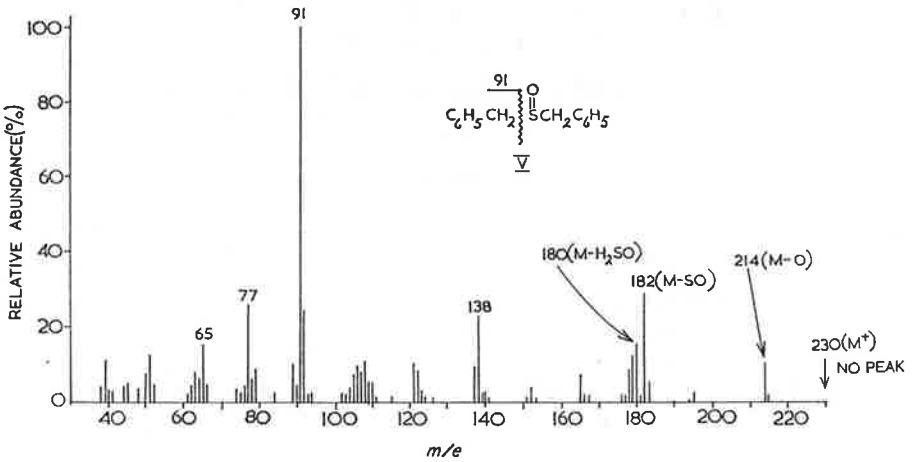
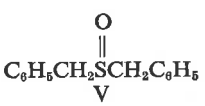
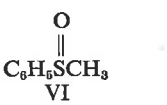


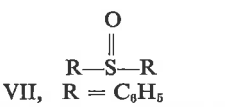
FIG. 3

of this composition may arise via allylic cleavage in the M–olefin species *c* to give *d* (*m/e* 63), but no metastable peaks are evident to substantiate this possibility. In all three spectra the most intense peaks are associated with fragments derived from one of the alkyl chains [e.g., *m/e* 43 ($C_3H_7^+$), *m/e* 41 ($C_3H_5^+$) and *m/e* 39 ($C_3H_3^+$) in Fig. 2].

Although the spectra of the purely aliphatic sulphoxides are devoid of abundant skeletal rearrangement fragments, this is not the case in the presence of the phenyl groups of dibenzyl sulphoxide (V); the spectrum (Fig. 3) contains abundant ions at *m/e* 182 ($C_{14}H_{14}^+$, M—SO, h.r.) and *m/e* 180 ($C_{14}H_{12}^+$, h.r.). In agreement with our earlier conclusions for disulphides[11] and aromatic thioethers,[1] the $[ABC]^+ \rightarrow [AC]^+$ reaction seems to be facilitated by sites of unsaturation in the vicinity of the bond cleavage.







[9] S. I. Goldberg and M. S. Sahli, *Tetrahedron Letters* 4441 (1965).

[10] I. D. Entwistle and R. A. W. Johnstone, *Chem. Comm.*, 29 (1965); see also C. Walling and L. Bollyky, *J. Org. Chem.* **29**, 2699 (1964) and W. Z. Herdt, *Ibid.* **30**, 3897 (1965).

[11] J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, C. Nolde, G. Schroll and D. H. Williams, *J. Chem. Soc.* in press.

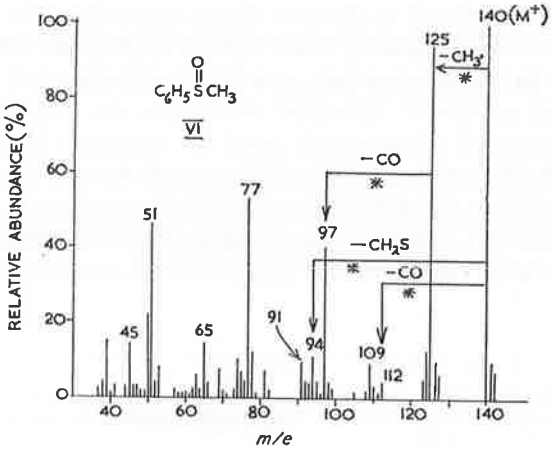


FIG. 4

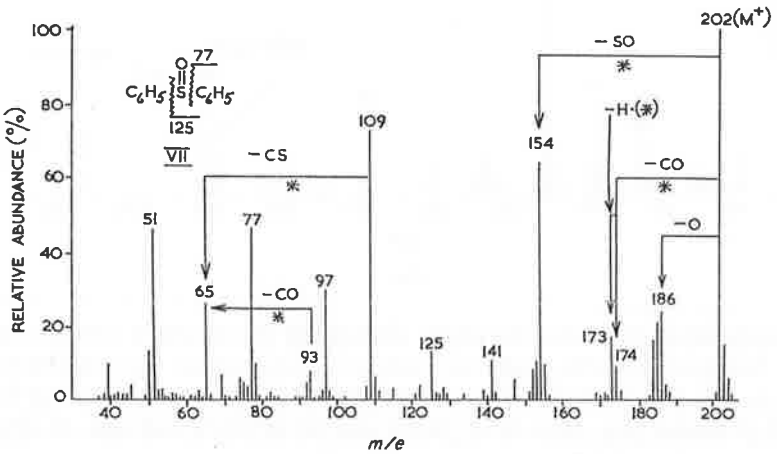


FIG. 5

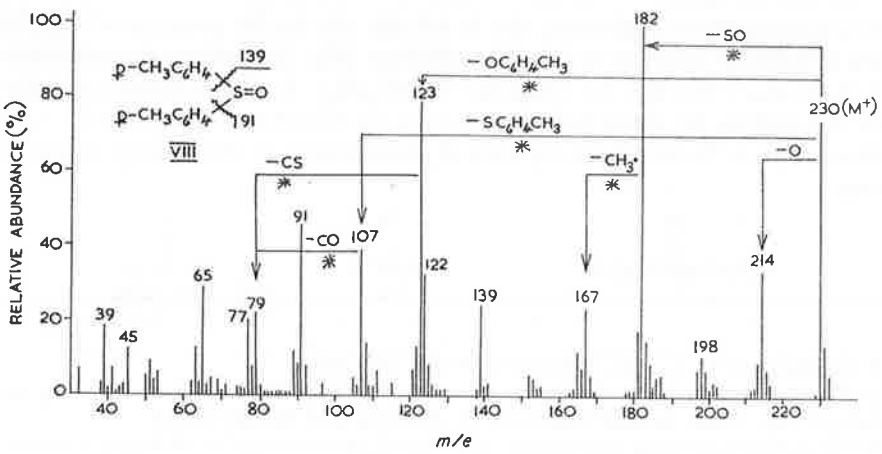


FIG. 6

The spectra (Figs. 4–6) of methyl phenyl sulphoxide (VI), diphenyl sulphoxide (VII) and di-*p*-tolyl sulphoxide (VIII) are remarkable for the abundance and diversity of the rearrangement ions which they contain. Only when both groups attached to the sulphoxide moiety are aromatic does the loss of SO give a very abundant ion (64% of the base peak in Fig. 5 and base peak in Fig. 6). Most noteworthy are the decomposition pathways which involve elimination of carbon monoxide (see Figs. 4–6); the transitions supported by appropriate metastable ions are indicated in the figures and pertinent high resolution data for VI and VII are given in Table 1.

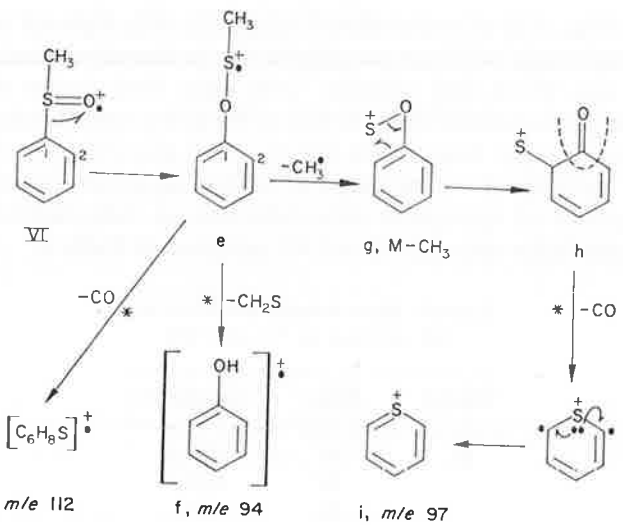
TABLE 1. HIGH RESOLUTION DATA FOR THE SPECTRA OF VI AND VII

Compd	Peak	Composition
VI	97	C_5H_5S
	94	C_6H_6O
	91	C_7H_7
VII	186	$C_{12}H_{10}S$
	174	$C_{11}H_{10}S$
	173	$C_{11}H_9S$
	154	$C_{12}H_{10}$
	141	$C_{11}H_9$
	125	C_6H_5SO
	109	C_6H_5S
	97	C_6H_5S

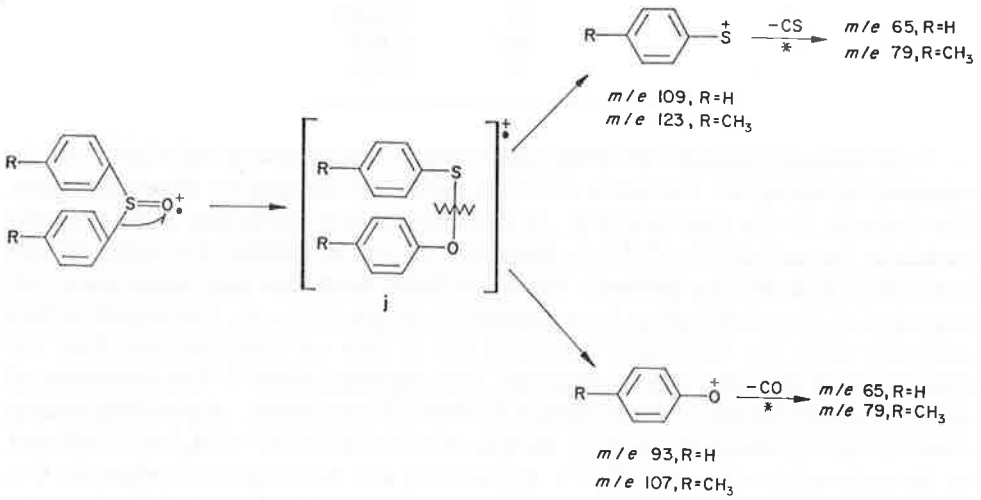
In all three compounds (VI–VIII) which contain the structural unit C_6H_4—S(=O)—, reactions involving the formation of C—O bonds are induced by electron impact. For example, in the spectrum (Fig. 4) of methyl phenyl sulphoxide (VI), both the molecular ion and the M—CH_3 ion eliminate CO, and in addition the molecular ion loses CH_2S in a one-step process. The C—O bond formation may occur via a 1,2-migration of the phenyl group from sulphur to oxygen (VI → e); the loss of carbon monoxide from the rearranged molecular ion is then no more unusual than the elimination of the same neutral fragment from diphenyl ether.[12] The formation of *m/e* 94 ($C_6H_6O^+$, perhaps ionized phenol, f) then follows simply. A plausible mechanism for the formation of *m/e* 97 by the loss of CO from the M—CH_3 ion is indicated by the sequence g → h → i ($C_5H_5S^+$). Routes may also be visualized in which the C-2 carbon atom of the aromatic ring is eliminated as CO. The formulation of *m/e* 97 ($C_5H_5S^+$) as the thiopyrylium cation i is reasonable in the light of the large delocalization energy of this ion as calculated using a simple molecular orbital method.[13] A 1,2-migration analogous to VI → e has previously been postulated to occur in some diaryl sulphones upon electron impact.[5]

Similarly, a number of transitions which are evident from the spectra (Figs. 5 and 6) of the diaryl sulphoxides VII and VIII support a 1,2-phenyl migration from sulphur to oxygen (see j). Simple S—O bond cleavage in j would then furnish *m/e* 109 and

[12] J. H. Beynon, G. R. Lester and A. E. Williams, *J. Chem. Phys.* **63,** 1861 (1959).
[13] J. Koutecky, *Coll. Czech. Chem. Comm.* **24,** 1609 (1959).



m/e 93 when R = H and *m/e* 123 and *m/e* 107 when R = CH_3 (see Figs. 5 and 6). The further decompositions of *m/e* 109 (Fig. 5) and *m/e* 123 (Fig. 6), by elimination of CS, and of *m/e* 93 (Fig. 5) and *m/e* 107 (Fig. 6) by elimination of CO are in good accord with this hypothesis.



Of the spectra of aliphatic sulphones (IX–XII) which have been determined, only that (Fig. 7) of dimethyl sulphone (IX) is not dominated by purely hydrocarbon fragment ions; in this case the base peak (*m/e* 79) corresponds to the loss of a methyl radical. High resolution measurements establish the composition of ions of lower abundance: *m/e* 45 (CHS), *m/e* 48 (5% of CH_4S and 95% of SO), *m/e* 63 (CH_3SO), *m/e* 64 (SO_2) and *m/e* 65 (HSO_2). In the spectra of diethyl sulphone (X), dipropyl sulphone (XI) and di-isobutyl sulphone (XII, Fig. 8), the base peaks occur at *m/e* 29 ($C_2H_5^+$), *m/e* 43 ($C_3H_7^+$) and *m/e* 57 ($C_4H_9^+$), respectively. It is interesting to note that whereas diethyl sulphone (X) gives a peak (10%) due to loss of C_2H_4 [but does not appreciably (<1%) eliminate C_2H_3], dipropyl sulphone (XI) loses both C_3H_6 and

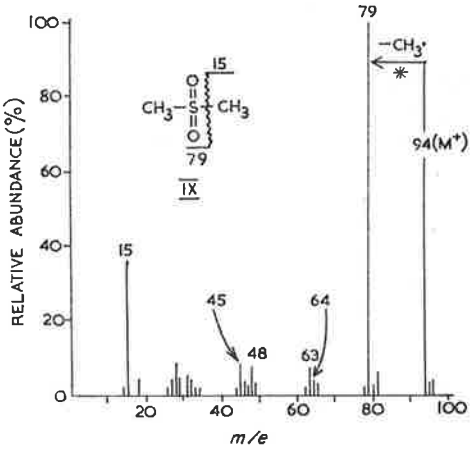


FIG. 7

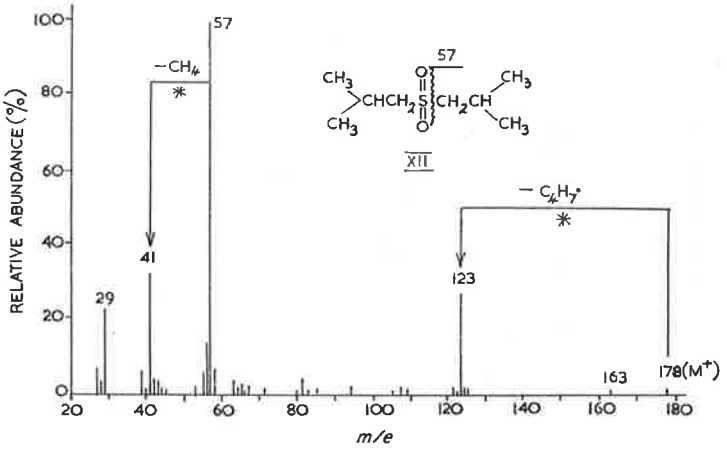


FIG. 8

C_3H_5 (peaks of relative abundance 11% and 8%, respectively) and di-isobutyl sulphone (XII) almost exclusively eliminates C_4H_7 (see Fig. 8), i.e., the tendency to eliminate the alkyl group with associated double hydrogen rearrangement to the charged fragment increases with increasing size of the alkyl group.

IX, R = CH_3 XI, R = n-C_3H_7

X, R = C_2H_5 XII, R = iso-C_4H_9

As in the case of sulphoxides, the complexities of skeletal rearrangement are evident in the spectra of sulphones (XIII–XV) containing a phenyl moiety directly attached to the functional group. The most unusual features of the spectra (Figs. 9 and 10) of methyl phenyl sulphone (XIII) and ethyl phenyl sulphone (XIV) are the decompositions of the molecular ions by losses of CH_2SO and C_2H_4SO, respectively, in one-step processes (high resolution data for XIII–XV are summarized in Table 2). The processes

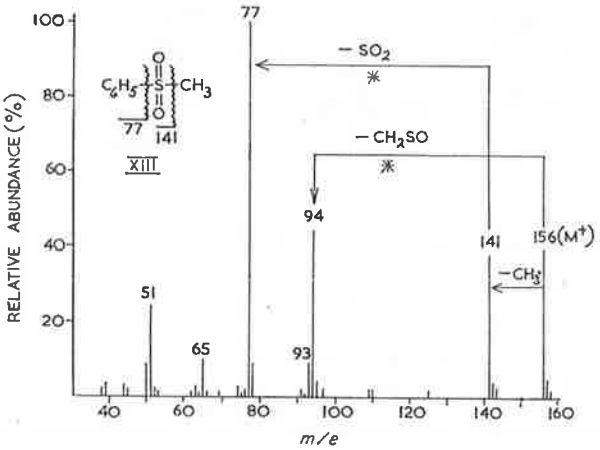


FIG. 9

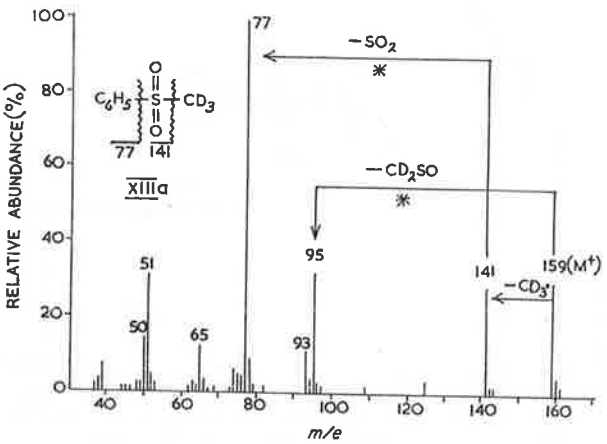


FIG. 9a

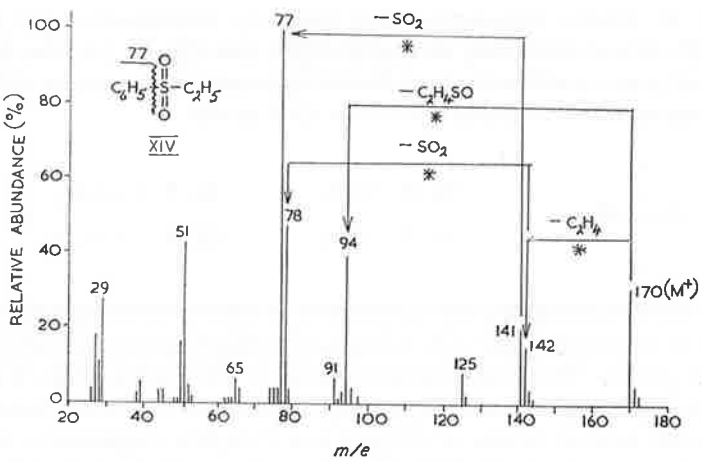


FIG. 10

are interpreted in terms of a 1,2-phenyl migration (XIII and XIV → k), as in the case of sulphoxides and of the diaryl sulphones of Meyerson, Drews and Fields.[5] In the spectrum (Fig. 9a) of trideuteromethyl phenyl sulphone (XIIIa), the *m/e* 94 ion ($C_6H_6O^+$) of Fig. 9 is almost quantitatively shifted to *m/e* 95 ($C_6H_5DO^+$), whereas *m/e* 93 ($C_6H_5O^+$) is not shifted. The rearrangement which leads to C—O bond formation does not appear to be a particularly high energy process, since the total ion current carried by the *m/e* 94 ions from XIII and XIV is increased slightly at lower energies (e.g., 15 eV spectra vs. 70 eV spectra).

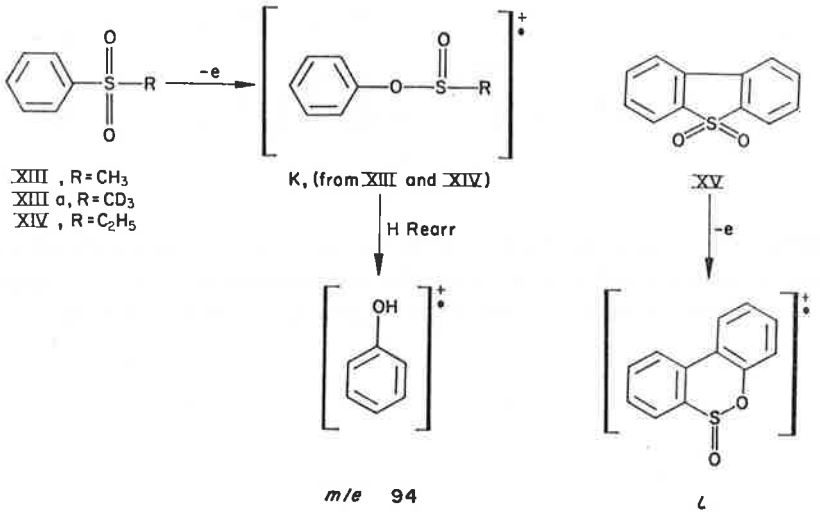


TABLE 2. HIGH RESOLUTION DATA FOR THE SPECTRA OF XIII–XV

Compd	Peak	Composition
XIII	94	C_6H_6O
XIV	141	$C_6H_5SO_2$
	125	C_6H_5SO
	94	C_6H_6O
	91	C_7H_7
XV	188	$C_{11}H_8SO$
	187	$C_{11}H_7SO$
	168	$C_{12}H_8O$
	160	$C_{10}H_8S$
	152	$C_{12}H_8$

The behaviour of simple diaryl sulphones has been so thoroughly documented by Meyerson *et al.*,[5] that it does not merit additional discussion here. However, it is noteworthy that dibenzothiophene dioxide (XV) not only decomposes by elimination of SO, but also by successive losses of carbon monoxide from the molecular ion (see Fig. 11) as established by high resolution measurements (Table 2). A C—O bond in

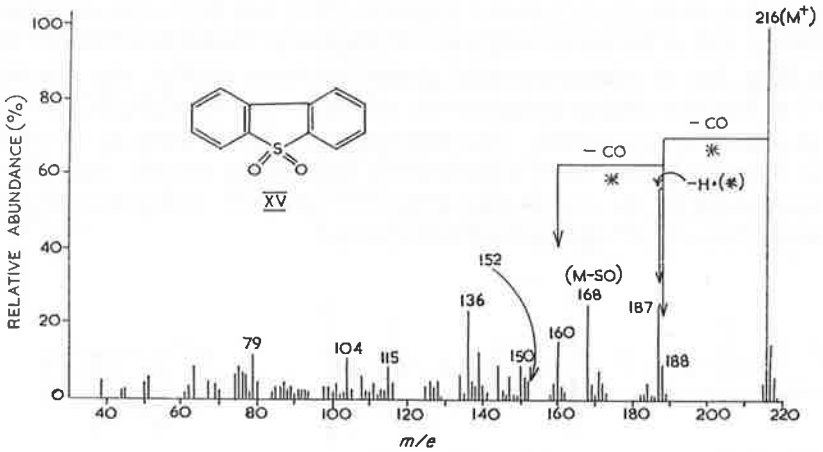
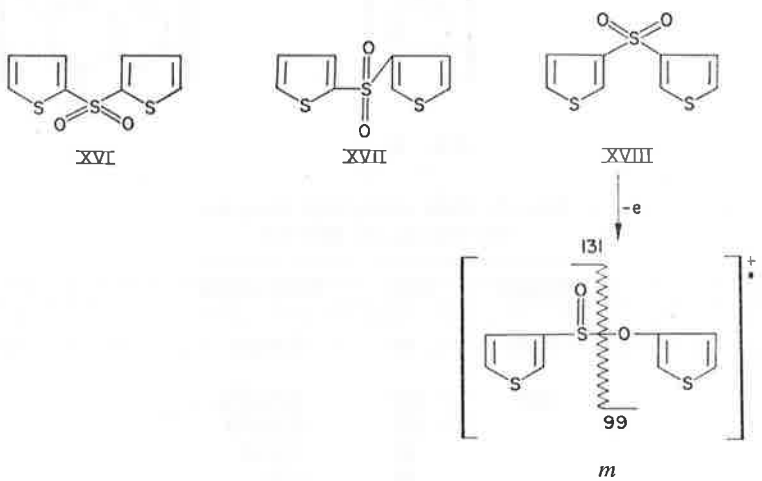


FIG. 11

the molecular ion of XV may be formed by a 1,2-shift (XV → I) and the process can obviously be repeated (either prior to or after the elimination of the first molecule of carbon monoxide) for the formation of the second necessary C—O bond.[13a]



The spectra of the dithienyl sulphones XVI–XVIII suggest that the 1,2-migration of a thienyl group from sulphur to oxygen upon electron impact occurs in a similar manner to the corresponding phenyl migration. All three spectra (see, for example, Fig. 12) contain abundant ions at *m/e* 131 and *m/e* 99 which can rise by S—O bond cleavage in the rearranged molecular ion m.

The results presented in this paper illustrate that although aliphatic sulphoxides and sulphones behave relatively simply upon electron impact, the corresponding aromatic compounds undergo well-defined skeletal reorganization. The nature of the

[13a] *Note added in proof*—This rearrangement has concurrently been observed by E. K. Fields and S. Meyerson [*J. Amer. Chem. Soc*, **88**, 2836 (1966)]. The authors wish to thank Dr. Meyerson for sending a copy of the manuscript to them prior to publication.

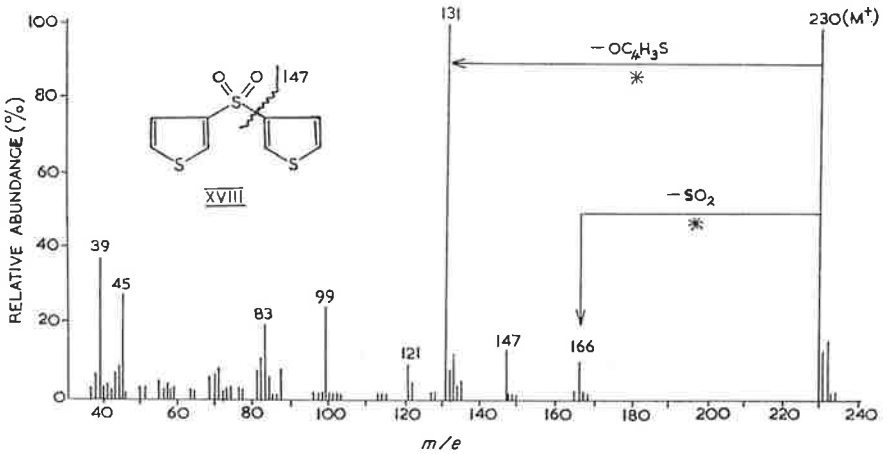


FIG. 12

reorganization is not only of mechanistic interest, but also a knowledge of the rearrangements is important to permit a secure interpretation of the spectra for analytical purposes.

EXPERIMENTAL

All mass spectra were determined on an AEI MS9 double focussing mass spectrometer operating at 70 eV and a source pressure of (1·0–5·0) × 10^{-7} mm Hg. Unless otherwise stated, samples were introduced into the source through a heated inlet system at a temperature of approximately 150°.

Dimethyl sulphoxide (I), di-*p*-tolyl sulphoxide (VIII) and dibenzothiophene dioxide (XV) were purified commercial samples. Previously published procedures were used for the preparation of di-n-propyl sulphoxide (II),[14] di-n-butyl sulphoxide (III),[14] di-isobutyl sulphoxide (IV),[15] dibenzyl sulphoxide (V),[16] diphenyl sulphoxide (VII),[17] dimethyl sulphone (IX),[14] diethyl sulphone (X),[14] di-n-propyl sulphone (XI),[14] and the dithienyl sulphones (XVI–XVIII).[18]

Di-isobutyl sulphone (XII) was prepared by the oxidation of di-isobutyl sulphoxide (IV) with H_2O_2 in AcOH. H_2O_2 in AcOH was also employed for the oxidation of thioanisole and d_3-thioanisole to methyl phenyl sulphoxide (VI), methyl phenyl sulphone (XIII) and trideuteromethyl phenyl sulphone (XIIIa). The same reagent furnished ethyl phenyl sulphone (XIV) from ethyl phenyl sulphide.

Acknowledgements—One of us (J. H. B.) is grateful for the award of an I.C.I. Fellowship. Thanks are expressed for a grant (to Aarhus University) from "Thomas B. Thriges fond" and to Dr. E. Jones for compounds XVI–XVIII.

[14] C. W. N. Cumper, J. F. Read and A. J. Vogel, *J. Chem. Soc.* 5323 (1965).
[15] D. Ll. Hammick and R. B. Williams, *J. Chem. Soc.* 211 (1938).
[16] A. J. Vogel and D. M. Cowan, *J. Chem. Soc.* 16 (1943).
[17] A. Schönberg, *Ber. Dtsch. Chem. Ges.* **56**, 2275 (1923).
[18] E. Jones and J. M. Moodie, *Tetrahedron* **21**, 2413 (1965).

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Studies in Mass Spectrometry

Part XVI.[1] Mass Spectra of Thiophenols

SVEN-OLOV LAWESSON, J. Ø. MADSEN and GUSTAV SCHROLL

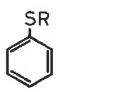
Department of Organic Chemistry, Chemical Institute, University of Aarhus, Aarhus C., Denmark

J. H. BOWIE and D. H. WILLIAMS

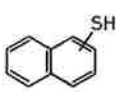
University Chemical Laboratory, Cambridge, England

A variety of thiophenols have been synthesised and their mass spectra determined and interpreted. The spectra are very useful from an analytical viewpoint, all compounds giving distinct molecular ions and the main fragmentations occurring without skeletal rearrangement. In some cases *ortho*-effects can indicate the relative orientation of substituents.

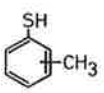
Although the mass spectra of phenols and naphthols have been widely studied and interpreted,[2–6] no studies of thiophenols and thionaphthols have appeared, except for the reported spectrum of thiophenol itself.[3,7] We have therefore undertaken a study of the behaviour of a variety of thiophenols



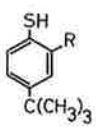
I, R=H
Ia, R=D



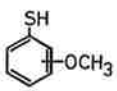
II, α-SH
III, β-SH



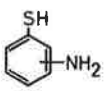
IV, (*ortho*)
V, (*meta*)
VI, (*para*)



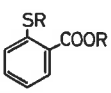
VII, R=H
VIII, R=CH3



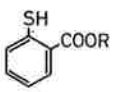
IX (*ortho*)
X (*meta*)
XI (*para*)



XII (*ortho*)
XIII (*para*)



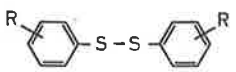
XIV, R=H
XIVa, R=D



XV, R=CH3
XVI, R=C6H5

under electron impact and the data are discussed in this paper and compared with the corresponding data (when available) for phenols.

In general, the mass spectra of the thiophenols I—XVI contain peaks due to traces of the disulphide which may be formed by oxidative dimerisation. At low pressures of the source ($\sim 1 \times 10^{-7}$ mm Hg) and heated inlet system, and at lower temperatures ($\sim 150°$) of the inlet system and source, peaks due to disulphides are small (0.1 % to 10 % relative abundance). Alternatively, high sample pressures and high temperatures lead to larger peaks from disulphides; the disulphide formulation (XVII) is substantiated by the observed fragmentation pattern.[8] The oxidative dimerisation may be greatly diminished or totally avoided if spectra are obtained by the direct inlet procedure. The coupling reaction [for which there is ample precedent, *e.g.*, *p*-toluenethiol (VI) may be oxidatively dimerised in high yield to *p*-tolyl disulphide in sulphuric acid solution employing Fe^{III} ions and air [9]] therefore occurs largely in the heated inlet system. The small peaks due to disulphides are omitted from the reported spectra (Figs. 1—9).



XVII

In the spectrum (Fig. 1) of thiophenol (I), the abundant M—1 ion (*m/e* 109) is formed by loss of approximately equal amounts of the hydrogen bound to sulphur and of ring hydrogens as indicated by the spectrum of S-d_1-thiophenol (Ia) (obtained by introducing the parent compound into the inlet system with deuterium oxide [10]). Metastable peaks * establish the decomposition of the molecular ion by loss of C_2H_2 and CS in one-step processes; the latter pathway leads to $C_5H_6^+$ (*m/e* 66) which decomposes to *m/e* 65 by expulsion of a hydrogen atom (see Fig. 1).

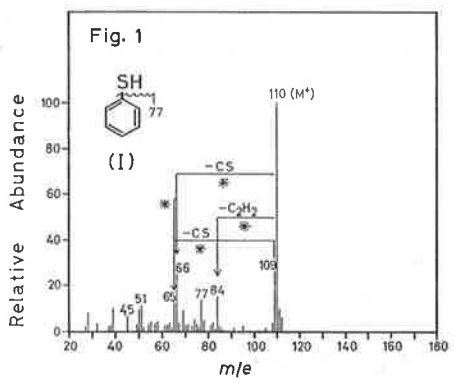


Fig. 1.

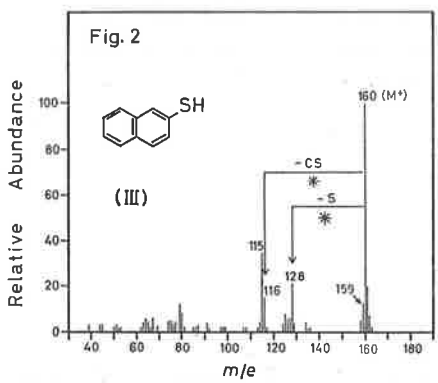


Fig. 2.

* Transitions supported by the presence of an appropriate metastable peak are indicated by an asterisk (*).

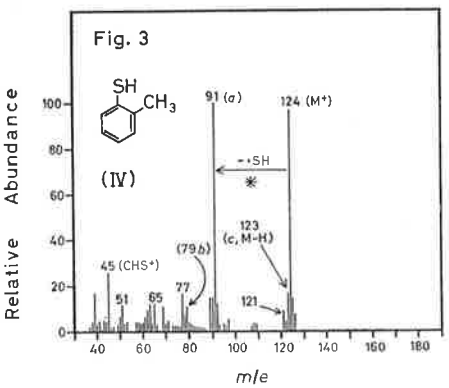


Fig. 3.

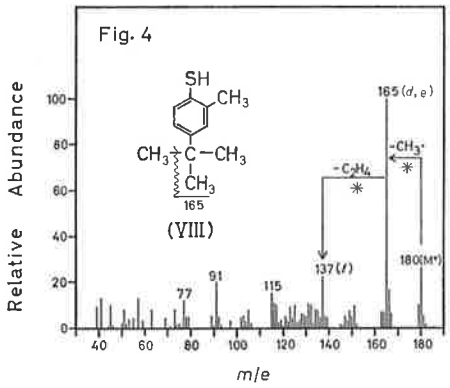
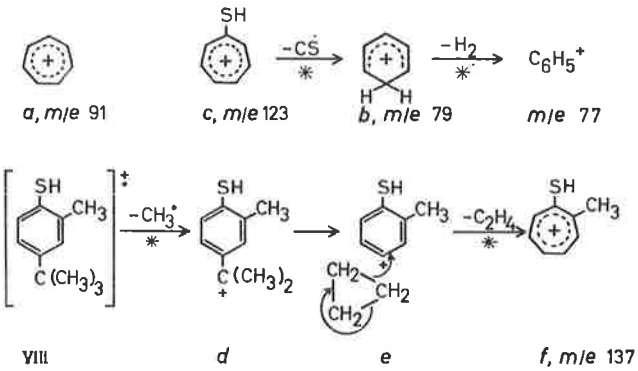


Fig. 4.

The spectra of 2,3-benzothiophenol (II) and 3,4-benzothiophenol (III) are similar, and therefore only that of III (Fig. 2) is reported here. Surprisingly, II and III decompose by loss of sulphur to a much larger extent than by loss of SH (see, for example, Fig. 2), whereas the reverse situation prevails in the spectrum (Fig. 1) of thiophenol (I). An appropriate metastable peak establishes that the *m/e* 115 ion (Fig. 2) arises, at least in part, by elimination of CS from the M−1 ion.

The spectra of the isomeric methyl thiophenols (IV—VI) are very similar and only that of the *ortho*-isomer (IV) is reproduced (Fig. 3). These spectra provide an interesting comparison with those of the corresponding methyl phenols (cresols),[2] which exhibit intense M−1 peaks, presumably due to the formation of hydroxytropylium ions. In contrast, the methyl thiophenols (see Fig. 3) furnish lower abundance M−1 ions and very abundant M−SH ions (*m/e* 91, corresponding to the tropylium ion *a*). The difference is possibly due to the greater stability of the SH radical relative to the OH radical. The *m/e* 79 ion ($C_6H_7^+$) is probably best represented[11] as the benzonium ion *b* and decomposes by loss of a hydrogen molecule (metastable peak at *m/e* 75.2 in the spectra of IV—VI) to *m/e* 77 ($C_6H_7^+$). Metastable peaks at *m/e* 50.8 in the spectra of all three isomers establish that *m/e* 79 arises *via* the elimination of CS from the M−1 ion which is represented as *c*. Appreciable M−3 ions (*m/e* 121) are also present in the spectra of IV—VI; presumably a common $C_7H_5S^+$ ion of enhanced stability is produced, but the nature of any such ion is not obvious.

The *p*-*t*-butylthiophenols VII and VIII show behaviour which is analogous to that of *t*-butylbenzene.[12] As a representative example, the spectrum of 2-methyl-4-*t*-butylthiophenol (VIII) is reproduced in Fig. 4. The base peak (*m/e* 165) is due to the anticipated loss of a methyl group, but this M−15 species then decomposes by loss of ethylene to *m/e* 137 as established by an appropriate metastable peak (*m/e* 113.6 obs., $137^2/165 = 113.7$). It has been proposed[12] on the basis of isotopic labelling experiments that the M−CH_3 ion from *t*-butylbenzene rearranges to a phenylated cyclopropane and the same



rearrangement (VIII→*d*→*e*) probably operates in the thiophenol VIII, leading ultimately to *f* (*m/e* 137).

A common feature of the spectra of the isomeric methoxythiophenols (IX—XI) lies in the successive eliminations of a methyl radical and CO from the molecular ions. Appropriate metastable peaks are found for these one-step transitions in all three spectra. While the initial product of CO elimination from the M—CH_3 ion *g* (*m/e* 125) may well be the cyclopentadienyl cation *h*(*m/e* 97), this probably rearranges further to give the highly resonance stabilised thiopyrylium cation *i* (*m/e* 97).[13,14] This fragmentation sequence is reminiscent of that observed for anisole itself,[15] and may be seen in the spectra (Figs. 5 and 6) of the *ortho*- and *para*-isomers (IX and XI) [the spectrum of the *meta*-isomer (X) is similar to that of the *para*-isomer (XI)]. It is noteworthy that the relative abundances of the M—CH_3 ions from the isomeric methoxythiophenols (IX—XI) are much less dependent on the relative orientation of SH and OCH_3 groups than in the corresponding dimethoxybenzenes [15] and methoxythioanisoles [16] (*i.e.*, quinoid M—15 ions such as *j* do not seem to be particularly favoured relative to non-conjugated M—15 ions such as *k* when

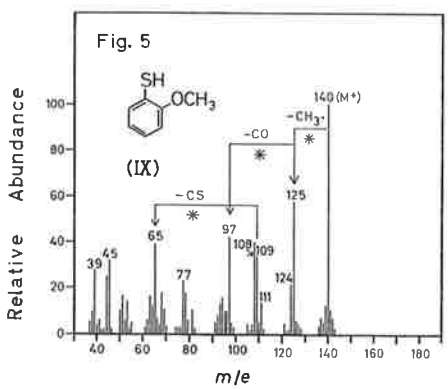


Fig. 5.

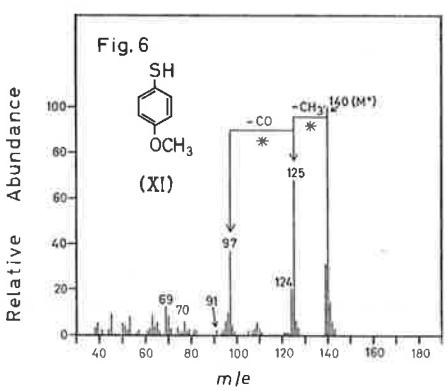
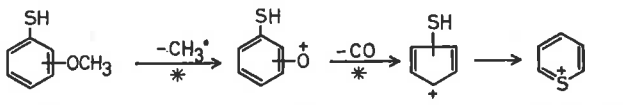


Fig. 6.



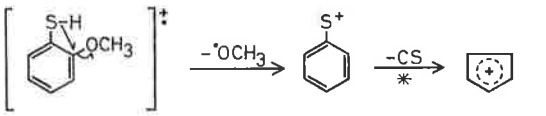
IX–XI *g*, *m/e* 125 *h*, *m/e* 97 *i*, *m/e* 97

j *k*

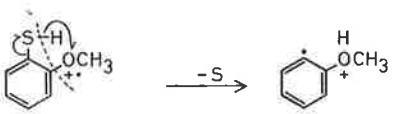
the electron-donating group is SH). This observation suggests that electron donation by SH to give ions such as *j* is relatively small.

Ortho-effects are apparently operative in the spectrum (Fig. 5) of *o*-methoxythiophenol (IX), which contains M—OCH_3 (*m/e* 109), M—CH_3OH (*m/e* 108, 30 %) and M—S (*m/e* 108, 70 %) peaks of considerably greater abundance than in the *meta*- and *para*-isomers (see Fig. 6). The M—OCH_3 ion is formulated as *l* because (i) the mechanism for the formation of *l* (IX→*l*) accounts for the necessity of an *adjacent* SH group and (ii) the M—OCH_3 ion decomposes by elimination of CS in a onestep process to *m/e* 65 as indicated by a metastable peak at *m/e* 38.8 ($65^2/109 = 38.8$); an identical metastable in the spectrum (Fig. 1) of thiophenol (I) supports the decomposition of the M—1 ion (*i.e.* *l*) from I by the same route. The loss of methanol can occur *via* a simple *ortho*-effect (see dotted lines in XIa), while the elimination of a sulphur atom may be facilitated by a hydrogen radical migration to oxygen (XIa→*m*).

Although the composition of *m* (and other ions from IX and XI) is established by high resolution measurements (summarised in Table 1), it is emphasised that the structure proposed is conjectural and, if *m* is formed, it may well rearrange further. It is noteworthy that the low abundance (2 %) *m/e* 91 ion from XI has the composition $C_7H_7^+$; its formation demands a methyl migra-



IX *l*, *m/e* 109 *m/e* 65



IX a *m*, *m/e* 108

Table 1. Compositions of some ions in the spectra (Figs. 5 and 6) of *o*-methoxythiophenol (IX) and *p*-methoxythiophenol (XI).

Compound	Ion	Composition
IX	108	C_6H_4S (30 %) C_7H_8O (70 %)
	109	C_6H_5S
	111	C_6H_7S
	124	C_6H_4SO
	125	C_6H_5SO
XI	69	C_3HS
	70	C_3H_2S
	91	C_7H_7
	97	C_5H_5S

tion. The occurrence of such ions is of obvious relevance in evaluating the possible use of the element mapping technique [17,18] in mass spectrometry.

The spectra of *o*-(XII)- and *p*-(XIII)-aminothiophenols are very similar and only that of the *p*-isomer (XIII) is reproduced (Fig. 7). High resolution measurements establish that the *m/e* 97 and *m/e* 98 ions correspond to $C_5H_5S^+$ and $C_5H_6S^+$, the latter being formed in a one-step process (metastable peak at *m/e* 76.8; $98^2/125 = 76.8$) from the molecular ion by elimination of HCN; this behaviour parallels that of aniline[3,19] indeed, *m/e* 93 ($C_6H_7N^+$, high resolution), formed by the loss of a sulphur atom, probably corresponds to the aniline molecular ion and decomposes by loss of HCN (metastable peak at *m/e* 46.8; $66^2/93 = 46.8$) to $C_5H_6^+$ (*m/e* 66, see Fig. 7). Metastable peaks also establish the sequence illustrated by the plausible structures *n*→*o*→*p*.*

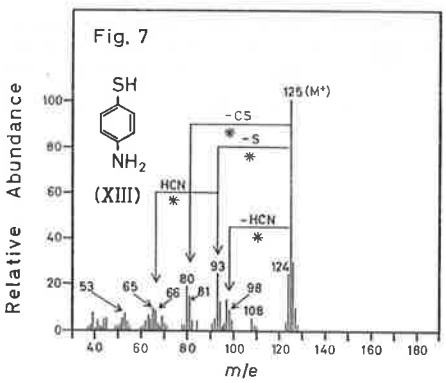


Fig. 7.

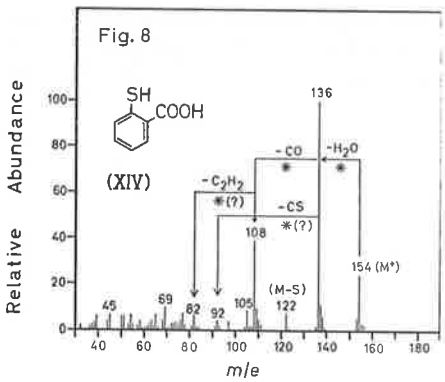
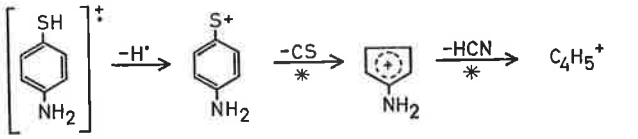


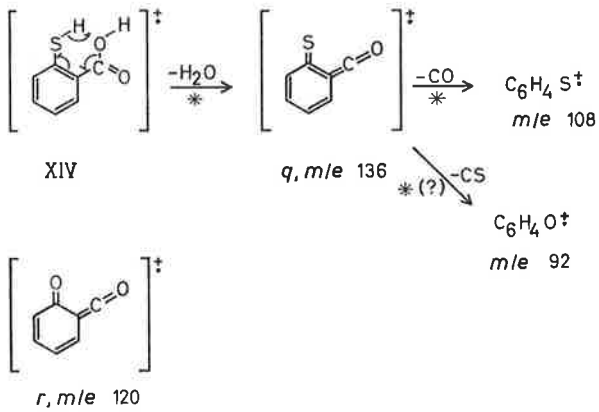
Fig. 8.

* The representation of $C_5H_6N^+$ (*m/e* 80) as a protonated pyridine, rather than as *o*, is equally feasible.



XIII *n*, *m/e* 124 *o*, *m/e* 80 (C_5H_6N, H.R.) *p*, *m/e* 53

The mass spectrum (Fig. 8) of thiosalicylic acid (XIV) resembles that of the corresponding phenol, salicylic acid,[20] insomuch as an *ortho*-effect permits the facile elimination of water (XIV → *q*). The ion *q* decomposes to a large extent by loss of CS (see Fig. 8).* In this connection it would be of interest to establish by O^{18}-labelling whether the corresponding ion (*r*) from salicylic acid eliminates the exocyclic or cyclic CO group, or a mixture of these two CO groups. The specific elimination of water in the manner indicated is established by the spectrum of O-d_2-XIV (XIVa) in which *m/e* 136 is not shifted.



XIV *q*, *m/e* 136 *r*, *m/e* 120

The spectrum (Fig. 9) of the methyl ester XV derived from thiosalicylic acid (XIV) is rationalised similarly and only the loss of methane from the molecular ion to give $C_7H_4O_2S^+$ (*m/e* 152, high resolution), presumably *via* an *ortho*-effect, merits comment. Similarly, the spectrum of the phenyl ester (XVI) contains by far the most abundant ion at *m/e* 94, corresponding to ionised phenol, which may also arise through the operation of an *ortho*-effect.

As regards analytical work, this study indicates that the mass spectra of thiophenols are valuable. The molecular ions are consistently distinct and skeletal rearrangement processes minimal among abundant ions. The presence of groups *ortho* to the SH function is frequently uncovered by the spectra.

* A metastable peak at *m/e* 62.2 corresponds either to the loss of CS from *m/e* 136 (*q*) ($92^2/136 = 62.23$) or to the elimination of acetylene from *m/e* 108 ($82^2/108 = 62.26$).

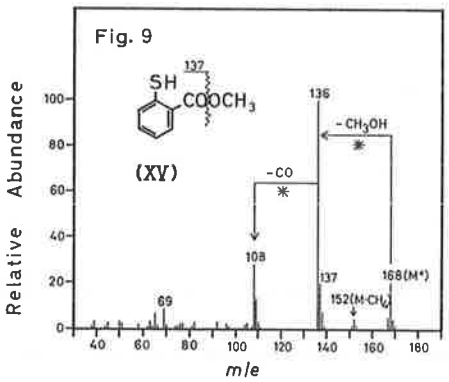


Fig. 9.

EXPERIMENTAL

All spectra were obtained using an AEI MS9 mass spectrometer operating at 70 eV. The reported spectra were obtained by introduction of the samples through a heated inlet system at temperatures ($\leq$ 150°C) and pressures ($\leq 2 \times 10^{-7}$ mm Hg) consistent with a minimum of disulphide formation.

Compounds, I, XII, XIII, XIV were purified commercial samples. Published procedures were employed for the syntheses of II,[21] III,[22] IV,[22] V,[23] VI,[24] IX,[25] X[26], XI,[27] XV,[28] and XVI.[29]

Acknowledgements. One of us (J.H.B.) wishes to thank I.C.I. for a Fellowship during the tenure of which this work was carried out. Thanks are expressed to the Consolidation Coal Company, Library, U.S.A., for samples of *p-t*-butylthiophenol (VII) and 2-methyl 4-*t*-butylthiophenol (VIII).

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STUDIES IN MASS SPECTROMETRY—XVII[1]

REARRANGEMENT PROCESSES IN SOME ESTERS CONTAINING UNSATURATED LINKAGES—THE ELIMINATION OF CO_2 FROM ESTERS

J. H. BOWIE and D. H. WILLIAMS
University Chemical Laboratory, Cambridge
and
P. MADSEN, G. SCHROLL and S.-O. LAWESSON
Dept. of Chemistry, Aarhus University, Aarhus, Denmark

(*Received* 2 *June* 1966)

Abstract—The mass spectra of a variety of propiolate, acetylenedicarboxylate, maleate, fumarate and cyanoacetate esters have been measured. The formation of ions via the elimination of carbon dioxide (with or without the associated loss of other groups) is quite common in these esters. The prevalence of such fragmentation processes, which are of obvious importance with respect to the element-mapping technique, is probably associated with the presence of double or triple bonds (in the vicinity of the ester function) which may be ionized by removal of an electron and thus provide an electron deficient site to which a group (alkyl, alkenyl, etc.) may migrate.

OF OBVIOUS relevance to the technique of element mapping,[2] is the rigorous evaluation of those processes occurring upon electron impact which involve the migration of atoms other than hydrogen. With reference to this problem, recent publications from our own[3,4] and other laboratories[5–8] have been concerned with (or have noted) the elimination of carbon dioxide from esters upon electron impact. In our own studies[3,4] only methyl and ethyl esters were examined, but processes involving the elimination of carbon dioxide with consequent skeletal rearrangement seemed particularly prevalent in those esters containing unsaturated linkages (e.g., C≡C[3] and C≡N[3,4] bonds) in the vicinity of the ester function . We have now synthesized and examined a variety of propiolates (HC≡CCOOR), acetylenedicarboxylates (ROOCC≡CCOOR), maleates and fumarates (ROOCCH=CHCOOR, *cis* or *trans*), cyanoacetates (N≡CCH_2COOR) and isopropylcyanoacetates [$(Me)_2$CHCH(CN)COOR] in the hope of evaluating the general scope of CO_2 elimination with or without associated loss of other groups) in these esters and the influence of the alkyl group (R).

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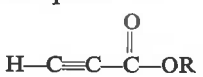
Methyl (I), ethyl (II), n-propyl (III), isobutyl (IV), s-butyl (V), allyl (VI) and benzyl (VII) propiolates were synthesized and their mass spectra determined. In each case the compositions of the M-44 and M-45 ions were determined by high resolution measurements. All the esters afforded M—CO_2 and M—HCO_2 ions, whose relative abundances are summarised in Table 1; it is emphasized that none of the hydrocarbon fragments quoted in the Table are present as intact units in the various esters prior to electron impact.



I, R = Me
II, R = Et
III, R = n-Pr
IV, R = iso-Bu
V, R = s-Bu
VI, R = CH_2—CH=CH_2
VII, R = CH_2-C_6H_5

Table 1. Relative abundances of M—CO_2 and M—CO_2H ions from propiolate esters (HC≡CCOOR)

R	R.A. (%) of M—CO_2 ion[a]	R.A. (%) of M—HCO_2 ion[a]
Me	20 (C_3H_4)	15 (C_3H_3)
Et	<1 (C_4H_6)[b]	10 (C_4H_5)[b]
Pr	2 (C_5H_8)[b]	8 (C_5H_7)
iso-Bu	<1 (C_6H_{10})[b]	3 (C_6H_9)[b]
s-Bu	1 (C_6H_{10})[b]	3 (C_6H_9)[b]
CH_2—CH=CH_2	4 (C_5H_6)[b]	8 (C_5H_5)
$CH_2C_6H_5$	34 (C_9H_8)	67 (C_9H_7)

[a] R.A. = relative abundance, the base peak arbitrarily being taken as 100: the compositions of the ions are given in parentheses.

[b] The peaks in the spectra corresponding to these integral masses were larger because of their doublet nature (as established by high resolution).

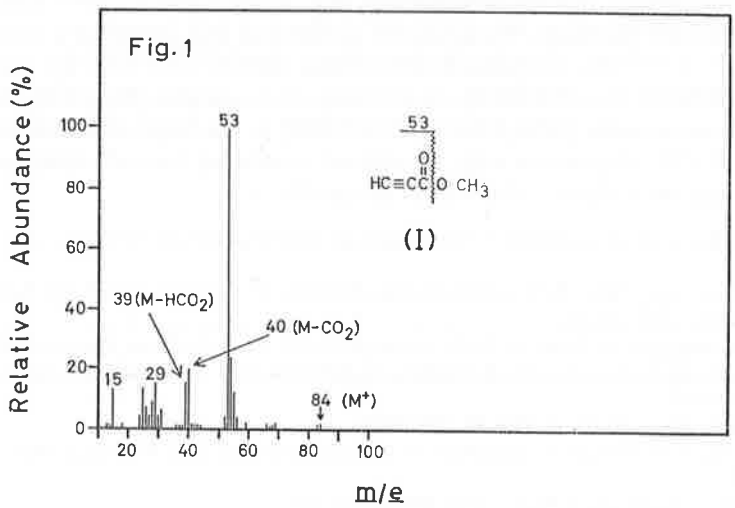


Fig. 1

Representative spectra are reported in detail in Figs. 1–3. The ion which formally corresponds to H—C≡C—C≡O$^+$ (*m/e* 53) either gives rise to the base peak or is ⩾90% of the base peak abundance in the spectra of I–VI (see Fig. 1 and Fig. 2). The spectrum (Fig. 2) of allyl propiolate (VI) is also noteworthy for the presence of an

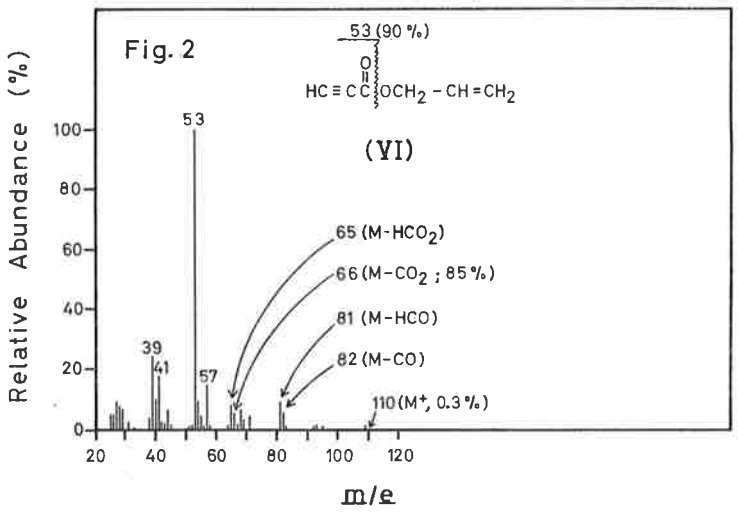


FIG. 2

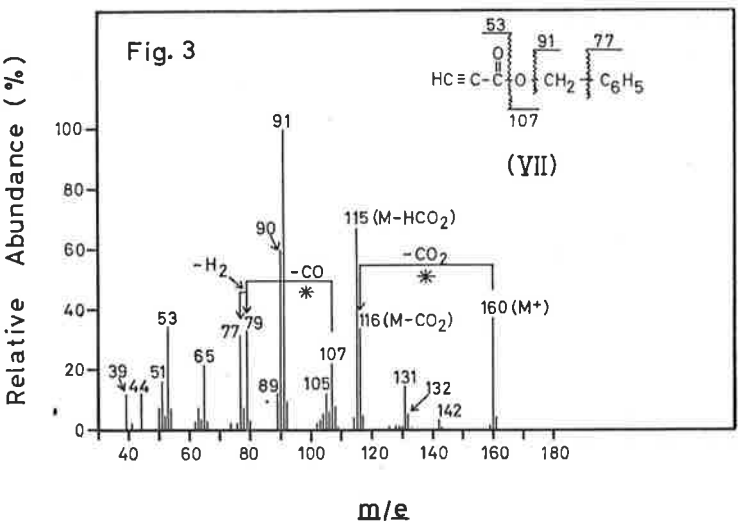
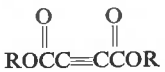


FIG. 3

M—CO ion [*m/e* 82, $C_5H_6O^+$, high resolution (H.R.)] which decomposes by loss of a hydrogen radical to *m/e* 81 ($C_5H_5O^+$, H.R.) as established by an appropriate metastable peak at *m/e* 80·0. A portion (10%) of the *m/e* 53 base peak of Fig. 2 is also due to a rearrangement ion ($C_4H_5^+$); a metastable peak at *m/e* 34·8 suggests that this ion can arise from the M—HCO species (*m/e* 81) by the elimination of carbon monoxide (calculated value, *m/e* 34·7). In the spectrum (Fig. 3) of the benzyl ester (VII), a

metastable peak at *m/e* 114·0 establishes that the M—HCO_2 ion (*m/e* 115) arises, at least in part, from the M—CO_2 ion by loss of a hydrogen radical.



VIII, R = Me
IX, R = Et
X, R = n-Pr
XI, R = iso-Pr
XII, R = n-Bu
XIII, R = iso-Bu
XIV, R = s-Bu
XV, R = CH_2—CH=CH_2

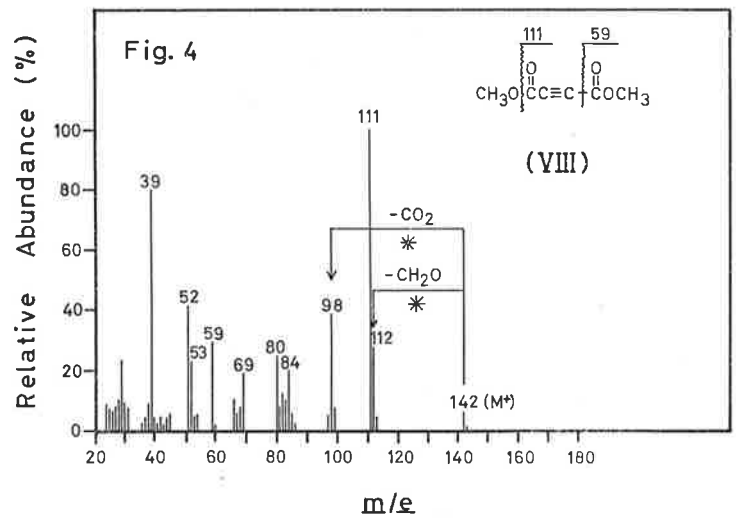


FIG. 4

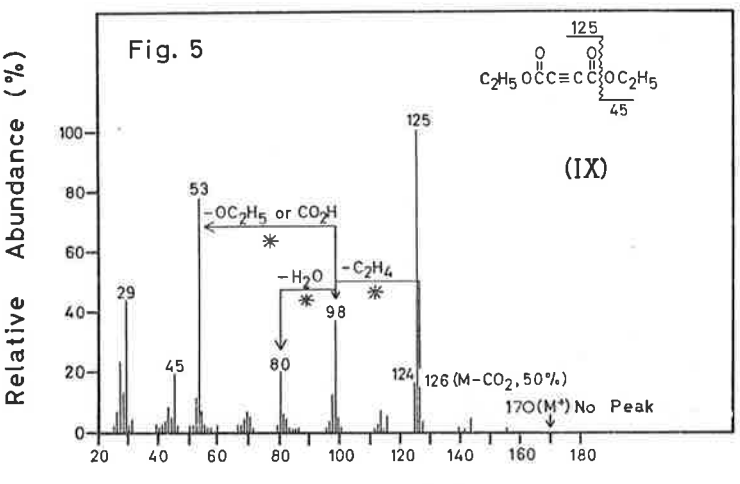
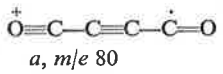


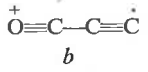
FIG. 5

Since the spectrum (Fig. 4) of dimethyl acetylenedicarboxylate (VIII) contains a M—CO_2 species,[3] it was of interest to study the prevalence of related ions from ethyl (IX), n-propyl (X), iso-propyl (XI), n-butyl (XII), isobutyl (XIII), s-butyl (XIV) and allyl (XV) esters. In the spectra of the esters (VIII–XIV) containing saturated alkyl groups, significant M—CO_2 ions appear only when R = CH_3 (Fig. 4) and R = C_2H_5 (Fig. 5). Other ions of unusual composition in the spectrum (Fig. 4) of the dimethyl

ester (VIII) are *m/e* 80 ($C_4O_2^+$, formally *a*) and *m/e* 52 (C_3O^+, formally *b*). Scheme 1 summarises some of the decomposition modes of diethyl acetylenedicarboxylate (IX) which involve skeletal rearrangement processes and are established by high resolution measurements and appropriate metastable peaks.[9]

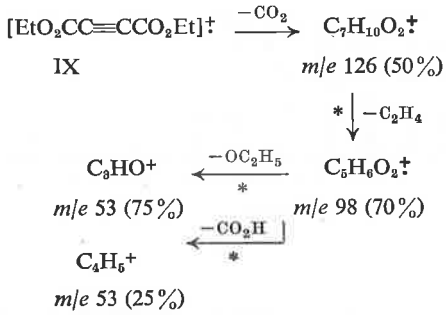


a, *m/e* 80

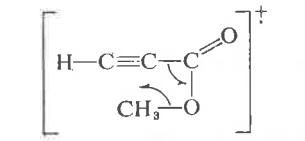


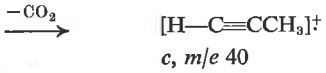
b

Scheme 1

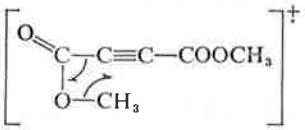


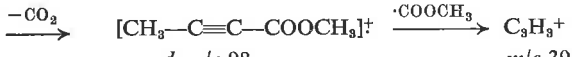
It is appropriate to consider possible mechanisms by which carbon dioxide may be eliminated from propiolates (I–VII) and dimethyl (VIII) and diethyl (IX) acetylenedicarboxylates. In the propiolate esters (I–VII), the alkyl group must migrate to one of the two acetylenic carbon aroms; a four-centre mechanism (e.g., I → *c*, *m/e* 40) appears most plausible and is analogous to the four-centre mechanism proposed by Brown and Djerassi[8] to account for the loss of carbon dioxide from some organic carbonates. A similar mechanism (VIII → *d*, *m/e* 98) probably operates in the decomposition of dimethyl acetylenedicarboxylate (VIII), since the spectrum (Fig. 4) contains an abundant ion at *m/e* 39 ($C_3H_3^+$), which may arise by elimination of a carbomethoxyl radical from *d*.





c, *m/e* 40





d, *m/e* 98 *m/e* 39

Skeletal rearrangement is very prevelant when diallyl acetylenedicarboxylate (XV) fragments under electron impact (the formation of most of the major ions between *m/e* 53 and *m/e* 97 involves the migration of groups other than hydrogen). The compositions of some ion which must arise via skeletal rearrangement in the spectrum (Fig. 6) are listed in Table 2. For purposes of clarity, the formal derivation of each rearrangement ion is indicated in the Table.

[9] The $C_5H_6O_2^+$ ion may, of course, arise also in part via a pathway which does not involve skeletal rearrangement and hence C_3HO^+ does not *necessarily* arise via a skeletal reorganisation pathway.

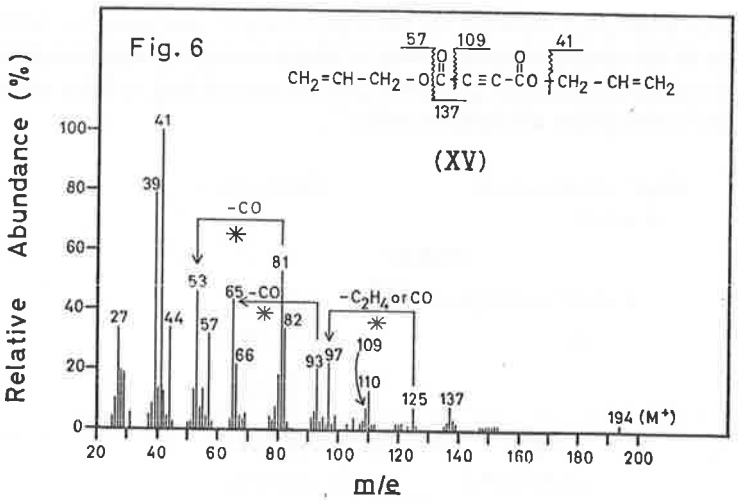
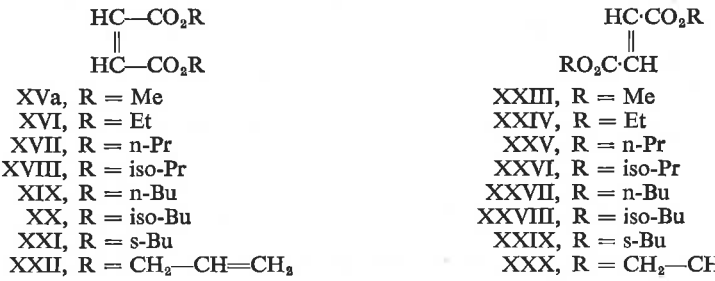


FIG. 6

TABLE 2. SKELETAL REARRANGEMENT IONS FROM DIALLYL ACETYLENEDICARBOXYLATE (XV)

Ion (*m/e*)	Composition	Formal derivation
125	$C_6H_5O_3$ (100%)	M − CO − CH_2—CH=CH_2
97	C_6H_9O (35%)	M − OOCC≡CCO − H
93	C_6H_5O (90%)	M − CO_2 − OCH_2—CH=CH_2
82	C_5H_6O (90%)	M − CO − COCH—CH=CH_2 (O)
81	C_5H_5O (90%)	M − CO − $COCH_2$—CH=CH_2 (O)
66	C_5H_6 (100%)	M − CO_2 − COCH—CH=CH_2 (O)
65	C_5H_5 (100%)	M − CO_2 − $COCH_2$—CH=CH_2 (O)
53	C_4H_5 (35%)	C_5H_5O − CO

It is noteworthy that all the rearrangement ions (with the exception of $C_6H_9O^+$) can formally be generated by a simple cleavage process coupled either with the elimination of CO or CO_2 (necessitating the migration of allyloxy and allyl groups, respectively). The complement to $C_6H_9O^+$ to account for *m/e* 97 is made up of $C_4HO_3^+$ (60%) and $C_5H_5O_2^+$ (5%); a strong metastable peak at *m/e* 75·4 suggests that these ions may arise, at least in part, from *m/e* 125 (Table 1) by the loss of C_2H_4 or CO, respectively (calculated metastable at *m/e* 75·3). Some other transitions established by the high resolution measurements and appropriate metastable peaks are summarized in Fig. 6. The most remarkable ions are $C_5H_5^+$ (*m/e* 65) and $C_5H_6^+$ (*m/e* 66) which formally consist of the carbon atoms of the acetylenic linkage and one allyl group.



XVa, R = Me
XVI, R = Et
XVII, R = n-Pr
XVIII, R = iso-Pr
XIX, R = n-Bu
XX, R = iso-Bu
XXI, R = s-Bu
XXII, R = CH_2—CH=CH_2

XXIII, R = Me
XXIV, R = Et
XXV, R = n-Pr
XXVI, R = iso-Pr
XXVII, R = n-Bu
XXVIII, R = iso-Bu
XXIX, R = s-Bu
XXX, R = CH_2—CH=CH_2

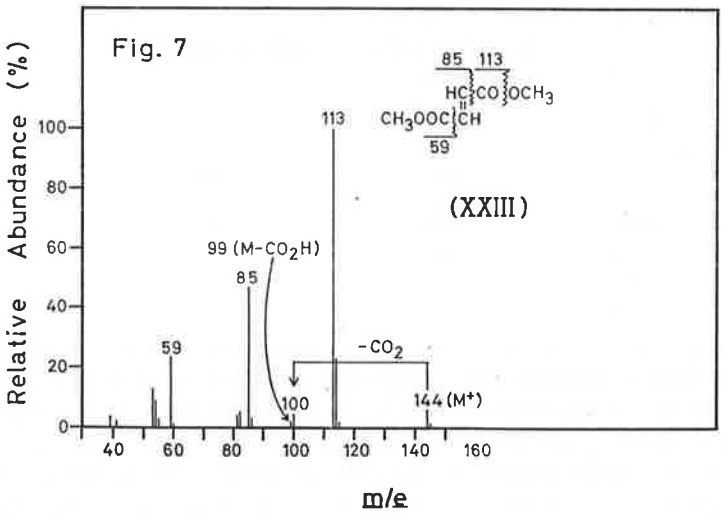
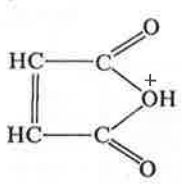


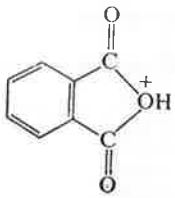
FIG. 7

The maleates and fumarates which have been synthesized and examined are summarized by the formulae XVa–XXX. Of the esters (XVa–XXI and XXIII–XXIX) containing saturated alkyl groups, only the methyl esters (XVa and XXIII) contain M—CO_2 ions (1% and 4% relative abundance, respectively), and M—CO_2H ions (0·3% and 2% relative abundance, respectively—see Fig. 7 for the spectrum of the *trans*-ester XXIII). In the spectrum (Fig. 7) of the *trans*-ester XXIII, *m/e* 99 is a singlet (M—CO_2H), but in the spectrum of the *cis*-isomer XVa is a doublet [M—CO_2H (10%) and $C_4H_3O_2$ (90%)]. The latter composition corresponds to the ion *e*, the analogue (*f*, *m/e* 149) of which is well authenticated in the spectra of phthalate esters.[10,11] However, an ion corresponding to *f* is of low abundance (0·5%) in the spectrum of dimethyl phthalate, although it is abundant in the spectra of higher esters.[10,11] Similarly, although the *m/e* 99 ion (*e*) is of very low relative abundance from dimethyl maleate (XV), it corresponds to the base peak from all the remaining dialkyl maleates [with the exception of the spectrum of di-iso-butyl maleate in which *m/e* 57 ($C_4H_9^+$) is the base peak and *m/e* 99 the second most abundant ion (65%)]. In addition the *m/e* 99 ion is abundant *but not the base peak* from all the corresponding fumarates (XXIV–XXIX). The relative abundances of *m/e* 99 are summarized for the two series in Table 3.

[10] F. W. McLafferty and R. S. Gohlke, *Analyt. Chem.* **31**, 2076 (1959).
[11] C. Djerassi and C. Fenselau, *J. Amer. Chem. Soc.* **87**, 5756 (1965).



e, *m/e* 99



f, *m/e* 149

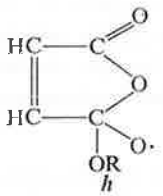
TABLE 3. RELATIVE ABUNDANCES OF *m/e* 99 IONS (*e*) FROM DIALKYL MALEATES AND DIALKYL FUMARATES

Alkyl group	Rel. Ab. *m/e* 99 (*e*) (Maleates)	Rel. Ab. *m/e* 99 (*e*) (Fumarates)
Me	3	0
Et	100	27
n-Pr	100	36
iso-Pr	100	65
n-Bu	100	43
iso-Bu	65	38
s-Bu	100	62

The situation summarized in Table 3 is *a priori* quite reasonable because the formation of *e* from a fumarate ester could require additional energy to cause isomerisation about the double bond. However, an attempt to illustrate the requirement of extra energy to form *e* from diethyl fumarate (XXIV) did not give an unambiguous result. Utilising the doublet nature of the *m/e* 99 peak [50% of $C_4H_3O_3^+$ (*e*) and 50% of M—$COOC_2H_5$] from diethyl fumarate (XXIV) at 70 eV to monitor the disappearance of *e* on decreasing the energy of the electron beam, it was observed that *m/e* 99 corresponded to *e* (35%) and M—COOEt (65%) at 20 eV, *e* (25%) and M—COOEt (75%) at approximately 15 eV, and solely to M—COOEt in the region of 13 eV. When diethyl maleate (XVI) was then added to the system as the lowest of these electron beam energies, the contribution from *e*, which reappeared on the oscilloscope, was barely significant.

Although the spectra of propyl and butyl maleates and fumarates appear to be free of skeletal rearrangement ions, two additional differences between the spectra of these closely related compounds merit comment. First, for any pair of esters (maleate and corresponding fumarate) of the formula $(CHCOOR)_2$, the ratio of the abundances of R^+ to $(R—H)^+$ ions is always greatest for the maleates (see Table 4). The formation of R^+ may be relatively more favourable from the *cis*-esters because of stabilization of the departing radical (formally *g*) as *h*. Second, the relative abundance of RO^+ fragments is always greater when the alkyl group R is α-branched (R = iso-propyl or s-butyl—Table 4).

g



h

TABLE 4. COMPARISON OF RELATIVE ABUNDANCES OF R^+, $(R—H)^+$ AND RO^+ IONS FROM PROPYL AND BUTYL MALEATES (*cis*) AND FUMARATES (*trans*)

R		Relative abundances			
		R^+	$(R—H)^+$	$R^+/(R—H)^+$	RO^+
n-Pr	*cis*	37	6	6·2	2
	trans	29	15	1·9	3
iso-Pr	*cis*	46	8	5·7	10
	trans	45	15	3·0	15
n-Bu	*cis*	60	17	3·5	1
	trans	42	75	0·56	1
iso-Bu	*cis*	100	24	4·2	1
	trans	55	58	0·95	1
s-Bu	*cis*	63	18	3·5	6
	trans	20	28	0·71	6

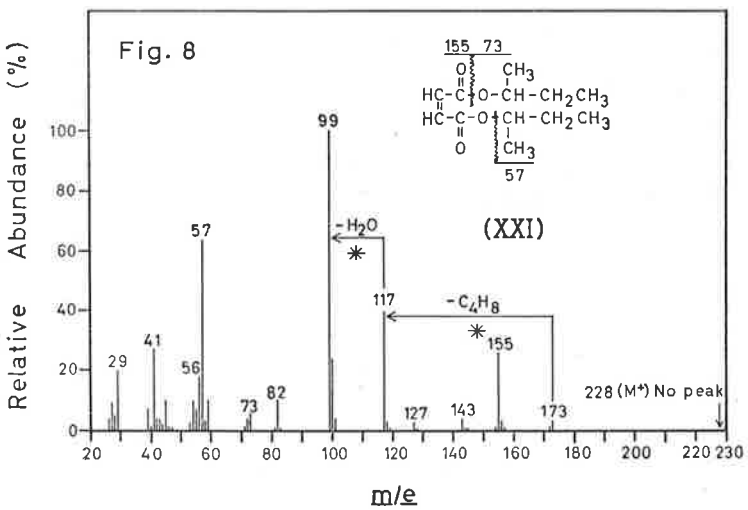


FIG. 8

Some of the general features discussed above may be seen on comparison of the spectra of s-butyl maleate (XXI, Fig. 8) and s-butyl fumarate (XXIX, Fig. 9), which are reported as representative spectra.

Diallyl maleate does not contain pronounced skeletal rearrangement ions in its spectrum, since the formation of *m/e* 41 (CH_2=CH—CH_2^+, base peak) and *m/e* 99 (*e*) is so favourable (cf. data accumulated in Tables 3 and 4). However, the spectrum (Fig. 10) of diallyl fumarate is much more interesting and has been extensively investigated by exact mass measurements (Table 5). Once more it is gratifying that all the major skeletal rearrangement fragments are derived by a simple bond cleavage coupled with CO or CO_2 elimination and an associated allyloxy or allyl migration. Where the origin of ions is not immediately obvious ($C_5H_5^+$ and $C_4H_7^+$), metastable peaks establish that these fragments arise from $C_5H_7^+$ and $C_5H_7O^+$ by the elimination of

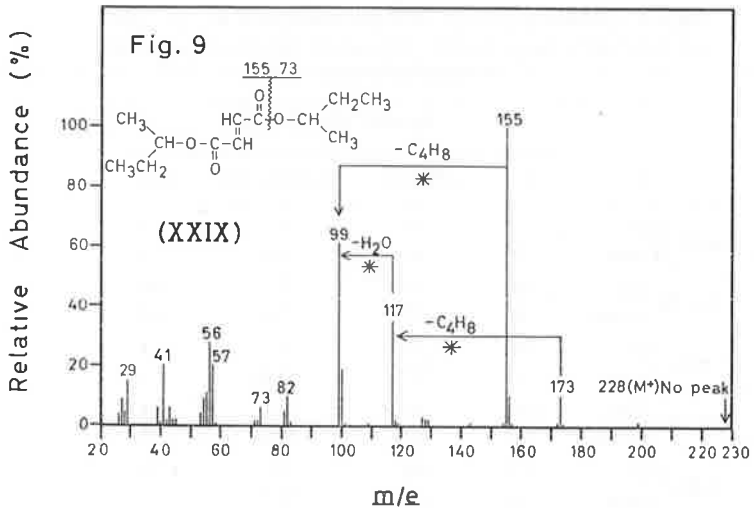


FIG. 9

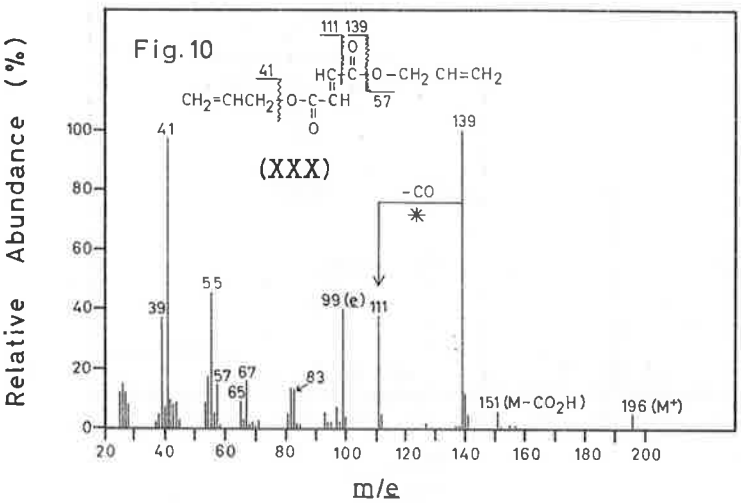
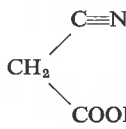


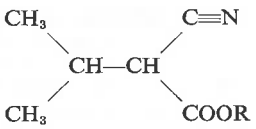
FIG. 10

TABLE 5. SKELETAL REARRANGEMENT IONS FROM DIALLYL FUMARATE (XXX)

Ion (*m/e*)	Composition	Formal derivation
151	$C_9H_{11}O_2$ (100%)	$M - CO_2H$
83	C_5H_7O (90%)	$M - CO - COCH_2CH{=}CH_2$
67	C_5H_7 (100%)	$M - CO_2 - COCH_2CH{=}CH_2$
65	C_5H_5 (100%)	$C_5H_7 - H_2$
55	C_4H_7 (25%)	$C_5H_7O - CO$



XXXI, R = n-Pr
XXXII, R = iso-Pr
XXXIII, R = n-Bu
XXXIV, R = iso-Bu
XXXV, R = s-Bu
XXXVI, R = t-Bu
XXXVII, R = CH_2—CH=CH_2
XXXVIII, R = Ph
XXXIX, R = $CH_2C_6H_5$



XL, R = n-Pr
XLI, R = iso-Pr
XLII, R = n-Bu
XLIII, R = iso-Bu
XLIV, R = s-Bu
XLV, R = t-Bu

H_2 and CO respectively. The driving force for the former reaction is perhaps the formation of a resonance stabilised cyclopentadienyl cation ($C_5H_5^+$).

A series of alkyl cyanoacetates (XXXI–XXXIX) and of alkyl isopropylcyanoacetates (XL–XLV) have been synthesized because methyl and ethyl cyanoacetates were previously observed to give M—CO_2H ions, while ethyl isopropylcyanoacetate eliminates CO_2 with associated expulsion of a hydrogen atom or of a methyl group of the isopropyl substituent.[4] High resolution measurements on the spectra of the simple cyanoacetates (N≡CCH_2COOR, XXXI–XXXIX) establish that analogous processes occur in the higher esters with the exception of t-butyl cyanoacetate (XXXVI) and phenyl cyanoacetate (XXXVIII); the tendency is particularly pronounced in the spectra of the allyl and benzyl esters (Table 6 and also Fig. 11). The spectrum of the benzyl ester in which the active methylene hydrogens have been replaced by deuterium establishes that the hydrogen expelled with CO_2 is derived almost exclusively from the benzyl group.

In the series of isopropylcyanoacetates [$(Me)_2CHCH(CN)COOR$, XL–XLV), the relative abundance of M—CO_2—CH_3 ions decreases with increasing size and increasing branching of R as summarised in Table 7. It is quite feasible that the tendency of

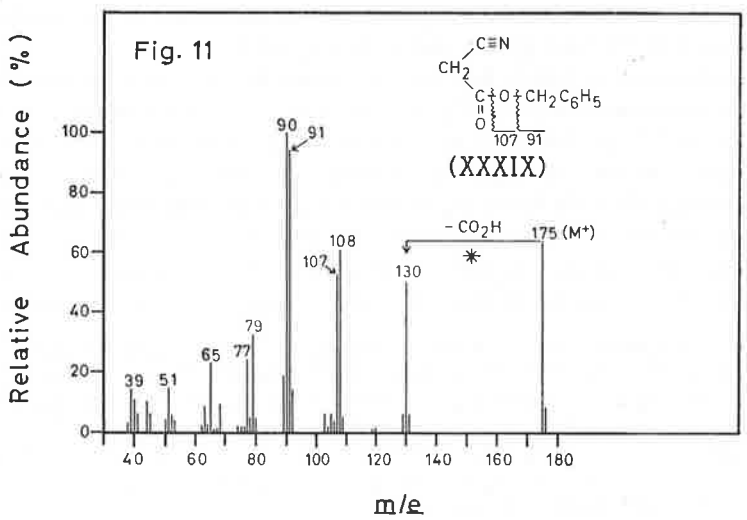


FIG. 11

TABLE 6. SOME SKELETAL REARRANGEMENT IONS FROM SIMPLE CYANOACETATES ($N{\equiv}C{-}CH_2COOR$)

R	M—CO_2H (Rel. Ab. %)	Other (Rel. Ab. %)
Me[4]	10	M—CO_2 (14)
Et[4]	10	—
n-Pr	3	M—CO_2—CH_3 (5)
		M—CO_2 (3)
iso-Pr	7	—
n-Bu	1	M—CO_2—CH_3 (5)
iso-Bu	1	M—CO_2—CH_3 (5)
		M—CO_2CH_2 (10)
s-Bu	1	—
t-Bu	—	—
CH_2—CH=CH_2	16	—
Ph	—	—
$CH_2C_6H_5$	50	—

TABLE 7. RELATIVE ABUNDANCE OF M—CO_2—Me IONS FROM ALKYL ISOPROPYLCYANOACETATES [$(Me)_2CHCH(CN)COOR$]

R	Et[a]	n-Pr	iso-Pr	n-Bu
Rel. Ab. %	27	5	2	1
R	iso-Bu	s-Bu	t-Bu	
Rel. Ab. %	2	1	0	

these M—CO_2—Me ions to decompose further may increase with increasing size and branching of R and hence their relative abundance is not a reliable measure of the preponderance of the rearrangement process. Unfortunately, the decomposition products of M—CO_2—Me species can have compositions which may also arise via simple cleavage pathways and hence it is not possible to evaluate this effect in these cases. However, the absence of appropriate metastable peaks which might establish any such decompositions of M—CO_2—Me ions, coupled with the drastic reductions in intensity of the M—CO_2—Me peaks, make it seem probable that the extent of the rearrangement does decrease with increasing size and branching of R.

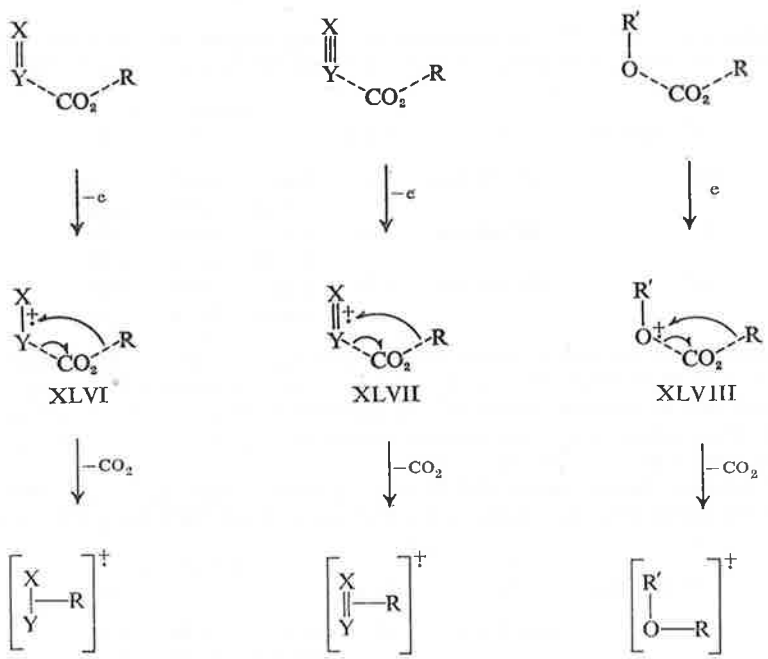
With all the information which has been gathered in the course of this study, some useful generalizations can probably now be made as to the tendency of esters to eliminate CO_2 or CO in $ABC^+ \rightarrow AC^+$ reactions upon electron impact. First, there do not appear to be any reported examples of *completely saturated* esters (RCOOR')[12] affording M—CO, M—CO_2 or M—CO_2H ions, although butyl propionate[11] and neo-pentyl esters[13] expel formaldehyde. However, all those esters which have been reported to undergo alkyl/aryl migrations with elimination of CO_2 (see Refs. 3–8 and the results reported in this paper) either contain double or triple bonds,

[12] For details of the mass spectra of such esters see R. Ryhage and E. Stenhagen (Edited by F. W. McLafferty) Chap. 3. "*Mass Spectrometry of Organic Ions*" Academic Press, New York (1963); R. Ryhage and E. Stenhagen, *Arkiv Kemi* **13**, 523 (1959); A. G. Sharkey, J. L. Shultz and R. A. Friedel, *Analyt. Chem.* **31**, 87 (1959); J. H. Beynon, R. A. Saunders and A. E. Williams, *Ibid.* **33**, 221, (1961) and F. M. Trent, F. D. Miller and G. H. Brown, *Appl. Spectroscopy* **15**, 64 (1961). The elimination of CO from formates [D. Van Raalte and A. G. Harrison, *Canada J. Chem.* **41**, 2054 (1963)] only of course requires hydrogen migration.

[13] D. R. Black, W. H. McFadden and J. W. Corse, *J. Phys. Chem.* **68**, 1237 (1964).

or lone pair electrons (in addition to those associated with the —COO-portion of the ester). It is therefore proposed that CO_2 elimination with associated group migration (other than hydrogen) is in general facilitated by removal of a π-electron (from a double or triple bond—see XLVI and XLVII, respectively, which Y---- C represents 1 or 2 σ-bonds) or of a lone pair electron to afford an electron deficient site to which the group can migrate. Particularly pertinent to this concept are the alkyl migrations recently found to occur in *saturated* dialkyl carbonates by Brown and Djerassi;[8] the electron deficient site to which the R group can migrate is then located on oxygen[8] (see XLVIII). Depending on the nature of the groups R and R′ and the nature of groups attached to the atoms X and Y, additional atoms may of course be expelled in association with the CO_2 elimination.

The concept is also useful in understanding the loss of formaldehyde from some saturated esters,[11,13] because in these cases the electron deficient site may be provided by ionisation within the carbonyl group. In addition, other esters which have been reported to lose CO_2 (neo-pentyl benzoate,[6] phenyl pivalate[5] and t-butyl benzoate[5])



contain unsaturation in aromatic rings. It is emphasised that generation of an electron deficient site by removal of lone-pair or π-electrons is not visualized as a prerequisite for skeletal rearrangement, since even saturated hydrocarbons may reorganise to some extent in this fashion upon electron impact,[14] but rather as a factor which will promote facile CO_2 elimination.

Although the unsaturated esters which we have investigated vary widely in structure, some useful general grends are indicated. In many cases (but not all), the tendency is for the methyl and ethyl esters to indergo CO_2 eliminations to a greater extent than propyl and butyl esters, probably because more alternative

[14] P. N. Rylander and S. Meyerson, *J. Amer. Chem. Soc.*, **78**, 5799 (1956).

reactions are open to the latter groups. Also it is obvious that allyl and benzyl esters studied are particularly prone to undergo $ABC^+ \rightarrow AC^+$ reactions, which is understandable in terms of units of unsaturation present in both "acid" and "alcohol" portions of the ester.[14a] Finally, although the composition of some ions initially suggest that their origins must be complex, simple cleavages with associated CO or CO_2 elimination from the ester group will usually account for their formation. Obviously, the possibility of analogous processes occurring must be borne in mind when natural products are examined by mass spectrometry.

EXPERIMENTAL

Mass spectra: an A.E.I. MS 9 mass spectrometer with the heated inlet system, and source, at a temp of 150–180°. High resolution measurements were performed at a resolution of 15,000 (10% valley definition).

All compounds were freshly distilled and their purities routinely checked by NMR and mass spectrometry. If any doubt remained as to the purity of a compound, this was additionally checked by VPC.

Alkyl propiolates. The following compounds were prepared by literature methods: I,[15] II,[16] IV[15] and VI.[17]

Compounds III, V and VII were synthesized by mixing propiolic acid with the corresponding alcohol (using conc H_2SO_4 as catalyst) and allowing the mixture to stand at room temp. for 1 week.

Compound	B.p.	Yield		Analysis (%) C	H
III	65°/50 mm	23%	Calc.	64·27	7·19
			Found	63·70	6·92
V	80°/66 mm	24%	Calc.	66·64	7·99
			Found	66·78	8·63
VII	122°/18 mm	25%	Calc.	74·99	5·03
			Found	74·54	5·51

Dialkyl acetylenedecarboxylates. The following compounds were prepared by literature methods: VIII,[18] IX,[18] X,[19] XI,[19] XII,[19] XIII[15] and XV.[17] Di-s-butyl acetylenedicarboxylate (XIV) was synthesized by heating acetylenedicarboxylic acid and s-butyl alcohol in benzene (with conc H_2SO_4 as a catalyst) under reflux for 2 hr (using a water separator); b.p. 88°/0·1 mm, yield 46%. (Found: C, 63·85; H, 8·04. Calc. C, 63·70; H, 8·02%.)

Dialkyl maleates. Diallyl maleate (XXII) was a purified commercial sample. The following compounds were prepared by literature methods: XV,[20] XVI,[21] XVII,[22] XIX[22] and XX.[22] Compounds

Compound	B.p.	Yield		Analysis (%) C	H
XVIII	104°/9 mm	85%	Calc.	59·98	8·05
			Found	59·98	8·09
XXI	130°/10 mm	79%	Calc.	63·13	8·83
			Found	62·93	8·61

[14a] In this respect, it is somewhat surprising that phenyl cyanoacetate (XXXVIII) does not furnish a skeletal rearrangement ion in its spectrum.

[15] I. F. Grove, *Ann. appl. Biol.* **35,** 38 (1948).

[16] K. V. Auwers, *Chem. Ber.* **65,** 146 (1932).

[17] C. D. Heaton and C. R. Noller, *J. Amer. Chem. Soc.* **71,** 2948 (1949).

[18] E. H. Huntress, T. E. Lesslie and J. Bornstein, *Org. Synth.* **32,** 55 (1952).

[19] G. H. Jeffrey and A. I. Vogel, *J. Chem. Soc.* 674 (1948).

[20] F. Adickes, *J. Prakt. Chem.* [2] **6,** 275 (1943).

[21] V. M. Mitchovitch, *Bull. Soc. Chim. Fr.* [5]. **4,** 1667 (1937).

[22] G. H. Jeffrey and A. I. Vogel, *J. Chem. Soc.* 658 (1948).

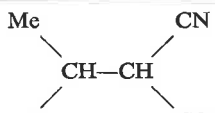
XVIII and XXI were synthesized by heating maleic acid and the appropriate alcohol (with conc H_2SO_4 as catalyst) under reflux in benzene for 2 hr using a separator to remove the water formed during the reaction.

Dialkyl fumarates. The following compounds were synthesized by literature methods: XXIII,[23] XXIV,[21] XXV,[22] XXVII,[22] XXVIII[22] and XXX.[24]

Compounds XXVI and XXIX were prepared in the same manner as that outlined above for the maleates.

Compound	B.p.	Yield		Analysis (%) C	H
XXVI	102°/9 mm	71%	Calc.	59·58	8·05
			Found	59·96	8·03
XXIX	127°/9 mm	67%	Calc.	63·13	8·83
			Found	63·51	8·83

Compound	B.p.	Yield		Analysis (%) C	H	N
XXXV	100°/10 mm	58%	Calc.	59·55	7·85	9·92
			Found	59·45	7·67	10·05
XXXVII	101°/10 mm	60%	Calc.	57·59	5·64	11·20
			Found	57·40	5·80	11·38
XXXVIII	m.p. 41°	12%	Calc.	67·07	4·38	8·69
			Found	66·78	4·29	8·84
XXXIX	115°/0·05 mm	63%	Calc.	68·56	5·18	8·00
			Found	68·65	5·12	8·21



	B.p.	Yield		Analysis (%) C	H
XL	103°/10 mm	63%	Calc.	63·88	8·94
			Found	63·41	8·88
XLI	93°/10 mm	63%	Calc.	63·88	8·94
			Found	63·53	8·82
XLII	115°/8 mm	58%	Calc.	65·54	9·35
			Found	65·66	9·32
XLIII	109°/10 mm	58%	Calc.	65·54	9·35
			Found	65·40	9·41
XLIV	104°/9 mm	68%	Calc.	65·54	9·35
			Found	65·55	9·41
XLV	96°/10 mm	60%	Calc.	65·54	9·35
			Found	65·42	9·18

[23] R. Anschütz, *Chem. Ber.* **12**, 2279 (1879).
[24] V. P. Golendefew, *J. Gen. Chem., U.S.S.R.* **10**, 1539 (1940).

Alkyl and aryl cyanoacetates. The following compounds were prepared by literature methods: XXXI,[25] XXXII,[26] XXXIII,[26] XXXIV[25] and XXXVI.[27] Compounds XXXV, XXXVII and XXXIX were synthesized by heating cyanoacetic acid and the appropriate alcohol (in benzene, using conc. H_2SO_4 as catalyst) under reflux for 2 hr (using a water separator). Compound XXXVIII was prepared by the general method outlined in Ref. 27.

Alkyl isopropylcyanoacetates. Compounds XL, XLI, XLII, XLIII and XLIV were prepared by alkylation of the Na salt of the cyanoacetate ester with isopropyl iodide in the alcohol corresponding to the ester. Compound XLV was available by alkylation of the Na salt of t-butyl cyanoacetate (prepared using NaH) with isopropyl iodide in dioxan.

Acknowledgement—The authors from Aarhus University wish to thank the Statens Almindelige Videnskabsfond for a grant.

[25] J. Guinchant, *Ann. Chim. Fr.* [9], **9**, 30 (1918).
[26] A. Karvonen, *Ann. acad. sci. Fennicae* **20**, 18 (1924).
[27] R. E. Ireland and M. Chaykovsky, *Org. Synth.* **41**, 5 (1961).

[Reprinted from the Journal of the American Chemical Society, 88, 4980 (1966).]

Studies in Mass Spectrometry. XIX.[1] Evidence for the Occurrence of Aromatic Substitution Reactions upon Electron Impact

J. Ronayne, D. H. Williams, and J. H. Bowie

Contribution from the University Chemical Laboratory, Cambridge, England.
Received June 20, 1966

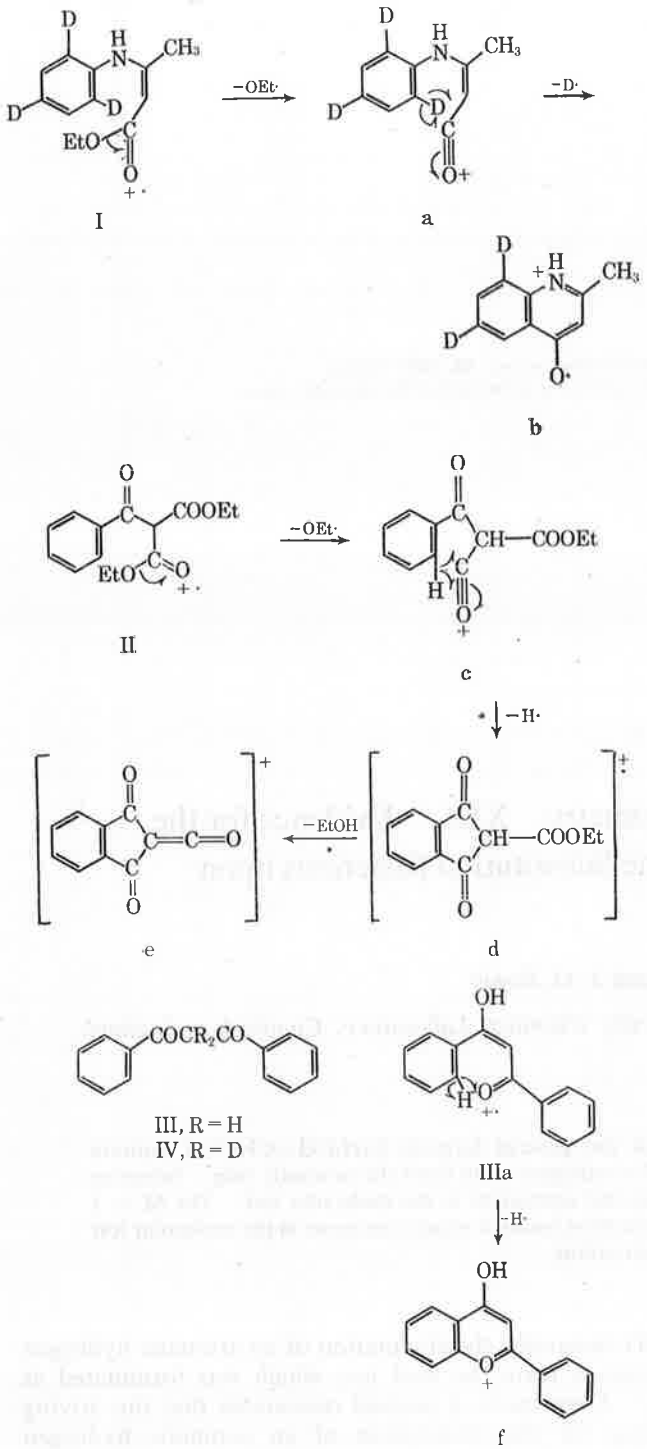
Abstract: The mass spectra of a number of compounds of the general formula $C_6H_5CH{=}CHCOR$ contain intense M − 1 peaks, which largely arise through the loss of a hydrogen atom from the aromatic ring. Selective deuteration experiments suggest that the phenyl hydrogens become equivalent in the molecular ion. The M − 1 species is probably formed *via* an intramolecular aromatic substitution reaction which can occur in the molecular ion and results in the formation of a relatively stable benzopyrylium cation.

In investigations of the behavior of β-keto esters,[2] β-diketones,[3] and enamines[4] upon electron impact we have uncovered reactions which are believed to correspond to intramolecular substitution reactions occurring in the mass spectrometer. Thus, ethyl 3-(2′,4′,6′-d_3-phenylamino)but-2-enoate (I) was shown to eliminate C_2H_5DO and C_2H_6O from its molecular ion in the ratio 85:15, and the loss of a deuterium atom from the aromatic ring was rationalized in terms of an intramolecular acylation of the aromatic ring by the acylium ion a to give the stabilized quinolinium ion b *via* loss of a deuterium atom.[4] Similarly, the successive losses of C_2H_5O, H, and C_2H_6O (as established by appropriate metastable peaks) from diethyl benzoylmalonate (II) demanded the elimination of an aromatic hydrogen atom to form the final ion, which was formulated as e.[2] Once more, it seemed reasonable that the driving force for the elimination of an aromatic hydrogen might be the intramolecular "Friedel–Crafts acylation" of the aromatic ring in the acylium ion c; ethanol could then be eliminated from d to furnish e.

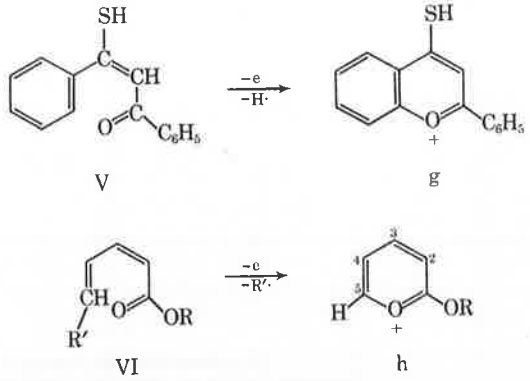
The second type of aromatic substitution reaction which we have suggested may occur upon electron impact involves the formation of a completely aromatic benzopyrylium ion.[3] Thus, dibenzoylmethane (III) exhibits a pronounced M − H ion in its spectrum, which still corresponds to the loss of a hydrogen atom from the molecular ion in the spectrum of the d_2 derivative IV. It was concluded that the driving force for the loss of the aromatic hydrogen atom, which is of necessity eliminated in the formation of the M − 1 species, lay in the formation of the oxonium ion f[3] from a molecular ion IIIa of III.

Reactions which bear some analogy to our sugges-

(1) Part XVIII: J. T. B. Marshall and D. H. Williams, *Tetrahedron*, in press.
(2) J. H. Bowie, D. H. Williams, S.-O. Lawesson, and G. Schroll, *J. Am. Chem. Soc.*, **87**, 5742 (1965).
(3) J. H. Bowie, D. H. Williams, S.-O. Lawesson, and G. Schroll, *J. Org. Chem.*, **31**, 1384 (1966).
(4) H. J. Jakobsen, S.-O. Lawesson, J. T. B. Marshall, G. Schroll, and D. H. Williams, *J. Chem. Soc.*, in press.

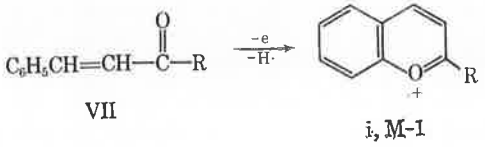


I a b II c d e III, R = H IV, R = D IIIa f



V g VI h

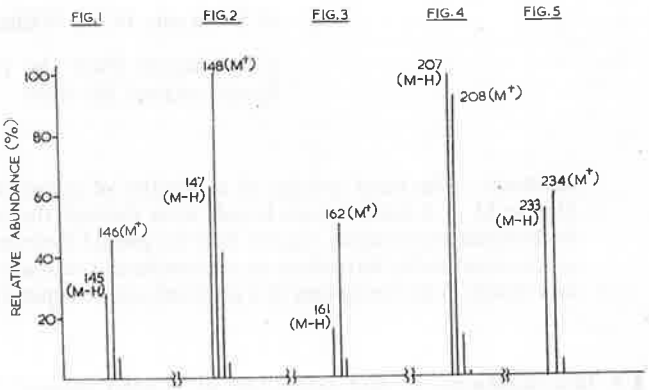
ing. Our aim was to show that abundant M − 1 ions are a fairly general feature of the mass spectra of such compounds and that the M − 1 ions are formed by loss of a hydrogen atom from the aromatic ring, presumably to give ions of the general formula i.



VII i, M-1

Discussion and Results

The compounds which have been investigated are summarized in formulas VIII–XII, and the molecular ion regions of their mass spectra are reproduced in Figures 1–5. It can be seen that M − 1 ions are



Figures 1–5. Molecular ion regions in the mass spectra of benzalacetone (VIII), cinnamic acid (IX), methyl cinnamate (X), benzalacetophenone (XI), and dibenzalacetone (XII), respectively.

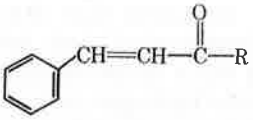
tions have recently been postulated to occur in other classes of compounds. Shannon and co-workers[5] have reported that thio derivatives of β-diketones such as V lose hydrogen in the mass spectrometer to form the postulated resonance-stabilized ion g. Vinylic 5,6-cleavage is important in the spectra of 2,4-dienoates (see VI), probably because aromatic oxonium ions such as h may be produced.[6]

Such reactions are of obvious chemical and diagnostic interest, and we have therefore undertaken a study of the mass spectra of a series of compounds of the general formula VII, with the aid of extensive dueterium label-

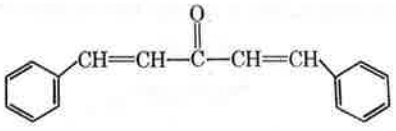
pronounced in the spectra of all these compounds. Surprisingly, only the M − 1 ion from the chalcone (XI) seems to have attracted attention previously[7,8] and only in one case[7] has there been an attempt to rationalize its formation, in terms of the structure j.

All the compounds studied are synthetically available from various base-catalyzed condensation reactions involving benzaldehyde. 2,4,6-d_3-Benzaldehyde (XV, d_1 = 2%, d_2 = 15%, d_3 = 83%) was therefore prepared from 2,4,6-d_3-aniline (XIII)[9] *via* the nitrile XIV.

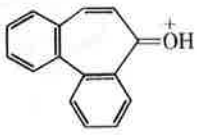
(5) S. H. H. Chaston, S. E. Livingstone, T. N. Lockyer, V. A. Pickles, and J. S. Shannon, *Australian J. Chem.*, **18**, 673 (1965).
(6) W. K. Rohwedder, A. F. Mabrouk, and E. Selke, *J. Phys. Chem.*, **69**, 1711 (1965).
(7) J. H. Beynon, G. R. Lester, and A. E. Williams, *J. Am. Chem. Soc.*, **63**, 1865 (1959).
(8) Y. Itagaki, T. Kurokawa, S. Sasaki, C.-T. Chang, and F.-C. Chen, *Bull. Chem. Soc. Japan*, **39**, 538 (1966).
(9) A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 241 (1946).



VIII, R = CH_3
IX, R = OH
X, R = OCH_3
XI, R = C_6H_5



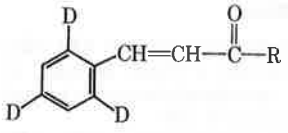
XII



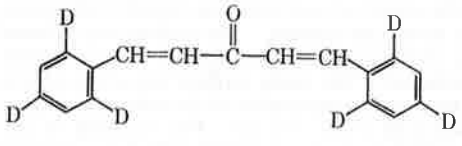
j

Appropriate condensation reactions then furnished the labeled derivatives VIIIa–XIIa.

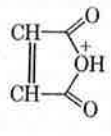
XIII XIV XV



VIIIa, R = CH_3
IXa, R = OH
Xa, R = OCH_3
XIa, R = C_6H_5



XIIa



k

The mass spectra of the deuterated derivatives contained M − H and M − D ions of approximately equal abundance. The ratios in which hydrogen atoms and deuterium atoms are expelled from the molecular ions of these derivatives are summarized in Table I. The calculations for each compound (VIIIa–XIa) are based upon an isotopic purity (d_1 = 2%, d_2 = 15%, d_3 = 83%) which was established from the mass spectrum of the common precursor 2,4,6-d_3-benzaldehyde (XV); the incorporation of two benzaldehyde molecules into dibenzalacetone (XIIa) leads to a calculated isotopic purity of d_3 = 1%, d_4 = 6%, d_5 = 25%, d_6 = 68%. The effects of ^{13}C isotopes have been obviated in the usual manner.[10] With the exception of methyl cinnamate (Xa), the calculations show that deuterium and hydrogen are lost in almost identical amounts. In all cases, the driving force for the loss of an aromatic deuterium atom is thought to be associated with the formation of an aromatic oxonium ion i. It is noteworthy that the formation of such ions requires the isomerization of a *trans* to a *cis* double bond in the mass spectrometer. However, such a transformation is known to be a facile process in 70-ev spectra as evidenced by the occurrence of abundant *m/e* 99 ions, corresponding to k, from dialkyl maleates *and* fumarates.[11]

Table I. Relative Proportions of Hydrogen and Deuterium Lost from the Molecular Ions of the Deuterated Compounds VIIIa–XIIa

Compound	Hydrogen lost, %	Deuterium lost, %
VIIIa	49	51
IXa	49	51
Xa	40	60
XIa	49	51
XIIa	49	51

Two explanations can account for the only *partial* loss of deuterium from the molecular ions of VIIIa–XIIa. First, it is possible that the hydrogen is lost from the aromatic ring from which deuterium is lost. Second, the hydrogen could be lost from some point in the molecule other than the phenyl ring of the styryl group. Since the results summarized in Table I are qualitatively the same for all the compounds (VIIIa–XIIa), the former explanation seemed more attractive. Additional deuterated derivatives have therefore been prepared to distinguish between these two possible explanations.

The compound selected for more exhaustive deuterium labeling was chalcone (XI, benzalacetophenone). d_5-Acetophenone (XVI, d_3 = 1.5%, d_4 = 16.5%, d_5 = 82%) was prepared by Friedel–Crafts acylation of d_6-benzene and on condensation with benzaldehyde afforded 2,3,4,5,6-d_5-benzalacetophenone (XIb). Chlorination of d_8-toluene gave d_6-benzal chloride (XVII), which was converted to d_6-benzaldehyde (XVIII, d_5 = 3%, d_6 = 97%) by hydrolysis; condensation of XVIII with acetophenone furnished the d_6 derivative (XIc). More exhaustive chlorination of d_8-toluene gave XIX which was converted to d_5-benzaldehyde (XX, d_4 = 3%, d_5 = 97%) *via* d_5-benzoic acid and d_5-benzyl alcohol; condensation of XX with acetophenone led to 2′,3′,4′,5′,6′-benzalacetophenone (XId). Finally, base-catalyzed exchange of acetophenone in deuteriomethanol gave d_3-acetophenone (XXI, d_2 = 2%, d_3 = 98%), which on condensation with benzaldehyde gave d_1-benzalacetophenone (XIe).

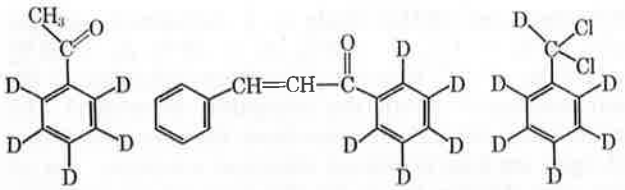
The results for the various labeled benzalacetophenones (XIa–XIe) are summarized in Table II. The figures establish that in the formation of the M − 1 ion from benzalacetophenone (XI), the hydrogen atom which is eliminated originates very largely (85%, if one assumes no isotope effect[12]) from the phenyl ring of the styryl group. It is gratifying that there is a clear distinction between the two aromatic rings of benzalacetophone (XI), only 6% of the M − 1 peak being formed by elimination of a hydrogen atom from the

(10) See, for example, K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 5.

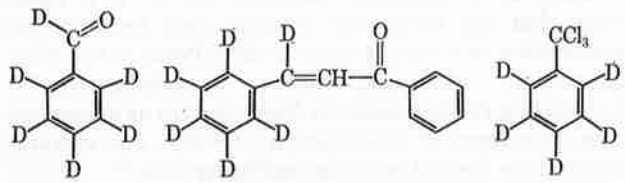
(11) J. H. Bowie, D. H. Williams, P. Madsen, G. Schroll, and S.-O. Lawesson, *Tetrahedron*, in press.

(12) In practice there will almost certainly be an isotope effect, but a fairly wide range of values has been observed for mass spectral processes so far investigated[13] and therefore no reliable estimate can be made for these cases. However, it is noteworthy that the results presented in Table II account completely for hydrogen lost in the formation of an M − 1 species by replacement of all 12 hydrogens by deuterium. The results therefore suggest that any isotope effect is small.

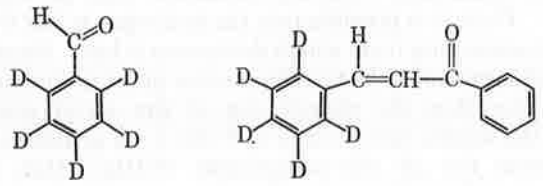
(13) J. K. Macleod and C. Djerassi, *Tetrahedron Letters*, 2183 (1966).



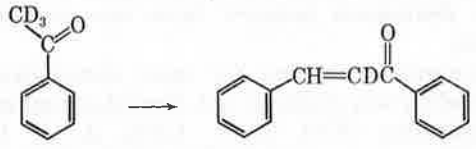
XVI XIb XVII



XVIII XIc XIX



XX XId



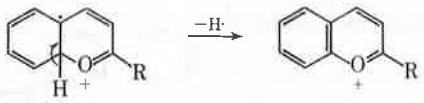
XXI XIe

phenyl ring of the benzoyl group (again assuming no isotope effect[12]). The β-hydrogen of the α,β-unsaturated ketone group is eliminated to a small extent (compare data for XIc and XId) but the α-hydrogen atom is not expelled to any significant extent in the formation of the M − 1 species.

Table II. Relative Proportions of Hydrogen and Deuterium Lost from the Molecular Ions of Deuterated Benzalacetophenones XIa–e

Compound	Hydrogen lost, %	Deuterium lost, %
XIa	49	51
b	94	6
c	6	94
d	15	85
e	100	0

The difference in the figures obtained when the styryl ring is labeled only in the *ortho* and *para* positions and when labeled completely correspond to complete equivalence of the aromatic hydrogens in this ring prior to the loss of a hydrogen atom from the molecular ion, if one assumes no isotope effect (*i.e.*, three-fifths of the 85% deuterium lost from the d_5 derivative XId is 51%, which corresponds exactly to the value observed for XIa). In view of our earlier conclusion that any isotope effect must be small (see ref 12), our experiments provide strong, but not unequivocal, evidence for randomization of these aromatic hydrogens prior to fragmentation. Such randomization could occur if, instead of loss of a hydrogen radical being concerted with C–O bond formation (see IIIa → f), l exists as a reaction intermediate and scrambling occurs in the styryl ring *via* a series of hydrogen shifts in l (prior to the loss of a hydrogen radical which affords i). Deuterium scrambling would not, of course, be observed in the labeled derivatives if only 1,3- and/or 1,5-hydrogen shifts occurred in l.[14] Attention is drawn to the contrasting absence of complete scrambling in the cyclization of the carbonium ion a to the ion-radical b.



l i, M−1

In summary, compounds of the general formula VII which we have investigated all show intense M − 1 peaks which are partly derived by expulsion of hydrogen from the aromatic ring. In the case of benzalacetophenone (XI), the hydrogen is lost almost exclusively from the styryl ring and, by analogy, this situation probably holds in the other compounds also. The results are consistent with (1) randomization of phenyl hydrogens in the molecular ion, and (2) formation of a relatively stable M − 1 oxonium ion i by means of an intramolecular aromatic substitution reaction.

Experimental Section

Mass spectra were obtained using an AEI MS 9 mass spectrometer operating at 70 ev and a source pressure of 0.1–0.5 × 10^{-6} mm. Samples were introduced through a heated inlet system at a temperature of approximately 150°.

Isotopic purities of condensation products from 2,4,6-d_3-benzaldehyde (XV) are in general based upon the isotopic purity of XV. In those cases where the isotopic purities of the condensation products could be directly checked, the results were the same as for the labeled benzaldehyde within 1%.

2,4,6-d_3-Benzaldehyde (XV). 2,4,6-d_3-Aniline (XIII, 4.5 g)[9] was diazotized and the diazotized solution added to a solution of cuprous cyanide in aqueous potassium cyanide. The mixture was refluxed on a water bath for 30 min, and the resulting yellow oil was separated by steam distillation. The crude product was extracted with ether (three 30-ml portions); evaporation of the ether extract gave crude 2,4,6-d_3-benzonitrile (XIV, 2.2 g). This material in dry ether (30 ml) was added to a suspension of anhydrous stannous chloride (8 g) in dry ether (70 ml) saturated with dry hydrogen chloride. The mixture was allowed to stand overnight. The resulting aldimine stannichloride was steam distilled and the crude product extracted with ether. Evaporation of the ether and distillation of the residue gave 2,4,6-d_3-benzladehyde [XV, 1.1 g, mol wt (mass spec) 109, d_1 = 2%, d_2 = 15%, d_3 = 83%].

2,4,6-d_3-Benzalacetone (VIIIa). 2,4,6-d_3-Benzaldehyde (XV, 70 mg) and acetone (120 mg) were condensed in the presence of 10% aqueous sodium hydroxide (1 ml). Ether extraction of the product and evaporation of the extract gave crude material (75 mg) which was purified by crystallization from ethanol to give 2,4,6-d_3-benzalacetone (VIIIa, mp 38–40°, mol wt (mass spec) 149, d_1 = 2%, d_2 = 15%, d_3 = 83%) as pale yellow plates. The isotopic purity was calculated from the M − CH_3 ion.

2,4,6-d_3-Cinnamic Acid (IXa). 2,4,6-d_3-Benzaldehyde (XV, 50 mg), malonic acid (100 mg), and pyridine (3 ml) were heated on a water bath for 2 hr. Dilute hydrochloric acid was then added until all the cinnamic acid had precipitated. The precipitate was isolated, washed well with water, and recrystallized from water to give 2,4,6-d_3-cinnamic acid [IXa, 56 mg, mp 122–124°, mol wt (mass spec) 151].

Methyl 2,4,6-d_3-Cinnamate (Xa). 2,4,6-d_3-Cinnamic acid (IXa, 20 mg) in ether (10 ml) was treated with a solution of diazomethane in ether until there was a persistent yellow color. The solution was allowed to stand overnight and the ether then evaporated. The

(14) The authors acknowledge helpful discussion with Dr. I. Fleming and Dr. W. J. Richter on the possible existence of l as a discrete reaction intermediate.

residue crystallized on standing to give methyl 2,4,6-d_3-cinnamate [Xa, 12 mg, mp 33–35°, mol wt (mass spec) 165, d_1 = 3%, d_2 = 14%, d_3 = 83%]. The isotopic purity was calculated from the M − OCH_3 ion.

2′,4′,6′-d_3-Benzalacetophenone (XIa). 2,4,6-d_3-Benzaldehyde (40 mg), acetophenone (40 mg), and absolute ethanol (3 ml) were mixed and 10% aqueous sodium hydroxide then added until the solution became cloudy. The mixture was shaken for 30 min, and the solid which separated from solution was then isolated by filtration. Recrystallization of the crude product from aqueous methanol gave 2′,4′,6′-d_3-benzalacetophenone [XIa, 65 mg, mp 55–57°, mol wt (mass spec) 211].

2,4,6,2′,4′,6′-d_6-Dibenzalacetone (XIIa). 2,4,6-d_3-Benzaldehyde (40 mg), acetone (10 mg), and absolute ethanol (3 ml) were mixed, and 10% aqueous sodium hydroxide (2 ml) was added. The mixture was shaken for 30 min and the solid product then isolated by filtration. The crude material was recrystallized from absolute ethanol giving 2,4,6,2′,4′,6′-d_6-dibenzalacetone [XIIa, mp 109–112°, mol wt (mass spec) 240, d_3 = 1%, d_4 = 6%, d_5 = 25%, d_6 = 68% as calculated from the isotopic purity of the precursor benzaldehyde].

2,3,4,5,6-d_5-Benzalacetophenone (XIb). 2,3,4,5,6-d_5-Acetophenone (XVI, d_3 = 1.5%, d_4 = 16.5%, d_5 = 82%) was prepared by a standard Friedel–Crafts reaction between d_6-benzene and acetic anhydride in the presence of aluminum chloride. This material (XVI) was then condensed with benzaldehyde as described previously to give XIb.

d_6-Benzaldehyde (XVIII). d_8-Toluene (2 ml) was heated gently under reflux and a rapid stream of chlorine passed into the solution in the presence of sunlight. When the temperature of the liquid had reached 208°, the reaction was stopped, and the resulting d_6-benzal chloride was hydrolyzed with aqueous 25% calcium hydroxide solution. The product was isolated *via* ether extraction and distilled to give d_6-benzaldehyde [XVIII, 1.0 g, mol wt (mass spec) 112, d_5 = 3%, d_6 = 97%]. The mass spectrum of the material showed it to be quite pure.

d_6-Benzlacetophenone (XIc). This material was prepared by condensation of d_6-benzaldehyde (XVIII) with acetophenone in the presence of 10% aqueous sodium hydroxide as previously described.

2,3,4,5,6-d_5-Benzaldehyde (XX). The chlorination of d_5-toluene (2 ml) was carried out as described for the preparation of d_6-benzaldehyde (XVIII), except it was continued until the temperature of the liquid had reached 232°. The resulting trichloride (XIX) was then hydrolyzed with 25% aqueous calcium hydroxide, and the d_5-benzoic acid was filtered off and dried. This material was then reduced to the alcohol with lithium aluminum hydride and the alcohol then oxidized to the corresponding aldehyde by refluxing in sunlight with N-chlorosuccinimide (1.3 g), pyridine (1.3 ml), and carbon tetrachloride (20 ml).[15] The mixture was acidified with dilute hydrochloric acid, and the organic layer was removed and washed well with water, 2 *N* sodium hydroxide (10 ml), and finally again with water (three 10-ml portions). The carbon tetrachloride solution was dried and evaporated and the residue purified by distillation to give 2,3,4,5,6-d_5-benzaldehyde [XX, 250 mg, mol wt (mass spec) 111, d_4 = 3%, d_5 = 97%].

2′,3′,4′,5′,6′-d_5-Benzalacetophenone (XId). This material was prepared by condensing d_5-benzaldehyde (XX) with acetophenone in the presence of 10% aqueous sodium hydroxide as previously outlined.

α-d_1-Benzalacetophenone (XIe). Benzaldehyde (40 mg) and 1′,1′,1′-d_3-acetophenone (XXI)[16] were condensed in the presence of 10% aqueous sodium deuteroxide (1 ml) and deuteriomethanol (3 ml), and the product was obtained as detailed previously.

Acknowledgment. J. R. gratefully acknowledges the receipt of a Science Research Council postgraduate award.

(15) M. F. Hebbelynck and R. H. Martin, *Experientia*, **5**, 69 (1949).
(16) D. S. Noyce, G. L. Woodward, and M. J. Jorgenson, *J. Am. Chem. Soc.*, **83**, 1162 (1961).

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STUDIES IN MASS SPECTROMETRY—XX[1]

BOND-FORMING REACTIONS OCCURRING IN THE FRAGMENTATION OF SOME α,β-UNSATURATED ESTERS AND NITRILES UPON ELECTRON IMPACT

D. H. WILLIAMS, R. G. COOKS, J. H. BOWIE
University Chemical Laboratory, Cambridge
and
P. MADSEN, G. SCHROLL and SVEN-OLOV LAWESSON
Dept. of Organic Chemistry, Aarhus University, Denmark

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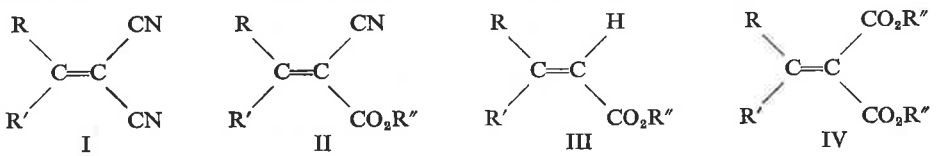
Abstract—Bond-forming reactions which occur in the decomposition of some α,β-unsaturated esters and nitriles upon electron impact are described. The reactions include bond formation between adjacent phenyl and cyanide substituents in structures of type A, and alkoxyl (or hydroxyl) migrations (probably by 1,3-shifts) in systems of type B, to give ions represented by C. A previously described cyclization reaction is shown to facilitate the expulsion of an *ortho*-substituent (at the site of cyclization) in a phenyl ring relative to the corresponding *meta*- and *para*-substituents.

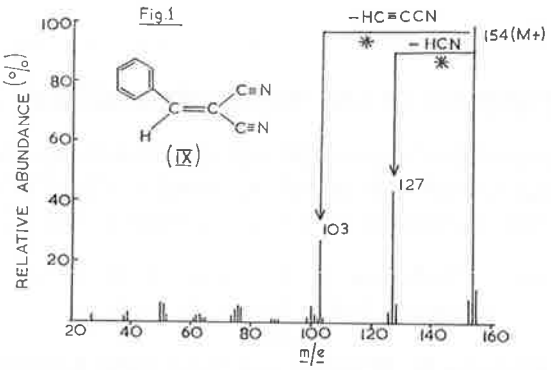
$C_6H_5C(R)=C(CN)R'$ (A) $\quad R(R')C=C(R'')CO_2R'''$ (B) $\quad R(R')\overset{+}{C}—OR'''$ (C)

REACTIONS occurring upon electron impact which necessitate bond formation between two atoms X and Y, where neither X nor Y is hydrogen, are of both practical and mechanistic interest. A recent review article[2] has summarized such reactions which have hitherto been reported. The present paper deals with some novel migrations of functional groups which are evident from the mass spectra of a variety of α,β-unsaturated nitriles and esters, represented in general by the structures I–IV.

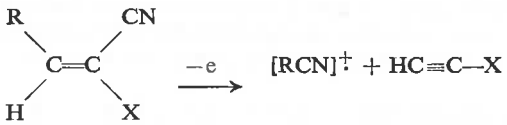


In compounds of the general formula I or II, when R or R′ is phenyl, ions formally corresponding to ionized phenyl cyanide are frequently observed in the spectra. Such ions vary greatly in relative abundance; also aromatic nuclei other than phenyl may participate in the reaction, as may be seen from the data compiled in Table 1. Among the compounds studied, the rearrangement is most prevalent in the spectrum (Fig. 1) of 1,1-dicyano-2-phenylethylene (IX), where the abundance of *m/e* 103 ($C_7H_5N^+$) attains 27% relative to the base peak molecular ion; an appropriate metastable peak establishes that *m/e* 103 is formed in a one-step process from the molecular ion. Although the product ion may conveniently be regarded as ionized phenyl cyanide, there is no evidence to favour C—C bond formation over C—N bond formation in this reaction. These examples appear to be the first reported ones in which an

[1] Part XIX, J. Ronayne, D. H. Williams and J. H. Bowie, *J. Am. Chem. Soc.* **88**, 4980 (1966).
[2] P. Brown and C. Djerassi, *Angew. Chem.* in press.

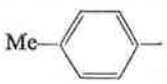
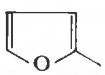
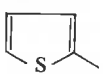
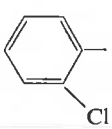


ion is generated with associated bond formation between 1,2-groups attached to a carbon-carbon double bond. The compounds (VI–VIII, X, XI) represented by the general formula II are of unknown stereochemistry, and we are therefore unable to judge whether a *cis*-relationship of the phenyl and cyanide groups is necessary for the rearrangement to occur. However, since *cis-trans* isomerization of double bonds is



V *a*

TABLE 1. RELATIVE ABUNDANCES OF IONS (*a*) IN THE SPECTRA OF COMPOUNDS OF THE GENERAL FORMULA V*

Compound			Composition of "*a*" (*m/e*)	Rel. Ab. (%)
No.	R	X		
VI	Ph	CO_2Et	C_7H_5N (*m/e* 103)	2
VII	Ph	CO_2H	C_7H_5N (*m/e* 103)	2
VIII		CO_2t-Bu	C_8H_7N (*m/e* 117)	3
IX	Ph	CN	C_7H_5N (*m/e* 103)	27
X		CO_2t-Bu	C_5H_3NO (*m/e* 93)	1
XI		CO_2t-Bu	C_5H_3NS (*m/e* 109)	5
XII		CN	C_7H_4NCl (*m/e* 137/139)	12/4

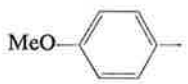
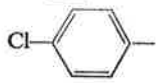
* The compositions of all ions reported in this paper have been established by high resolution measurements. Decomposition processes which are substantiated by appropriate metastable peaks are signified in the figures by an asterisk (*).

known to be a facile process upon electron-impact,[3] a *cis*-relationship would not seem to be a likely prerequisite. The occurrence of this rearrangement process is consistent with the generalization[3] that skeletal rearrangement is frequently facilitated by the proximity of highly unsaturated groups, and with the known propensity[4–6] of nitriles to undergo bond-forming reactions on electron impact.

A second rearrangement process which has been observed involves the migration of an alkoxyl or OH group in the mass spectral fragmentation of compounds represented by the general formulae II–IV. In the general case the reaction is probably best represented as a 1,3-alkoxyl (or OH) shift (XIII → *b*), followed by bond fission as indicated to give *c*.[7]

The compounds which have been found to undergo this fragmentation reaction upon electron impact are listed in Table 2, which also gives the relative abundances

TABLE 2. RELATIVE ABUNDANCES OF IONS (*c*) FORMED BY ALKOXYL OR HYDROXYL MIGRATION IN THE SPECTRA OF SOME α,β-UNSATURATED ESTERS AND ACIDS OF THE GENERAL FORMULA XIII

No.	R	Compound R′	R″	Composition of *c* (*m/e*)	Rel. Ab. (%)
VI	Et	Ph	CN	$C_9H_{11}O$ (*m/e* 135)	5
VII	H	Ph	CN	C_7H_7O (*m/e* 107)	9
XIV	Me	Ph	CN	C_8H_9O (*m/e* 121)	12
XV	H	Ph	H	C_7H_7O (*m/e* 107)	3
XVI	Me	Ph	H	C_8H_9O (*m/e* 121)	2
XVII	Et	Ph	CO_2Et	$C_9H_{11}O$ (*m/e* 135)	28
XVIII	Et		CO_2Et	$C_{10}H_{13}O_2$ (*m/e* 165)	5
XIX	Et		CO_2Et	$C_9H_{10}OCl$ (*m/e* 169/171)	2/0·6
XX	Et		CO_2Et	$C_9H_{10}OCl$ (*m/e* 169/171)	14/5
XXI	Et		CO_2Et	$C_9H_{10}OCl$ (*m/e* 169/171)	14/5
XXII	Et	Me	CN	C_4H_9O (*m/e* 73)	1
XXIII	Et	EtO	CO_2Et	$C_5H_{11}O_2$ (*m/e* 103)	2

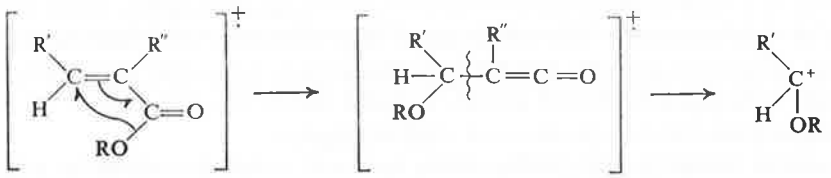
[3] J. H. Bowie, D. H. Williams, P. Madsen, G. Schroll and S.-O. Lawesson, *Tetrahedron* **23**, 305 (1967).

[4] R. Beugelmans, D. H. Williams, H. Budzikiewicz and C. Djerassi, *J. Am. Chem. Soc.* **86**, 1386 (1964).

[5] J. H. Bowie, R. Grigg, D. H. Williams, S.-O. Lawesson and G. Schroll, *Chem. Comm.* 403 (1965).

[6] J. H. Bowie, R. Grigg, S.-O. Lawesson, P. Madsen, G. Schroll and D. H. Williams, *J. Am. Chem. Soc.* **88**, 1699 (1966).

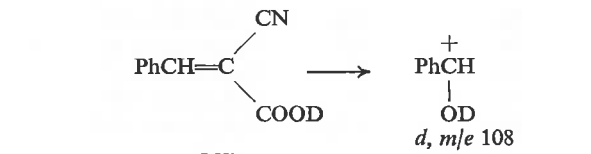
[7] In the representation of concerted processes (e.g., XIII→*b*), the use of a fishhook is not intended to imply any preference for a homolytic process over a heterolytic one.



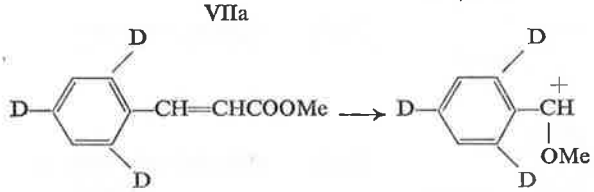
XIII *b* *c*

and compositions of the product ions. The stereochemistry of compounds VI, VII, XIV and XXII is unknown.

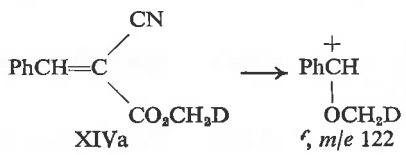
Although high resolution measurements establish all the proposed migrations, additional evidence has been forthcoming from deuterium labelling in a number of cases. Thus the 9% peak at *m/e* 107 in the spectrum of the acid VII is shifted to *m/e* 108 (*d*) in the spectrum of the O-d_1-acid VIIa, and the *m/e* 121 rearrangement ion from methyl cinnamate XVI is shifted to *m/e* 124 (*e*) in the spectrum of the d_3-derivative XVIa.[8] Similarly, the *m/e* 121 ion in the spectrum (Fig. 2) of methyl α-cyanocinnamate (XIV) is shifted to *m/e* 122 (*f*) in the spectrum of the d_1-derivative XIVa, while the *m/e* 135 ion from diethyl benzalmalonate (XVII, see Fig. 3) is quantitatively shifted to *m/e* 138 (*g*) in the spectrum of the d_3-derivative XVIIa.



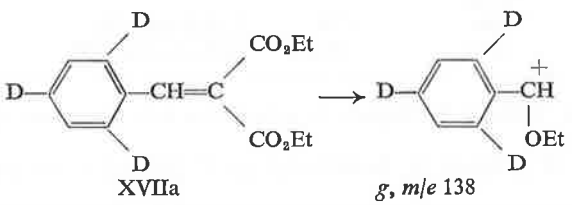
VIIa *d*, *m/e* 108



XVIa *e*, *m/e* 124



XIVa *f*, *m/e* 122

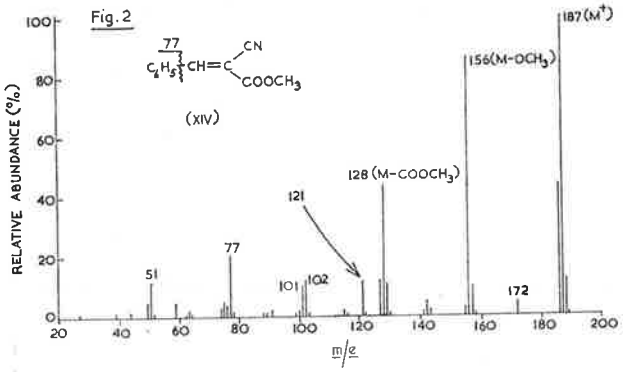


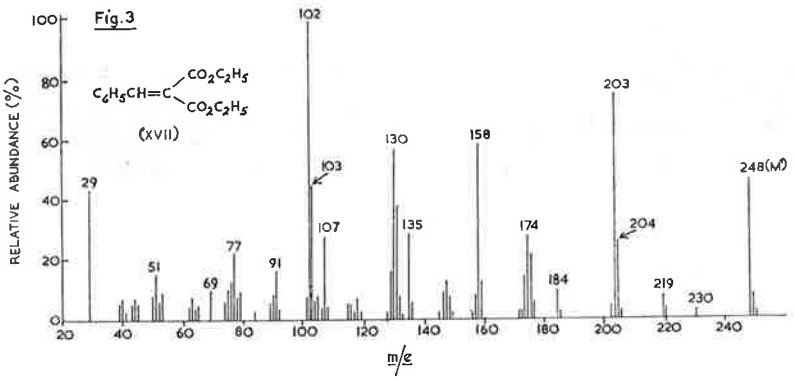
XVIIa *g*, *m/e* 138

[8] The product ions are represented as benzyl cations merely for convenience, and no preference is implied for these structures over the ring expanded hydroxy- or alkoxy-tropylium ions.[9]

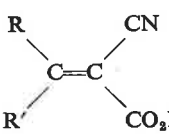
[9] For examples of tropylium ion formation in the mass spectrometer, see H. M. Grubb and S. Meyerson in (F. W. McLafferty ed.) *Mass Spectrometry of Organic Ions* Chap. 10. Academic Press, New York (1963).

A number of aliphatic α,β-unsaturated ethyl esters which have been examined (XXIV–XXVIII) do not give ions corresponding to ethoxyl migrations, and indeed the data collected in Table 2 suggest that a β-phenyl substituent on the double bond

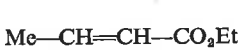




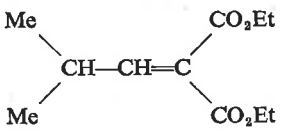
facilitates the production of the rearrangement ions (attention is drawn to the low relative abundance of the rearrangement ions from the aliphatic esters XXII and XXIII). This behaviour may be understood in terms of the favourability of the appropriate bond cleavage in *b* when *R′* is a phenyl substituent, to produce benzyl cations or tropylium ions. However, the possibility of a 1,5-alkoxyl or 1,5-hydroxyl shift (XXIX → *h*), followed by a 1,3-hydrogen shift (*h* → *i*) and subsequent cleavage (*i* → *j*) cannot be excluded when a phenyl substituent is conjugated with the double bond.[10]



XXIV, R = R′ = Me
XXV, R = R′ = Et
XXVI, R = H, R′ = iso-Pr
(or R = iso-Pr, R′ = H)

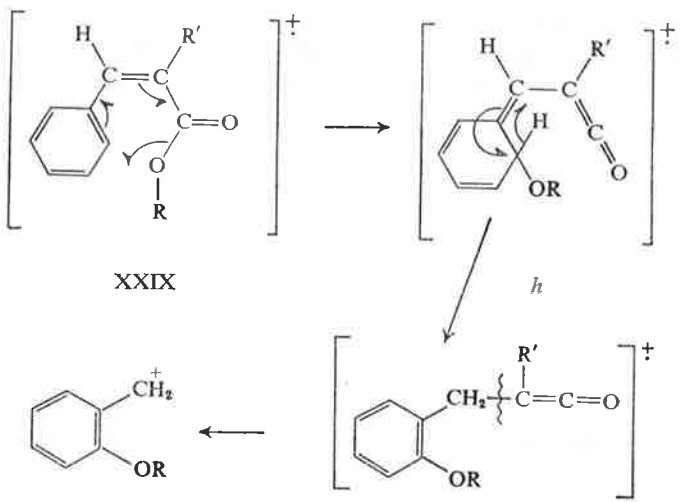


XXVII



XXVIII

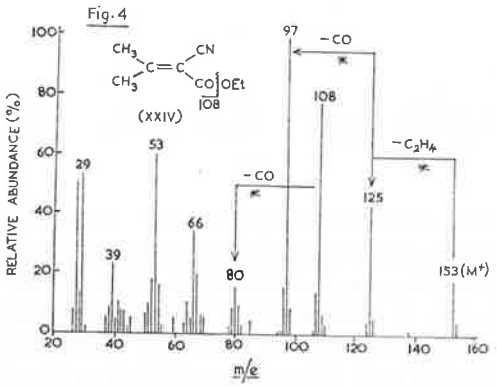
[10] In *trans*-cinnamates, the operation of a 1,5-shift (XXIX → *h*) would of course require isomerization about the double bond prior to rearrangement.



XXIX *h*

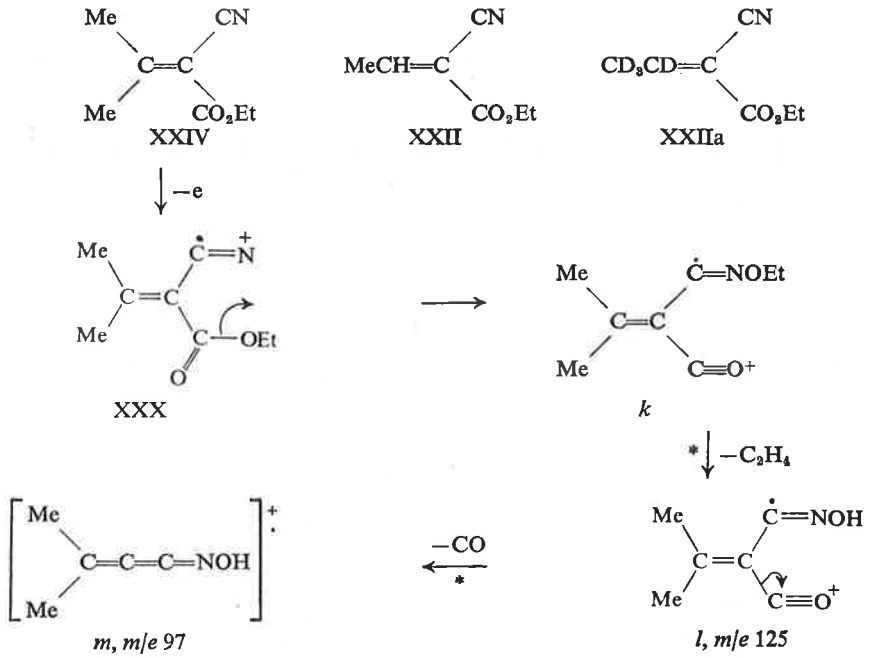
j *i*

The effect of varying the energy of the electron beam (down to a nominal 11 eV) on both the cyanide (V → *a*) and ethoxyl (XIII → *b* → *c*) migrations has been determined. In the compounds examined at low energies (IX, XXI, XXII), the total ion current carried by the rearrangement fragments was sensibly constant.

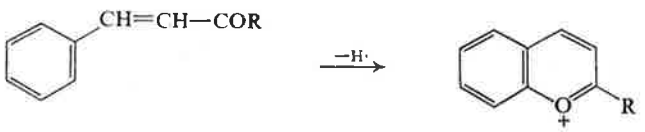


The close proximity of cyanide and carboethoxy groups, when attached to the same sp^2-hybridized carbon atom (see II), may on occasions lead to abundant M—C_2H_4—CO rearrangement ions. This behaviour is illustrated by reference to the spectrum (Fig. 4) of ethyl isopropylidenecyanoacetate (XXIV), in which appropriate metastable peaks establish the origin of the base peak (*m/e* 97, $C_5H_7NO^+$) from the molecular ion via successive losses of ethylene (to *m/e* 125, $C_6H_7NO_2^+$) and carbon monoxide. Similarly, in the spectrum of the ethylidene derivative XXII, *m/e* 83 ($C_4H_5NO^+$, 16% of the M—OC_2H_5 base peak) arises *via* the successive losses of C_2H_4 and CO from the molecular ion; the spectrum of the d_4-derivative XXIIa establishes that the ethylene is expelled from the ethyl group of the ester. These processes demand the migration of an oxygen atom, presumably as an OEt or OH group. Since a neighbouring cyanide group bound to the sp^2-hybridized carbon atom seems

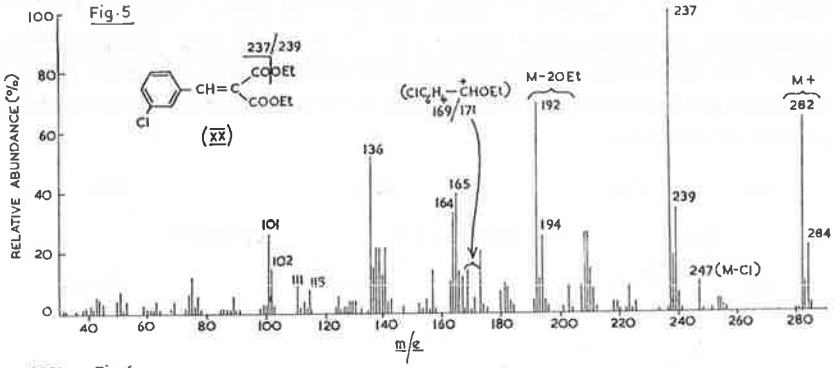
to be necessary for this reaction to occur, one possible representation of the process may be illustrated by the sequence XXX → *k* → *l* → *m* (*m/e* 97). The loss of ethylene from XXIV after ionization to give the acid, followed by a OH migration to the nitrile function might also be entertained since no loss of carbon monoxide is found to precede the expulsion of ethylene.

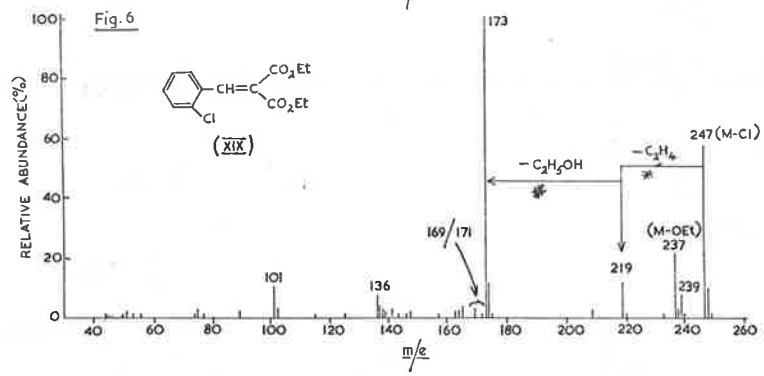


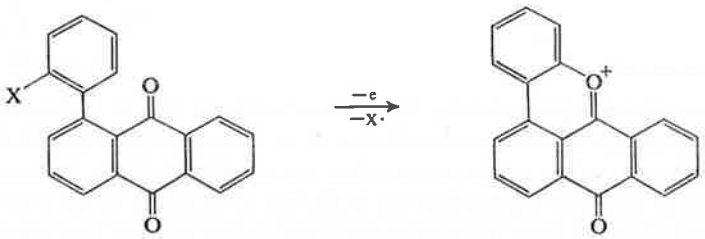
In some systems represented by the general formula XXXI it has recently been shown[1] that abundant M-1 ions arise via loss of an aromatic hydrogen atom, probably with the production of an aromatic oxonium ion *n*. Waight[11] has demonstrated that such cyclization reactions can lead to the facile loss of an *ortho*-substituent (XXXII → *o*). Since deuterium labelling has established that hydrogen is not lost specifically from the *ortho*-position in the reaction typified by XXXI → *n*,[1] it was of interest to determine whether chlorine was preferentially eliminated from the *ortho*-isomer XIX relative to the *meta*- and *para*-isomers XX and XXI. Whereas the spectra of the *m*- and *p*-isomers are virtually identical (see, for example, Fig. 5), that of the *o*-isomer XIX (Fig. 6) contains no molecular ion, but exhibits a relatively abundant M—Cl ion, the further decomposition of which provides (at least in part) both *m/e* 219 and the base peak (*m/e* 173). These observations strongly indicate a facile chlorine radical elimination via cyclization (XIX → *p*) only in the *o*-isomer.



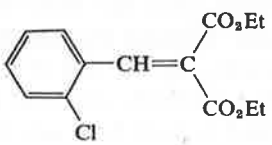
[11] E. S. Waight, Symposium on *Newer Physical Methods in Structural Chemistry*, Oxford (1966).



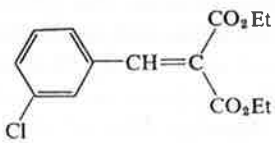




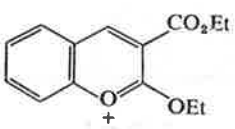
XXXII *o*



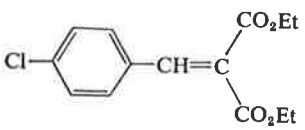
XIX



XX



p



XXI

While the elimination upon electron impact of stable neutral species (e.g., CO) from organic molecules with bond-formation between the terminal portions can no longer be regarded as very unusual,[2] the possible migration of groups in concerted electrocyclic reactions (e.g., XIII → *b* or XXIX → *h*) appears to be a rarer phenomenon, examples of which are of great mechanistic interest. However, it is emphasized that if the ionization process is regarded as occurring by removal of a π-electron from the olefinic double bond of XIII, then the alkoxyl (or hydroxyl) migration may be visualized to occur to a benzylic carbonium ion centre, in analogy to other cases.[11a]

Acknowledgement—A grant from Statens almindelige videnskabsfond (to S.-O. L.) is gratefully acknowledged.

EXPERIMENTAL

All mass spectra were determined using an AEI MS 9 mass spectrometer operating at 70 eV and a source pressure of approximately 1×10^{-7} mm Hg. Samples were introduced through a heated inlet system (at approximately 150°) or by the direct insertion technique.

Compound XV was obtained commercially. We have previously[12] reported the preparation of VIII, X and XI.

Diethyl *m*-chlorobenzalmalonate (XX) was prepared by condensation of *m*-chlorobenzaldehyde with diethylmalonate, yield 28%, b.p. 135°/0·5 mm, n_D^{25} 1·5380. (Found: C, 59·33; H, 5·38; Cl, 12·50. Calc. for $C_{14}H_{15}O_4Cl$: C, 59·49; H, 5·36; Cl, 12·71%.)

The following Knoevenagel products were prepared by reported methods (compound and Ref. given), VI,[13] VII,[14] IX,[15] XII,[15] XIV,[16] XVI,[17] XVII,[18] XVIII,[19] XIX,[20] XXI,[21] XXII,[22] XXIII,[23] XXIV,[24] XXV,[25] XXVI,[26] XXVII,[27] XXVIII.[28]

The isotopically labelled ester XIVa was prepared by condensation of benzaldehyde with monodeuterated methyl cyanoacetate, which was obtained from the acid by esterification with diazomethane in a dioxane-deuterium oxide mixture.[29] Yield 89%, m.p. 87–88°.

Ethyl d_4-ethylidenecyanoacetate (XXIIa) was prepared by condensation of d_4-acetaldehyde with ethyl cyanoacetate, yield 69%, b.p. 99°/11 mm., n_D^{25} 1·4456.

The spectrum of the deuterated acid VIIa was obtained by introducing the acid VII into the spectrometer in the presence of D_2O.[30]

Methyl 2,4,6-d_3-cinnamate (XVIa) was prepared by a previously described[1] procedure. Diethyl 2,4,6-d_3-benzalmalonate (XVIIa) was available from the condensation of 2,4,6-d_3-benzaldehyde[1] with diethyl malonate.

[11a] R. G. Cooks and D. H. Williams, *Chem. Comm.* 51 (1967).
[12] S.-O. Lawesson, E. H. Larsen and H. J. Jacobsen, *Arkiv. Kemi* **23**, 453 (1965).
[13] W. Baker and A. Lapworth, *J. Chem. Soc.* **127**, 563 (1925).
[14] A. Lapworth and J. A. McRae, *J. Chem. Soc.* **121**, 1700 (1922).
[15] B. B. Corson and R. W. Stoughton, *J. Am. Chem. Soc.* **50**, 2828 (1928).
[16] B. B. Corson and R. W. Stoughton, *J. Am. Chem. Soc.* **50**, 2835 (1928).
[17] P. Pfeiffer, I. Engelhardt and W. Alfuss, *Liebig's Ann.* **467**, 178 (1928).
[18] R. Anschütz, *Liebig's Ann.* **354**, 124 (1907).
[19] E. Knoevenagel, *Chem. Ber.* **31**, 2594 (1898).
[20] P. E. Gagnon and L. Gravel, *Canad. J. Research*, **8**, 600 (1933).
[21] E. E. Pratt and E. Werble, *J. Am. Chem. Soc.* **72**, 4638 (1950).
[22] K. V. Auwers, *Chem. Ber.* **56**, 1182 (1923).
[23] L. Claisen, *Chem. Ber.* **26**, 2731 (1893).
[24] G. Komppa, *Chem. Ber.* **33**, 3532 (1900).
[25] K. V. Auwers, *Chem. Ber.* **56**, 1184 (1923).
[26] F. D. Popp and A. Catala, *J. Org. Chem.* **26**, 2738 (1961).
[27] F. R. Goss, C. K. Ingold and J. F. Thorpe, *J. Chem. Soc.* **123**, 3352 (1923).
[28] S. B. Schryver, *J. Chem. Soc.* **63**, 1344 (1893).
[29] K. J. van de Merwe, P. S. Steyn, and S. H. Eggers, *Tetrahedron Letters* 3923 (1964).
[30] J. S. Shannon, *Austral. J. Chem.* **15**, 265 (1962).

Mass Spectra and Organic Analysis. Part VIII.[1] The Mass Spectra of Piperitone, the Piperitols, and Related Products

By **A. F. Thomas** and **B. Willhalm**, Research Laboratory, Firmenich & Cie, Geneva, Switzerland
J. H. Bowie, University Chemical Laboratory, Cambridge

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Mass Spectra and Organic Analysis. Part VIII.[1] The Mass Spectra of Piperitone, the Piperitols, and Related Products

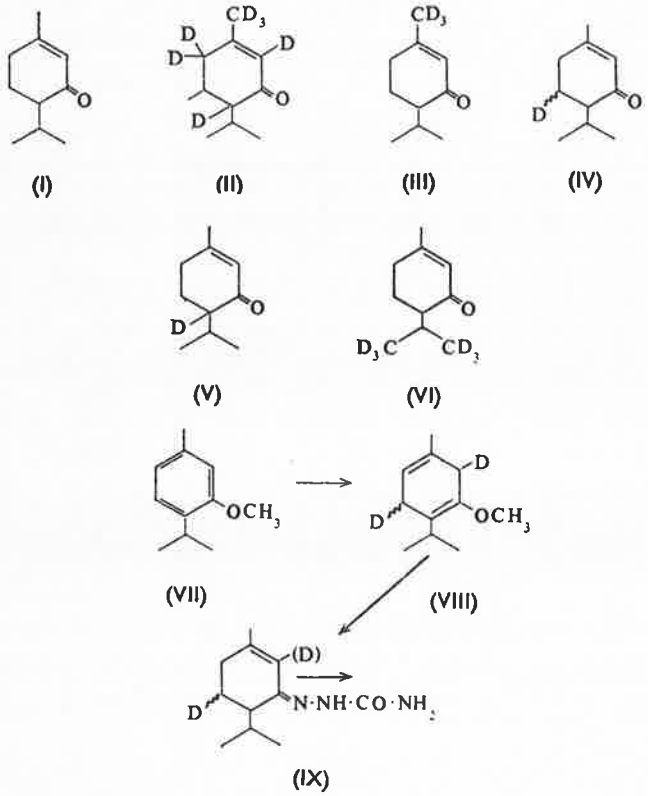
By **A. F. Thomas** and **B. Willhalm**, Research Laboratory, Firmenich & Cie, Geneva, Switzerland
J. H. Bowie, University Chemical Laboratory, Cambridge

With the aid of deuteriation studies and exact mass measurements, structures for the ions observed in the mass spectra of piperitone and *cis*- and *trans*-piperitol are given, and related to the simpler 3-methylcyclohexenone and 3-methylcyclohexenol. Keto–enol interconversions within the mass spectrometer are shown to be unlikely. The loss of methyl attached to a double bond in the 3-methylcyclohexenols is described. The piperitol spectra are highly dependent on the condition of the mass spectrometer so far as the loss of water is concerned.

THIS Publication describes the results obtained with some unsaturated analogues of our previously reported menthones [2] and menthols.[1] There are not many analyses of mass spectra of cyclic αβ-unsaturated ketones outside the steroid field,[3] although von Sydow has published the spectra of four unsaturated ketones including piperitone.[4]

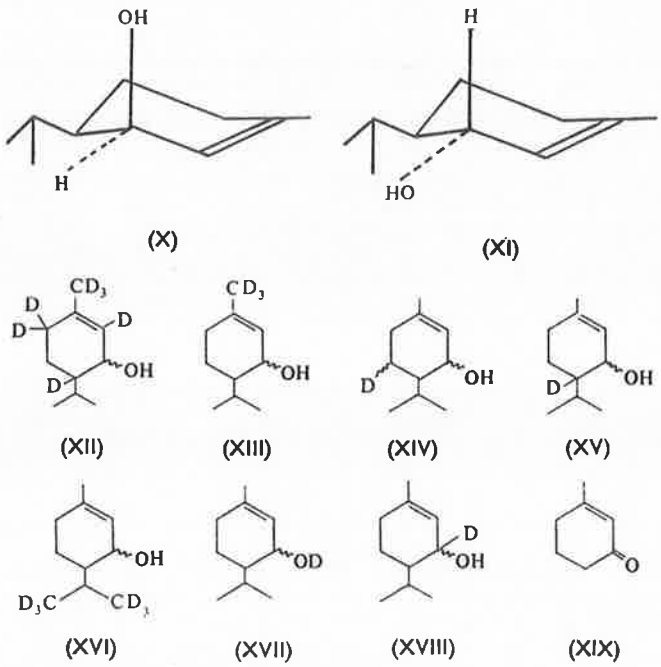
Preparation of Materials.—The deuteriated piperitones (II) and (VI) were available from our previous work.[2] Reaction of trideuteriomethylmagnesium iodide with cryptone [5] led to a mixture of *cis*- and *trans*-1-hydroxymenth-2-ene deuteriated in the C-7 methyl group, oxidation of which [6] gave the piperitone (III). Thymol methyl ether (VII) was reduced with sodium and deuterioethanol in heavy ammonia [7] to (VIII), then treatment with semicarbazide gave a piperitone semicarbazone (IX) that was decomposed, the resulting dideuteriated piperitone being back-exchanged with water to give (IV). A study of the rate of deuterium exchange of piperitone in alkaline heavy water showed the expected more rapid exchange of the axial C-4 hydrogen than the others (Figure 1). Examination of the rate of change of the mass spectroscopic fragment at *m/e* 82 (not involving C-4; see below) showed that most of the deuterium

[1] Part VII, A. F. Thomas and B. Willhalm, *J. Chem. Soc.* (*B*), 1966, 219.
[2] B. Willhalm and A. F. Thomas, *J. Chem. Soc.*, 1965, 6478.
[3] R. H. Shapiro and C. Djerassi, *J. Amer. Chem. Soc.*, 1964, **86**, 2825.
[4] E. von Sydow, *Acta Chem. Scand.*, 1964, **18**, 1099.
[5] Cf. A. S. Galloway, J. Dewar, and J. Read, *J. Chem. Soc.*, 1936, 1595.
[6] J. P. Bain, B.P. 761,686; J. P. Bain, A. B. Booth, and E. A. Klein, U.S.P. 2,863,882 (*Chem. Abs.*, 1959, **53**, 8194); *idem.* 2,827,499 (*Chem. Abs.*, 1958, **52**, 14,719); J. P. Bain, A. B. Booth, and W. Y. Gary, U.S.P. 2,894,040 (*Chem. Abs.*, 1959, **53**, 22,067).
[7] Cf. A. J. Birch, *J. Chem. Soc.*, 1944, 432.

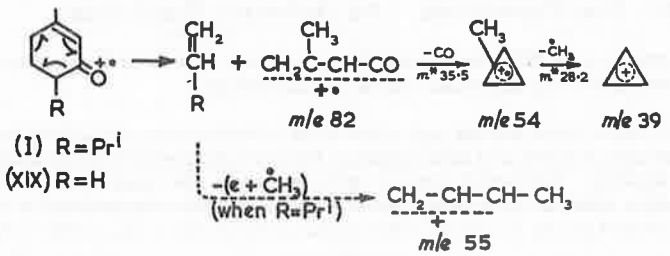


incorporated in the first 20—30 min. went into this position (Figure 1), leading to (V).

Reduction of piperitone by lithium aluminium hydride in ether at room temperature is reported to give a mixture of 36% *cis*- and 64% *trans*-piperitol (X) and (XI).[8] We found a slightly higher proportion of (X), the n.m.r. spectrum of which confirmed the stereochemical assignment, a coupling constant of 6 c./sec. being observed between the vinyl hydrogen on C-2 and the carbinol hydrogen on C-3, consistent with the dihedral angle of about 40° observed on Dreiding models with the conformation shown in (X).[9]



In addition to the deuteriated piperitols (XII)—(XVI) corresponding to the piperitones (II)—(VI), we prepared (XVIII) by reduction of piperitone with lithium aluminium deuteride, and (XVII) by direct exchange in the mass spectrometer itself (cf. ref. 1).



Scheme 1

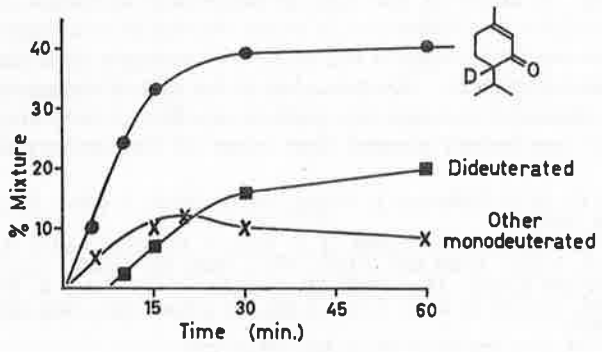


FIGURE 1

Mass Spectrum of Piperitone (Figure 2).—The principal fragment is at *m/e* 82, and arises as shown in Scheme 1 * by a retro-Diels–Alder fission, this idea being supported by the mass spectra of the deuteriated piperitones, and the behaviour of 3-methylcyclohex-2-enone (XIX) which, unlike piperitone (I), exhibits a strong metastable peak at about *m/e* 61·2 associated with this fission. The subsequent fate of the fragment at *m/e* 82 is shown

* All the fragments of piperitone and the piperitols that are discussed were checked by exact mass measurements, and, unless otherwise stated, consist almost entirely of the C, H, and O composition expected for the formulæ given.

[8] A. K. Macbeth, B. Milligan, and J. S. Shannon, *J. Chem. Soc.*, 1953, 901; use of sodium borohydride in alcohol leads to extensive 1,4-reduction, cf. M. E. Cain, *J. Chem. Soc.*, 1964, 3532.

[9] M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11.

by the existence of metastable peaks corresponding to loss of first CO, then methyl. Most of the fragment at *m/e* 55 that does not contain oxygen (70% of the total)

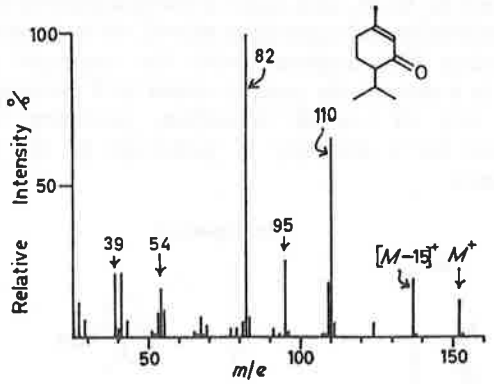


FIGURE 2

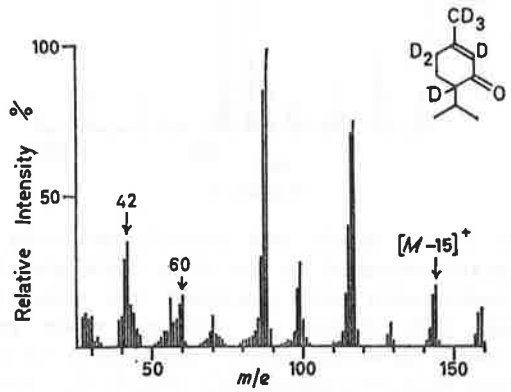


FIGURE 3

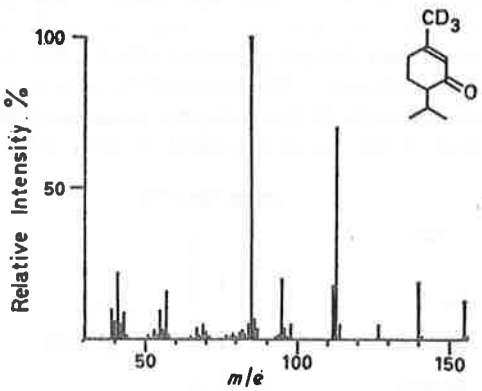
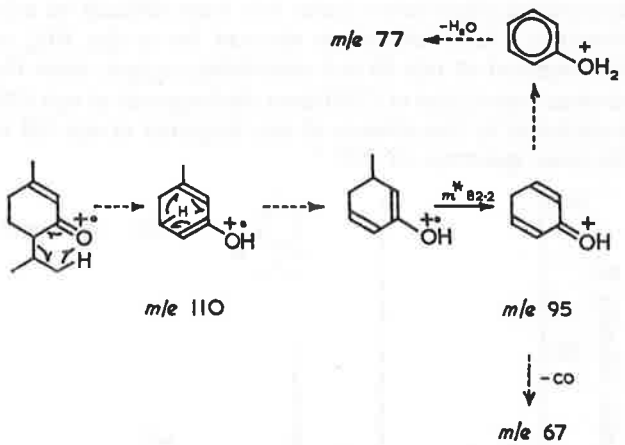


FIGURE 4

appears to arise from the neutral olefin of this fragmentation, and apart from this the fragments in Scheme 1 are almost the only ones unaffected in either position or intensity by deuteriation of the side-chain (VI).

* We recently established the existence of both possible enol ions of 3-methylcyclohexanone as fragments in the mass spectrometer. They have quite different fragmentation patterns, which we shall treat elsewhere. These facts are unrelated to known keto–enol rearrangements in the inlet system of certain mass spectrometers,[13,14] but argue against the occurrence of repeated keto–enol transitions such as are sometimes invoked to account for observed mass spectrometric fissions (*e.g.*, in ref. 15).

The only other important fragmentation path taken by piperitone results from an initial γ-hydrogen transfer (" McLafferty rearrangement ") [10] involving the side-chain (Scheme 2) analogous to what has been abundantly demonstrated with menthone.[2,11] It will be noted that this fragment at *m/e* 110 is the enol ion of 3-methylcyclohex-2-enone (XIX), but its fate in the mass spectrometer is quite different from that of the ketone; it loses the methyl group attached to C-1, the resulting fragment at *m/e* 95 shifting to 96 in (IV), (V), and (VI), to *m/e* 99 in (II), but remaining at 95 in (III). One explanation is that a rearrangement of the enol occurs by hydrogen transfer from C-5 as shown in Scheme 2.



Scheme 2

This constitutes an experimental confirmation of the logical theoretical assumption in accord with ionisation potential considerations,[12] that an enol is formed in the McLafferty rearrangement, and that it does not rapidly rearrange to the ketone,* in analogy to the experimental evidence supplied by Pitts *et al.*[16] in connection with the corresponding photochemical reaction.[17]

Loss of methyl from piperitone probably occurs by the same mechanism as we have suggested for menthone [2] (Scheme 3).

The $C_8H_{12}O^+$ ion at *m/e* 124 is formed, as the deuteri-

[10] F. W. McLafferty, *Analyt. Chem.*, 1959, **31**, 82; leading references to this reaction in: H. Fritz, H. Budzikiewicz, and C. Djerassi, *Chem. Ber.*, 1966, **99**, 35; C. Djerassi and L. Tökes, *J. Amer. Chem. Soc.*, 1966, **88**, 536.

[11] H. Budzikiewicz, C. Djerassi, and D. H. Williams, " Interpretation of Mass Spectra of Organic Compounds," Holden-Day, San Francisco, 1964.

[12] S. Meyerson and J. D. McCollum, *Adv. Analyt. Chem. and Instrum.*, 1963, **2**, 187.

[13] K. Biemann, " Mass Spectrometry, Organic Chem. Applications," McGraw-Hill, 1962, p. 218.

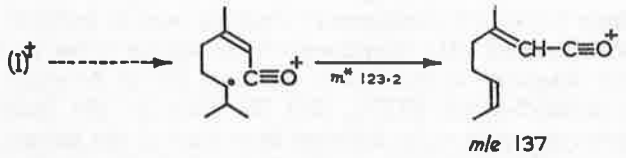
[14] E. Lund, H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 1528; C. Djerassi, R. H. Shapiro, and M. Vandewalle, *ibid.*, 1965, **87**, 4892; H. Budzikiewicz and C. Djerassi, *Chem. and Ind.*, 1965, 1697.

[15] F. Weiss, A. Isard, A. Lautz, G. Bonnard, J. Sarpinet, and R. Husson, *Bull. Soc. chim. France*, 1965, 3677.

[16] J. N. Pitts, J. K. Foote, and J. K. S. Wan, *Photochem. and Photobiol.*, 1965, **4**, 323; G. R. McMillan, J. G. Calvert, and J. N. Pitts, *J. Amer. Chem. Soc.*, 1964, **86**, 3602.

[17] R. G. W. Norrish and M. F. S. Appleyard, *J. Chem. Soc.*, 1934, 874.

ated compounds [notably (IV)] show, by loss of carbons 5 and 6 without hydrogen transfer.



Scheme 3

Simple loss of an isopropyl radical will give rise to the ion at *m/e* 109, and, although a metastable peak at about *m/e* 87 can be correlated with loss of ethylene from the fragment at *m/e* 137, the mass spectra of the deuteriated piperitones make this very difficult to substantiate. Also difficult to account for is the 10% of the fragment at *m/e* 95 not containing oxygen, since the obvious source (loss of CHO from the fragment at *m/e* 124) is excluded by the absence of any fragment at *m/e* 101 in the mass spectrum of (VI).

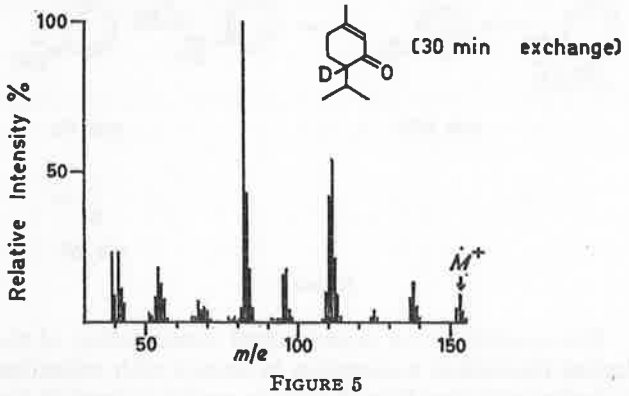


FIGURE 5

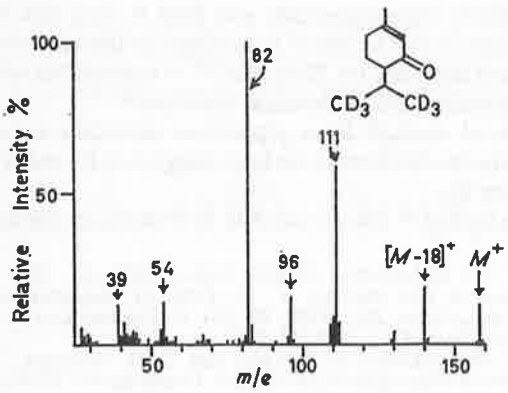


FIGURE 6

The small fragment at *m/e* 67 occurs in all the 3-methylcyclohex-2-enones we have so far examined, and could be ascribed to the $C_5H_7^+$ ion (although we have not checked this with exact mass measurements) possibly arising, like the small fragment at *m/e* 77, from the fragment at *m/e* 95.

It is well known that the lower fragments become less and less specific (with the exception of those belonging to the clear-cut degradations described). For instance, the fragment at *m/e* 55 is 70% C_4 (mostly from C-4, 5, 8, and 9; cf. Scheme 1), 30% being $C_3H_3O^+$. The fragment at *m/e* 41 is even less specific. The deuteriated compound (VI) exhibits fragments at every mass number from *m/e* 41 to 46, and, since 3-methylcyclohex-2-enone has practically no fragment at *m/e* 41, we feel justified in associating this fragment with the isopropyl group. There is a metastable peak at about 37·2 corresponding to a *m/e* 41 ⟶ 39 transition, providing further evidence for a diversity of pathways to the lighter fragments.

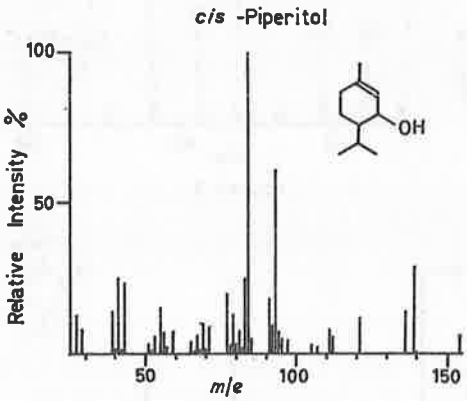


FIGURE 7

Mass Spectra of cis- *and* trans-*Piperitol.*—At first, the spectra measured on the Atlas CH-4 and A.E.I. MS-9 instruments were practically the same, *trans*-piperitol (XI) (Figure 8) showing much greater $[M - 18]^+$, $[M - 18 - 15]^+$, and $[M - 18 - 43]^+$ fragments than *cis*-piperitol (X) (Figure 7). Early in our experiments, however, we were obliged to change the filament in our Atlas instrument. On previous occasions we had noticed a very marked catalytic dehydration and dehydrogenation effect after insertion of a new cathode unit. We followed this effect by successive measurements of the α-ionone mass spectrum, and found that it always disappeared entirely after 48 hr.

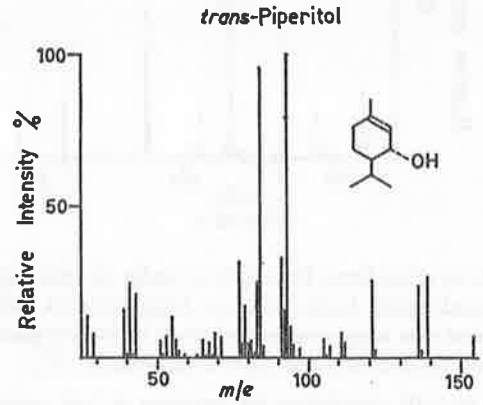


FIGURE 8

For the first time we now used a cathode unit that was not entirely new, but was a repaired unit in which only the rhenium filament had been changed, and we were surprised to find no catalytic effect at all in the α-ionone

spectrum. We concluded that the surface of the ceramic part of the new cathode units had been responsible for this effect. Furthermore, we found that the piperitol spectra were similar to previous ones, but some five months later (after a total lifetime of this cathode unit of about 1 year) we noticed for both piperitols a markedly lower tendency to form dehydration fragments (the three mentioned at the start of this paragraph). Nearly 1 year later (total lifetime of the cathode unit about 2 years) the relative intensities of these dehydration fragments had further diminished (Figures 9 and 10), that might be accounted for by a trace of acid or other catalyst on the walls of the capillary, since on other occasions we have stored *trans*-piperitol for some months without alteration.

There are two main breakdown paths in the piperitol mass spectra, one being through the initial loss of water mentioned. Although a precise calculation is probably not justified in the case of the heptadeuteriated piperitols (XII) (since it is unlikely that the loss was entirely by electron bombardment), the fragments at *m/e* 140—144 do, in fact, fit a loss of CD_3 and HDO with the new

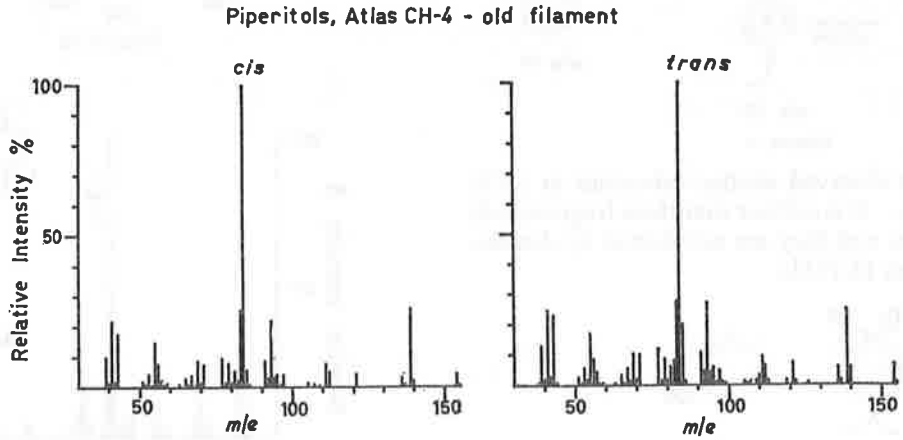


FIGURE 9 FIGURE 10

trans-piperitol still giving more dehydration fragments than the *cis*-isomer. The piperitols are so far the only substances we have found to show such striking differences in their mass spectra, other spectra remaining very similar to the earlier ones. We also carried out some experiments with varying source temperatures in the MS-9 instrument, and found that, contrary to what might intuitively be expected, raising the source temperature resulted in a lowering of the proportion of the dehydration fragments (Table 1), thus supporting the

TABLE 1 *

Relative intensity (% base fragment) of various ions at different source temperatures

	M^+	$M - 15^+$	$M - 18^+$	$M - 33^+$	$M - 61^+$
75°c	16	33	36	21	100
150°c	17	38	41	25	100
350°c	5	35	26	23	94

* The figures of the mass spectra of deuteriated piperitols and the values quoted in Table 1 refer only to *cis*-piperitol. Similar values are found with *trans*-piperitol, but with a higher proportion of dehydration fragments.

notion that the dehydration is catalytic rather than thermal or arising from electron bombardment. *cis*-Piperitol has been reported to be unstable,[18] but we have found both *cis*- and *trans*-piperitol to be thermally stable, being largely unchanged after passage over glass helices up to 300°. Nevertheless, on one occasion after collection from a Carbowax column and storage in the dark in a sealed capillary tube, a sample of *trans*-piperitol had been dehydrated entirely, an observation

filament on the Atlas instrument. Subsequent measurements were all made with the repaired filament, but examination of *cis*- and *trans*-(XV) showed that, at the same time as Figures 9 and 10 were recorded, neither piperitol lost water by 1,2-elimination to any extent.

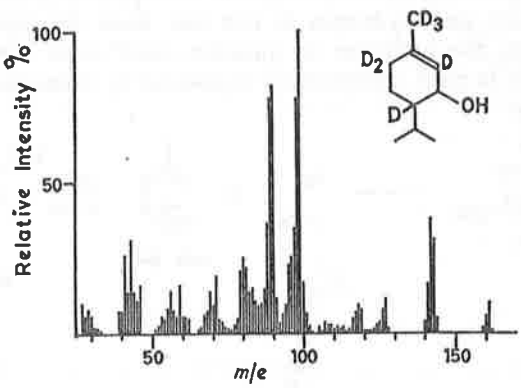
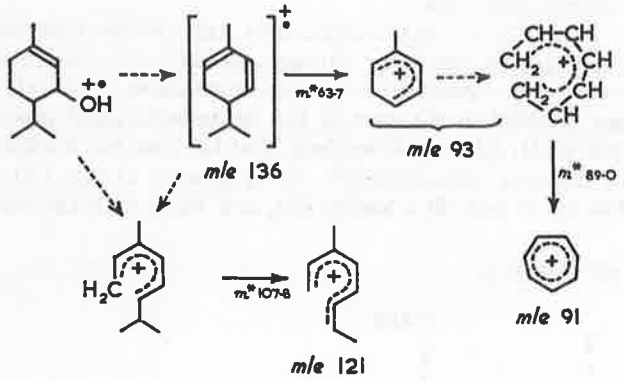


FIGURE 11

Since no hydrogen is lost from any of the methyl groups or from C-5, and *trans*-piperitol does not 1,2-eliminate water to any appreciable extent, it appears that most of the remainder must come from C-6, although the importance of the fragment at *m/e* 121 suggests that the $[M - 18]^+$ fragment is not merely the α-phellandrene ion.[19] A further point requiring explanation is the

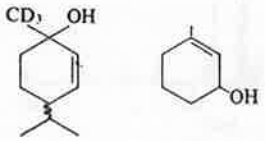
[18] J. Read and J. Walker, *J. Chem. Soc.*, 1934, 308.
[19] A. F. Thomas and B. Willhalm, *Helv. Chim. Acta*, 1964, **47**, 475.

loss of deuterium from the methyl group on C-1 in the formation [from (XIII)] of the fragment corresponding to *m/e* 93. Scheme 4 provides one explanation of



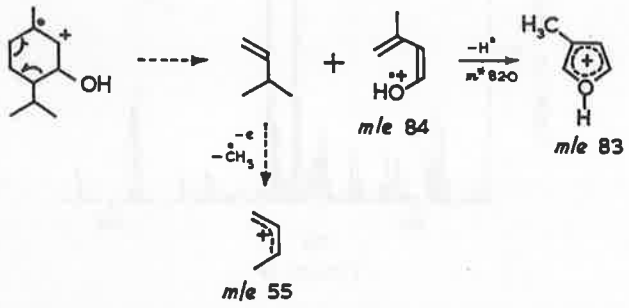
Scheme 4

this, and we have observed similar behaviour in (XX) (both *cis* and *trans*). It is evident that these fragments do not contain oxygen, and they are not shifted by deuteriation on the oxygen (XVIII).



(XX) (XXI)

The second main breakdown path of the piperitols leads by way of a retro-Diels–Alder fission (Scheme 5) to the main fragment at *m/e* 84. Loss of a hydrogen from this fragment gives *m/e* 83, and, since the methyl group retains all its hydrogen in this reaction [compound (XIII)] and hydrogen is not lost from the hydroxyl group, the hydrogen in question must come from C-6 which is most conveniently explained by formation of a furan.



Scheme 5

The most difficult problem in the mass spectra of the piperitols is to account for the loss of the methyl group, which is only the one attached to C-1 [(XII), (XIII), and (XVI)]. It is reasonable to suppose that the C-3–C-4 bond is the weakest in the piperitol molecule, and its fission may lead, as we have shown above, directly to the " retro-Diels " fragment. Should this not happen, stabilisation of the radical-ion through loss

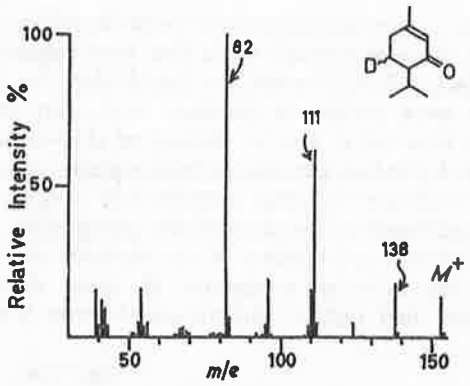


FIGURE 12

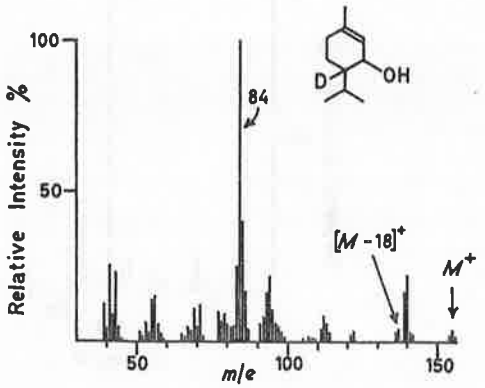


FIGURE 13

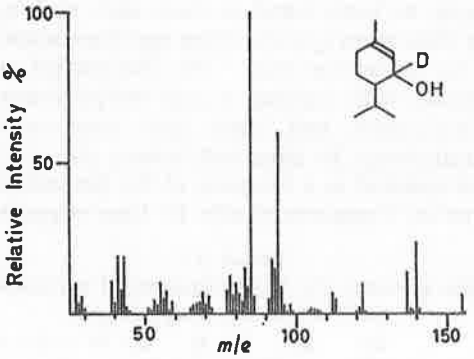


FIGURE 14

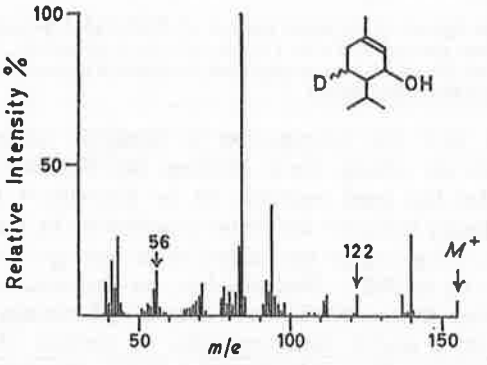


FIGURE 15

of a methyl radical from the isopropyl group does not occur, and cyclisation to the cyclobutane in which the methyl removed is both allyl and quaternary (Scheme 6a)

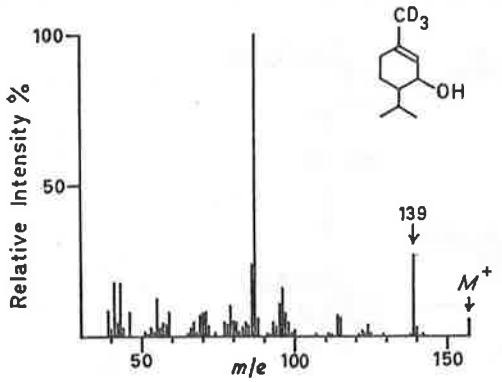


FIGURE 16

is a possible explanation of the results. The alternative, involving initial hydrogen transfer from C-3, does not account for the lack of stereochemical preference in this fission, but otherwise accounts satisfactorily for the fragments observed (Scheme 6b).

Several small fragments arise from mass 139 such as at *m/e* 97 (loss of C_3H_6), and a small proportion of the fragment at *m/e* 111 (loss of C_2H_4), the latter moving to *m/e* 117 in (XVI) but remaining at *m/e* 111 in (XIII). The fragment at *m/e* 71 can be associated with *m/e* 139, too, since there is a metastable peak at about *m/e* 36·3 that does not move in (XIII) but shifts to slightly lower *m/e* in (XIV), corresponding to a change of *m/e* 140 ⟶ 71. This fragment at *m/e* 71 must therefore be associated with a double hydrogen transfer, one of which comes mostly from the terminal carbon of the side-chain in (XVI), and the other presumably from the adjacent carbon, since it does not come from any of the positions we have labelled. Scheme 6 also shows a possible genesis for this ion. It is possible that 3-methylcyclohex-2-enol (XXI) undergoes loss of methyl in the same way [unlike the corresponding ketone (XIX)], the " retro-Diels " reaction being relatively small (Figure 18), but we have not checked that the carbon lost is really the methyl attached to the double bond in (XXI), and, indeed, cyclohex-2-enol exhibits a relatively strong

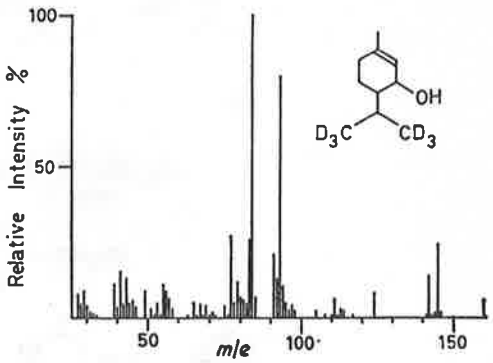


FIGURE 17

$[M - 15]^+$ fragment arising by loss of C-6 adjacent to the carbinol group (personal communication from Dr. R. T. Aplin, who has confirmed this by deuteriation studies).

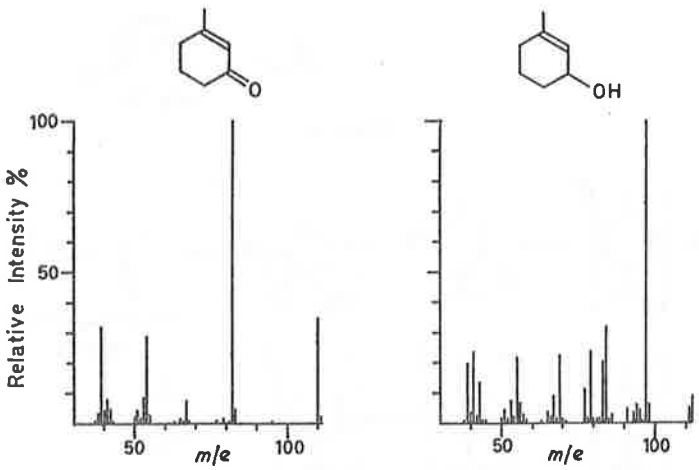


FIGURE 18

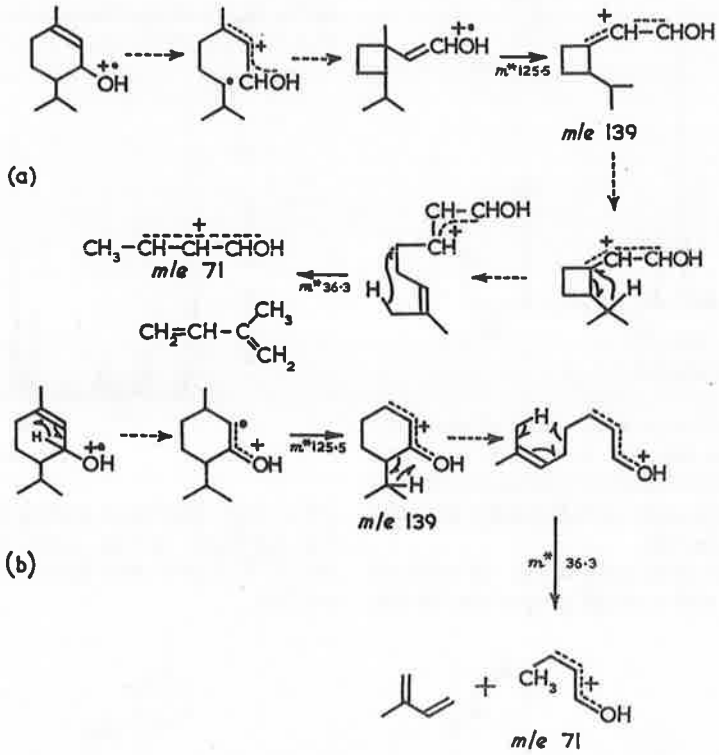
Scheme 6a bears some resemblance to a previous idea [18] of two of us (A. F. T., B. W.) (Scheme 7a) for the formation of the $[M - 43]^+$ fragment from menth-4(8)-ene which has recently been criticised by Weinberg and Djerassi,[20] who propose two successive double bond migrations.* We feel that it is unlikely that two such rearrangements occur with the speed required, since the very existence of the retro-Diels fission points to a highly specific directing influence of the double bond in cyclic systems, although we realise that, if no readily available fission can occur directly, a rearrangement possibility exists. A possibility not considered by Weinberg and

* Our mechanism for the $[M - 15]^+$ fragment is clearly wrong in the light of these results.

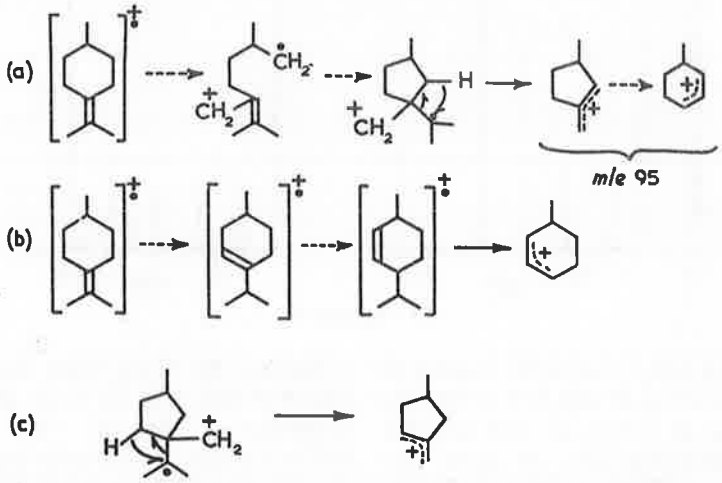
[20] D. S. Weinberg and C. Djerassi, *J. Org. Chem.*, 1966, **31**, 115.

Djerassi is that recyclisation does occur, but with hydrogen transfer preferentially from the alternative carbon (C-5) to the extent of 60—80%, 15—30% coming from C-2 following Scheme 7c.*

they do not have a very important fragment at *m/e* 43 exhibiting instead the fragment at *m/e* 60 characteristic of acetic acid, and at *m/e* 93 and 121, characteristic of many terpenes.



Scheme 6



Scheme 7

Piperitol Acetates.—We have also examined the mass spectra of the piperitol acetates, but we feel that they are extensively decomposed thermally before becoming subjected to electron bombardment, since, although they give small fragments associated with the piperitols,

* *Note added in proof:* We have since shown that Scheme 7b is probably correct in this case (B. Willhalm and A. F. Thomas, *Helv. Chim. Acta*, in the press).

EXPERIMENTAL

Mass spectra were generally measured as previously described,[2] or on an A.E.I. model MS-9. High-resolution measurements were on the latter, resolution being one part in 12,000 with 10% valley definition.

Preparative gas chromatography was carried out on a fully automatic Carlo Erba " Fractovap P " using 1—5-ml. injections on a column 2 m. × 20 mm. packed with

Carbowax on Chromosorb A in series with a 4 m. × 10 mm. column packed with Carbowax on Chromosorb W.* Analytical gas chromatographic and other apparatus was as previously described. [2,4,6,7-$^2H_7$]Piperitone (II) and [9,10-$^2H_6$]piperitone were made as previously described.[2]

1-[$^2H_3$]*Methyl-4-isopropylmenth-2-en-1-ol* (XX) (cf. ref. 5).—A synthetic mixture (prepared as described in ref. 21) of 4-isopropylcyclohex-2-enone (cryptone) and 4-isopropylcyclohex-3-enone was separated by preparative gas chromatography. Cryptone (0·75 g.) in dry ether (5 ml.) was added to [$^2H_3$]methylmagnesium iodide (made from 1·0 g. of [$^2H_3$]methyl iodide) in dry ether. Decomposition of the complex with ammonium chloride solution and isolation of the product with pentane gave a mixture of *cis*- and *trans*-1-[$^2H_3$]methyl-4-isopropylmenth-2-ene, from which samples of the individual compounds were separated by gas chromatography. Less than 1% of the isomers had less than three ^2H.

[7-$^2H_3$]*Piperitone* (III).[6]—The crude mixture (0·3 g.) of *cis*- and *trans*-(XX) was added to well-stirred sodium bichromate (0·2 g.) in water (0·8 ml.) and 50% sulphuric acid (0·5 ml.), and the piperitone isolated in pentane; isotopic purity >97%.

4-*Isopropyl-5-methoxy-1-methyl*[3,6-$^2H_2$]*cyclohexa-1,4-diene* (VIII) (cf. ref. 7).—Thymol methyl ether (kindly supplied by Dr. E. Sundt) (0·5 g.) in ethan[^2H]ol was reduced with sodium in liquid [$^2H_3$]ammonia following the method previously described,[2] and the product isolated with pentane and purified by gas chromatography; isotopic purity 95% [$^2H_2$].

[5ξ-^2H]*Piperitone* (IV).—The crude dihydrothymol(VIII) was heated with semicarbazide hydrochloride (0·2 g.) and sodium acetate (0·3 g.) in alcohol (5 ml.). Dilution with water caused [2,5-$^2H_2$]piperitone semicarbazone (0·15 g.) to precipitate. After steam-distillation with 10% aqueous sulphuric acid, the piperitone was isolated in pentane and back-exchanged by warming with dilute sodium hydroxide. It was finally purified, after isolation in pentane, by gas chromatography; isotopic purity 96%.

Deuterium Exchange of Piperitone.—Piperitone (0·6 g.) was added to dioxan (20 ml.) and deuterium oxide (20 g.) in which a small pellet of sodium had been dissolved. At intervals, 5 ml. of solution was withdrawn and rapidly shaken with pentane and deuterium oxide (1 ml.), the pentane layer then being washed with water (2 × 2 ml.) to neutrality. Drying and concentration of the pentane gave piperitones with the isotopic content shown in Table 2.

TABLE 2

Contents (%) of ^2H in piperitone

Time (min.)	Atoms of ^2H 0	1	2	3	4	5	6	7
5	85	15	—	—	—	—	—	—
10	57	38	4·7	—	—	—	—	—
15	50	43	7	—	—	—	—	—
30	33	47	16	3	—	—	—	—
60	20	49	20	7	2	—	—	—
210	—	15	29	27	20	8	1	—
1080	—	—	—	6	15	31	37	11

The piperitols were made by reduction of the corresponding piperitone with lithium aluminium hydride in ether. The *cis*- and *trans*-isomers were separated by gas chromatography; 44% *cis*- and 56% *trans*-piperitol were observed on undeuteriated material.

[3-^2H]*Piperitol.*—This was prepared similarly, using lithium aluminium deuteride.

We should like to thank Mr. C. Pellegrin for assistance with the experimental work. We have received continuous encouragement from Dr. Max Stoll and the directors of Firmenich & Cie throughout this investigation.

[6/965 *Received, July 29th*, 1966]

* We are greatly indebted to Dr. E. Palluy for the preparation of this highly successful column.

[21] G. Stork and S. R. Dowd, *J. Amer. Chem. Soc.*, 1963, **85**, 2178.

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AUSTRALIAN JOURNAL OF CHEMISTRY

ELECTRON IMPACT STUDIES

I. HIGH RESOLUTION MASS SPECTRA OF SOME UNSATURATED CYCLIC KETONES

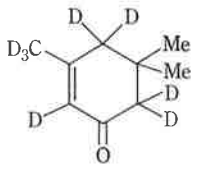
By J. H. Bowie†

[*Manuscript received December* 23, 1965]

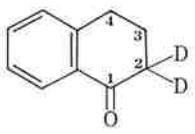
Summary

The mass spectra of some 2-cyclohexen-1-ones, tetralones, and indanones have been investigated. The characteristic fragmentation processes, substantiated by appropriate metastable peaks, exact mass measurements, and in some cases by deuterium labelling studies, greatly facilitate the determination of both the type of system and the position of substituents on that system.

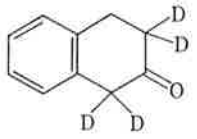
Although the mass spectra of cyclic ketones have been studied (cf.[1,2]), the spectra of the synthetically important cyclohex-2-en-1-ones, tetralones, and indanones, with the exception of carvone,[3] have not been reported. This paper deals with the interpretation of the mass spectra (Table 1 and Figures 2, 4–6) of cyclohex-2-en-1-one (I), isophorone (II), 3,5,5-trimethylcyclohex-3-en-1-one (IV), 1- and 2-tetralone (V and VIII), 3-ethoxycarbonyl-1-tetralone (VII), 1- and 2-indanone (X and XI), and 1-ethoxycarbonyl-2-indanone (XII).



(III)



(VI)



(IX)

The composition of all fragment ions mentioned in this paper have been established by exact mass measurements; specific structures have been assigned primarily to produce a self-consistent rationale for the interpretation of the spectra and are to be regarded as formal representations only.

† University Chemical Laboratory, Cambridge, U.K.; present address: Department of Organic Chemistry, University of Adelaide.

[1] Budzikiewicz, H., Djerassi, C., and Williams, D. H., "Interpretation of Mass Spectra of Organic Compounds." pp. 17–26, 140–61. (Holden Day: San Francisco 1964.)

[2] Budzikiewicz, H., Djerassi, C., and Williams, D. H., "Structural Elucidation of Natural Products by Mass Spectrometry." (Holden Day: San Francisco 1964.) Vol. 2, pp. 50–94.

[3] Reed, R. I., in "Mass Spectrometry of Organic Ions." (Ed. F. W. McLafferty.) p. 668. (Academic Press: New York 1963.)

TABLE 1

MASS SPECTRA

Only peaks greater than 2% of the base peak (arbitrarily taken as 100%) are recorded

(I)	*m/e*	37	38	39	40	41	42	43	50	51	52	53	54	55	66	67	68	69
	I (%)	3	8	26	22	9	10	8	4	5	3	7	3	8	5	5	100	6
	m/e	96(M)	97															
	I (%)	21	4															
(III)	*m/e*	39	40	41	42	43	44	45	46	51	52	53	54	55	56	57	58	59	60
	I (%)	9	12	17	23	13	10	8	7	4	5	4	7	7	12	12	15	17	17
	m/e	68	69	70	71	72	73	74	78	79	80	81	82	83	84	85	86	87	88
	I (%)	3	6	7	7	7	6	5	4	4	5	6	6	8	15	14	26	70	100
	m/e	89	90	99	100	101	102	103	111	112	113	114	115	116	117	118		
	I (%)	9	4	5	5	6	9	10	8	11	8	7	7	6	5	4		
	m/e	126	127	128	129	130	131	143	144	145	146	147						
	I (%)	4	4	4	5	7	8	4	9	22	24	4						
(VI)	*m/e*	39	40	43	50	51	52	63	64	65	66	67	74	75	76	77	78	79	89
	I (%)	10	7	3	8	12	8	14	10	8	6	3	5	5	5	9	7	6	24
	m/e	90	91	92	103	104	116	117	118	119	120	128	129	130	131	132		
	I (%)	64	16	16	4	10	14	16	100	25	13	4	7	11	22	22		
	m/e	133	134	147	148(M)	149												
	I (%)	22	5	12	70	13												
(VII)	*m/e*	39	50	51	63	65	77	89	90	91	115	116	117	118	127	144	145		
	I (%)	6	4	5	3	9	3	9	16	10	23	12	20	13	7	19	100		
	m/e	146	173	218(M)	219														
	I (%)	13	7	17	4														
(IX)	*m/e*	39	40	41	44	51	52	53	58	59	62	63	64	65	66	77	78	79	80
	I (%)	6	3	3	3	7	6	3	3	6	3	6	6	6	3	4	10	13	5
	m/e	89	90	92	93	94	95	103	104	105	106	107	116	117	118	119	120		
	I (%)	3	3	5	6	4	3	5	27	70	100	12	3	10	8	10	20		
	m/e	121	122	133	134	147	148	149	150	151									
	I (%)	14	5	3	3	4	17	44	53	12									
(X)	*m/e*	39	50	51	52	62	63	74	75	76	77	78	89	101	102	103	104	105	
	I (%)	6	11	18	5	4	8	8	7	14	20	29	6	3	15	36	70	9	
	m/e	130	131	132(M)	133														
	I (%)	12	36	100	11														
(XI)	*m/e*	38	39	50	51	52	61	62	63	64	65	74	75	76	77	78	79	89	103
	I (%)	6	12	13	24	10	5	8	13	4	4	8	7	8	19	38	6	7	36
	m/e	104	105	132(M)	133														
	I (%)	100	16	34	6														
(XII)	*m/e*	39	43	44	45	46	50	51	52	62	63	65	74	75	76	77	78	79	89
	I (%)	8	7	54	26	13	14	19	8	5	10	4	5	4	6	14	26	4	6
	m/e	102	103	104	105	132	133	158	159										
	I (%)	4	29	100	13	57	9	5	3										

($d_5 = 7$; $d_6 = 16$; $d_7 = 37$; $d_8 = 40\%$)

($d_2 = 3$; $d_3 = 38$; $d_4 = 49\%$)

The mass spectrum (see Table 1) of cyclohex-2-en-1-one (I) is readily interpretable, and is summarized in Figure 1.†

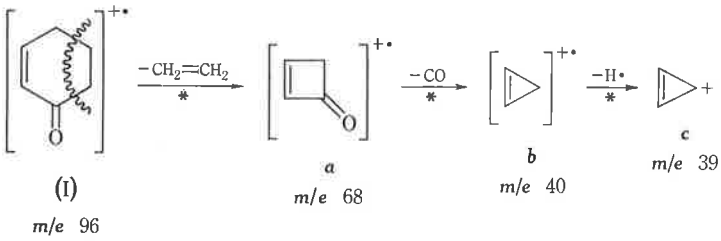


Fig. 1

This is a general fragmentation process for alkylcyclohex-2-en-1-ones and is even the most preponderant process for 5-isopropyl-3-methylcyclohex-2-en-1-one (piperitone)[4] which can also undergo a highly favoured McLafferty rearrangement[5] to oxygen. A further example which illustrates this process is the mass spectrum (Fig. 2) of isophorone (II). The interpretation of this spectrum has been aided by

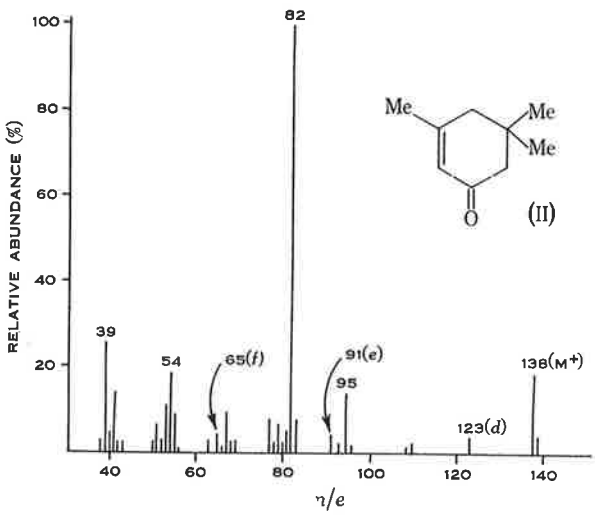


Fig. 2

a series of high resolution measurements, and from a consideration of the mass spectrum (Table 1) of isophorone-d_8 (III). It should be noted here that, even for compounds containing only C, H, and O, exact mass measurements are essential for unequivocal interpretation of the spectra, and this will be apparent several times throughout the course of this paper.

† An asterisk represents the presence of an appropriate metastable ion for the process indicated.

[4] Bowie, J. H., and Thomas, A. F., unpublished data.

[5] McLafferty, F. W., "Determination of Organic Structures by Physical Methods." pp. 129–49. (Academic Press: New York 1962.)

The most important fragmentation of the isophorone molecular ion (II, *m/e* 138) is the loss of isobutene, followed by elision of carbon monoxide, then a hydrogen radical (all processes substantiated by appropriate metastable ions), which parallels the fragmentation of cyclohex-2-en-1-one itself. Additional fragmentation of

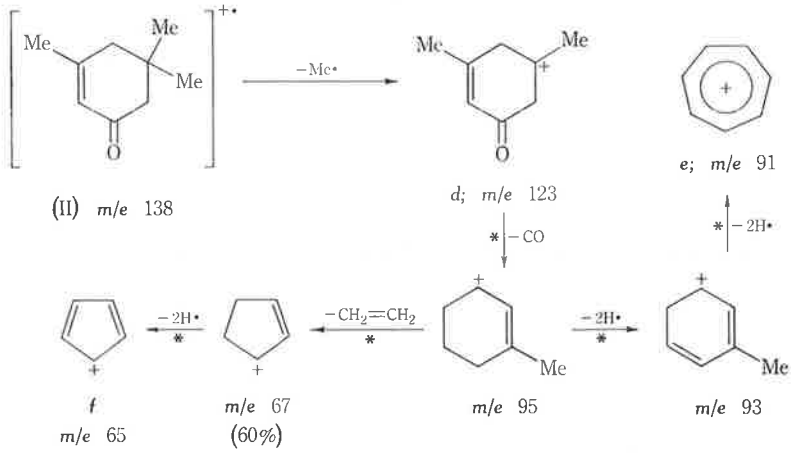


Fig. 3

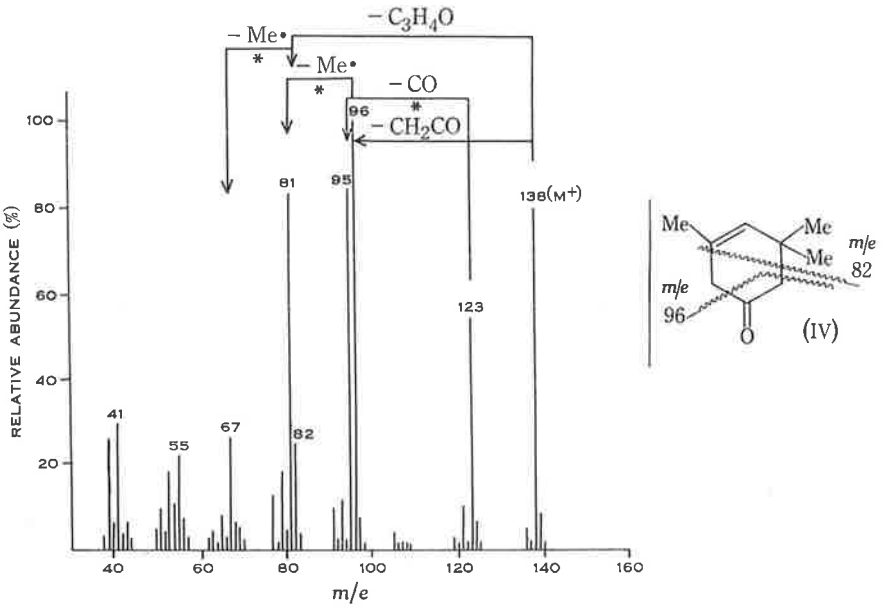


Fig. 4

(II, *m/e* 138) involves the specific loss of Me· from the five position [from the spectrum of the d_8 derivative (III)] to form *d* (*m/e* 123), while further fragmentation of this species ultimately furnishes *m/e* 91, probably the stable tropylium cation *e*, and *m/e* 65, represented as the cyclopentadienyl cation *f* (Fig. 3).

The utility of mass spectroscopy in distinguishing between cyclohex-2-en-1-ones and cyclohex-3-en-1-ones can be demonstrated by a comparison of the spectra (Figs. 2 and 4) of isophorone (II) and 3,5,5-trimethylcyclohex-3-en-1-one (IV). An inter-

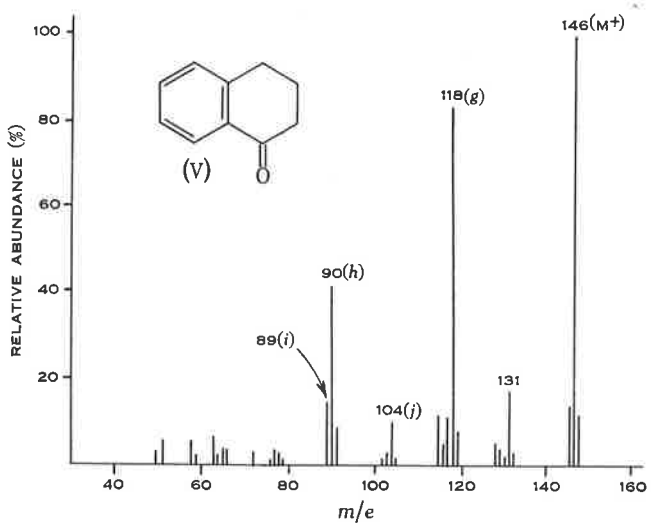


Fig. 5

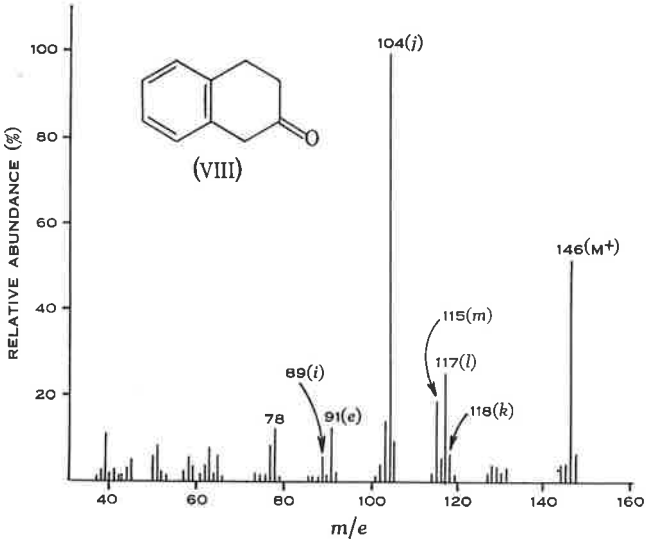


Fig. 6

pretation of the mass spectrum of (IV) is summarized in Figure 4. In this case, the base peak (*m/e* 96, M—42) arises by elision of ketene from the molecular ion, while a minor fragmentation is associated with loss of C_4H_3O from the molecular ion by

unfavourable vinylic cleavage, probably to furnish the cyclopropene derivative $C_6H_{10}^{+\cdot}$ (*m/e* 82, M—56) which loses Me· by allylic cleavage to form the stable cation $C_5H_7^+$, *m/e* 67 (see Fig. 4).

1- and 2-Tetralone (V and VIII) behave differently upon electron impact. Their spectra (Figs. 5 and 6) are interpreted in Figures 7 and 8, and an interpretation of the spectrum (Fig. 5) of 1-tetralone was aided by the spectrum of its d_2 derivative (VI).

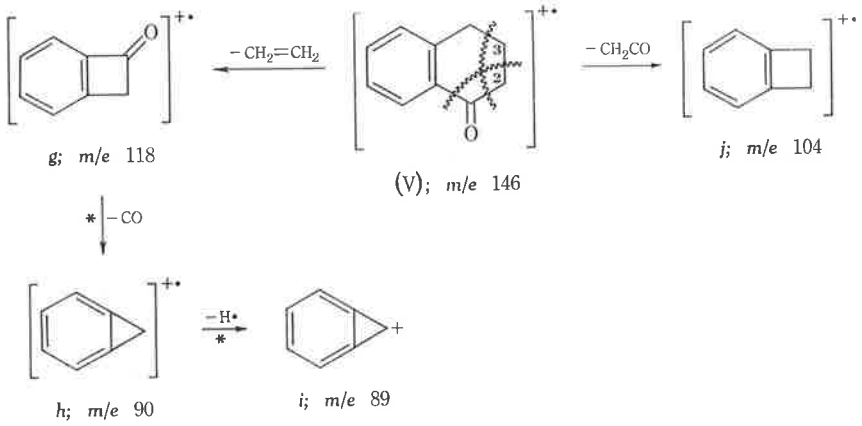


Fig. 7

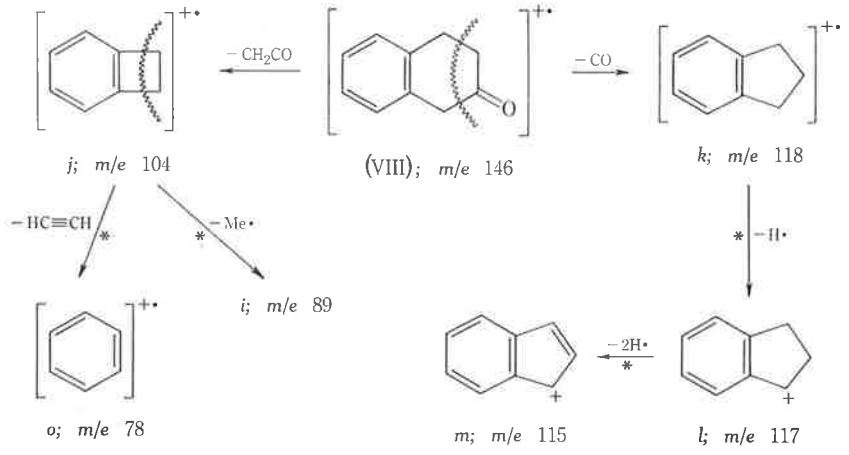


Fig. 8

It follows from the spectrum of the 1-tetralone-d_2 (VI), that the loss of ethylene from the molecular ion (V) comes exclusively from the 2,3-position to form *g* (*m/e* 118); the fragmentation concludes with the plausible formation of the benzocyclopropenyl cation *i* (*m/e* 89). The loss of a methyl radical from the 1-tetralone molecular ion is pronounced (17% of the base peak) whereas analogous losses of Me· in the spectra of (I), (VIII), (X), and (XI) are either absent, or very small.

The 1-tetralone-d_2 molecular ion (*m/e* 148) loses 15, 16, and 17 mass units equally, showing that this loss of Me· is a random process possibly involving all saturated centres. Such a process should be contrasted with the loss of a Me· from the molecular ion of cyclohexanone which occurs by α-cleavage and specific hydrogen rearrangement.[6]

Although alkyl substituted 1-tetralones should follow this general fragmentation pattern, caution should be taken in extending the analogy, since 3-ethoxycarbonyl-1-tetralone (VII) (see Table 1) fragments primarily via the ester group, and only loses ethoxycarbonylethylene to a small extent to give 70% (high resolution) of *m/e* 118 (13% of the base peak) as *g*, which is not of diagnostic value in this case.

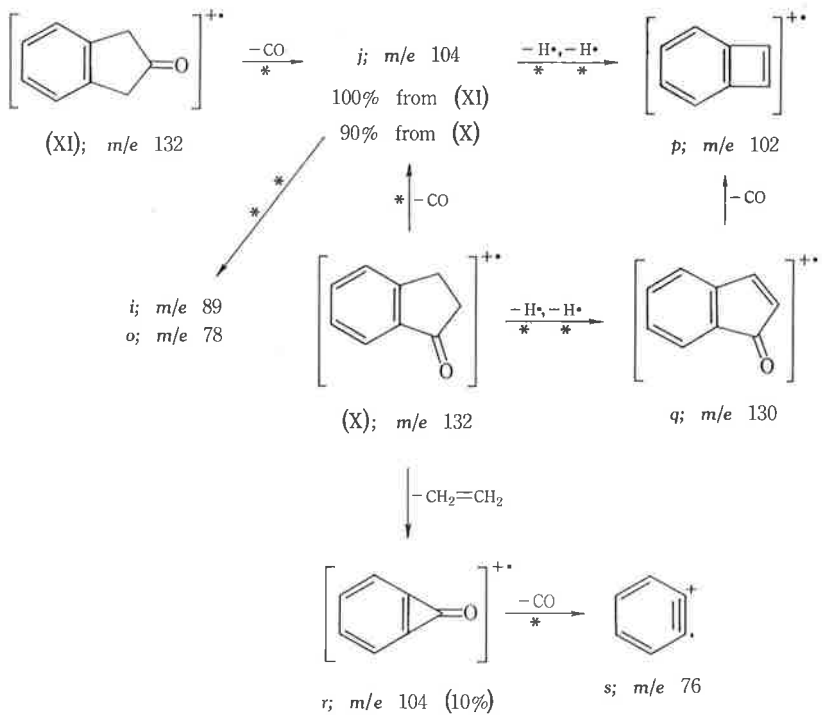


Fig. 9

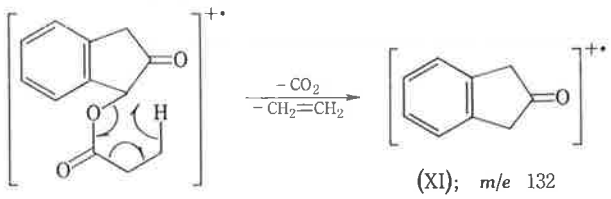
2-Tetralone (VIII) behaves characteristically on electron impact, and the fragmentation is summarized in Figure 6 and Figure 8.

In this case, favoured loss of ketene from the molecular ion (*m/e* 146) forms an ion *j* (*m/e* 104), whose representation as the benzocyclobutene molecular ion is supported by its fragmentation to the benzocyclopropenyl cation *i* (*m/e* 89) and the benzene radical ion *o* (*m/e* 78). Additional support for the above formulation is forthcoming from the spectrum (Table 1) of the 2-tetralone-d_4 (IX) in which the analogous ion, *m/e* 106, loses some HC≡CD to furnish *m/e* 79, indicative of a cyclic

[6] Williams, D. H., Budzikiewicz, H., Pelah, Z., and Djerassi, C., *Mh. Chem.*, 1964, **95**, 166.

structure. A minor fragmentation is elision of carbon monoxide from the molecular ion to form *k*, *m/e* 118, with the final formation of the indene cation *m* (*m/e* 115).

The mass spectra (Table 1) of 1- and 2-indanone (X and XI) show some interesting features, and are summarized in Figure 9. The only apparent visual difference between the two spectra is that the molecular ion of 1-indanone carries more of the total ion current than that of 2-indanone, while the 1-indanone molecular ion is able to lose two H· to form the 1-indenone radical ion *p* (*m/e* 130) which the other isomer cannot do. The other important difference is that the loss of *m/e* 28 from the 1-indanone molecular ion (*m/e* 132) is a doublet corresponding to loss both of CO (90%) to *j* (*m/e* 104) and ethylene (10%) to *r* (*m/e* 104). 2-Indanone, on electron impact, loses only CO to form the benzocyclobutene radical ion *j* (*m/e* 104) which fragments in the normal manner.



(XII); *m/e* 204 (XI); *m/e* 132

Fig. 10

Finally, the mass spectrum (Table 1) of 1-ethoxycarbonyl-2-indanone (XII) is notable for the characteristic loss of the ester group with concomitant hydrogen rearrangement to carbon to give the 2-indanone molecular ion (*m/e* 132) (Fig. 10). The distinction between hydrogen migration to carbon and to oxygen is assured as the resulting spectrum of *m/e* 132 is very similar to that of 2-indanone, and is substantiated by all the appropriate metastable ions. This spectrum should be contrasted with that of 3-ethoxycarbonyl-1-tetralone (VII), in which no analogous rearrangement is observed.

Experimental

All spectra were determined using an A.E.I. MS9 mass spectrometer operating at 70 eV and with the heated inlet system and source at a temperature of approximately 150°.

All compounds were tested for purity either by gas chromatography or by nuclear magnetic resonance spectroscopy, and the labelled compounds were prepared by the general method of Djerassi *et al.*[7]

Acknowledgment

Grateful acknowledgment is made to Dr D. H. Williams for helpful discussion. This work was carried out during the tenure of an I.C.I. Fellowship.

[7] Williams, D. H., Wilson, J. M., Budzikiewicz, H., and Djerassi, C., *J. Am. chem. Soc.*, 1963, **85**, 2091.

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AUSTRALIAN JOURNAL OF CHEMISTRY

ELECTRON IMPACT STUDIES

II.† MASS SPECTRA OF QUERCETAGETIN DERIVATIVES

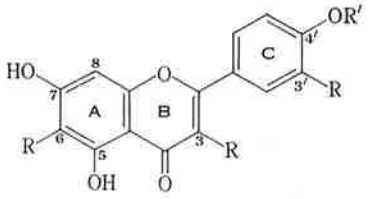
By J. H. Bowie‡§ and D. W. Cameron‡

[*Manuscript received March* 15, 1966]

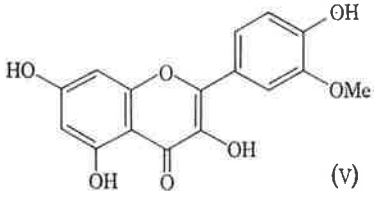
Summary

The mass spectra of 11 quercetagetin derivatives are reported and discussed. The spectra are generally simple and amenable to analysis. A number of fragmentation processes have been substantiated by exact mass measurements, appropriate metastable ions, and deuterium labelling.

Although the mass spectra of flavone[1] (I), apiginin[2] (II), acacetin[2] (III), and isorhamnetin[3] (V) have been discussed, no detailed investigation of a specific family of flavones has been reported. The purpose of this paper is to establish a relationship between the structures of derivatives of quercetagetin (IV) and their fragmentation patterns produced on electron impact.



	R	R′
(II)	H	H
(III)	H	Me
(IV)	OH	H



(V)

The spectra of eleven quercetagetin derivatives are reported in Table 1 and Figures 1–4. All ions having an abundance of 5% or more of the base peak (100%) are recorded in Table 1. The presence of an asterisk (*) in either the text or a figure indicates the presence of an appropriate metastable ion for the process indicated. Although exact mass measurements establish the compositions of some of the fragment ions discussed (see Table 3 below), specific formulae have been depicted merely to relate the fragmentation pattern to the structure of the intact molecule, and are intended to be formal representations only. The isotopic purity of compounds (VII), (IX), and (XIV) is indicated in Table 1.

† Part I, *Aust. J. Chem.*, 1966, **19**, 1619.

‡ University Chemical Laboratory, Cambridge, U.K.

§ Present address: Department of Organic Chemistry, University of Adelaide.

[1] Barnes, C. S., and Occolowitz, J. L., *Aust. J. Chem.*, 1964, **17**, 975.

[2] Reed, R. I., and Wilson, J. M., *J. chem. Soc.*, 1963, 5949.

[3] Pelter, A., Stainton, P., and Barber, M., *J. heterocyclic Chem.*, 1965, **2**, 262.

Fig. 1

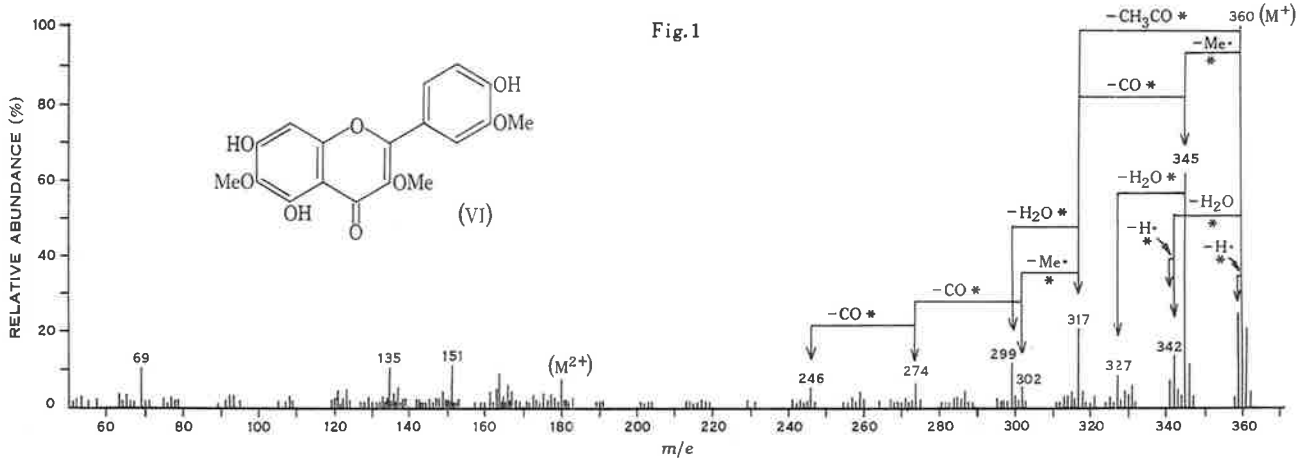

RELATIVE ABUNDANCE (%)
m/e
(VI)
HO
MeO
OMe
OH
OMe
OH
O
$-CH_3CO*$
360 (M^+)
$-Me\cdot$
$-CO*$
$-H_2O*$
$-H_2O$
$-H\cdot$
$-CO*$
$-Me\cdot$
$-CO*$
$-H\cdot$
345
317
342
299
327
302
274
246
69
135
151
(M^{2+})

Fig. 2

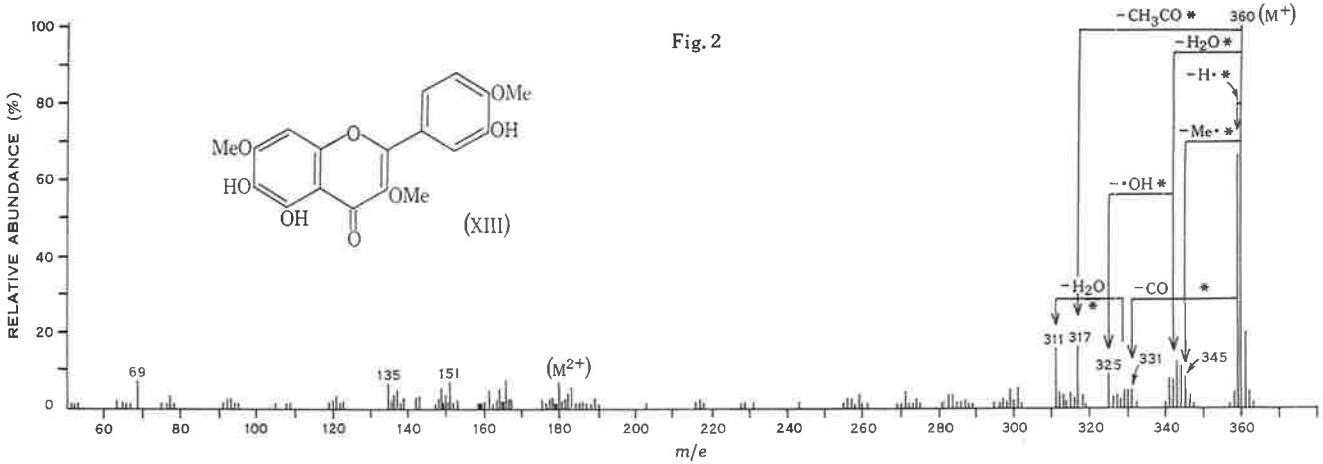

RELATIVE ABUNDANCE (%)
m/e
(XIII)
MeO
HO
OH
OMe
OMe
OH
O
$-CH_3CO*$
360 (M^+)
$-H_2O*$
$-H\cdot*$
$-Me\cdot*$
$-\cdot OH*$
$-H_2O$
$-CO$
311
317
325
331
345
69
135
151
(M^{2+})

Fig. 3

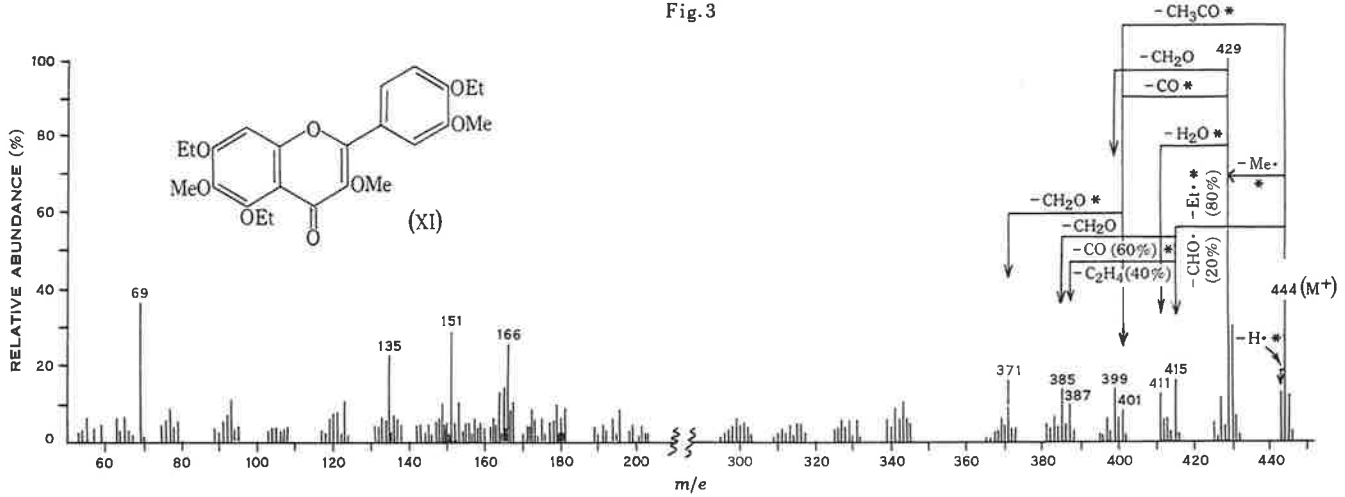

RELATIVE ABUNDANCE (%)
m/e
(XI)
EtO
MeO
OEt
OMe
OMe
OEt
O
69
135
151
166
371
385
387
399
401
411
415
429
444 (M+)
-CH3CO *
-CH2O
-CO *
-H2O *
-Me· *
-Et· * (80%)
-CHO· (20%)
-CH2O *
-CH2O
-CO (60%) *
-C2H4 (40%)
-H· *

Fig. 4

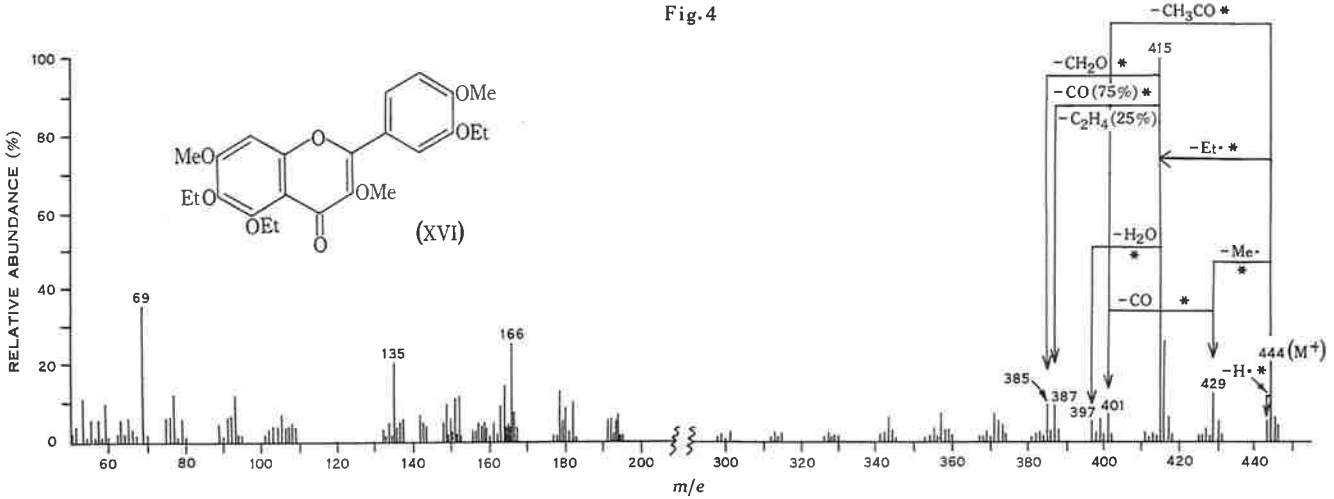
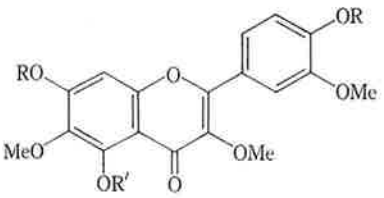

RELATIVE ABUNDANCE (%)
m/e
(XVI)
MeO
EtO
OEt
OMe
OMe
OEt
O
69
135
166
385
387
397
401
415
429
444 (M+)
-CH3CO *
-CH2O *
-CO (75%) *
-C2H4 (25%)
-Et· *
-H2O *
-Me· *
-CO *
-H· *

TABLE 1

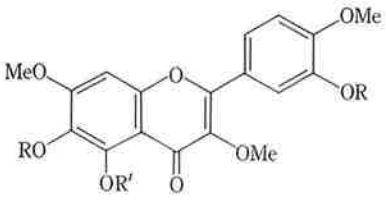
MASS SPECTRA OF QUERCETAGETIN DERIVATIVES

Because of the complexity of the spectra of compounds (IX) and (XIV), only the high mass range is recorded

(IV)	*m/e*	69	76	77	79	122	123	136	137	150	289	317	318(M)	319		
	I (%)	24	6	8	8	7	6	11	12	11	8	23	100	18		
(VII)	*m/e*	69	70	77	93	108	109	119	120	121	122	123	135	136	137	149
	I (%)	13	6	7	9	9	9	8	12	15	8	14	35	19	14	13
	m/e	150	151	152	163	164	165	167	168	246	247	274	275	299	300	
	I (%)	8	41	17	13	26	12	12	9	7	6	9	8	21	18	
	m/e	301	302	317	318	319	327	328	331	332	341	342	343	345	346	
	I (%)	8	7	28	27	12	10	9	9	6	9	18	17	55	54	
	m/e	347	348	359	360	361	362	363	($d_0 = 44$, $d_1 = 35$, $d_2 = 18$, $d_3 = 2\%$)							
	I (%)	29	9	12	99	100	53	16								
(VIII)	*m/e*	69	76	78	93	135	136	142	149	151	152	163	165	167	171	175
	I (%)	26	13	12	8	8	10	7	17	13	14	12	39	6	7	7
	m/e	177	178	180	181	194	315	327	331	341	343	345	355	357	359	
	I (%)	11	21	12	12	16	6	9	6	7	6	15	12	9	7	
	m/e	369	370	373	374	375	387	388(M)	389	390						
	I (%)	19	8	85	19	6	15	100	23	6						
(IX)	*m/e*	369	370	371	372	373	374	375	376	377	378	387	388	389	390	
	I (%)	7	9	18	19	26	46	52	37	16	6	12	44	84	100	
	m/e	391	392	393	394						($d_0 = 17$, $d_1 = 33$, $d_2 = 37$,					
	I (%)	69	37	14	6						$d_3 = 22$, $d_4 = 7$, $d_5 = 4\%$)					
(X)	*m/e*	69	76	93	143	149	158	165	167	172	187	195	201	329	341	343
	I (%)	10	6	6	8	14	8	15	16	12	17	9	8	8	8	6
	m/e	344	357	359	369	371	383	384	387	388	401	402(M)	403			
	I (%)	11	7	6	7	11	10	5	100	24	35	66	15			
(XII)	*m/e*	69	93	135	151	153	299	317	326	331	341	342	343	345	346	
	I (%)	10	5	6	9	5	7	10	6	7	6	18	7	44	8	
	m/e	359	360	361	387	401	402	403	444	445	486(M)	487				
	I (%)	29	94	21	7	9	57	12	100	28	13	5				
(XIV)	*m/e*	369	370	371	372	373	374	375	376	377	378	387	388	389	390	
	I (%)	6	13	22	26	42	67	49	31	13	6	9	43	84	100	
	m/e	391	392	393	394						($d_0 = 17$, $d_1 = 33$, $d_2 = 37$,					
	I (%)	68	38	67	8						$d_3 = 22$, $d_4 = 7$, $d_5 = 4\%$)					
(XV)	*m/e*	69	77	79	89	91	92	93	121	135	142	149	150	151	153	163
	I (%)	36	10	7	6	6	6	9	7	19	7	11	6	8	15	10
	m/e	164	166	179	181	192	299	313	329	343	344	345	357	359	369	
	I (%)	19	17	12	11	9	6	6	6	9	8	6	7	16	7	
	m/e	371	372	387	388	389	401	402	415	416(M)	417					
	I (%)	11	6	100	28	7	31	13	8	54	16					
(XVII)	*m/e*	69	77	93	135	149	151	153	311	317	325	342	343	345	359	360
	I (%)	14	6	5	7	6	9	6	9	6	6	6	8	6	39	26
	m/e	401	402	403	444	486(M)	487									
	I (%)	16	100	24	9	10	5									

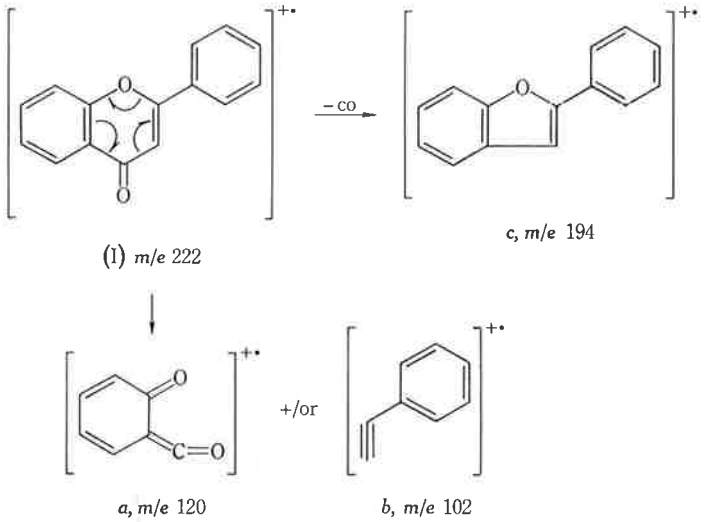


	R	R′
(VI)	H	H
(VII)	D	D
(VIII)	Me	H
(IX)	CD_3	H
(X)	Me	Me
(XI)	Et	Et
(XII)	Ac	Ac



	R	R′
(XIII)	H	H
(XIV)	CD_3	H
(XV)	Et	H
(XVI)	Et	Et
(XVII)	Ac	Ac

The retro Diels–Alder process [(I) → *a*+*b*] and the loss of carbon monoxide from the molecular ion [(I) → *c*] are important decomposition modes[1] in the mass spectra of flavone[1] (I), apiginin[2] (II), and acacetin[2] (III), but are of minor importance in that of the more highly substituted flavone, isorhamnetin[3] (V) (see Fig. 5).



(I) *m/e* 222 *c*, *m/e* 194

a, *m/e* 120 *b*, *m/e* 102

Fig. 5[1]

The quercetagetin derivatives ((IV) and (VI–XVII)) do not fragment in this way on electron impact. Instead, the molecular ion, which is always pronounced, loses radicals (R = H·, Me·, or Et·) from several of the oxygen substituents to form stable cations $(M-R)^+$. Invariably, the loss of one of these radicals is especially favoured, sufficiently so, sometimes, to lead to the base peak of the spectrum. The study of a variety of *O*-alkyl derivatives (Table 2), together with the deuteration experiments to be discussed, shows that this process is associated with either the

oxygenated substituent at C6 or at C3′. The former possibility seems more likely on structural grounds, since, as illustrated in Figure 6, it may be facilitated by the formation of a quinonoid cation, no analogous formation being possible in the case of C3′. (The substituents R in Figures 6 and 7 are not necessarily the same and

TABLE 2

RELATIVE ABUNDANCE OF M−R IONS IN THE SPECTRA OF QUERCETAGETIN DERIVATIVES
(Expressed as percentage of the base peak)

Compound	(IV)	(VI)	(VIII)	(X)	(XI)	(XIII)	(XV)	(XVI)
M−H·	23	24	15	35	13	66	8	5
M−Me·	—	62	85	100	100	9	31	12
M−Et·	—	—	—	—	16	—	100	100

may be H, Me, or Et.) These observations suggest that, for *O*-alkyl quercetagetin derivatives, the nature of the substituent at C6 may readily be determined by mass spectrometry.

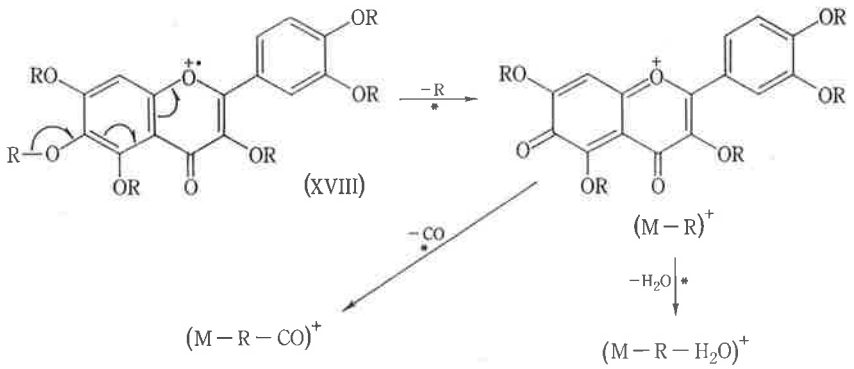


Fig. 6

Quinonoid structures similar to that in Figure 6 can be written for elimination either from the C3 substituent (Fig. 7) or from the C8 (in the case of flavones containing a C8 alkoxyl group). The former is not an observed process for quercetagetin derivatives, for reasons that will be discussed later, nor for isorhamnetin[3] (V) [where the (M−H·) ion constitutes only 10% of the molecular ion (base peak)]. Preliminary results suggest, on the other hand, that the latter is a major fragmentation pathway for flavones containing C8 but not C6 substituents.[4] The number of compounds in this category that have been examined, however, is insufficient for generalization at this stage.

These observations are illustrated by the following examples. The isomeric jaceidin[5,6] (VI) and oxyayanin B[7] (XIII) behave differently on electron impact.

[4] Bowie, J. H., unpublished data.

[5] Farkas, L., Hörhammer, L., Wagner, H., Rösler, H., and Gurniak, R., *Chem. Ber.*, 1964, **97**, 610.

[6] Bowie, J. H., and Cameron, D. W., *J. chem. Soc.*, 1965, 5651.

[7] King, F. E., King, T. J., and Stokes, P. J., *J. chem. Soc.*, 1954, 4587.

The major difference between the two spectra (Figs. 1 and 2) lies in the fragmentation through differing substituents at C6 (see Fig. 6 and Table 2); other fragmentations are indicated in Figures 1 and 2. The compositions of all the major ions in the

TABLE 3

EXACT MASS MEASUREMENTS IN THE SPECTRA OF COMPOUNDS (VI), (XI), AND (XVI)

(VI) *m/e*	Composition	(XI) *m/e*	Composition	(XVI) *m/e*	Composition
342	$C_{18}H_{14}O_7$	415	$C_{22}H_{23}O_8$ (80%)	415	$C_{22}H_{23}O_8$
327	$C_{17}H_{11}O_7$		$C_{23}H_{27}O_7$ (20%)	401	$C_{22}H_{25}O_7$
317	$C_{16}H_{13}O_7$	401	$C_{22}H_{25}O_7$	397	$C_{22}H_{21}O_7$
302	$C_{15}H_{10}O_7$	387	$C_{21}H_{23}O_7$ (60%)	387	$C_{21}H_{23}O_7$ (75%)
299	$C_{16}H_{11}O_6$		$C_{20}H_{19}O_8$ (40%)		$C_{20}H_{19}O_8$ (25%)
274	$C_{14}H_{10}O_6$	166	$C_{12}H_6O$ (45%)	385	$C_{21}H_{21}O_7$
246	$C_{13}H_{10}O_5$		$C_8H_6O_4$ (55%)	166	$C_{12}H_6O$ (50%)
151	$C_8H_7O_3$				$C_8H_6O_4$ (50%)
135	$C_8H_7O_2$ (65%)			135	$C_8H_7O_2$ (30%)
	$C_7H_3O_3$ (35%)				$C_7H_3O_3$ (70%)
69	C_4H_5O (20%)			69	C_4H_5O (65%)
	C_3HO_2 (80%)				C_3HO_2 (35%)

spectrum (Fig. 1) of jaceidin (VI) have been established by exact mass measurements (see Table 3). Another noteworthy fragmentation mode common to both spectra (Figs. 1 and 2) is the concerted loss of an acetyl radical from the various molecular

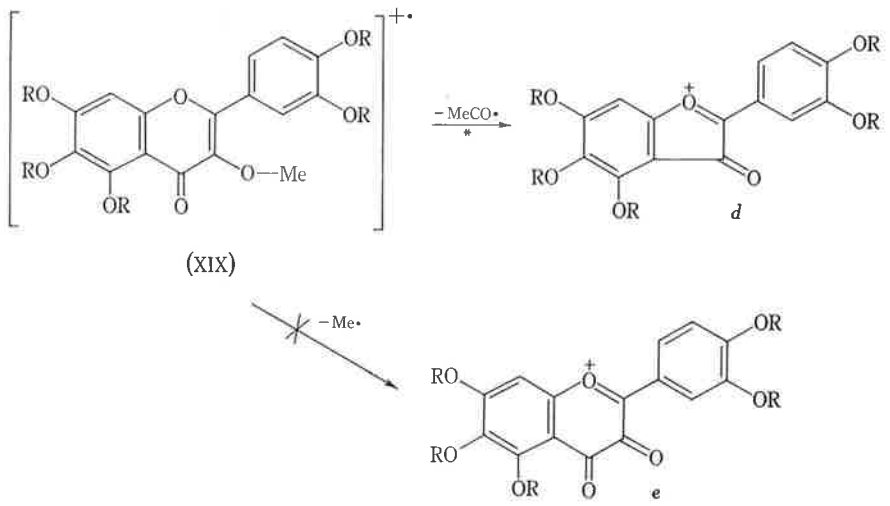


Fig. 7

ions (*m/e* 360) (these processes are substantiated by metastable ions at *m/e* 287·8). This process [(M—CH_3CO), substantiated by a metastable ion] is also noted in the spectra of (XI), (XII), (XVI), and (XVII), but is not substantiated by metastable ions in the spectra of (VIII), (X), or (XV). The concerted loss of an acetyl radical

has not been observed in the mass spectra of either simple methoxybenzenes[8] or flavones,[1–3] and a possible explanation is that this loss originates from the 3-position to form the M−43 cation, possibly *d*. Such a process (Fig. 7) would explain why the plausible loss of a radical from the C3 substituent (cf. Fig. 6) to form *e* is not observed, presumably because of the inherent instability of the *o*-quinonoid intermediate *e*, thus resulting in the concerted elimination of an acetyl radical (Me· +CO) from the various molecular ions. If such a process (XIX → *d*) is observed in the mass spectrum of an *O*-alkylquercetagetin, the presence of a methoxyl substituent at C3 may be tentatively assigned. The region *m/e* 100 → 200 in both these spectra and in those of the other quercetagetin derivatives is composed generally of small peaks due to doubly charged ions and fragment ions (Table 3) which are of little diagnostic value for structural studies, and will not be discussed further in this paper.

Small but significant ions arising from the loss of the elements of water from both molecular ions and fragment ions are observed in all spectra (Figs. 1–4 and Table 1) examined: such processes have been observed previously.[3] To attempt to ascertain the sites of elimination of water, the mass spectra (Table 1) of the deuterium-labelled compounds (VII) [prepared by introducing (VI) into the source with deuterium oxide[9]], (IX) and (XIV) [prepared by treating (VI) and (XIII) respectively with diazomethane and deuterium oxide[10]] were examined. Because of the incomplete labelling of these compounds (see Table 1 for the isotopic purities), results were ambiguous regarding the loss of water. However, examination of the spectra (Table 1) of the labelled pentamethyl ethers (IX and XIV) and the unlabelled (VIII) clearly shows loss of CH_3· from the molecular ion of (IX), and CD_3· from that of (XIV), thereby confirming that either the C6 or C3′ substituent is involved in the decomposition. This fact, when combined with the above evidence (Table 2 and Figure 6) lends additional support to the fragmentation outlined in Figure 6.

It should be noted here that incorporation of deuterium[9] into jaceidin (VI) by the direct insertion technique yields a d_2 but almost no d_3 derivative, whereas similar treatment of quercetagetin pentamethyl ether (VIII) gives less than 5% incorporation of deuterium. Caution should therefore be exercised when using this technique to estimate the number of phenolic hydroxyl groups in a flavone where strong hydrogen bonding interactions may occur.

The mass spectra (Table 1, Figs. 3 and 4) of the methyl ethers (VIII) and (X), and the ethyl ethers (XI), (XV), and (XVI) clearly illustrate the applicability of the general fragmentation processes summarized in Figures 6 and 7. The spectra of triethyl jaceidin (XI) and triethyl oxyayanin B (XVI) are reproduced in Figures 3 and 4, and illustrate the ease with which these two compounds may be differentiated. Exact mass measurements establish the compositions of the major ions in the spectra of (XI) and (XVI) (see Table 3). The two acetates triacetyl jaceidin (XII) and triacetyl oxyayanin B (XVII) behave unexceptionally on electron impact (Table 1), exhibiting significant molecular ions, which lose three ketene units to furnish the molecular ions of the parent compounds (VI) and (XIII), which fragment

[8] Barnes, C. S., and Occolowitz, J. L., *Aust. J. Chem.*, 1963, **16**, 219.

[9] Shannon, J. S., *Aust. J. Chem.*, 1962, **15**, 265.

[10] Van der Merwe, K. J., Steyne, P. S., and Eggers, S. H., *Tetrahedron Lett.*, 1964, 3923.

as described previously (Figs. 1 and 2). Finally the mass spectrum (Tables 1 and 2) of quercetagetin (IV) exhibits the molecular ion as base peak, a substantial M—H· cation, and an M—CHO· cation (metastable at *m/e* 262·8); consistent with the above generalizations.

In summary, mass spectrometry can be used to determine the type of oxygen substituent at C6 in quercetagetin derivatives and possibly in other flavones of known high-oxygenation pattern. It thereby complements chemical and spectroscopic methods[6,11,12] used in investigating the nature of oxygen substituents at other positions on the flavone nucleus.

Experimental

All spectra were determined by the direct insertion technique using an A.E.I. MS9 mass spectrometer operating at 70 eV, with a source temperature of 200–250°. Exact mass measurements were carried out at a resolution of 14,000 (10% valley definition) to an accuracy of 15 p.p.m.; heptacosafluorotributylamine was used to provide reference masses. All compounds cited have been previously described.[5–7] Quercetagetin was synthesized by demethylation of jaceidin with constant boiling hydrogen iodide in acetic anhydride; oxyayanin B and jaceidin were converted into the labelled quercetagetin pentamethyl esters (IX) and (XIV) by methylation with diazomethane and deuterium oxide.[10]

Acknowledgments

We are indebted to Drs T. J. King and J. W. W. Morgan for supplying us with many flavone samples. One of us (J.H.B.) is grateful for the award of an I.C.I. Fellowship.

[11] Jurd, L., in "The Chemistry of Flavonoid Compounds." (Ed. T. A. Geissman.) pp. 107–155. (Pergamon Press: Oxford 1962.)

[12] Massicot, J., and Marthé, P., *Bull. Soc. chim. Fr.*, 1962, 1962.

ARKIV FÖR KEMI

UTGIVET AV

KUNGL. SVENSKA VETENSKAPSAKADEMIEN

Band 26 nr 33

E. DYNESEN, S.-O. LAWESSON, G. SCHROLL, J. H. BOWIE and

R. G. COOKS

Electron impact studies. III

Mass spectra of substituted 9,10-dihydrophenanthrenes

ALMQVIST & WIKSELL

STOCKHOLM

GÖTEBORG • UPPSALA

1967

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Electron impact studies. III

Mass spectra of substituted 9,10-dihydrophenanthrenes

By E. Dynesen, S.-O. Lawesson, G. Schroll, J. H. Bowie and R. G. Cooks

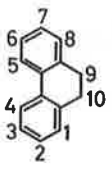
ABSTRACT

The mass spectra of twenty substituted 9,10-dihydrophenanthrenes are reported and discussed. The spectra exhibit pronounced molecular ions and characteristic fragmentation patterns. The absence of skeletal rearrangement ions in the spectra of these compounds allow mass spectrometry to be used for analytical purposes. In some cases, "ortho-effects" can indicate the relative orientation of substituents in the tricyclic system.[1]

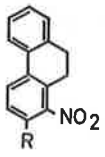
Although the mass spectra of several phenanthrenes and 9,10-dihydrophenanthrenes are recorded [1] no systematic study of the mass spectra of 9,10-dihydrophenanthrenes has been reported. The mass spectra of 9,10-dihydrophenanthrene (I) and the substituted 9,10-dihydrophenanthrenes (II–XXII) are reported in Table 1 and Figs. 1–10. The appearance of an asterisk (*) in either the text or a figure depicts the presence of an appropriate metastable ion for the process indicated. Although exact mass measurements establish the compositions of many ions, it is stressed that specific structures have been written for fragment ions to relate the fragmentation processes to the structure of the intact molecule. Such structures are intended to be nominal representations only.

The major fragment ions present in the mass spectrum (Fig. 1) of 9,10-dihydrophenanthrene (I) are also found in the spectra of the substituted 9,10-dihydrophenanthrenes (II–XXII). The fragmentations of I are summarised in Fig. 1. The molecular ion (*m/e* 180, base peak) readily loses hydrogen to form the stable phenanthrene radical ion (*m/e* 178) which fragments further by loss of acetylene to *m/e* 152, probably the biphenylene radical ion *a*. Alternatively, the 9,10-dihydrophenanthrene molecular ion may decompose by elision of a methyl radical to form the stable fluorene cation *b*, *m/e* 165. This ion, which is absent in the spectrum (Table 1) of phenanthrene (XXIII) (but present in the spectra of alkylphenanthrenes [1], is observed in the mass spectra of all the 9,10-dihydrophenanthrenes studied, and is therefore indicative of saturation at C–9 and C–10 when there are no more than three substituents (and no alkyl substituents) on this tricyclic system.

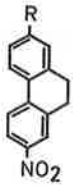
[1] Part II of this series is: Bowie, J. H., and Cameron, D. W., Austral. J. Chem. *19*, 1627 (1966).



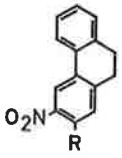
(I)



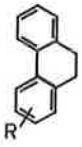
(II) R = H
(III) R = NH_2
(IIIa) R = ND_2
(IV) R = $NHCOCH_3$



(V) R = H
(VI) R = NH_2
(VII) R = $NHCOCH_3$

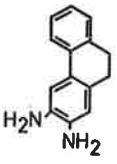


(VIII) R = H
(IX) R = Br
(X) R = I
(XI) R = NH_2
(XII) R = $NHCOCH_3$

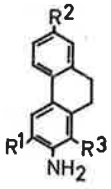


(XIII) R = 2-$NHCOCH_3$
(XIV) R = 2-$NHCOCF_3$
(XV) R = 3-$NHCOCH_3$
(XVI) R = 4-$NHCOCH_3$

(XVII) R = H
(XVIII) R = D



(XIX)



(XX) $R^1 = NO_2 R^2 = H, R^3 = NO_2$
(XXI) $R^1 = H, R^2 = R^3 = NO_2$
(XXII) $R^1 = R^2 = NO_2, R^3 = H$

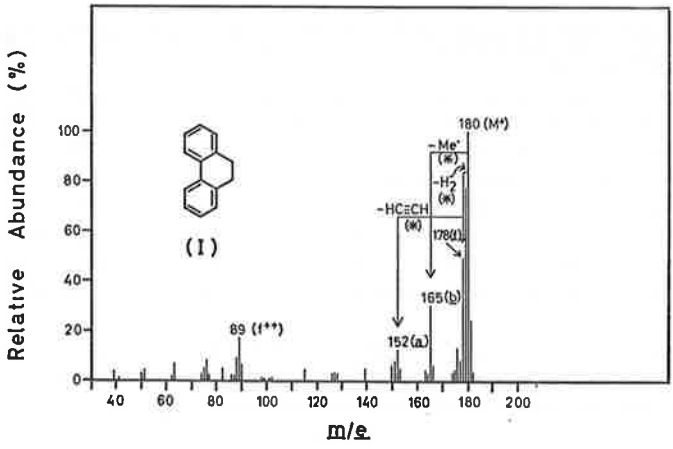


Fig. 1

Table 1.[a] Mass spectra of substituted 9,10-dihydrophenanthrenes.

IIa) *m/e*	95.5	96.5	151	152	153	163	164	165	166	167	177						
I (%)	8	12	12	15	6	6	6	40	14	6	11						
	178	179	180	192	193	194	195	205	206	222	223						
	21	12	9	16	26	22	9	74	21	11	100						
	224	225	240	241	242	$d_0 = 70$; $d_1 = 27$; $d_2 = 3$ %[b]											
	34	7	82	35	7												
VII) *m/e*	43	44	47	48	49	55	57	67	69	71	81	82	87	95	97	109	
I (%)	20	10	35	18	10	24	20	10	20	12	15	9	16	16	12	11	
	111	123	135	137	149	152	163	165	166	177	178	180	193				
	7	7	7	9	7	7	6	26	7	6	8	7	15				
	194	195	208	209	210	240	250	252	282 (M)	283							
	45	9	10	11	21	100	6	20	55	10							
X) *m/e*	76	98	99	151	152	165	166	176	177	178	179	257	258	259			
I (%)	6	9	6	7	7	8	7	22	15	60	11	10	6	9			
	273	275	303	304	305	306											
	5	5	100	16	96	15											
X) *m/e*	47	76	84	85	151	165	176	177	178	179	305	349	351 (M)				
I (%)	9	7	6	5	5	7	15	10	37	6	9	6	100				
	352																
	16																
XI) *m/e*	47	96.5	152	165	166	167	178	193	194	195	240 (M)	241					
I (%)	6	7	8	21	7	9	5	5	29	5	100	19					
XIII) *m/e*	43	152	165	166	177	178	193	194	195	196	237 (M)	238					
I (%)	8	7	15	5	6	6	13	31	100	18	82	15					
XVIII) *m/e*	96.5	97	105	152	165	166	167	180	181	192	193	194	195				
I (%)	8	7	6	6	57	19	8	7	7	15	28	20	9				
	208	209	210	211	212	213	214	$d_0 = 28$, $d_1 = 41$, $d_2 = 23$									
	9	10	64	100	68	24	5	$d_3 = 7$, $d_4 = 1$ %[b]									
XX) *m/e*	139	140	150	151	152	153	163	164	165	166	177	178					
I (%)	14	6	5	16	19	9	17	19	51	19	13	11					
	190	191	192	193	203	204	205	206	207	208	220	221					
	10	25	37	18	33	20	21	7	8	6	11	13					
	222	233	238	249	250	267	268	269	285 (M)	286							
	11	10	5	5	6	14	100	17	93	15							
XXI) *m/e*	82.5	95.5	139	151	152	163	164	165	166	176	177						
I (%)	8	11	6	7	11	14	15	37	11	11	21						
	178	180	190	191	192	193	203	204	205	220	221	222					
	11	7	17	18	19	14	15	35	7	6	6	18					
	237	250	267	268	269	285 (M)	286										
	11	5	14	100	16	57	9										
XXII) *m/e*	152	163	164	165	166	177	178	180	190	191	192						
I (%)	8	9	9	26	11	5	6	11	6	7	13						
	193	194	209	223	239	240	255	285 (M)	286								
	23	6	12	5	17	6	21	100	15								
XXIII) *m/e*	76	87	88	151	152	176	177	178 (M)	179								
I (%)	7	6	8	5	5	14	8	100	14								

[a] All ions greater than 5 % of the base peak (100 %) are recorded.
[b] Isotopic purities.

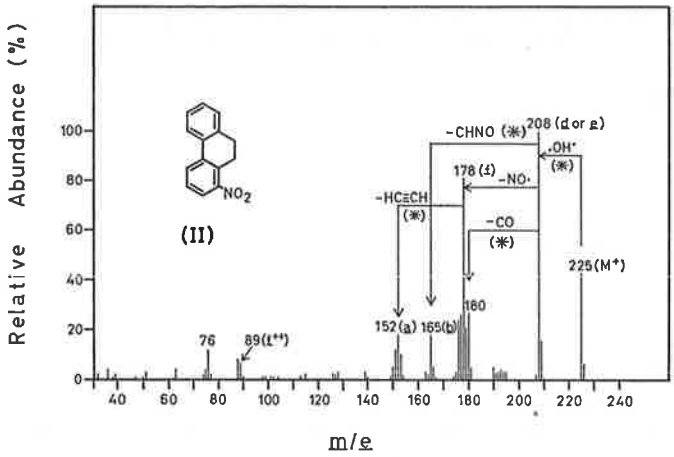


Fig. 2

a, m/e 152 b, m/e 165

The mass spectra (Figs. 2–4) of 1-nitro- (II), 2-nitro- (V), and 3-nitro-9,10-dihydrophenanthrene (VIII) may be used to differentiate the three compounds. The decomposition modes exhibited by V and VIII on electron impact are summarised in Figs. 3 and 4 and high resolution measurements establish the compositions of *m/e* 195, 179, 178 and 152 in the spectrum of V. Of the compounds studied, the 9,10-dihydrophenanthrenes (V–VII) containing a nitro group at C–2 (or C–7) have larger

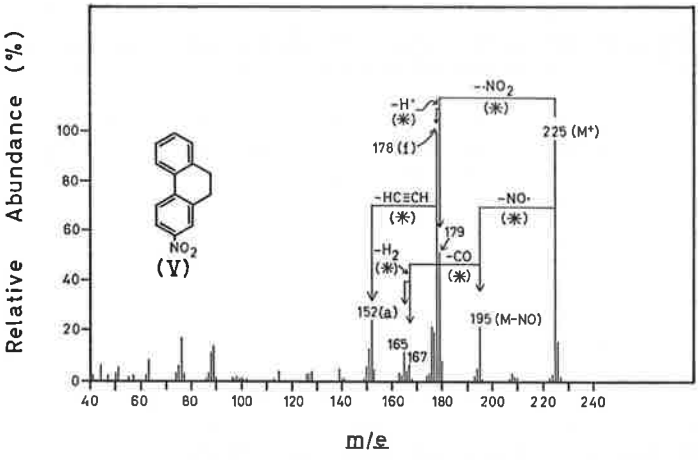


Fig. 3

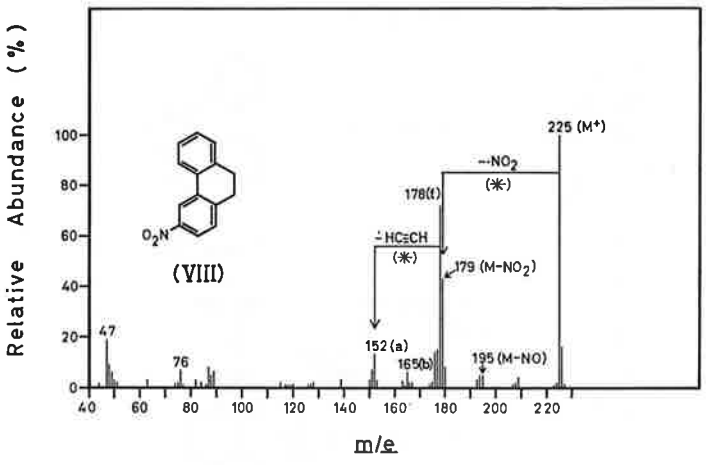


Fig. 4

M–NO ions than those compounds (VIII–XI) having the substituent at C–3 (or C–6). Although the partial rearrangement of the nitro groups of many organic compounds to nitrite on electron impact has been observed previously [2], it is not clear in this case whether the enhanced rearrangement at C–2 is due to conjugate or steric effects. Nevertheless, a comparison of the spectra (Table 2) of compounds containing such substituents (when a 1-nitro group is absent) illustrates the analytical applicability of this observation.

The spectrum (Fig. 2) of 1-nitro-9,10-dihydrophenanthrene (II) is entirely different from those already considered, primarily because of the "ortho-effect" [3] operating between the substituent at C–1 and the hydrogen groups at C–10.[1] This effect is noted in the spectra of all 9,10-dihydrophenanthrenes containing a nitro group at C–1, and is therefore diagnostic for this substituent. The fragmentations of II on electron impact are summarised both in Scheme 1 and Fig. 2. The base peak of the spectrum is due to the loss of a hydroxyl radical from the molecular ion (*m/e* 225) which presumably proceeds by a concerted elimination mechanism, as no analogous effect is noted when an amino group is present at C–1 (see later). No distinction can be made between an elimination occurring via the nitro group of II (to *d*, *m/e*

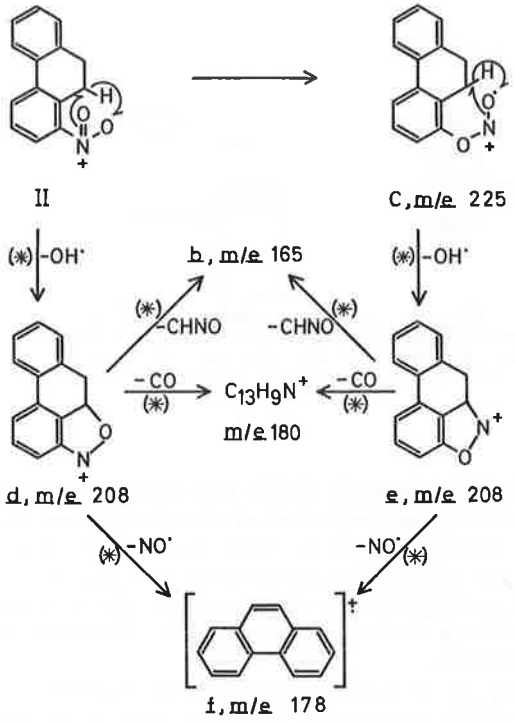
Table 2. Relative abundance of M–NO· ions in the spectra of 2- and 3-nitro-9,10-dihydrophenanthrenes.

2-NO_2	V	VI	VII	XXII	XXI[a]
M-NO· as % of base peak	23	16	20	22	1
3-NO_2	VIII	IX	X	XI	XII
M-NO· as % of base peak	5	4	3	2	1

[a] Compound XXI in addition contains a nitro group adjacent to C-9.

[1] A different "ortho-effect" is noted in the spectrum of 1-nitronaphthalene where it has been proposed [4, 5] that the molecular ion may rearrange to the 8-nitroso-1-naphthol radical ion, which then decomposes by elision of carbon monoxide.

Scheme 1[1]



208) or through the rearranged nitrite group of *c*, *m/e* 225 (to *e*, *m/e* 208), as either of these species (*d* or *e*) could in principle eliminate carbon monoxide (to *m/e* 180) or NO· (to the phenanthrene molecular ion). When this "ortho-effect" operates, the loss of NO· from the molecular ion is negligible.

The main features of the spectra of the mononitro-9,10-dihydrophenanthrenes are retained in the spectra of the more highly substituted nitro-9,10-dihydrophenanthrenes. The spectra (Figs. 5, 6 and Table 1) of the three isomeric nitroamino-9,10-dihydrophenanthrenes (III, VI and XI) clearly illustrate the ease with which the 1-nitro group may be detected. The fragmentations of III and VI are summarised in Figs. 5 and 6 and the interpretation of the spectrum (Fig. 5) of III has been aided by the spectrum (Table 1) of N-d_2-III (IIIa) which was produced by introducing III directly into the source with deuterium oxide [6]. It can be seen that the isotope label is completely retained in the [M–OH·] ion (supporting the mechanisms illustrated in Scheme 1) whereas the [M–35] ion (M–OH·–H_2O) has lost approximately 10 % of the label, showing that the loss of water from the (M–OH·) ion is a random process involving hydrogens attached to both nitrogen and carbon. It is also of interest to note that the only significant difference between the spectra (Fig. 6 and Table 1) of VI and XI lies in the relative abundances of the M–NO ions (Table 2), and it follows that the "ortho-effect" operative between the adjacent nitro and amino groups of

[1] The compositions of all ions mentioned in Scheme 1 have been determined by exact mass measurements.

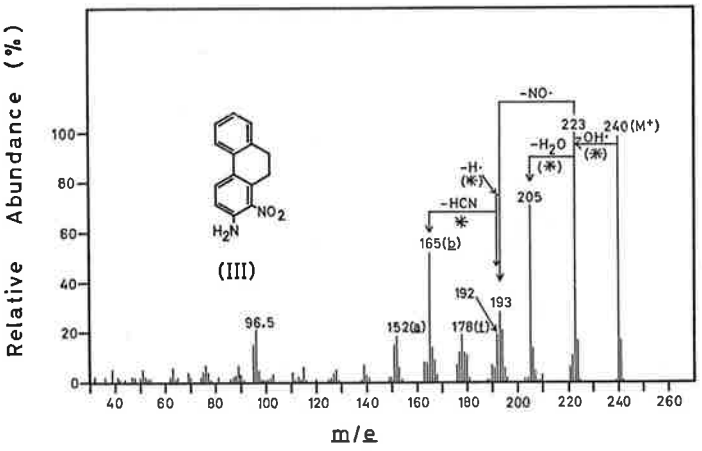


Fig. 5

XI is very small. The spectra (Table 1) of the three isomeric dinitroamino-9,10-dihydrophenanthrenes also follow the above pattern, with the two isomers (XX and XXI) containing 1-nitro substituents being easily recognisable. However, the spectra (Tables 1 and 2) of XX and XXI are almost identical, and consequently the generalisation (Table 2) concerning the detection of a 2-nitro group by the relative abundance of its M–NO ion, is not applicable to compounds already containing a 1-nitro substituent, presumably because of the facile decomposition which may proceed through this substituent.

When the amino substituent of III is replaced by an acetamido group (which on electron impact may readily decompose by elision of ketene), pronounced loss of a hydroxyl radical from the M–CH_2CO ion (see Scheme 1) is now observed. The mass spectra (Figs. 7 and 8, Table 1) of the three isomeric acetamidonitro 9,10-dihydrophenanthrenes (IV, VII and XII) show this effect clearly. The fragmentations

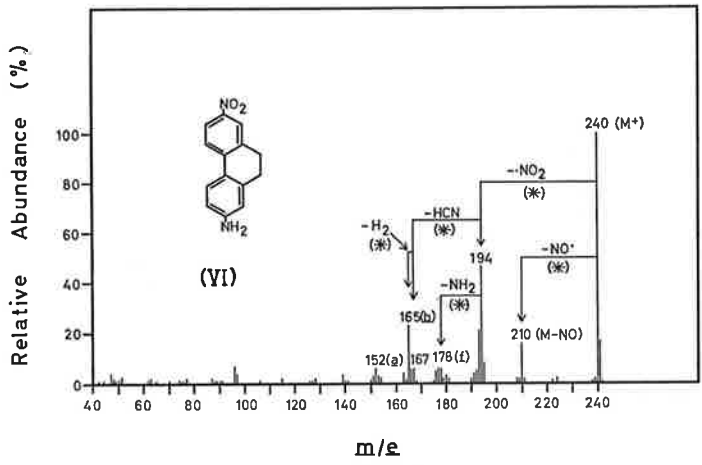


Fig. 6

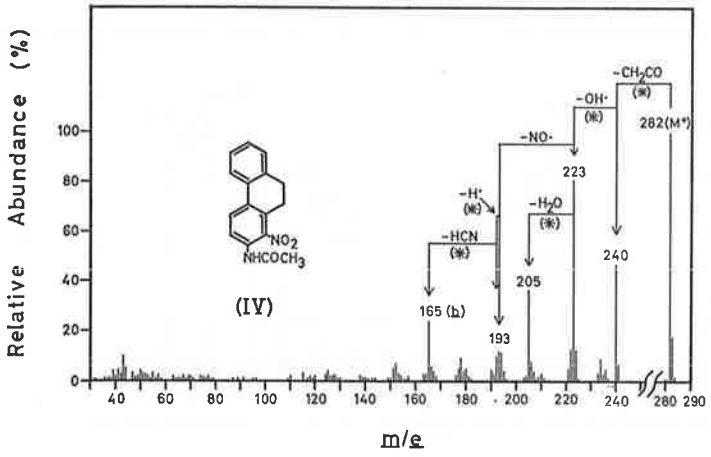


Fig. 7

of IV and XII are summarised in Figs. 7 and 8. 2-Bromo- and 2-iodo-3-nitro-9,10-dihydrophenanthrene (IX and X) behave unexceptionally on electron impact (Table 1), exhibiting the fragmentation modes (M–halogen–NO_2) or (M–NO_2–halogen) to furnish the stable phenanthrene molecular ion (*f*, *m/e* 178), together with abundant *m/e* 165 (*b*) ions characteristic of the 9,10-dihydrophenanthrene system.

The two isomeric diamino-9,10-dihydrophenanthrenes (XVII and XIX) behave identically on electron impact, showing that the "ortho-effect" operating between the two amino groups is more pronounced than that operating between the 1-amino substituent and the hydrogen substituents of C–10 in the spectrum (Fig. 9) of XVII. The loss of the elements of ammonia from the molecular ion (*m/e* 210) involves the loss of three hydrogen atoms attached to nitrogen to give *m/e* 193, possibly *g*, as evidenced by the spectrum (Table 1) of N-d_4-1,2-diamino-9,10-dihydrophenanthrene

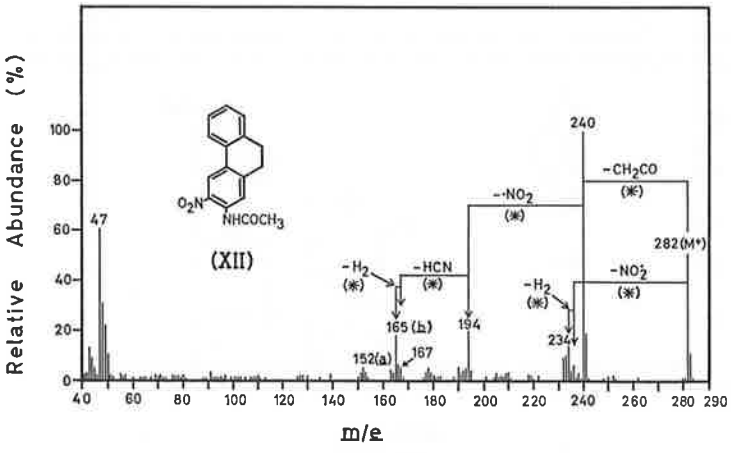


Fig. 8

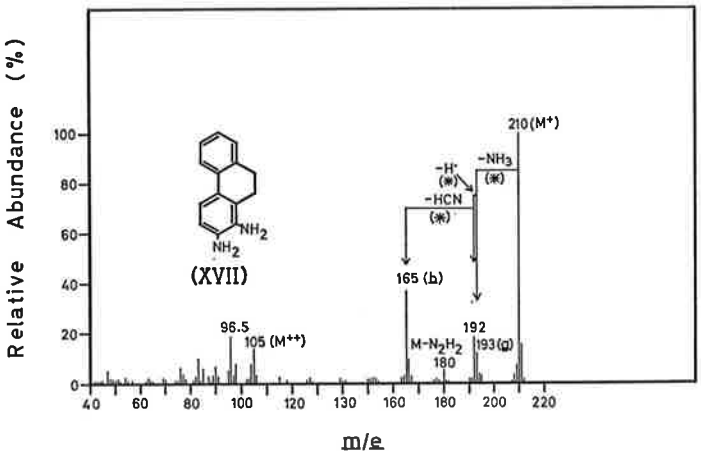
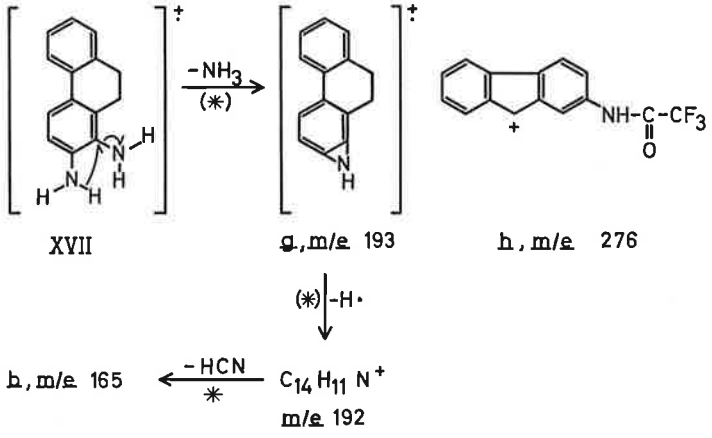


Fig. 9

(XVIII) (produced by introducing XVII directly into the source with deuterium oxide [6]. This behaviour is analogous to that exhibited by *o*-phenylene diamine on electron impact [7]. Further fragmentations of XVII and XIX are indicated in Fig. 9. The compositions of the major ions (*m/e* 193, 192, 180 and 165) in the spectrum of XIX have been established by h.r. measurements.



The spectra of the three acetamido-9,10-dihydrophenanthrenes are similar (see Table 1 for the spectrum of XIII), showing the molecular ion as the base peak, with pronounced elision of ketene to give the corresponding amino-9,10-dihydrophenanthrene radical ion. A very different situation is observed in the spectrum (Fig. 10) of 2-trifluoracetamido-9,10-dihydrophenanthrene (XIV). Here, and in other compounds containing the trifluoroacetyl group [8], elimination of $COCF_2$ with concomitant fluorine rearrangement is not an observed process. Instead, the molecular ion (*m/e* 291) is very pronounced and indeed is so stable that loss of a methyl radical from the

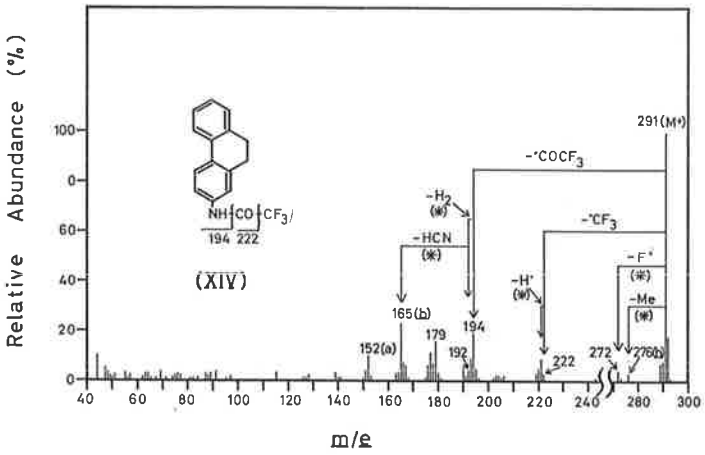


Fig. 10

molecular ion (to *h*, *m/e* 276) is observed. Other fragmentations are unexceptional, and are summarised in Fig. 10.

In summary, mass spectrometry is of considerable use in the determination of both the type and position of substituents on the 9,10-dihydrophenanthrene system, and complemented by other spectroscopic techniques, should aid structure elucidation in this field.

Experimental

All mass spectra were obtained on an A.E.I. MS 9 mass spectrometer operating at 70 eV. Samples were introduced directly into the source which was maintained at a temperature of 150–180°. Exact mass measurements were determined at a resolution of 14.000 (10 % valley definition) using heptacosafluorotributylamine to provide reference masses.

9,10-Dihydrophenanthrene (I) was a purified commercial sample. A previously published procedure [9] was used to prepare 2-nitro-9,10-dihydrophenanthrene (V). By acetylation of 2-amino-9,10-dihydrophenanthrene 2-acetylamino-9,10-dihydrophenanthrene (XIII) was obtained [9].

Most products utilized for mass spectrometry were analytical specimens, proved to be homogeneous by thin layer chromatography and other methods.

The following eighteen compounds were prepared for the first time. For physical and analytical data, see Table 3. II and VIII were prepared by deamination of III and XI, respectively. Hydrolysis of IV, VII and XII gave III, VI and XI, respectively. Nitration of XIII produced IV, VII and XII. IX and X were prepared from XI according to Sandmeyer. XIV was prepared by trifluoroacetylation of 2-amino-9,10-dihydrophenanthrene. XV and XVI were prepared by acetylation of the corresponding amines. XVII and XIX were prepared by reduction of III and XI, respectively. XX was obtained by hydrolysis of the corresponding N tosylderivative. XXI and XXII were prepared by hydrolysis of the corresponding N-acetyl derivatives.

Table 3. Analyses.

Compound	Mp. °C	Received			Calculated		
		C	H	N	C	H	N
II	68.6–69.6	74.65	4.79	6.40	74.65	4.92	6.22
III	123.8–125	69.95	5.19	11.93	69.99	5.03	11.66
IV	170.8–172.8	67.88	5.07	9.91	68.07	5.00	9.92
VI	138.2–139.8	69.73	5.44	11.76	69.99	5.03	11.66
VII	215.5–216.8	67.89	5.14	10.14	68.07	5.00	9.92
VIII	81.2–82	75.18	4.86	6.31	74.65	4.92	6.22
IX[a]	124 –125.8			4.47			4.61
X[b]	104 –105			4.01			3.99
XI	157 –158.5	69.70	5.42	11.87	69.99	5.03	11.66
XII	177 –179	68.35	4.50	9.88	68.07	5.00	9.92
XIV	144 –145.5	65.67	4.06	4.98	65.98	4.16	4.81
XV	140 –142	80.71	5.95	6.10	80.98	6.37	5.90
XVI	156.6–159	80.44	6.16	6.58	80.98	6.37	5.90
XVII	212 –214	78.31	6.43	13.30	79.96	6.71	13.32
XIX	142 –142.6			13.67			13.32
XX	236 –238	59.01	3.83	14.41	58.94	3.89	14.73
XXI	225.5–227	58.50	3.74	14.79	58.94	3.89	14.73
XXII	269 –269.5	58.65	3.83	14.95	58.94	3.89	14.73

[a] Analysis: (Br) Rec. 25.94; calc. 26.28.
[b] Analysis: (J): Rec. 35.72; calc. 36.14.

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Department of Chemistry, Aarhus University, Aarhus C, Denmark (E. D., S.-O. L., G. S.)

Univeristy Chemical Laboratory, Lensfield Rd., Cambridge, United Kingdom (J. H. B., R. G. C.)

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Skeletal Rearrangement on Electron Impact[1]

By J. H. BOWIE

(*Department of Organic Chemistry, University of Adelaide, South Australia*)

R. G. COOKS

(*University Chemical Laboratory, Lensfield Rd., Cambridge*)

S.-O. LAWESSON, P. JAKOBSEN, and G. SCHROLL

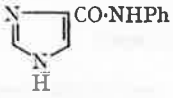
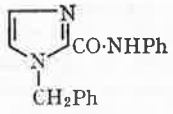
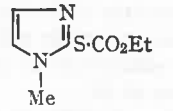
(*Department of Organic Chemistry, Aarhus University, Aarhus C., Denmark*)

THE loss of CO and CO_2 with associated skeletal rearrangement has been shown to occur when certain organic compounds containing carbonyl groups are subjected to electron impact.[2] This is an important feature of mass spectrometry and must be carefully documented because of its obvious relevance to the "element mapping" technique.[3]

Further examples of skeletal rearrangements involving the loss of CO or CO_2 are listed in the Table. The compositions of all rearrangement ions have been established by exact mass measurements and in six cases the decompositions are definitely confirmed by appropriate metastable ions (indicated by the presence of an asterisk). In the case of (VII), ^{18}O labelling establishes that the CO lost comes from the ketone moiety, in agreement with similar loss of the ketone group in both methyl and ethyl acetoacetate.[4] It is possible that similar eliminations occur in compounds (IV—VI). The possibility of thermal rearrangement in the case of (XII) has been excluded by obtaining the spectrum by the direct inlet procedure at 60°.

Many of the rearrangement ions mentioned fragment further upon electron impact, and full details of all spectra will be published later.

TABLE

Compound	Rearranged ion	Relative abundance (% of base peak)	Migrating group
(I) $MeCO_2{\cdot}CH_2{\cdot}CH{=}CH_2$	$M - CO$ $M - CHO$	2 2	Me
(II) $MeCO_2{\cdot}CH_2{\cdot}C{\equiv}CH$	$M - CO$	4	Me
(III) $PhCO_2{\cdot}CH_2{\cdot}CH{=}CH_2$	$M - CO_2H$	6	
(IV) $MeCO{\cdot}CH_2{\cdot}CO_2Pr^n$	$M - CO$	2	Me
(V) $MeCO{\cdot}CH_2{\cdot}CO_2Pr^i$	$M - CO$	3	Me
(VI) $MeCO{\cdot}CH_2{\cdot}CO_2{\cdot}CH_2{\cdot}CH{=}CH_2$	$M - CO$	2	Me
(VII) $MeCO{\cdot}CH_2{\cdot}CO_2Ph$	$M - CO$ (*)	7	Me
(VIII) $MeCO{\cdot}NH{\cdot}COMe$	$M - CO$ (*)	24	Me
(IX) 	$M - CO$ (*)	8	Ph
(X) 	$M - CO$ (*)	2	PhNH
(XI) 	$M - CO$ (*) $M - C_4H_3N_2O$ (*)	5 37	PhNH
(XII) 	$M - CO_2$	4	Et

(*Received, July 11th*, 1966; *Com.* 475.)

[1] Previous paper in this series: I. R. C. Bick, J. H. Bowie, and G. K. Douglas, *J. Org. Chem.*, submitted for publication.

[2] J. H. Bowie, R. Grigg, D. H. Williams, S.-O. Lawesson, and G. Schroll, *Chem. Comm.*, 1965, 403; J. H. Bowie, R. Grigg, S.-O. Lawesson, P. Madsen, G. Schroll, and D. H. Williams, *J. Amer. Chem. Soc.*, 1966, **88**, 1699; J. H. Bowie, D. H. Williams, P. Madsen, G. Schroll, and S.-O. Lawesson, *Tetrahedron*, submitted for publication; M. Fischer and C. Djerassi, *Chem. Ber.*, 1966, **99**, 750; W. H. McFadden, K. L. Stevens, S. Meyerson, A. J. Karabatsos, and C. E. Orzech, *J. Phys. Chem.*, 1965, **69**, 1742; P. Natalis and J. L. Franklin, *ibid.*, p. 2935; P. Brown and C. Djerassi, *J. Amer. Chem. Soc.*, in the press.

[3] K. Biemann, *Pure Appl. Chem.*, 1964, **9**, 95; K. Biemann, P. Bommer, and D. M. Desiderio, *Tetrahedron Letters*, 1964, 1725.

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ELECTRON IMPACT STUDIES

VI.* MASS SPECTRA OF ESTERS AND THIOESTERS. SKELETAL REARRANGEMENT ON ELECTRON IMPACT

By J. H. Bowie,† R. G. Cooks,‡ P. Jakobsen,§ S.-O. Lawesson,§ and G. Schroll§

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Summary

The mass spectra of representative series of simple alkyl acetoacetates, alkyl acetothioacetates, and some unsaturated esters derived from unsaturated alcohols or phenols are reported and discussed. The fragmentation schemes have been established by high resolution measurements, appropriate metastable ions, and by deuterium and ^{18}O labelling. Many of the spectra show significant skeletal rearrangement fragments arising from either loss of carbon monoxide or carbon dioxide.

The occurrence of skeletal rearrangement fragments has been observed in the mass spectra of β-diketones,[1,2] cyanoacetates,[3] α,β-unsaturated esters,[4] ethyl acetoacetates,[5] and in other groups of compounds containing carbonyl functions.[6–10] The presence of such fragments in the mass spectra of simple compounds is not only of importance in the understanding of fragmentation modes, but is also of obvious relevance to the element mapping technique.[11]

* Part V, *Chem. Commun.*, 1966, 539.
† Department of Organic Chemistry, University of Adelaide.
‡ University Chemical Laboratory, Lensfield Road, Cambridge, England.
§ Department of Organic Chemistry, Aarhus University, Aarhus C, Denmark.

[1] Bowie, J. H., Grigg, R., Williams, D. H., Lawesson, S.-O., and Schroll, G., *Chem. Commun.*, 1965, 403.
[2] Bowie, J. H., Lawesson, S.-O., Schroll, G., and Williams, D. H., *J. org. Chem.*, 1966, **31**, 1384.
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[10] Teeter, R. M., Tenth Annual Conference on Mass Spectrometry, A.S.T.M. Committee E-14, New Orleans, La., 1962, p. 51.
[11] Biemann, K., *Pure appl. Chem.*, 1964, **9**, 95; Biemann, K., Bommer, P., and Desiderio, D. M., *Tetrahedron Lett.*, 1964, 1725.

TABLE 1

MASS SPECTRA OF ESTERS AND THIOESTERS

All ions greater than 2% of the base peak (arbitrarily taken as 100%) are recorded

(I)	*m/e*	27	28	29	39	41	42	43	44	58	59	60	61	69	84	85	102	103
	I (%)	14	10	8	6	11	15	100	16	10	13	23	17	15	25	32	12	20
	m/e	115	144(M^+)															
	I (%)	3	3															
(II)	*m/e*	28	39	41	42	43	44	57	58	59	69	84	85	87	102	103	116	
	I (%)	6	8	14	11	100	19	10	10	15	15	23	27	5	16	13	2	
	m/e	144(M^+)																
	I (%)	3																
(III)	*m/e*	27	28	29	39	41	42	43	44	55	56	57	58	60	69	84	85	103
	I (%)	18	10	21	7	38	20	100	16	7	76	25	10	10	20	25	35	30
	m/e	116	143	158(M^+)														
	I (%)	3	2	4														
(IV)	*m/e*	27	28	29	39	41	42	43	44	56	57	58	85	103				
	I (%)	25	18	13	12	34	25	100	43	14	10	13	14	5				
(V)	*m/e*	27	28	29	39	41	42	43	44	55	56	57	58	59	60	69	73	85	87
	I (%)	20	16	25	14	26	15	38	24	14	14	31	15	25	10	25	18	100	25
	m/e	102	103	129	158(M^+)													
	I (%)	15	37	3	2													
(VI)	*m/e*	27	28	29	39	41	43	44	56	57	58	59	60	69	84	85	103	
	I (%)	8	9	10	6	30	56	20	10	35	8	100	4	26	34	22	14	
	m/e	158(M^+)																
	I (%)	2																
(VIII)	*m/e*	27	28	29	39	41	43	44	55	56	57	58	67	69	71	81	82	85	99
	I (%)	18	4	14	19	24	100	23	12	8	65	14	19	6	6	9	38	7	18
	m/e	103																	
	I (%)	7																	
(XII)	*m/e*	27	28	39	41	42	43	69	76	84	85	86	118	160(M^+)					
	I (%)	8	15	5	12	11	97	8	11	10	100	5	12	24					
(XIV)	*m/e*	27	28	29	39	41	43	55	56	57	61	69	84	85	86	90	118		
	I (%)	8	9	8	4	13	65	5	20	8	4	7	10	100	5	10	2		
	m/e	174(M^+)																	
	I (%)	13																	
(XV)	*m/e*	27	28	29	39	41	43	56	57	58	61	69	84	85	86	89	90	118	
	I (%)	6	9	11	4	13	66	8	20	7	10	7	9	100	5	5	10	8	
	m/e	119	146	174(M^+)															
	I (%)	5	4	18															
(XVI)	*m/e*	27	28	29	39	41	42	43	55	56	57	58	69	84	85	90	91	118	
	I (%)	12	13	19	12	38	6	32	8	11	100	12	4	5	56	17	7	43	
	m/e	119	174(M^+)	175															
	I (%)	14	25	3															

TABLE 1 (*Continued*)

(XVII)	*m/e*	26	27	28	29	37	38	39	40	41	42	43	45	46	54	56	58	59	69
	I (%)	28	39	11	10	20	30	80	15	64	20	100	56	4	9	9	9	11	26
	m/e	73	74	85	125	168(M^+)													
	I (%)	13	7	14	3	2													
(XVIII)	*m/e*	39	41	42	43	56	57	71	72	100(M^+)									
	I (%)	9	10	4	100	10	15	2	2	2									
(XIX)	*m/e*	39	43	44	55	56	70	98(M^+)											
	I (%)	18	100	3	5	4	4	2											
(XXI)	*m/e*	39	41	51	77	91	105	106	117	122	123	162(M^+)							
	I (%)	6	6	8	20	2	100	9	6	3	2	12							
(XXII)	*m/e*	39	40	41	51	52	53	77	78	79	80	81	91	97	105	106	157	158	
	I (%)	19	10	23	24	7	18	54	4	52	24	40	4	15	100	9	3	2	
	m/e	202(M^+)																	
	I (%)	9																	
(XXIII)	*m/e*	39	50	51	63	65	76	77	93	94	105	106	198(M^+)						
	I (%)	19	9	26	5	13	4	45	3	3	100	13	12						

TABLE 2

EXACT MASS MEASUREMENTS IN THE MASS SPECTRA OF COMPOUNDS (I)–(XXII)

Compound	*m/e*	Composition	Compound	*m/e*	Composition
(I)	43	C_2H_3O(80%), C_3H_7(20%)	(VII)	69	C_3HO_2(50%), C_5H_9(50%)
	102	$C_5H_{10}O_2$(65%), $C_4H_6O_3$(35%)		43	C_2H_3O(70%), C_3H_7(30%)
	103	$C_4H_7O_3$	(IX)	114	$C_6H_{10}O_2$
(II)	43	C_2H_3O(80%), C_3H_7(20%)	(X)	164	$C_{10}H_{12}O_2$
	102	$C_4H_6O_3$(60%), $C_5H_{10}O_2$(40%)		58	C_3H_6O
	103	$C_4H_7O_3$	(XI)	118	$C_5H_{10}OS$(85%), $C_4H_6O_2S$(15%)
(III)	43	C_2H_3O(70%), C_3H_7(30%)	(XII)	43	C_2H_3O(60%), C_3H_7(40%)
	56	C_4H_8		118	$C_4H_6O_2S$
	69	C_3HO_2	(XIII)	43	C_2H_3O(55%), C_3H_7(45%)
	85	$C_4H_5O_2$		118	$C_4H_6O_2S$
	103	$C_4H_7O_3$		132	$C_6H_{12}SO$
	116	$C_6H_{12}O_2$	(XV)	43	C_2H_3O
(IV)	43	C_2H_3O(95%), C_3H_7(5%)		146	$C_7H_{14}OS$
(V)	43	C_2H_3O(95%), C_3H_7(5%)	(XVIII)	72	$C_4H_{10}O$
(VI)	43	C_2H_3O	(XIX)	70	C_4H_8O
	59	C_3H_7O	(XXI)	117	C_9H_9
	69	C_3HO_2		122	$C_7H_6O_2$
	84	$C_4H_4O_2$	(XXII)	80	C_6H_8
(VII)	142	$C_7H_{10}O_3$		81	C_6H_9
	128	$C_8H_{16}O$		91	C_7H_7
	110	C_8H_{14}		97	C_6H_9O
	99	$C_6H_{11}O$		105	C_7H_5O
	85	C_5H_9O(70%), $C_4H_5O_2$(30%)		157	$C_{12}H_{13}$
	81	C_6H_9		158	$C_{12}H_{14}$

Because of our interest in the skeletal rearrangement ions observed in the mass spectra of ethyl acetoacetates[5] we have investigated the relative abundance of such ions in the spectra of the alkyl acetoacetates (I)–(X) and have extended this study to include the alkyl acetothioacetates (XI)–(XVII) and the unsaturated esters (XVIII)–(XXIII). Some of this work has been reported in a previous communication;[12] we wish here to report the work in full.

$CH_3COCH_2CO_2R$

R	R
(I) Pr^n	(VI) Bu^t
(II) Pr^i	(VII) 1-ethylcyclohexyl
(III) Bu^n	(VIII) 1-isopropylcyclohexyl
(IV) Bu^i	(IX) allyl
(V) Bu^s	(X) CH_2Ph

$CH_3COCH_2C(=O)SR$

R	R
(XI) Et	(XVI) Bu^t
(XII) Pr^n	(XVII) allyl
(XIII) Pr^i	
(XIV) Bu^n	
(XV) Bu^s	

Throughout this paper, an asterisk (*) denotes the presence of a metastable ion for the process indicated. The compositions of many fragment ions have been established by exact mass measurements and these are summarized in Table 2. The spectra of compounds (VII), (IX), (X), (XI), and (XIII) are recorded in Figures 1–5 (pp. 694–6) while the spectra of all other compounds are recorded in Table 1.

TABLE 3

RELATIVE ABUNDANCES (%) OF FRAGMENT IONS IN THE SPECTRA OF THE ALKYL ACETOACETATES (I)–(VI)

Compound	M^+	$M-CO$	$M-CH_2CO$	$M-(R-2H\cdot)$	$M-RO\cdot$	$C_3HO_2^+$ *m/e* 69	R^+	$R-H\cdot$	$C_3H_7O^+$ *m/e* 59	CH_3CO^+ *m/e* 43
(I)	2	1	8	20	32	15	20	15	12	80
(II)	3	2	12	13	27	15	20	11	14	80
(III)	4	—	2	30	35	20	25	76	—	100
(IV)	—	—	—	5	15	2	10	15	—	100
(V)	—	—	—	37	100	25	31	26	15	35
(VI)	—	—	—	15	22	25	35	10	100	55

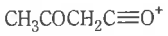
The mass spectra of methyl and ethyl acetoacetate have been discussed previously.[5] In the spectra of (I)–(X), the loss of ketene from the molecular ion to form enolic fragment ions (a significant process in the spectrum of ethyl acetoacetate), is either very small or absent, e.g. in the spectrum of the propyl derivative (I), the $M-CH_2CO$ ion constitutes 65% of *m/e* 102 (12% of the base peak); in the n-butyl derivative (III) only 2% of the base peak, while no loss of ketene is observed in the spectra of the other butyl derivatives (IV)–(VI). When R is a larger alkyl group than ethyl, the acetyl cation (*m/e* 43) is always pronounced, and processes occur which involve loss (from the molecular ion) of (1) the alkyl residue with double hydrogen rearrangement to give an ion corresponding to *a*,[13] together with (2) loss of an alkoxyl radical to yield *b* (*m/e* 85). The presence of the M^+-ROH ion (*m/e* 84) is

[12] Bowie, J. H., Cooks, R. G., Jakobsen, P., Lawesson, S.-O,. and Schroll, G., *Chem. Commun.*, 1966, 539.

[13] Bowie, J. H., Lawesson, S.-O., Schroll, G., and Williams, D. H., *J. org. Chem.*, 1966, **31**, 1792.

noted in the spectra of (I)–(III) and (VI), but not in those of (IV) and (V). No explanation can be offered for this anomalous observation. The general features of the spectra of (I)–(VI) are summarized in Tables 1 and 3. The relative abundance of skeletal rearrangement ions in the spectra of (I)–(VI) correspondingly decreases

a

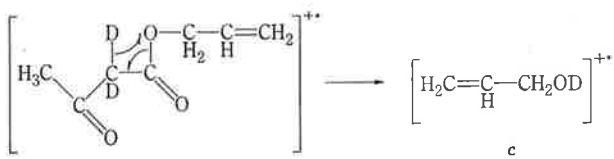


b

with increasing size of the alkoxyl group. Although small rearrangement ions are noted (Table 3) for the propyl derivatives (I) and (II), no skeletal rearrangements are observed in the spectra of the butyl derivatives (III)–(VI). When the alkoxyl group contains a saturated ring system as in (VII) and (VIII), the mass spectra are not characteristic of β-keto esters, apart from exhibiting ions corresponding to the acetyl cation (70% of *m/e* 43) and to *b* [30% of *m/e* 85 (Table 2)]. Instead fragment ions are present which arise primarily from the alkoxyl group, which after initial cleavage, has retained the charge. This is illustrated by the spectrum (Fig. 1) of (VII), while the compositions of the various fragment ions in this spectrum are summarized in Table 2.

Significant differences are observed in the spectra of β-keto esters containing unsaturation in the alkoxyl group. Skeletal rearrangement ions due to loss of carbon monoxide from the molecular ions are again observed, especially in the case of (X) (R = $PhCH_2$) where this ion constitutes 13% of the base peak. ^{18}O labelling[5,14] indicates that the carbon monoxide expelled originates from the ketone moiety (Fig. 3).

The benzyloxy cation (*m/e* 107) in this spectrum (Fig. 3) must at least partly arise by loss of $MeCH_2CO\cdot$ from the skeletal rearrangement ion (*m/e* 164) as this decomposition is evidenced by an appropriate metastable ion at *m/e* 70·1. Fragment ions due to the presence of the benzyl alcohol and allyl alcohol radical ions (*m/e* 108 and 58) are prominent in the spectra (Figs. 2 and 3) of (IX) and (X). As the genesis of such ions requires H rearrangement, (IXa) was synthesized (by direct D_2O exchange with (IX)) and its mass spectrum compared with that of (IX). The peak at *m/e* 58 in Figure 2 moves to *m/e* 59 while that at *m/e* 57 is not affected. This is consistent with deuterium transfer via a four-membered transition state, viz. (IXa) → *c*:



(IXa) *c*

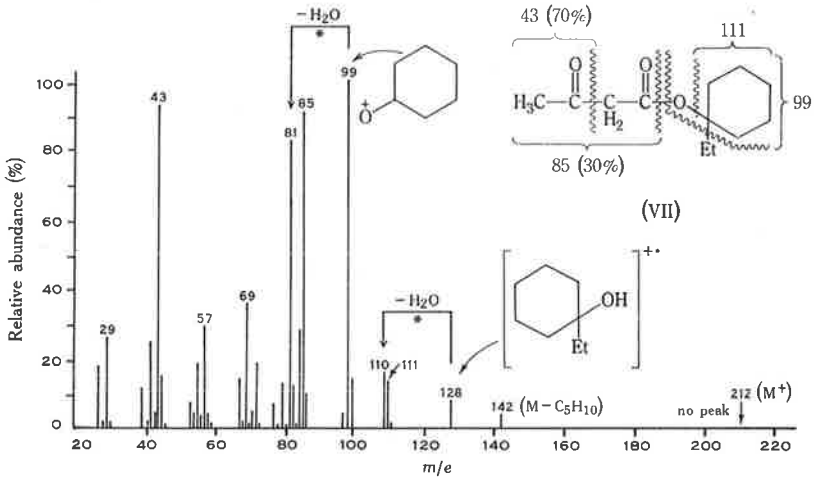
The mass spectra (Figs. 4 and 5, Table 1) of the thioesters (XI)–(XVI) bear some resemblance to the analogous β-keto esters. Because of the thermal decomposition that these compounds undergo at elevated temperatures, all spectra were determined by the direct insertion procedure using a source temperature of 50°. The spectra

[14] Richter, W. J., Senn, M., and Burlingame, A. R., *Tetrahedron Lett.*, 1965, 1235.

are generally simple and readily interpretable. The mass spectra of (XI) and (XIII) are illustrated in Figures 4 and 5, while the major fragmentations of (XI)–(XVII) are summarized in Table 3.

The elision of ketene from the molecular ion to form enolic fragment ions, which is a preponderant process for ethyl acetoacetates, is neither observed in the spectrum of ethyl acetothioacetate (XI) nor in those of (XII)–(XVI). Instead, ready loss of the alkylthio radical by α-cleavage to C=O to furnish *b* (*m/e* 85) is the preponderant

Fig. 1



process in these spectra. The formation of the thiol radical ion ($RSH^{+\cdot}$) by hydrogen rearrangement is an observed process in all spectra. Comparison of the mass spectra of (XII) and of the labelled compound $CH_3COD_2C(=O)SPr^n$ (XIIa) (prepared analogously to (IXa)) shows a shift of *m/e* 76 to *m/e* 77. This indicates that $Pr^nSH^{+\cdot}$ (*m/e* 76) is formed by hydrogen transfer via a four-membered transition state. The analogous alcohol radical ion does not generally occur in the mass spectra of simple alkyl acetoacetates, but can be seen in cases where charge stabilization of the alcohol radical ion may occur, e.g. (IX) and (X). Here, as in the case of β-keto esters, skeletal rearrangement fragments are observed, their relative abundances decreasing as the size of the alkylthio group increases (Table 4). Strangely, no skeletal rearrangement ions are observed in the spectrum (Table 1) of the allyl derivative (XVII). Further fragmentations are summarized in Table 4 and Figures 4 and 5.

RCOOR′

	R	R′
(XVIII)	Me	allyl
(XIX)	Me	propargyl
(XX)	Ph	Me
(XXI)	Ph	allyl
(XXII)	Ph	cyclohex-2-enyl
(XXIII)	Ph	Ph

Finally, because of the skeletal rearrangement ions which are observed in the spectra of α,β-unsaturated esters,[4] the spectra of the unsaturated esters (XVIII)–

(XXIII) were determined. The general fragmentations (Table 1) of these compounds on electron impact are unexceptional and follow the normal ester decomposition modes.[15] The skeletal rearrangement ions are summarized in Table 4, p. 697. Neither

Fig. 2

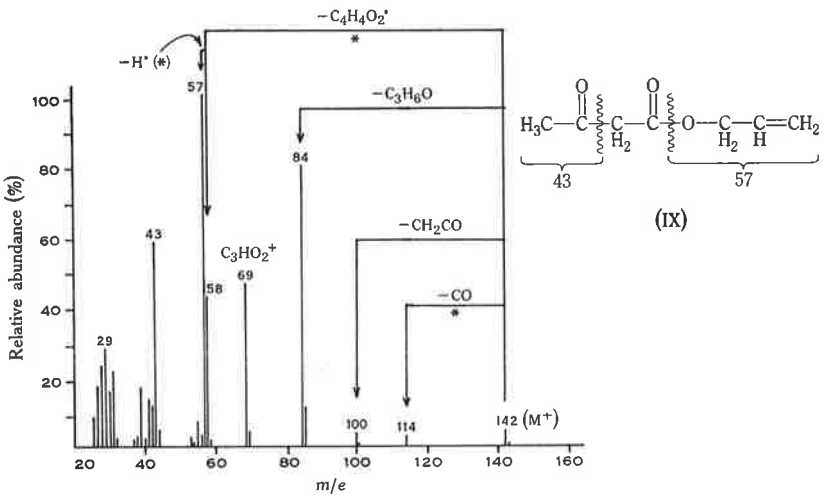
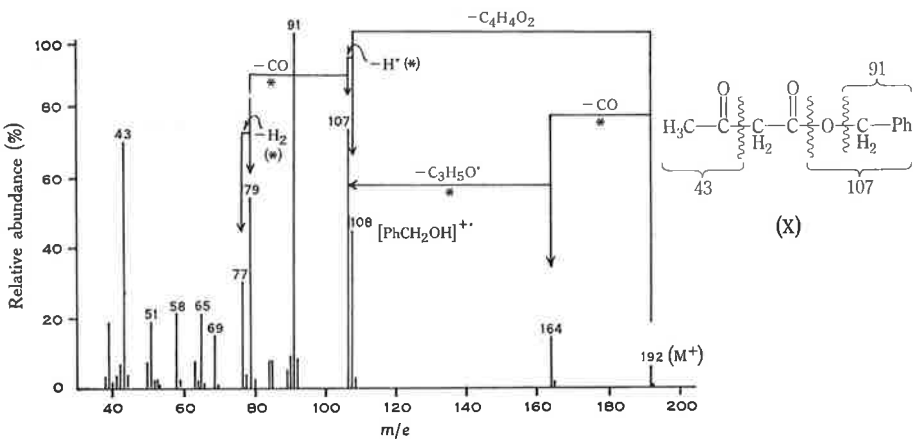


Fig. 3



methyl[16] nor phenyl benzoate (XX and XXIII) show any rearrangement ions in their spectra. The mass spectra of compounds containing R = Me and R′ = allyl or propargyl (XVIII and XIX) exhibit M−CO ions whereas (XXI) and (XXII) (R = Ph, R′ = allyl and cyclohex-2-enyl) exhibit M−CO_2 and M−CO_2H rearrangement ions. The spectrum (Table 1) of (XXII) is also noteworthy for the occurrence

[15] Budzikiewicz, H., Djerassi, C., and Williams, D. H., "Interpretation of Mass Spectra of Organic Compounds." pp. 10–17. (Holden-Day: San Francisco 1964.)

[16] "Catalog of Mass Spectral Data." Spectrum No. 1752. American Petroleum Institute Research Project 44. (Carnegie Institute of Technology: Pittsburg, Pa.)

of a further skeletal rearrangement ion at *m/e* 91, $C_7H_7^+$ by high resolution (5% of the base peak), whose representation as the tropylium cation is substantiated by the decomposition

$$m/e\ 91 \xrightarrow[*]{-HC\equiv CH} m/e\ 65\ (C_5H_5^+\ \text{H.R.})$$

The compositions of all skeletal rearrangement ions indicated in Table 5 have been established by exact mass measurement.

Fig. 4

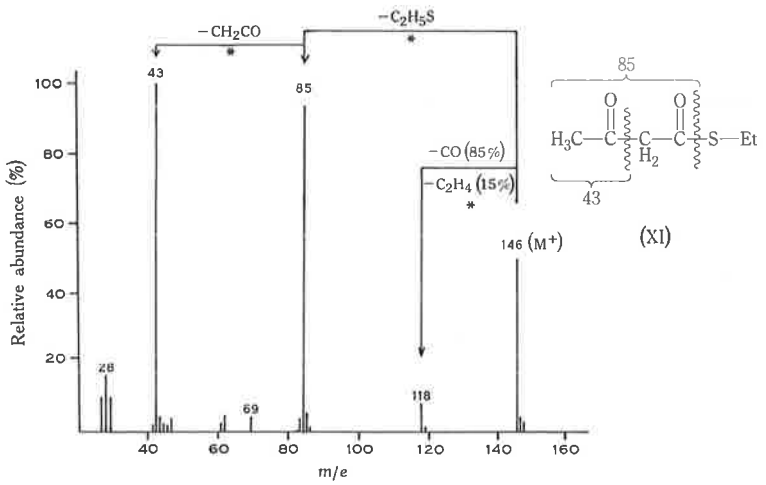
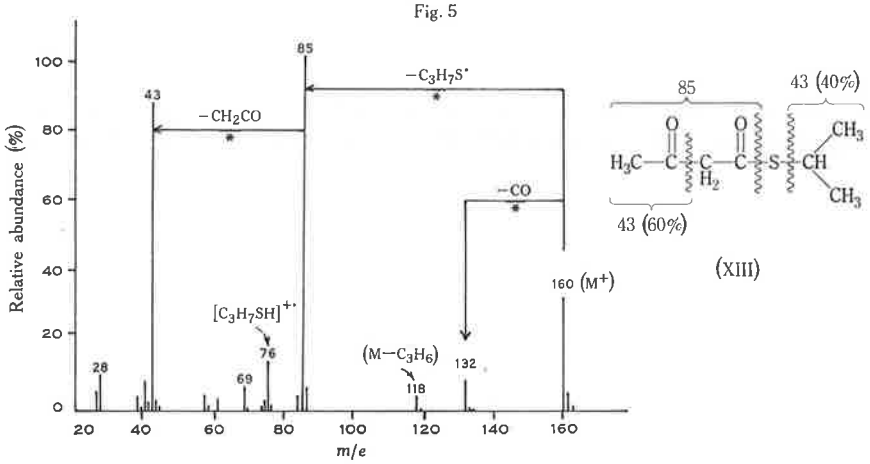


Fig. 5



It has been suggested[4] that skeletal rearrangements which involve loss of CO or CO_2 apparently occur because removal of the π-electrons from double bonds (C=C or C=O) generates electron deficient centres which may then be utilized to promote C–C or C–O bond formation in reactions of the type $[ABC]^+ \rightarrow [AC]^+$.

Experimental

The spectra of the β-keto esters and the unsaturated esters were determined on a Hitachi Perkin–Elmer RMU-6D mass spectrometer, with samples being introduced into the source through a heated inlet system at a temperature of approximately 150°. The thio compounds were measured by the direct insertion procedure on an AEI MS9 mass spectrometer using a source temperature not in excess of 55°. Exact mass measurements were carried out with the MS9, at a resolution of 14,000 (10% valley definition), using heptacosafluorotributylamine to provide reference masses.

Table 4

Relative abundances (%) of fragment ions in the spectra of the thioesters (XI)–(XVI)

Compound	M+	M−CO	M−(R–H·)	RSH	M−RS·	R+	MeCO+
(XI)	35	4	2	7	93	12	100
(XII)	24	—	12	11	100	49	58
(XIII)	23	11	2	12	100	45	49
(XIV)	13	—	3	10	100	8	65
(XV)	17	4	8	10	100	18	66
(XVI)	25	—	43	17	56	100	22

Table 5

Relative abundances (%) of skeletal rearrangement ions in the spectra of compounds (XVIII)–(XXIII)

Rearranged Ion	(XVIII)	(XIX)	(XX)	(XXI)	(XXII)	(XXIII)
$M-CO$	2	4	—	—	—	—
$M-CO_2$	—	—	—	1	1	—
$M-HCO_2$	—	—	—	6	3	—

All liquid samples were distilled twice, if necessary further purified by gas chromatography. Purity was routinely checked by gas chromatography, and n.m.r. and mass spectrometry.

Compounds (XX) and (XXIII) were purified commercial samples; (I)–(VI), (IX), and (X) were prepared from diketene and the appropriate alcohol.[17,18] The following compounds were prepared by reported procedures: (VII) and (VIII),[19] (XVIII),[20] (XIX),[21] (XXI),[22] and (XXII).[23] Compounds (XI)–(XVII) were prepared from diketene and the corresponding thiols (experimental details will be published elsewhere).

Acknowledgments

One of us (R.G.C.) is grateful for the award of an Elsie Ballot Fellowship. A grant from Statens Almindelige Videnskabsfond (to S.-O.L.) is gratefully acknowledged. The mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

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Thiophen Chemistry. Part XIII.[1] Mass Spectra of Substituted Thiophens

By J. H. Bowie, Department of Organic Chemistry, University of Adelaide, South Australia
R. G. Cooks, University Chemical Laboratory, Cambridge
S.-O. Lawesson and C. Nolde, Aarhus University, Denmark

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By J. H. Bowie, Department of Organic Chemistry, University of Adelaide, South Australia
R. G. Cooks, University Chemical Laboratory, Cambridge
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The mass spectra of thirty-two substituted thiophens are reported and discussed. The compounds fragment in a well defined manner on electron impact; fragmentation processes have been substantiated by exact mass measurements and appropriate metastable ions. All mass spectra exhibit pronounced molecular ions, while skeletal rearrangement ions are present in many of the spectra. In general, isomeric thiophens containing substituents in either the 2- or 3-position cannot be differentiated by mass spectrometry.

THE mass spectra of thiophen [2] and alkylthiophens [3,4] have been discussed. This Paper deals with the mass spectra of thirty-two substituted thiophens, and is complementary to papers on hydroxythiophens [5] and t-butoxythiophens.[5a]

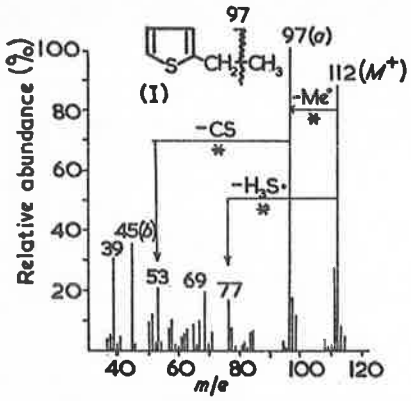


FIGURE 1

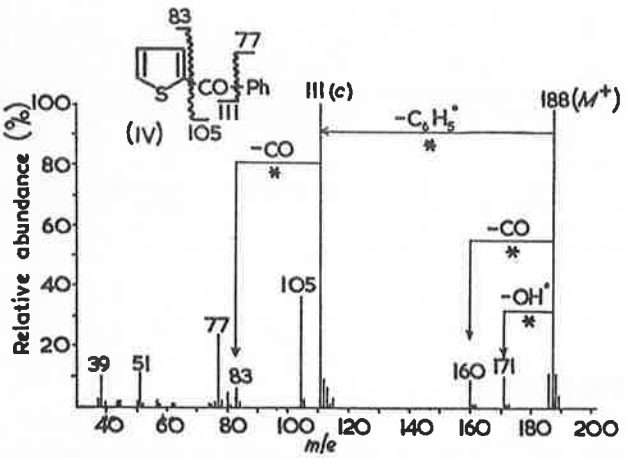
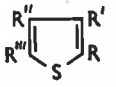


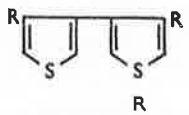
FIGURE 2

The mass spectra of the thiophens (I)—(XXXII) are reported in Figures 1—8 and Table 1. The compositions of many ions have been determined by exact mass measurements (Table 2); transitions substantiated by an appropriate metastable peak are indicated by an asterisk (in text and Figures). Structures written for fragment ions are nominal only, but are intended to relate the fragmentation processes to the structure of the intact molecule (*e.g.*, it has been suggested that the furan molecular ion does not have the ground-state structure [6]).



	R	R′	R″	R‴
(I)	Et	H	H	H
(II)	CHO	H	H	H
(III)	COMe	H	H	H
(IV)	COPh	H	H	H
(V)	OCOPh	H	H	H
(VI)	CH_2Ph	H	H	H
(VII)	Ph	H	H	H
(VIII)	Ph	H	Ph	H
(IX)	Ph	H	H	Ph
(X)	Cl	H	H	H
(XI)	Cl	H	H	Cl
(XII)	Br	H	H	H
(XIII)	H	Br	H	H
(XIV)	Br	Br	H	H
(XV)	Br	H	Br	H

	R	R′	R″	R‴
(XVI)	Br	H	H	Br
(XVII)	H	Br	Br	H
(XVIII)	Br	Br	Br	H
(XIX)	Br	Br	H	Br
(XX)	Br	Br	Br	Br
(XXI)	CO_2H	H	H	H
(XXII)	H	CO_2H	H	H
(XXIII)	Br	H	H	CO_2H
(XXIV)	H	Br	CO_2H	H
(XXV)	H	Br	H	CO_2H
(XXVI)	Br	Br	H	CO_2H
(XXVII)	Br	CO_2H	H	Br
(XXVIII)	Br	H	Br	CO_2H
(XXIX)	Br	Br	CO_2H	Br
(XXX)	NH_2	CO_2Et	OH	H



(XXXI) R = H
(XXXII) R = Br

Empirical rules relating the structures of alkylthiophens to their fragmentation patterns have been reported.[2] Several modifications to these rules are now necessary. First, it has been noted [4] that in general, the molecular ion of an alkylthiophen will be greater than 50% of the base peak (always *a*, *m/e* 97 for alkylthiophens) only when the substituents are methyl. Exceptions to this generalisation have been noted,[4] and the mass spectrum (Figure 1) of 2-ethylthiophen shows a further exception to this rule. Here the molecular ion constitutes 87% of the base peak. The compositions of the major peaks have been established by exact mass

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[4] I. W. Kinney and G. L. Cook, *Analyt. Chem.*, 1952, **24**, 1391.

[5] R. Grigg, H. J. Jakobsen, S.-O. Lawesson, M. V. Sargent, G. Schroll, and D. H. Williams, *J. Chem. Soc.* (*B*), 1966, 331.

[5a] H. J. Jakobsen, G. Schroll, S.-O. Lawesson, D. A. Lightner, A. M. Duffield, and C. Djerassi, *Arkiv Kemi*, in press.

[6] W. H. Pirkle, *J. Amer. Chem. Soc.*, 1965, **87**, 3022.

TABLE 1

Mass spectra of thiophens *

(II)	*m/e*	37	38	39	45	50	57	58	69
	I (%)	6	8	41	26	4	6	6	3
	m/e	81	82	83	84	111	112(*M*)		113
	I (%)	6	4	13	6	100	84		8
	m/e	114							
	I (%)	4							
(III)	*m/e*	37	38	39	42	43	45	57	58
	I (%)	4	12	29	5	17	18	16	13
	m/e	69	81	82	83	97	98	111	112
	I (%)	5	4	5	36	2	1	100	18
	m/e	113	126(*M*)		127	128			
	I (%)	10	82		9	5			
(V)	*m/e*	27	38	39	45	50	51	53	55
	I (%)	14	6	14	31	21	50	5	21
	m/e	56	69	71	76	77	78	99	105
	I (%)	5	5	10	8	73	14	6	100
	m/e	106	204(*M*)						
	I (%)	35	10						
(VI)	*m/e*	39	40	45	50	51	53	63	65
	I (%)	13	4	22	4	10	4	7	7
	m/e	69	73	77	89	91	96	97	98
	I (%)	5	5	7	6	10	6	67	5
	m/e	99	115	127	128	129	141	147	173
	I (%)	3	10	4	10	20	10	7	85
	m/e	174(*M*)		175	176				
	I (%)	100		14	5				
(VIII)	*m/e*	39	45	50	51	63	69	77	89
	I (%)	13	8	8	13	10	5	11	11
	m/e	102	115	118	121	134	139	165	189
	I (%)	6	9	6	14	10	3	5	8
	m/e	191	202	203	234	235	236(*M*)		237
	I (%)	12	10	5	13	8	100		20
	m/e	238							
	I (%)	6							
(IX)	*m/e*	39	45	50	51	63	69	77	89
	I (%)	13	9	8	13	10	3	6	3
	m/e	115	118	121	135	165	189	191	202
	I (%)	8	8	17	6	3	3	4	9
	m/e	203	221	234	235	236(*M*)		237	238
	I (%)	3	2	9	5	100		20	6
(X)	*m/e*	37	38	39	45	50	57	58	59
	I (%)	10	10	38	40	3	18	19	4
	m/e	69	73	79	81	82	83	84	85
	I (%)	8	8	9	8	6	75	5	3
	m/e	118(*M*)		119	120(*M*)		121	122	
	I (%)	100		8	33		2	2	
(XII)	*m/e*	37	38	39	44	45	49	50	57
	I (%)	10	12	25	6	25	5	6	23
	m/e	58	69	81	82	83	84	85	117
	I (%)	12	3	16	12	42	3	3	3
	m/e	119	162(*M*)		163	164(*M*)		165	166
	I (%)	3	100		8	98		5	4
(XIV)	*m/e*	37	38	44	45	49	50	56	69
	I (%)	15	13	5	19	5	4	6	3
	m/e	81	82	83	117	119	135	137	161
	I (%)	22	34	5	12	12	6	6	28
	m/e	162	163	164	240(*M*)		241	242(*M*)	
	I (%)	2	28	2	72		4	100	
	m/e	243	244(*M*)		245	246			
	I (%)	7	77		3	3			

(XIX)	*m/e*	37	38	44	45	48	56	57	67
	I (%)	53	10	45	10	19	8	27	7
	m/e	68	78	79	80	81	82	115	116
	I (%)	14	10	30	90	95	6	8	19
	m/e	117	118	122	123	126	135	137	138
	I (%)	8	19	8	8	10	8	8	8
	m/e	159	160	161	162	163	195	197	199
	I (%)	39	42	34	38	3	3	6	3
	m/e	238	239	240	241	242	243	244	318
	I (%)	15	55	30	100	18	57	5	17
	m/e	320	321	322	323	324			
	I (%)	47	4	44	3	19			
(XXIII)	*m/e*	37	38	39	44	45	49	50	53
	I (%)	33	44	50	10	44	9	7	11
	m/e	57	58	69	80	81	82	83	117
	I (%)	41	5	10	4	35	66	13	11
	m/e	119	161	163	178	180	189	190	191
	I (%)	11	6	6	2	2	81	5	83
	m/e	192	193	206	207	208	209	210	
	I (%)	6	4	97	6	100	8	5	
(XXVIII)	*m/e*	36	37	38	44	45	49	53	56
	I (%)	7	37	16	16	36	11	7	7
	m/e	57	68	69	79	80	81	82	83
	I (%)	13	7	23	7	15	48	22	7
	m/e	97	109	116	117	118	119	122	124
	I (%)	7	11	9	11	8	11	8	7
	m/e	125	135	137	149	151	160	161	162
	I (%)	10	8	6	6	6	33	30	33
	m/e	163	197	240	241	242	243	244	256
	I (%)	30	6	11	8	20	7	10	3
	m/e	258	260	267	268	269	270	271	284
	I (%)	5	3	28	4	52	6	30	50
	m/e	285	286	287	288	289	290		
	I (%)	4	100	6	53	5	4		
(XXIX)	*m/e*	36	37	44	45	56	68	69	79
	I (%)	13	14	24	20	6	11	8	10
	m/e	80	81	82	83	115	116	123	125
	I (%)	53	53	11	4	12	12	8	8
	m/e	159	160	161	162	163	195	197	237
	I (%)	40	23	43	34	6	5	5	10
	m/e	238	239	240	241	284	286	288	316
	I (%)	8	24	14	9	5	10	5	6
	m/e	318	320	322	336	338	345	346	347
	I (%)	21	21	8	3	3	26	6	63
	m/e	348	349	350	351	362	363	364	365
	I (%)	6	63	6	28	38	5	100	8
	m/e	366	367	368	369				
	I (%)	98	6	43	4				

* All peaks greater than 2% of the base peak (arbitrarily taken as 100%) are recorded.

TABLE 2

Exact mass measurements in spectra of compounds (I)—(XXXI)

Cpd.	m/e	Compn.	Cpd.	m/e	Compn.
(I)	45	CHS	(XXI)	100	C_4H_4OS
	53	C_4H_5	(XXII)	71	C_3H_3S
	67	C_5H_7		72	C_3H_4S
	69	C_3HS		100	C_4H_4OS
	77	C_6H_5		45	CHS
	85	C_4H_5S	(XXIII)	178/180	C_4H_3OSBr
(II)	50	C_4H_2	(XXVIII)	256/258/260	$C_4H_2OSBr_2$
	57	C_3HS			
	58	C_3H_2S	(XXIX)	334/336/338/340	C_4HOSBr_3
(III)	97	C_5H_5S			
(IV)	160	$C_{10}H_8S$	(XXX)	40	C_2H_2N
(VII)	89	C_7H_5		45	C_2H_5O
	102	C_8H_6		68	C_3H_2NO
	115	C_9H_7		72	C_2H_2NS (60%), C_3H_6NO (10%), $C_3H_4O_2$ (30%)
	121	C_7H_5S		73	C_3H_5NS
	128	$C_{10}H_8$		85	$C_3H_3NO_2$
	134	C_8H_6S		86	C_3H_4NS
(XI)	57	C_2HS		87	C_3H_5NS (70%), C_3H_3OS (30%)
	69	C_3H_2S		115	C_4H_5NOS
	73/75	C_2H_2Cl		142	$C_5H_4NO_2S$
	79	CSCl		143	$C_5H_5NO_2S$
	81	C_4HS (50%), CSCl (50%)	(XXXI)	77	C_6H_5
	82	C_4H_2S		108	C_6H_4S
(XII)	45	CHS		121	C_7H_5S
	57	C_3HS		127	$C_5H_3S_2$
	69	C_3HS		134	C_8H_6S
	83	C_4H_3S		140	$C_6H_4S_2$

measurements (Table 2). Secondly, it is inferred [2] that the presence of the thioformyl cation, *b* (*m/e* 45) in the mass spectrum of a thiophen indicates that either the C(2) or C(5) atom is bonded to hydrogen. This is not the case, as *b* (*m/e* 45) is present in the mass spectra (Figure 6 and Table 1) of all 2,5-disubstituted thiophens when either C(3) or C(4) is bound to hydrogen.

The mass spectra (Table 1 and Figure 2) of the acylthiophens (II)—(IV) exhibit base peaks due to the formation of the acylium cation *c*. Such behaviour is analogous to that observed for acylbenzenes.[7,8] Further loss of carbon monoxide from *c* forms the thienyl cation (*m/e* 83) which may then decompose either by loss of acetylene (probably to *d*, *m/e* 57) or CS (to the cyclopropenyl cation, *m/e* 39).

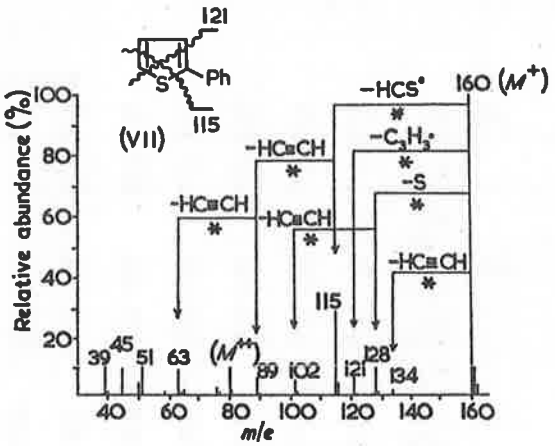


FIGURE 3

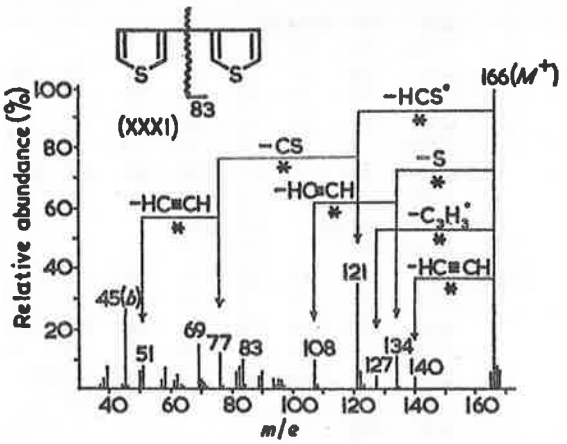


FIGURE 4

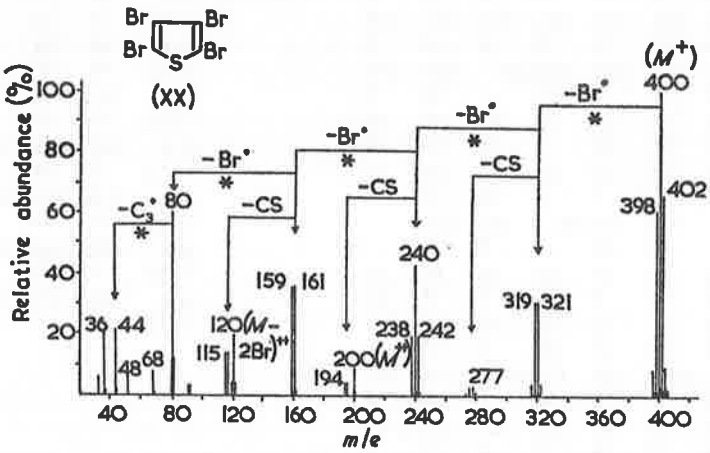


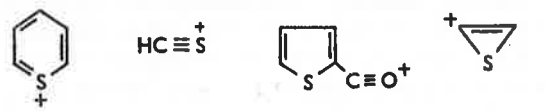
FIGURE 5

The mass spectra (Table 1 and Figure 2) of the acylthiophens (II)—(IV) exhibit base peaks due to the formation of the acylium cation *c*. Such behaviour is analogous to that observed for acylbenzenes.[7,8] Further loss of carbon monoxide from *c* forms the thienyl cation (*m/e* 83) which may then decompose either by loss of acetylene (probably to *d*, *m/e* 57) or CS (to the cyclopropenyl cation, *m/e* 39).

[7] V. H. Dibeler, R. M. Reese, and F. L. Mohler, *J. Chem. Phys.*, 1957, **26**, 304.

[8] S. Meyerson and P. N. Meyerson, *J. Amer. Chem. Soc.*, 1957, **79**, 1058.

The spectra of the acylthiophens (III) and (IV) are notable for the presence of skeletal rearrangement ions



a, *m/e* 97 *b*, *m/e* 45 *c*, *m/e* 111 *d*, *m/e* 57

which originate by loss of carbon monoxide with concomitant rearrangement of either Me (in III) or Ph

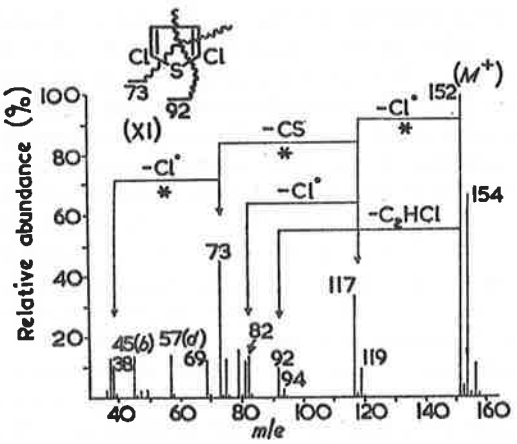


FIGURE 6

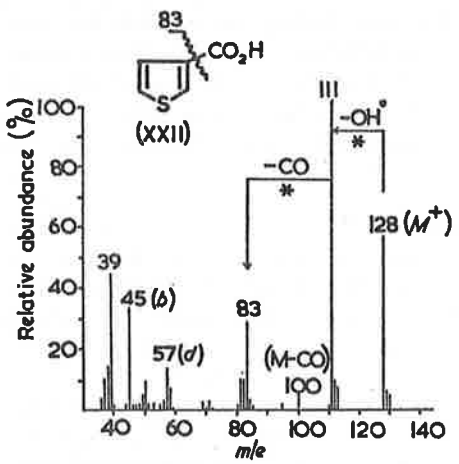


FIGURE 7

(in IV). This process is especially marked in the spectrum (Figure 2) of the phenyl derivative (IV), where it is substantiated by the presence of an appropriate metastable ion. This process has been reported,[9] and skeletal rearrangements involving the loss of CO or CO_2 from carbonyl compounds have been observed.[10-16] As analogous ions are rarely noted in the spectra of acylbenzenes [7,8] (benzophenone is an exception), it seems plausible, in this case, that their genesis should be by migration of the methyl or phenyl group to the electron-deficient heteroatom. As supporting evidence for this statement, it has been shown that the sulphur atoms in sulphides,[17] disulphides,[18] sulphones,[19,20] and sulphoxides [20] are involved in both skeletal rearrangements and molecular-ion rearrangements.

The spectra of the monosubstituted derivatives (V) and (VI) are recorded in Table 1. The spectrum of 2-benzylthiophen (VI), analogously to those of the alkylthiophens, shows pronounced β-cleavage to the

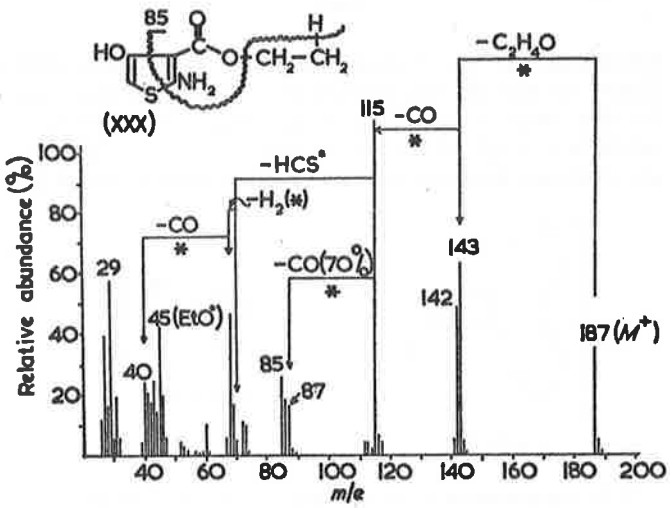


FIGURE 8

thiophen ring to form *a*, *m/e* 97 (67% of the base peak) whilst β-cleavage to the benzene ring to form the tropylium cation (*m/e* 91, $C_7H_7^+$) is minimal (10% of the base peak).

A very different situation is observed when the phenyl group is directly attached to the thiophen ring, as in (VII)—(IX). Here, the molecular ion may fragment in a variety of ways, and this is illustrated by the spectrum (Figure 3) of 2-phenylthiophen (VII). The fragmentation modes are summarised in the Scheme (structures are nominal) while high-resolution measurements (Table 2) confirm the compositions of the major fragment ions.

The most striking fragmentation of (VII) on electron impact involves the loss of sulphur from the molecular ion to give a species which may be represented as the phenylcyclobutadiene ion radical *h*. Corresponding loss of the heteroatom is not noted in the spectra of

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[10] J. H. Bowie, R. Grigg, S.-O. Lawesson, P. Madsen, G. Schroll, and D. H. Williams, *Chem. Comm.*, 1965, 403.
[11] J. H. Bowie, R. Grigg, S.-O. Lawesson, P. Madsen, G. Schroll, and D. H. Williams, *J. Amer. Chem. Soc.*, 1966, **88**, 1699.
[12] J. H. Bowie, D. H. Williams, P. Madsen, G. Schroll, and S.-O. Lawesson, *Tetrahedron*, 1967, **23**, 305.
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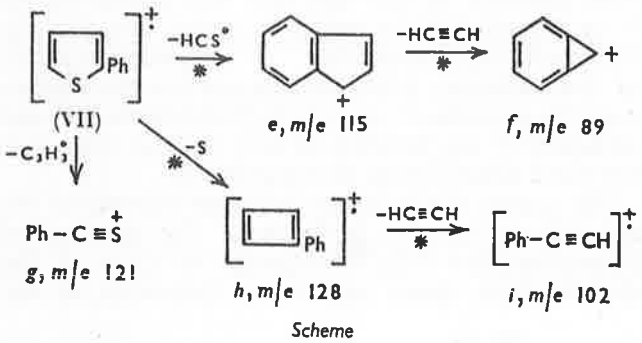
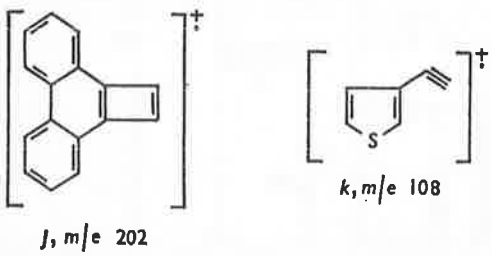
furan [21] or pyrrole,[22] again reflecting the unique properties of sulphur compounds when subjected to electron impact. This effect is more pronounced in the



Scheme

spectra of the two diphenylthiophens (VIII) and (IX) (Table 1) and ββ′-thienylthiophen (XXXI; Figure 4). In the case of 2,5-diphenylthiophen (IX) hydrogen sulphide instead of sulphur is lost from the molecular ion probably to form the condensed system *j* (*m/e* 202).



It is noteworthy that the mass spectra (Table 1) of the two diphenyl derivatives (VIII) and (IX) are almost identical (apart from small differences in the relative abundances of ions). Although it is reasonable that the spectrum of (VIII) should exhibit an M — HCS ion (*m/e* 191), such behaviour should not be exhibited in the spectrum of the 2,5-diphenyl analogue (IX). An M — HCS ion is observed in this spectrum, indicating that a phenyl migration has taken place to carbon [possibly C(3)] in order to allow this decomposition to occur. Such behaviour is not without precedent; thioannulenes fragment in this manner on electron impact,[23] while 2-phenylthiophen can be photochemically converted into 3-phenylthiophen.[24]

The mass spectrum (Figure 4) of (XXXI) is similar to those of the phenylthiophens (VII)—(IX) in that little α-cleavage (to yield the thienyl cation *m/e* 83) is observed. The prominent process is M^+ — HCS· — CS to form *m/e* 77 ($C_6H_5^+$) whose representation as the phenyl cation is supported by its characteristic loss of acetylene (substantiated by a metastable ion) to *m/e* 51 ($C_4H_3^+$). The process M^+ — S — CH≡CH [to *k* (*m/e* 108)] is again significant, so it appears that loss of sulphur from a thiophen system on electron impact occurs when a stable aromatic system is directly attached to the thiophen ring.

A wide variety of halogenated thiophens have been synthesised and their mass spectra determined. All the possible isomeric bromothiophens (XII)—(XX) were available, as well as the two chlorothiophens (X) and (XI). It is not possible to distinguish between the isomeric halogenothiophens by mass spectrometry, as their spectra are very similar. Consequently only one example of each series is recorded in Table 1. These spectra are readily interpretable, and in most cases the molecular ion is the base peak [except in (XIX) where the M^+ — Br· ion constitutes the base peak]. The major fragmentation process in the bromo-derivatives is M^+ — *n*Br·, where *n* equals the number of bromine substituents. The spectrum (Figure 5) of tetrabromothiophen (XX) illustrates this feature and demonstrates the ease with which bromine radicals are lost from heterocyclic systems on electron impact. The situation is more complex in the spectra of the chlorothiophens (X) and (XI). Here, as expected, C–Cl rupture is not as prominent as C–Br cleavage and this is reflected in the spectrum (Figure 6) of 2,5-dichlorothiophen (XI). In this spectrum, loss of the second chlorine radical is not favoured; instead the process M^+ — Cl· — CS — Cl· is preponderant. The compositions of the major ions in this spectrum have been established by exact mass measurements (Table 2), and the presence of *b* (*m/e* 45) in this spectrum should be noted.

The spectra (Figure 7) of the two thiophencarboxylic acids (XXI) and (XXII) are notable for two reasons. First, they are identical; secondly, they contain skeletal rearrangement ions due to the loss of CO with accompanying OH migration. The latter observation is striking because aryl carboxylic acids have not been observed to undergo skeletal rearrangement of this sort, and because both isomers undergo the rearrangement to the same extent. If the sulphur atom is involved in this rearrangement (which surely it must) then this indicates that C–S cleavage (in XXII) may have taken place in the molecular ion to allow OH migration to S. If this is so, then the molecular ion does not have the ground-state structure (cf. furan [6]).

To extend this investigation we studied some bromothiophencarboxylic acids (XXIII)—(XXIX). Again the spectra of the isomers are indistinguishable, and the main fragmentation is M^+ — OH· — CO — *n*Br·. All compounds have significant M — CO rearrangement ions and these processes are substantiated by appropriate metastable ions in the spectra of (XXVII) and (XXVIII). The relative abundances of these ions are in Table 3. There is no apparent correlation between relative abundance and structure, and it seems plausible that this is due to some type of rearrangement of the molecular ion.

Having now determined the fragmentation modes for a series of simple thiophen derivatives (see above and refs. 2—5*a*), we wish to see whether they can be extended (in combination with exact mass measurements) to

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[22] H. Budzikiewicz, C. Djerassi, A. H. Jackson, G. W. Kenner, D. J. Newman, and J. M. Wilson, *J. Chem. Soc.*, 1964, 1949.
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[24] H. Wynberg and H. van Driel, *J. Amer. Chem. Soc.*, 1965, **87**, 3999; *Chem. Comm.*, 1966, 203.

explain the spectrum of a complex thiophen (*e.g.*, XXX). This molecule on electron impact might be expected to fragment by concerted loss of ethanol by the "*ortho*-effect" [25] which operates for salicylates and anthranilates [25] and also for thiophen derivatives.[5] After this initial loss of ethanol, the spectrum should be that of a simple thiophen. The spectrum of (XXX) is illustrated and interpreted in Figure 8, and the high-resolution measurements are recorded in Table 2. The spectrum does not reflect the above expectations; instead the molecular ion specifically fragments by loss of C_2H_4O from the ester to give the corresponding formylthiophen (*m/e* 143) which fragments as earlier described. The overall process is $M^+ - C_2H_4O - CO - HCS^{\cdot} - H_2 - CO$ as indicated in Figure 8 and Table 2. The reason for this anomaly is not clear, but it is apparently an effect of the two *ortho*-substituents, and therefore care should always be exercised when extending simple fragmentation schemes to explain the spectra of complex molecules.

TABLE 3

Relative abundances of skeletal rearrangement ions in the mass spectra of thiophencarboxylic acids

Cpd.	(XXI)	(XXII)	(XXIII)	(XXIV)	(XXV)
$M - CO$ (%)	4	4	2	2	2
Cpd.	(XXVI)	(XXVII)	(XXVIII)	(XXIX)	
$M - CO$ (%)	5	5	6	3	

EXPERIMENTAL

Mass spectra were determined on a Hitachi–Perkin-Elmer RMU-6D mass spectrometer operating at 70 ev, with an inlet and source temperature of approximately 150°. Exact mass measurements were carried out at a resolution of 14,000 (10% valley definition) with an A.E.I. MS9 mass spectrometer with heptacosafluorotributylamine to provide reference masses. Exact mass measurements were correct to within 15 p.p.m.

Compounds were routinely checked for purity by nuclear magnetic resonance spectroscopy, mass spectrometry, and vapour-phase chromatography.

Compound (XII) was a purified commercial sample and the following compounds were prepared by reported procedures: I,[26] II,[27] III,[28] IV,[29] V,[30] VI,[31] VII,[32] VIII,[33] IX,[34] X,[35] XI,[36] XIII,[36] XIV,[37] XV,[38] XVI,[37] XVII,[39] XVIII,[37] XIX,[37], XX,[37] XXI,[40] XXII,[41] XXIII,[42] XXIV,[43] XXV,[38] XXVI,[42], XXVII,[44] XXVIII,[43] XXIX,[45] XXX,[46] XXXI,[47] and XXXII.[48]

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[6/1356 *Received, October 24th*, 1966]

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Electron Impact Studies. Part VIII.[1] Mass Spectra of Substituted Azobenzenes; Aryl Migration on Electron Impact

By **J. H. Bowie** and **G. E. Lewis**, Department of Organic Chemistry, University of Adelaide, South Australia
R. G. Cooks, University Chemical Laboratory, Lensfield Road, Cambridge

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Electron Impact Studies. Part VIII.[1] Mass Spectra of Substituted Azobenzenes; Aryl Migration on Electron Impact

By **J. H. Bowie** and **G. E. Lewis**, Department of Organic Chemistry, University of Adelaide, South Australia
R. G. Cooks, University Chemical Laboratory, Lensfield Road, Cambridge

The spectra of thirty-eight substituted azobenzenes are reported and discussed. The molecular ions are observed as pronounced peaks throughout, and the fragmentation processes are substantiated by exact mass measurements and by the presence of appropriate metastable ions. An approximately linear relationship is shown to exist between the relative ease of cleavage of C–N bonds in 3- and 4-monosubstituted azobenzenes and Hammett σ-values for those substituents, suggestive of some correlation between this mass-spectrometric process and ground-state chemistry. Without exception, the mass spectra of azobenzenes show the presence of skeletal rearrangement ions due to biphenylene, or substituted biphenylene radical ions.

ALTHOUGH the mass spectra of diazoethane,[2] diazocarbonyl compounds,[3] and azoferrocenes [4] have been discussed, no systematic survey of substituted azobenzenes has been reported. This Paper is concerned with the interpretation of the mass spectra (Table 1; Figures 1—6, 8—10) of the azobenzenes (I)—(XXXVIII). Although the compositions of many ions have been

[1] Part VII, J. H. Bowie, R. G. Cooks, P. Jakobsen, S.-O. Lawesson, and C. Nolde, preceding Paper.

[2] "Catalog of Mass Spectra Data," American Petroleum Institute Research Project 44, Carnegie Institute of Technology, Pittsburgh, spectrum no. 765.

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TABLE 1

Mass spectra of substituted azobenzenes; all ions greater than 2% of the base peak (arbitrarily taken as 100%) are recorded

(IX)	*m/e*	38	39	50	51	63	64	74	75
	I (%)	6	9	30	41	12	9	9	26
	m/e	76	77	78	90	105	106	152	153
	I (%)	31	100	8	5	30	4	16	4
	m/e	155	156	157	158	183	185	232	234
	I (%)	38	5	40	4	16	15	2	2
	m/e	260(*M*)		261	262(*M*)		263		
	I (%)	33		7	32		6		
(X)	*m/e*	38	39	50	51	52	57	62	63
	I (%)	8	11	22	58	6	7	6	11
	m/e	64	68	69	74	75	76	77	78
	I (%)	6	4	10	9	52	8	100	5
	m/e	94	95	96	105	123	124	151	152
	I (%)	5	93	11	22	38	3	3	4
	m/e	170	171	172	200(*M*)		201		
	I (%)	13	8	3	54		14		
(XI)	*m/e*	38	39	50	51	63	64	74	75
	I (%)	6	7	40	40	11	8	10	12
	m/e	76	77	78	105	127	151	152	153
	I (%)	66	100	9	32	5	7	19	4
	m/e	203	204	231	232	280	308(*M*)		309
	I (%)	66	8	30	2	3	93		14
(XIII)	*m/e*	30	39	50	51	63	64	74	75
	I (%)	6	7	28	33	7	9	6	15
	m/e	76	77	78	92	105	122	150	151
	I (%)	21	100	8	8	33	12	4	2
	m/e	152	227(*M*)		228				
	I (%)	5	30		5				
(XIV)	*m/e*	38	39	41	50	51	52	63	64
	I (%)	5	22	5	5	26	10	9	9
	m/e	65	66	77	78	91	92	93	105
	I (%)	50	8	34	5	7	100	11	3
	m/e	120	121	141	152	167	168	197(*M*)	
	I (%)	32	4	3	2	5	3	53	
	m/e	198							
		11							
(XV)	*m/e*	39	41	42	50	51	52	53	63
	I (%)	13	6	5	13	35	9	4	12
	m/e	64	65	66	76	77	76	79	80
	I (%)	13	26	5	9	75	18	42	5
	m/e	90	91	104	105	106	107	134	135
	I (%)	8	10	6	6	100	10	23	3
	m/e	141	152	167	182	197	211(*M*)		212
	I (%)	3	5	2	2	2	51		9
(XVI)	*m/e*	39	42	50	51	52	63	64	65
	I (%)	10	38	10	32	6	11	5	8
	m/e	76	77	78	79	80	90	91	92
	I (%)	8	58	20	23	4	8	16	9
	m/e	93	104	105	106	118	119	120	121
	I (%)	6	6	21	30	8	13	100	13
	m/e	148	151	152	153	180	181	196	197
	I (%)	17	2	3	2	2	2	2	2
	m/e	225(*M*)		226					
	I (%)	73		16					
(XVII)	*m/e*	39	42	50	51	52	63	65	76
	I (%)	7	5	5	18	4	9	18	7
	m/e	77	78	90	91	92	104	105	106
	I (%)	50	15	14	100	12	23	33	4
	m/e	115	119	129	152	153	154	155	165
	I (%)	6	6	6	7	9	5	14	7
	m/e	167	180	181	196	197	210	224	
	I (%)	10	6	8	96	17	13	7	
	m/e	301(*M*)		302					
	I (%)	83		18					
(XVIII)	*m/e*	39	45	50	51	63	64	69	76
	I (%)	7	6	16	36	13	5	8	9
	m/e	77	78	82	91	105	107	108	134
	I (%)	100	8	6	11	26	5	7	38
	m/e	135	152	162	210	213	239(*M*)		240
	I (%)	5	5	4	3	4	49		8
(XXI)	*m/e*	39	50	51	63	65	75	76	77
	I (%)	9	12	30	4	23	6	10	100
	m/e	78	104	105	121	122	148	151	152
	I (%)	8	4	13	15	2	4	4	3
	m/e	181	198	209	226(*M*)				
	I (%)	2	2	2	15				
(XXII)	*m/e*	39	50	51	64	65	76	77	78
	I (%)	5	9	20	5	13	11	100	8
	m/e	91	93	105	106	121	122	131	141
	I (%)	7	9	28	6	36	5	3	3
	m/e	151	152	153	177	181	198	209	225
	I (%)	3	13	8	7	7	6	6	2
	m/e	254(*M*)		255					
	I (%)	25		5					
(XXVIII)	*m/e*	39	41	51	63	65	66	89	90
	I (%)	17	6	9	9	42	3	9	7
	m/e	91	92	119	152	165	166	167	195
	I (%)	100	9	11	8	8	7	8	3
	m/e	210(*M*)		211					
	I (%)	36		6					
(XXXI)	*m/e*	38	39	50	51	52	63	64	65
	I (%)	6	6	6	9	7	17	34	10
	m/e	76	77	78	79	92	93	107	108
	I (%)	6	73	13	6	52	7	100	13
	m/e	135	136	156	184	199	227	242(*M*)	
	I (%)	40	6	3	3	3	3	58	
	m/e	243							
	I (%)	13							
(XXXII)	*m/e*	39	50	51	63	64	74	75	76
	I (%)	9	36	7	17	19	9	58	67
	m/e	77	92	106	122	123	150	151	
	I (%)	10	27	8	100	16	60	7	
	m/e	272(*M*)		273					
	I (%)	48		8					
(XXXV)	*m/e*	39	50	51	63	64	65	66	74
	I (%)	12	22	20	12	9	42	5	9
	m/e	75	76	77	93	111	112	113	114
	I (%)	50	22	14	25	100	10	37	5
	m/e	121	122	139	140	141	149	151	152
	I (%)	37	4	60	6	24	13	3	21
	m/e	153	181	215	216	232	234	260(*M*)	
	I (%)	4	9	8	5	2	2	42	
	m/e	261	262(*M*)						
	I (%)	7	16						
(XXXVI)	*m/e*	39	50	51	63	76	77	78	104
	I (%)	4	8	21	5	18	100	8	6
	m/e	105	106	167	181	182	209	226	255
	I (%)	40	3	6	43	5	4	3	2
	m/e	256	257	286(*M*)		287			
	I (%)	2	2	36		7			

TABLE 1 (*Continued*)

(XXXVII)	*m/e*	50	51	76	77	78	105	126	127
	I (%)	6	24	6	100	12	20	10	7
	m/e	139	151	152	153	168	180	181	204
	I (%)	3	8	77	12	4	20	4	3
	m/e	227	257	258	285	362(*M*)		363	
	I (%)	3	58	10	3	40		11	
(XXXVIII)	*m/e*	39	50	51	64	65	75*	76	77
	I (%)	7	4	20	5	5	6	4	100
	m/e	78	89	90	105	106	121	139	152
	I (%)	10	11	10	27	4	6	4	6
	m/e	165	166	167	194	228	239	241	271
	I (%)	56	44	9	17	3	3	3	50
	m/e	272	299	376(*M*)		377			
	I (%)	11	5	40		13			

(XL)*	*m/e*	50	51	52	63	64	77	78	92
	I (%)	5	14	5	8	12	10	12	31
	m/e	101	120	126	127	128	137	138	144
	I (%)	6	6	12	100	15	9	14	5
	m/e	145	155	156	263	264	265	266	
	I (%)	8	13	5	7	19	30	5	

($^3H_1 = 13$; $^3H_2 = 34$; $^3H_3 = 53\%$)

* Because of the complexity of this spectrum only peaks of abundance greater than 5% of the base peak are recorded.

established by exact mass measurements (Table 2), the structures of these are generally not known. However, nominal structures have been written in order that the fragmentation processes may be related to (or rationalised with) the structures of the intact molecules. The presence of a metastable ion for a process (indicated either in the text or a Figure) is depicted by an asterisk (*).

TABLE 2

Exact mass measurements in the spectra of (I)—(XXXIX)

Cpd.	*m/e*	Composition
(I)	105	$C_6H_5N_2$
	128	$C_{10}H_8$
	152	$C_{12}H_8$
	153	$C_{12}H_9$
	154	$C_{12}H_{10}$
(IV)	165	$C_{13}H_9$
	167	$C_{13}H_{11}$
(XII)	92	C_6H_4O (80%) C_6H_6N (20%)
	105	$C_6H_5N_2$
	122	$C_6H_4NO_2$
	150	$C_6H_4N_2O_2$
	152	$C_{12}H_8$
(XVII)	104	C_7H_6N
	105	C_7H_7N (90%) $C_6H_5N_2$ (10%)
(XXI)	93	C_6H_7N (45%) C_6H_5O (55%)
	105	$C_6H_5N_2$
	121	$C_7H_5O_2$
	153	$C_{12}H_9$
	181	$C_{13}H_9N_2$ (60%) $C_{13}H_9O$ (40%)
	198	$C_{13}H_{10}O_2$
(XXIV)	103	$C_7H_3O_2$
	104	$C_7H_4O_2$
	105	$C_6H_5N_2$
	121	$C_7H_5O_2$ (95%) C_6H_9O (5%)
	149	$C_9H_9O_2$
	150	$C_9H_{10}O_2$
	151	$C_{12}H_7$
(XXIV)	152	$C_{12}H_8$
	153	$C_{12}H_9$
	177	$C_9H_9N_2O_2$
	181	$C_{13}H_9O$
(XXVI)	65	C_5H_5
	93	C_6H_5O (95%) C_6H_7N (5%)
	105	$C_6H_5N_2$
	142	$C_{11}H_{10}$
	152	$C_{12}H_8$
	169	$C_{12}H_9O$
	170	$C_{12}H_{10}O$
(XXVII)	92	C_6H_4O
	141	$C_{11}H_9$
	169	$C_{12}H_9O$
(XXXI)	171	$C_{12}H_{11}O$
	199	$C_{13}H_{11}O_2$
(XXXIII)	93	C_6H_7N
	105	$C_6H_5N_2$ (60%) C_7H_5O (40%)
	106	C_7H_6O
	142	C_6H_5Br
	170	C_6H_5OBr
(XXXIV)	171	C_6H_6NBr
	173	
(XXXV)	93	C_6H_5O (90%) C_6H_7N (10%)
	121	$C_7H_5O_2$
(XXXVI)	226	$C_{18}H_{10}$
	256	$C_{18}H_{12}N_2$
(XXXIX)	64	C_5H_4
	92	C_6H_4O
	143	$C_{10}H_9N$

The purpose of this study was to investigate the basic fragmentation processes for substituted azobenzenes, to ascertain whether the position of the substituents on the benzene rings may be determined by mass spectrometry, and to study the nature and genesis of any skeletal rearrangement ions.

(I)

(II) 2-Me	(XIV) 4-NH_2	(XXV) 2-OH
(III) 3-Me	(XV) 4-NHMe	(XXVI) 4-OH
(IV) 4-Me	(XVI) 4-NMe_2	(XXVII) 4-OMe
(V) 2-Cl	(XVII) 4-N(Me)CH_2Ph	(XXVIII) 2,2'-Me_2
(VI) 3-Cl	(XVIII) 4-SCN	(XXIX) 3,3'-Me_2
(VII) 4-Cl	(XIX) 2-CO_2H	(XXX) 4,4'-Me_2
(VIII) 3-Br	(XX) 3-CO_2H	(XXXI) 4,4'-$(OMe)_2$
(IX) 4-Br	(XXI) 4-CO_2H	(XXXII) 4,4'-$(NO_2)_2$
(X) 4-F	(XXII) 2-CO_2Et	(XXXIII) 4-Br-2-OMe
(XI) 4-I	(XXIII) 3-CO_2Et	(XXXIV) 4-Br-2'-OMe
(XII) 3-NO_2	(XXIV) 4-CO_2Et	(XXXV) 4-Cl-2'-CO_2H
(XIII) 4-NO_2		

PhN=N·(p-C_6H_4)·N=NPh (XXXVI)
PhN=N·(p-C_6H_4)·(p-C_6H_4)·N=NPh (XXXVII)
PhN=N·(p-C_6H_4)·CH_2·(p-C_6H_4)·N=NPh (XXXVIII)
2-MeO·C_6H_4·N=N·2-naphthyl (XXXIX)

Azobenzenes fragment in a well defined and characteristic manner on electron impact. In general, the position of substituents on the benzene rings cannot be distinguished by mass spectrometry, except for the cases of 2-OMe and 2-CO_2Et substituents which exhibit

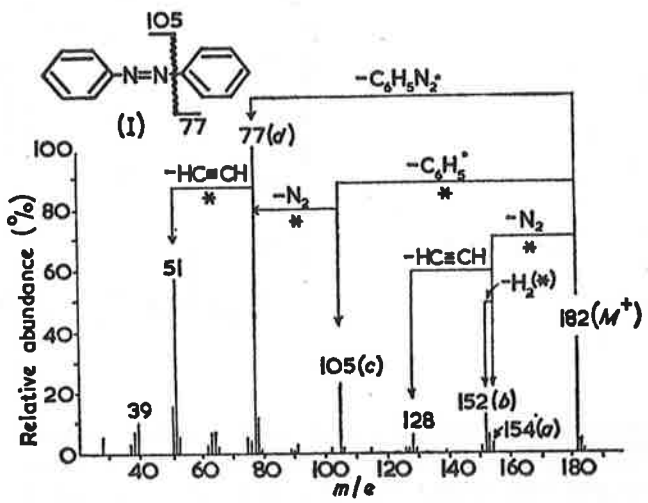


FIGURE 1

[a] F. W. McLafferty, "Mass Spectrometry of Organic Ions," Academic Press, New York, 1963, p. 337.

significant " *ortho*-effects " (see ref. 5). Without exception, all azobenzenes show skeletal-rearrangement ions in their mass spectra. These ions arise by loss of nitrogen (together with the various substituents) from the molecular ions.

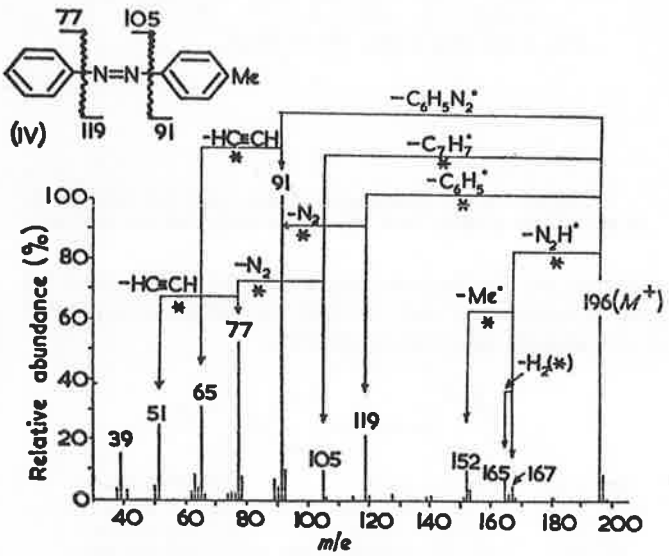
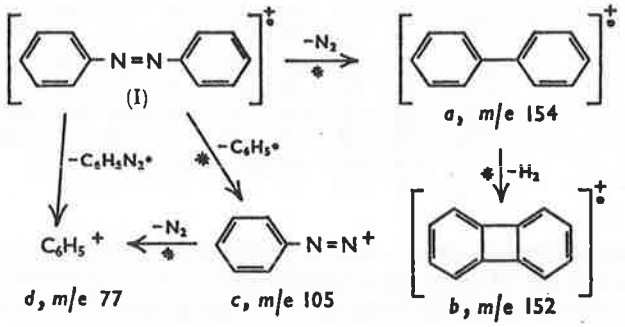


FIGURE 2

The mass spectrum (Figure 1) of azobenzene (I) illustrates characteristic fragmentation processes which are common to all azobenzene derivatives. These processes are summarised in Scheme 1 and Figure 1. The preponderant process is cleavage of the C–N bond to give both *d* (*m/e* 77) and *c* (*m/e* 105). The cation *c* may further decompose by loss of nitrogen to furnish the phenyl cation *d* (*m/e* 77). The most striking feature in the spectrum of azobenzene is the presence of the skeletal rearrangement ions *a* (*m/e* 154) and *b* (*m/e* 152). Skeletal rearrangements of this type have not been reported for nitrogen compounds, but are common in the spectra of diaryl disulphides,[6] diaryl sulphones,[7,8]



Scheme 1

and diaryl sulphoxides.[8] It is assumed[6] that their genesis occurs by ionisation of a double bond in the aromatic ring to furnish electron-deficient centres which are available for the attack of the incipient radical. It should be noted that these rearrangements are all low-energy processes; in the case of azobenzene they occur even at an energy of 15 ev.

The monosubstituted azobenzenes (II)—(XXVII) behave similarly on electron impact. The spectra of (IV), (VII), (XXIV), (XXVI), and (XXVII) are in Figures 2—6, and those of (IX)—(XI), (XIII)—(XVIII), (XXI), and (XXII) are in Table 1. Because of the similarity of the spectra of the isomeric monosubstituted azobenzenes (small differences are sometimes observed

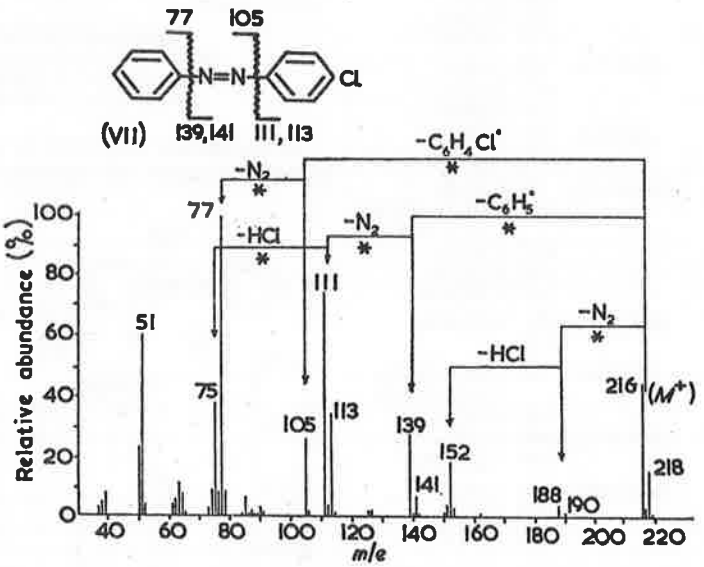


FIGURE 3

[6] J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, G. Schroll, and D. H. Williams, *J. Chem. Soc.* (*B*), 1966, 946.

[7] S. Meyerson, H. Drews, and E. K. Fields, *Analyt. Chem.*, 1964, **36**, 1294.

[8] J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, C. Nolde, and D. H. Williams, *Tetrahedron*, 1966, **22**, 3515.

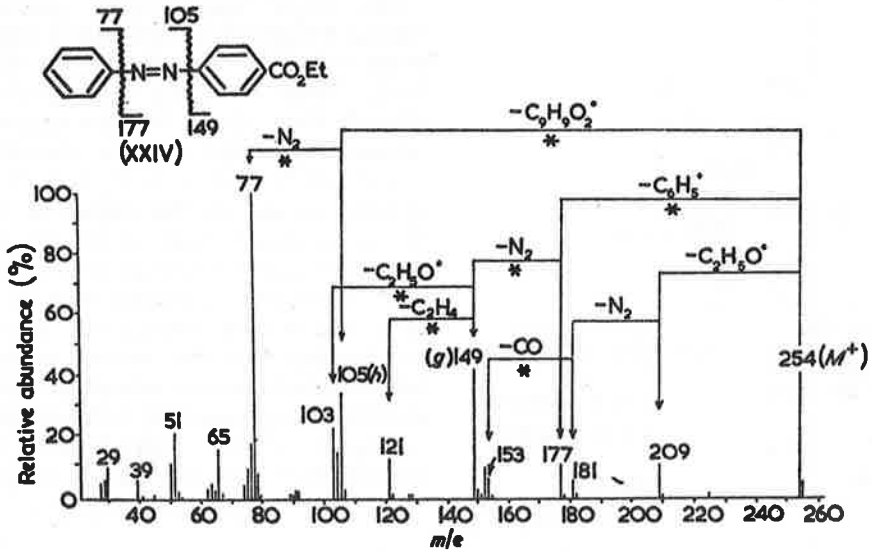


FIGURE 4

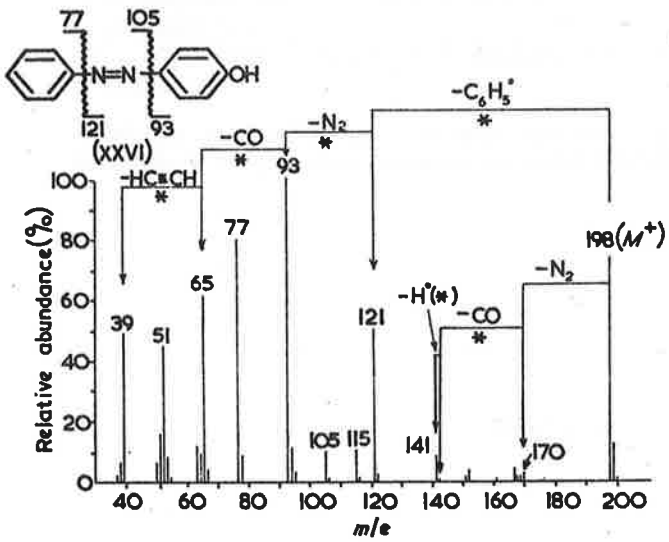


FIGURE 5

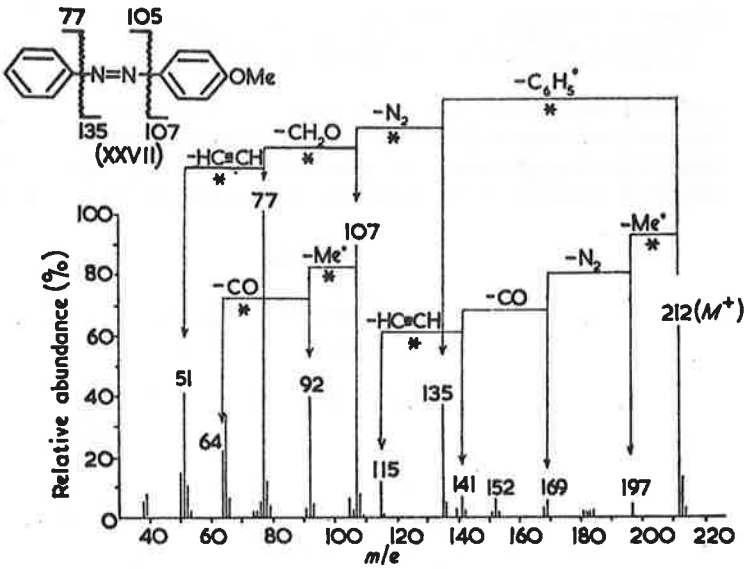
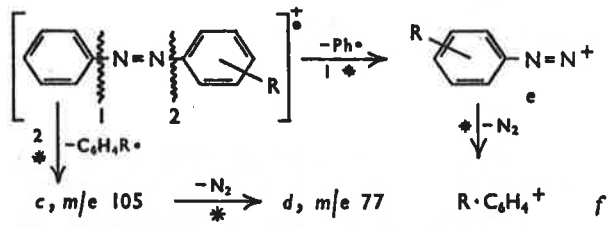


FIGURE 6

in the relative abundances of some ions) only the spectrum of the *para*-isomer of each group is reported in Table 1. As a compendium of the fragmentation



Scheme 2

processes of substituted benzenes is available,[9] no discussion of these processes is necessary here. Instead, particular processes are indicated in Figures 2—6 and a general summary is recorded in Scheme 2.

The skeletal rearrangements observed for the various monosubstituted azobenzenes generally occur by different fragmentations depending on the nature of the substituent. However, all fragmentations involve the loss of nitrogen. These fragmentations are summarised in Figures 2—6. The biphenylene radical ion *b* (*m/e* 152) is observed in all mass spectra, and is often produced by the general process $M^+ - (R^\bullet + H^\bullet + N_2)$ (*e.g.*, the monohalogenoazobenzenes), the relative decomposition order depending on the nature of the substituent. The compositions of many of the fragment ions involved in these rearrangements have been established by exact mass measurements (Table 2). It is of interest to

[9] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, San Francisco, 1964.

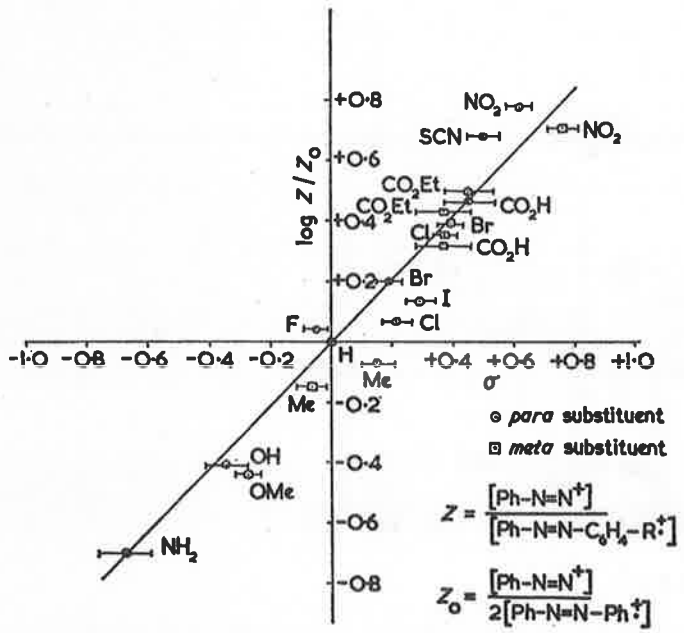


FIGURE 7 Correlation of Hammett σ-values with the relative abundances of PhN=N⁺ ions (*m/e* 105) in the spectra of *meta*- and *para*-monosubstituted azobenzenes ($\rho = 1{\cdot}05 \pm 0{\cdot}1$)

consider the similar spectra (Figure 5) of the monohydroxyazobenzenes (XXV) and (XXVI) where skeletal rearrangement processes of increased complexity are observed because of the tendency of the phenol (R = OH) to fragment preferentially by loss of carbon monoxide rather than by loss of a hydroxyl radical.[10] In this case the skeletal rearrangement process is mainly $M^+ - N_2 - CO - H^{\cdot} - HC{\equiv}CH$, as shown by exact mass measurements (Table 2). Even here, a small peak due to *b* (*m/e* 152) is observed in the spectrum.

The major fragmentation processes indicated in Scheme 2 originate by cleavage of either C–N bond (processes 1 and 2). Examination of the spectra (Figures 2—6; Table 1) of the monosubstituted azobenzenes (II)—(XXVII) shows that the relative extents of these processes [*i.e.*, the relative abundances of the ions *c* (Ph–N=N⁺) and *e* (R–C_6H_4–N=N⁺) in the various spectra] depend on the nature of the substituent R. It has previously been shown for acetophenones and benzophenones [11,12] that electron impact fragmentations may be related to ground-state processes. In these cases, the relative abundances of the acetyl (*m/e* 43) and benzoyl (*m/e* 105) cations in the various spectra may be quantitatively related to Hammett σ-values by plotting an expression log Z/Z_0 against σ. The theoretical aspects of this treatment have been discussed by McLafferty.[12] For the case of acetophenones,

$$Z = \frac{\text{Rel. abundance of MeCO}^+ \text{ in the spectrum of R–C}_6\text{H}_4\text{–CO–Me}}{\text{Rel. abundance of the molecular ion}}$$

and

$$Z_0 = \frac{\text{Rel. abundance of MeCO}^+ \text{ in the spectrum of acetophenone}}{\text{Rel. abundance of the acetophenone molecular ion}}$$

This treatment may be adopted for *meta*- and *para*-monosubstituted azobenzenes, with respect to either of the ions *c* (Ph–N=N⁺) or *e* (R–C_6H_4–N=N⁺). In each case a correction must be made to the Z_0 term, as two ions *c* are produced from the azobenzene molecular ion (see Figure 7). For ion *c*, the plot (Figure 7) of log Z/Z_0 against σ shows an approximately linear correlation. A similar plot for the various ions *e* gives an inverse

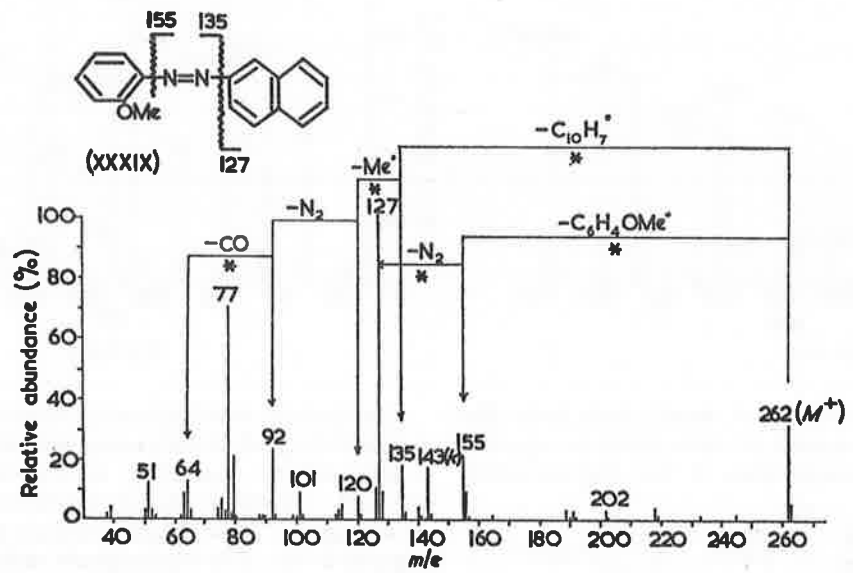


FIGURE 8

[10] T. Aczel and H. E. Lumpkin, *Analyt. Chem.*, 1960, **32**, 1819.
[11] F. W. McLafferty, *Analyt. Chem.*, 1959, **31**, 477.
[12] M. M. Bursey and F. W. McLafferty, *J. Amer. Chem. Soc.*, 1966, **88**, 4484.

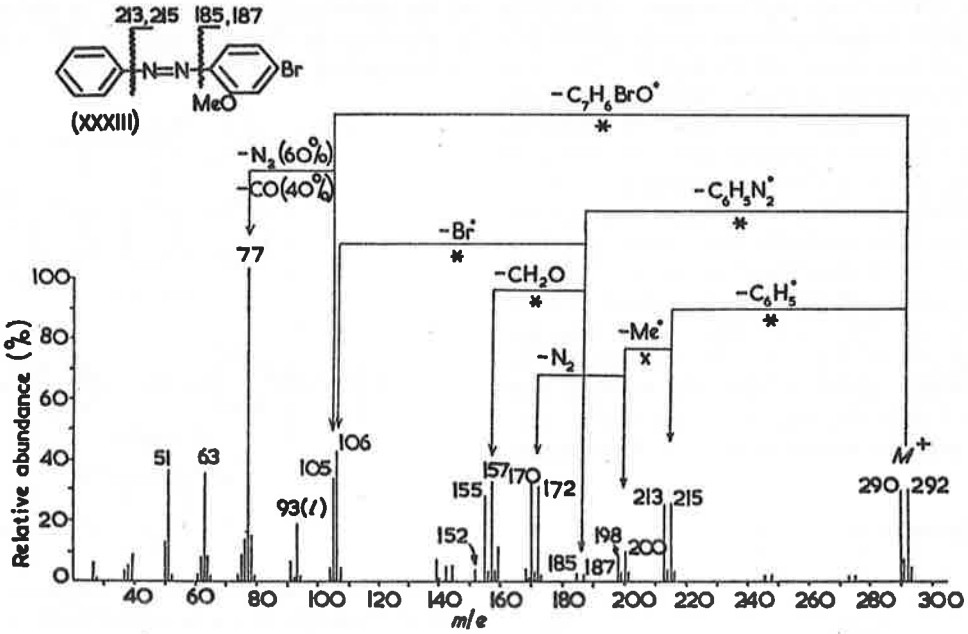


FIGURE 9

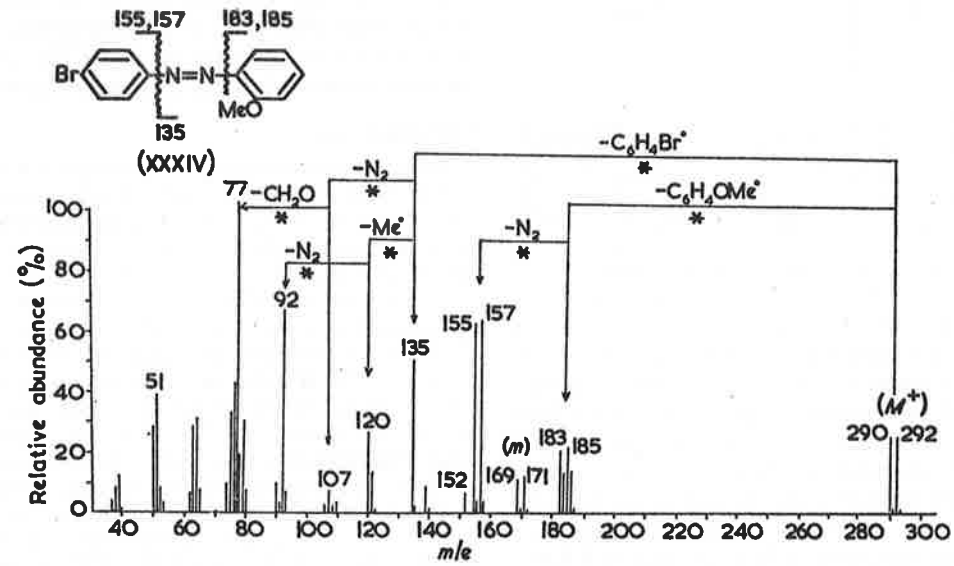
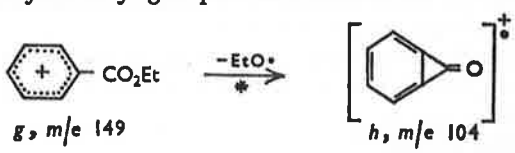


FIGURE 10

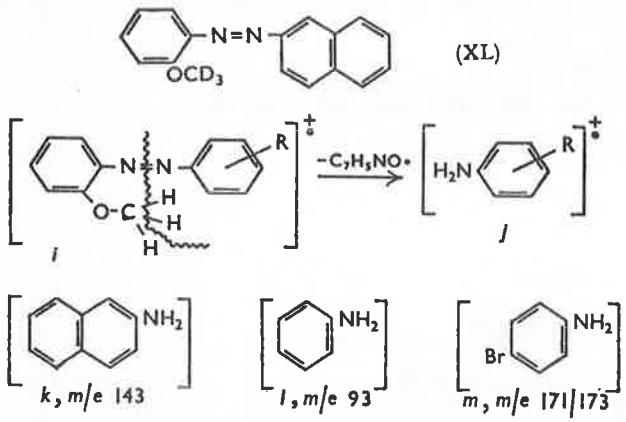
slope (to that in Figure 7). However, in this case the scatter of points is more pronounced, presumably because of the different stabilities of the ions *e*. Therefore C–N cleavages suffered by monosubstituted azobenzenes on electron impact are related semiquantitatively to solution chemistry.

There are two series of monosubstituted azobenzenes in which the spectra of the *ortho*-isomers are subtly different from those of the other isomers. In the case of the ethoxycarbonyl derivatives (XXII)—(XXIV), the major difference between the spectrum of the *para*-isomer (XXIV) (Figure 4) and the *ortho*-isomer (XXIII) (Table 1) is that the ion *g* (*m/e* 149) (44% of the base peak; Figure 4), together with its fragment ions *m/e* 104 (probably *h*) and *m/e* 103 (C_7H_3O), is entirely absent in the spectrum of the *ortho*-isomer. The reason for this difference is not clear; nevertheless, the observation may be used to detect the presence of the 2-ethoxycarbonyl group in an azobenzene.



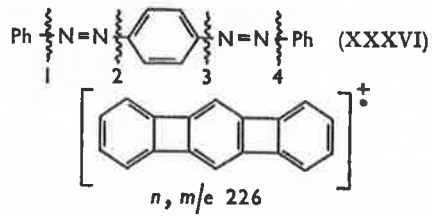
A more positive distinction can be made for a 2-methoxy substituent, because an additional ion appears in the spectra of 2-methoxyazobenzenes which is absent in the spectra of the 4-methoxy-analogues. The spectrum of 4-methoxyazobenzene (XXVII) is illustrated in Figure 6. 2-Methoxyazobenzene was not available,

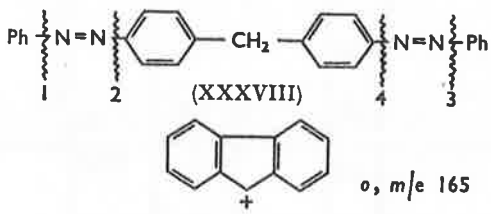
but the spectra of the naphthyl analogue (XXXIX) and the substituted 2-methoxyazobenzenes (XXXIII) and (XXXIV) are reproduced in Figures 8—10. The spectrum of a 2-methoxyazobenzene shows a significant peak due to the amine radical ion *j* which is produced by N=N cleavage with two hydrogens from the methoxyl group transferring to the β-nitrogen atom (see *i* ⟶ *j*). This has been substantiated by the spectrum of the trideuterio-derivative (XL) (see Table 1 for isotopic purities) where *k* (*m/e* 143) shifts quantitatively to *m/e* 144 and 145 (from a comparison of the isotopic purities of both these peaks and the molecular ion). Such ions are observed in Figures 8—10 [*viz.*, in the spectra of (XXXIX), (XXXIII), and (XXXIV), the relevant ions are *k* (*m/e* 143), *l* (*m/e* 93), and *m* (*m/e* 171/173), respectively] and are characteristic of the 2-methoxyl-substituent.



The spectra (Table 1) of the symmetrically disubstituted azobenzenes (XXVIII)—(XXXII) are unexceptional in that C–N cleavage (Scheme 2) produces the same ion *e* from both sides of the molecule. The spectra (Table 1; Figures 9 and 10) of the unsymmetrically disubstituted azobenzenes (XXXIII)—(XXXV) are more complex because C–N fission by processes 1 and 2 (Scheme 2) produces different ions *e* which fragment independently according to the nature of the substituent. The spectra (Figures 9 and 10) of the two bromo-2-methoxyazobenzenes (XXXIII) and (XXXIV) illustrate the ease with which isomers containing both substituents on one ring can be differentiated from those containing one substituent on each ring. All exact mass measurements for these spectra are recorded in Table 2.

Finally, the spectra (Table 1) of compounds containing two azo linkages show some interesting features. Compound (XXVI) fragments characteristically by the cleavages 1—4 [see (XXXVI)] with the ultimate formation of the phenyl cation *d* (*m/e* 77). A rearrangement peak is observed in this spectrum at $M - N_4H_4$ probably corresponding to an ion *n* (*m/e* 226).





The compound (XXXVIII) fragments in a slightly different manner [1—4 in (XXXVIII)] on electron impact, with the formation of an ion *m/e* 166 ($C_{13}H_{10}^{+\cdot}$) which on the loss of a hydrogen radical yields the fluorene cation *o* (*m/e* 165; 56% of the base peak). All processes indicated for the spectra of (XXXVI) and (XXXVIII) are substantiated by appropriate metastable ions.

EXPERIMENTAL

All mass spectra were determined with a Hitachi–Perkin-Elmer RMU-6D mass spectrometer operating at 75 ev. The spectra of the monosubstituted azobenzenes were carefully measured under identical instrument conditions, *viz.*, source and inlet system at 150° ± 5°, and identical sample pressures. The spectra of other azobenzenes were determined with the inlet system and source between 200 and 250°. Exact mass measurements were determined with an A.E.I. MS 9 mass spectrometer using a resolution of 14,000 (10% valley definition) with heptacosafluorotributylamine providing the reference masses. All exact mass measurements were correct to 15 p.p.m.

All the compounds employed were available from previous investigations, as indicated: (I)—(IV) and (XXVIII)—(XXX);[13] (V)—(VII), (XI), and (XIX)—(XXIV);[14] (VIII)—(X), (XXVI), (XXVII), (XXXI), and (XXXII);[15] (XII) and (XIII);[16] (XIV)—(XVII);[17] (XXV), (XXXIII), (XXXIV), and (XXIX);[18] (XXXVI) and (XXXVII);[19] (XXXV);[20] (XXXVIII).[21]

The labelled compound (XL) was prepared by the fusion of *o*-nitrophenyl trideuteriomethyl ether (cf. ref. 22) ($^2H_1 = 11$; $^2H_2 = 35$; $^2H_3 = 51\%$) and 2-naphthylamine with sodium hydroxide (cf. ref. 18).

One of us (R. G. C.) acknowledges the award of an Elsie Ballot Fellowship.

[6/1408 *Received, November 4th*, 1966]

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[16] G. M. Badger, C. P. Joshua, and G. E. Lewis, *Austral. J. Chem.*, 1965, **18**, 1639.
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ELECTRON IMPACT STUDIES—IX[1]

MASS SPECTRA OF ARYLSULPHINYLAMINES SKELETAL REARRANGEMENT ON ELECTRON IMPACT

J. H. BOWIE

Department of Organic Chemistry, The University of Adelaide, Adelaide, South Australia

F. C. V. LARSSON, G. SCHROLL, S.-O. LAWESSON

Department of Organic Chemistry, The University of Aarhus, Aarhus C, Denmark

and

R. G. COOKS

University Chemical Laboratory, Lensfield Road, Cambridge, England

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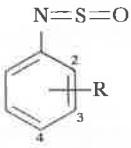
Abstract—The mass spectra of sixteen arylsulphinylamines are reported and discussed. The spectra exhibit pronounced molecular ions and large skeletal rearrangement fragments. The fragmentation modes have been substantiated by high resolution measurements, appropriate metastable ions and deuterium labelling studies. In several cases 'ortho effects' enable the determination of both the position and nature of the ortho substituent in substituted sulphinylanilines.

THE MASS spectra of thiophenols,[2] arylthioethers,[3] disulphides,[4] sulphones[5-8] and sulphoxides[5,6] have been reported. Large rearrangement ions are observed in the spectra of diaryl disulphides, arylsulphones and arylsulphoxides. Although the mass spectra of two perfluoroalkyl sulphinylamines have recently been determined,[9] no study of arylsulphinylamines has been reported.

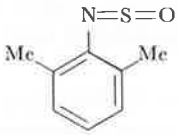
Because of our interest in the skeletal rearrangement processes which are observed in the spectra of sulphones[5-8] and sulphoxides[5,6] we have synthesized a series of sulphinylamines and have determined their mass spectra. This paper is concerned with the investigation of the mass spectra (Figs 1–8 and Table 1) of the sulphinylamines I–XVI. Although exact mass measurements (Table 2) establish the compositions of many fragment ions in the spectra, specific structures written for fragment

[1] Part VIII. J. H. Bowie, R. G. Cooks and G. E. Lewis, *J. Chem. Soc.* (B), in press.
[2] J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, G. Schroll and D. H. Williams, *Acta. Chem. Scand.* in press.
[3] J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen and D. H. Williams, *J. Chem. Soc.* (B), 951 (1966).
[4] J. H. Bowie, D. H. Williams, S.-O. Lawesson, J. Ø. Madsen, C. Nolde and G. Schroll, *J. Chem. Soc.* (B), 946 (1966).
[5] S. Meyerson, H. Drews and E. K. Fields, *Analyt. Chem.* **36**, 1294 (1964).
[6] J. Ø. Madsen, C. Nolde, S.-O. Lawesson, G. Schroll, J. H. Bowie and D. H. Williams, *Tetrahedron Letters* 4377 (1965).
[7] J. H. Bowie, D. H. Williams, S. O. Lawesson, J. Ø. Madsen, C. Nolde and G. Schroll. *Tetrahedron* **22**, 3515 (1966).
[8] E. K. Fields and S. Meyerson, *J. Am. Chem. Soc.* **88**, 2836 (1966).
[9] M. Lustig, *Inorg. Chem.* **5**, 1317 (1966).

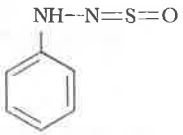
ions are nominal only, but serve to relate the fragmentation modes to the structure of the molecule in the ground state.[10,11] The presence of an asterisk either in the text or a figure represents the presence of an appropriate metastable ion for the process indicated.



	R
I	H
II	2-Cl
III	3-Cl
IV	4-Cl
V	2-CO_2Me
VI	3-CO_2Me

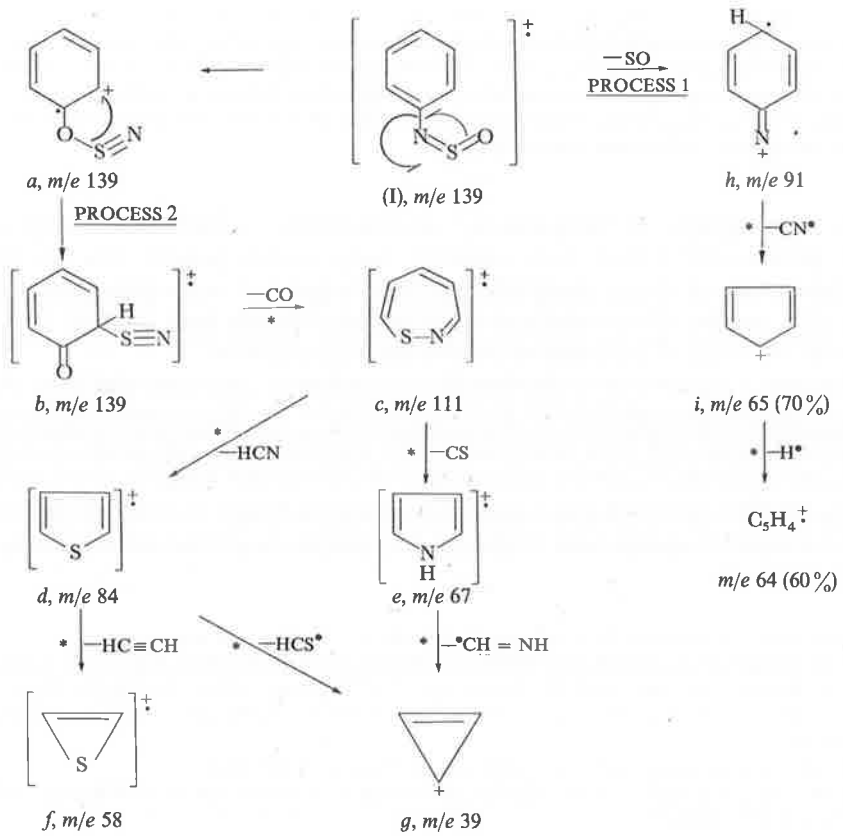


VII	2-Me
VIII	3-Me
IX	4-Me
X	2-OMe



XI	2-OCD_3
XII	3-OMe
XIII	4-OMe
XIV	3-NSO

Scheme 1



[10] J. Monigny, L. Brakier and L. D'or, *Bull. Classe, Sci. Acad. roy. Belg.* **48**, 1002 (1962).
[11] W. H. Pirkle, *J. Am. Chem. Soc.* **87**, 3022 (1965).

TABLE 1. MASS SPECTRA OF SULPHINYLAMINES*

III *m/e*	37	38	39	45	48	49	50	51	52	61	62	63	64	73	74	75	83	89	90	98	
I(%)	19	24	33	25	14	7	12	9	6	13	21	48	24	10	8	16	7	13	52	7	
	99	101	110	111	112	118	120	125	127	138	139	140	145	$173(M^+)$							
	24	12	56	8	4	11	4	13	13	100	12	6	4	63							
	174	$175(M^+)$																			
	4	24																			
IV *m/e*	37	38	39	45	48	49	50	51	52	61	62	63	64	65	73	74	75	83	89	90	
I(%)	15	19	31	15	13	6	15	9	4	12	23	54	29	8	12	8	14	6	12	54	
	91	92	98	99	100	101	110	111	118	120	125	127	129	138	139	140	145				
	4	4	5	15	4	7	49	6	12	3	20	23	6	100	7	5	6				
	$173(M^+)$	174	$175(M^+)$																		
	54	4	20																		
VI *m/e*	15	29	37	38	39	45	48	50	51	52	59	62	63	64	69	75	76	77	78	80	
I(%)	18	9	10	12	47	12	13	20	13	8	13	11	54	30	6	8	10	8	12	21	
	83	90	92	110	111	138	139	166	167	168	182	$197(M^+)$	198	199							
	14	30	11	34	13	68	6	100	16	7	10	58	8	4							
VIII *m/e*	37	38	39	45	48	50	51	52	53	62	63	64	65	66	75	77	78	79	80	81	
I(%)	5	11	57	13	13	18	34	24	9	8	18	13	30	10	12	36	38	18	12	11	
	85	91	92	97	98	104	105	110	124	125	126	136	137	138	139	152					
	10	18	38	16	19	24	6	16	24	19	6	8	5	38	6	8					
	$153(M^+)$	154	155																		
	100	9	5																		
XI† *m/e*	26	27	28	30	37	38	39	44	45	48	50	51	52	53	54	62	63	64	65	66	
I(%)	10	24	12	15	12	19	30	18	9	10	40	76	47	16	8	18	58	50	22	20	
	67	75	76	77	78	79	80	93	94	95	96	97	98	106	107	108	110	120	121		
	7	8	10	10	96	24	18	20	17	12	12	8	28	100	10	6	8	25	51		
	122	123	124	138	139	169	170	171	172	$d_0 = 14$,	$d_1 = 33$,										
	40	31	19	18	8	10	25	27	14	$d_2 = 36$,	$d_3 = 17\%$.										
XIV *m/e*	37	38	39	45	48	50	51	52	64	65	75	76	77	78	90	91	92	96	97	98	
I(%)	25	34	47	22	100	26	26	26	26	15	15	29	52	20	6	16	14	8	26	18	
	104	110	123	124	125	126	138	152	167	172	$200(M^+)$										
	20	6	8	55	8	8	21	32	3	3	20										
XV *m/e*	38	39	48	50	51	52	53	63	64	65	76	77	78	89	90	91	92	104	106		
I(%)	5	16	7	7	10	7	6	9	5	14	5	12	5	6	4	36	12	10	7		
	117	118	134	135	139	146	148	150	151	152	$167(M^+)$	168									
	19	11	7	5	5	6	8	100	10	13	46	5									
XVI *m/e*	38	39	48	49	50	51	52	63	65	74	76	77	78	105	$154(M^+)$						
I(%)	6	12	10	9	22	47	10	5	8	8	6	100	16	16	5						

* All peaks greater than 2% of the base peak (arbitrarily 100%) are recorded.

† Because of the complexity of this spectrum only peaks greater than 5% of the base peak are recorded.

TABLE 2. EXACT MASS MEASUREMENTS IN THE SPECTRA OF I–XV

Compound	*m/e*	Composition	Compound	*m/e*	Composition
I	62	C_5H_2	IX	91	C_7H_7 (40%)
	63	C_5H_3 (95%)			C_6H_5N (60%)
		C_4HN (5%)		92	C_6H_6N
	64	C_5H_4 (60%)		98	C_5H_6S
		C_4H_2N (40%)		104	C_7H_6N
	65	C_5H_5 (70%)		105	C_7H_7N
		C_4H_3N (30%)		110	C_5H_4NS
	67	C_4H_5N		124	C_6H_6NS
	84	C_4H_4S		125	C_6H_7NS
	91	C_6H_5N		136	C_7H_6NS
	111	C_5H_5NS		138	C_6H_4NOS
II	63	C_4HN (15%)	X	66	C_5H_6 (50%)
		C_5H_3 (85%)			C_4H_4N (50%)
	73	C_3H_2Cl		78	C_5H_4N
	75	C_3H_2Cl (25%)		93	C_6H_7N (70%)
		C_6H_3 (75%)			C_6H_5O (30%)
	83	C_4H_3S		98	C_4H_4NS
	90	C_6H_4N		110	C_5H_4NS
	98	C_5H_3Cl (60%)		106	C_6H_4NO
		C_4H_2OS (40%)		120	C_7H_6NO
	99	C_5H_4Cl		121	C_7H_7NO
	110	C_5H_4NS		138	C_6H_4NOS
	125/127	C_6H_4NCl		139	C_6H_5NOS
	138	C_6H_4NOS	XII	141	C_6H_7NOS
V	63	C_5H_3	XIII	64	C_5H_4 (50%)
	78	C_5H_4N			C_4H_2N (30%)
	83	C_4H_3S			SO_2 (20%)
	90	C_6H_4N		66	C_4H_4N (50%)
	110	C_5H_4NS			C_5H_6 (50%)
				69	C_3HS
				78	C_5H_4N

The spectrum (Fig. 1) of sulphinylaniline (I)† is remarkable for its skeletal rearrangement ions, and these are summarized in Scheme 1. Exact mass measurements (Table 2) confirm the compositions of all major fragment ions, but it is stressed that the structures drawn for fragment ions are nominal.

Sulphinylaniline (I) fragments by two distinct pathways on electron impact. Loss of SO (by N–S cleavage) from the molecular ion I, (*m/e* 139) gives an ion *h*, *m/e* 91 which fragments by loss of $CN^{\bullet}$ to produce the cyclopentadienyl cation *i* (*m/e* 65) (Process 1). However, the major features of the spectrum are produced by a molecular ion rearrangement, which is a low energy process, even occurring at a nominal 10 eV. Loss of carbon monoxide from the molecular ion (Process 2) necessitates C—O bond formation, possibly of the type I → *a* (similar processes have been observed in the spectra of sulphones and sulphoxides.[5,6] The loss of carbon monoxide from *a* is then

† Since this paper went to press, the spectrum of sulphinylaniline has been reported; see B. E. Job, *Chem. Commun.* 44 (1967).

no more unusual than the loss of carbon monoxide from diaryl ethers.[12, 13] The structure of *m/e* 111 (produced by elision of carbon monoxide from the molecular ion) must be cyclic (possibly *c*), as it may decompose by loss of either HCN or CS to the thiophene and pyrrole ion radicals (*d*, *m/e* 84 and *e*, *m/e* 67 respectively). The structures of *d* and *e* are supported by their characteristic fragmentation patterns (Scheme 1).[14, 15]

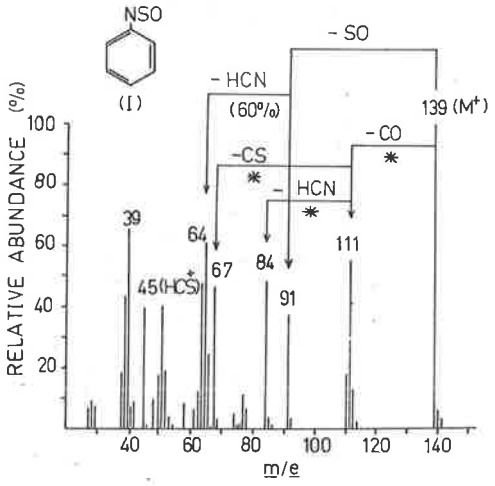


FIG. 1.

The spectra of the substituted sulphinylanilines II–XV retain some of the features of the spectrum of sulphinylaniline, but in general, the fragmentations will also involve the substituent. These features are illustrated by the mass spectra (Fig. 2 and Table 1) of the three chlorosulphinylanilines (II–IV). In the spectrum (Fig. 2) of 2-chlorosulphinylaniline (II), processes 1 and 2 (Scheme 1) are modified by the presence of the chloro substituent, viz. Process 1, M^+—SO—$Cl^\bullet$—HCN [instead of M^+—SO—$CN^\bullet$—$H^\bullet$ (Scheme 1)]; process 2, M^+—$Cl^\bullet$—CO [instead of M^+—CO (Scheme 1)]. The compositions of the major fragment ions in this spectrum have been determined by exact measurements (Table 2). It is of interest to note that the spectra of the three chloro compounds are very similar, a further illustration that halogen substituents seldom give rise to "ortho-effects" in mass spectrometry.

A different modification to Scheme 1 may be seen in the very similar spectra (Fig. 3 and Table 1) of the 2- and 3-methoxycarbonylsulphinylanilines (V, VI). Here, the loss of the entire ester group precedes the fragmentations by processes 1 and 2, and it can now be seen that these two processes may originate from either an odd electron (Fig. 1) or an even electron species (Fig. 3).

[12] J. H. Beynon, G. R. Lester and A. E. Williams, *J. Chem. Phys.* **63**, 1861 (1959).

[13] J. H. Beynon, *Mass Spectrometry and its Applications to Organic Chemistry* pp. 272–273. Elsevier, Amsterdam, (1960).

[14] H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds* p. 231. Holden-Day, San Francisco (1964).

[15] H. Budzikiewicz, C. Djerassi, A. H. Jackson, G. W. Kenner, D. J. Newman and J. M. Wilson, *J. Chem. Soc.* 1949 (1964).

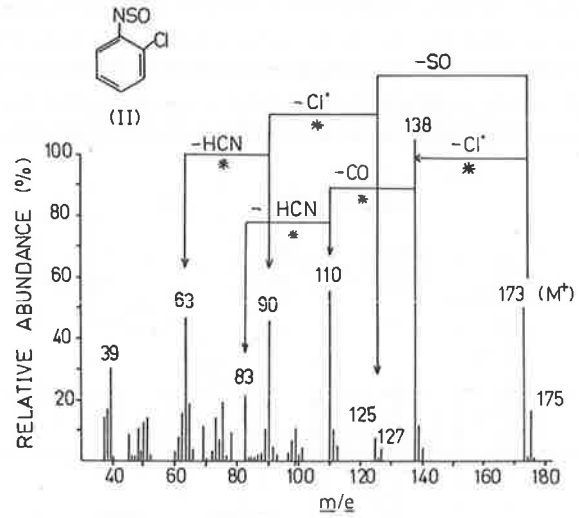


FIG. 2.

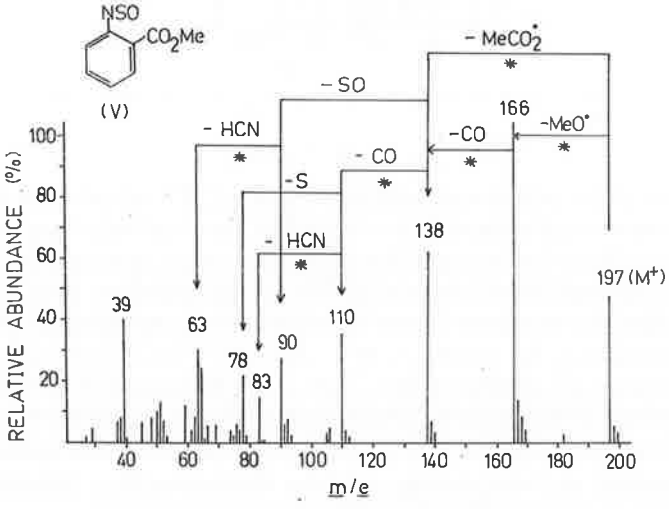


FIG. 3.

The spectra (Figs. 4 and 5, Table 1) of the methylsulphinylanilines differ markedly depending on the position of the substituent. The spectra (Fig. 4, Table 1) of the 3- and 4-methyl derivatives VIII and IX follow the general fragmentation patterns of substituted sulphinylanilines and the fragmentation modes are illustrated in Fig. 4. The major difference between the two spectra lies in the loss of the methyl radicals from the various molecular ions, viz. 83% of the base peak in the spectrum of IX, 37% in that of VIII. This observation reflects the enhanced stability of the cation *j*, *m/e* 138 produced on elimination of a methyl radical from the *p*-position. Similar effects are observed in the spectra of methylanisoles[16, 17] and methylthioanisoles.[3]

[16] C. S. Barnes and J. L. Occolowitz, *Austral. J. Chem.* **15**, 219 (1963).

[17] Z. Pelah, J. M. Wilson, M. Ohashi, H. Budzikiewicz and C. Djerassi, *Tetrahedron* **19**, 2233 (1963).

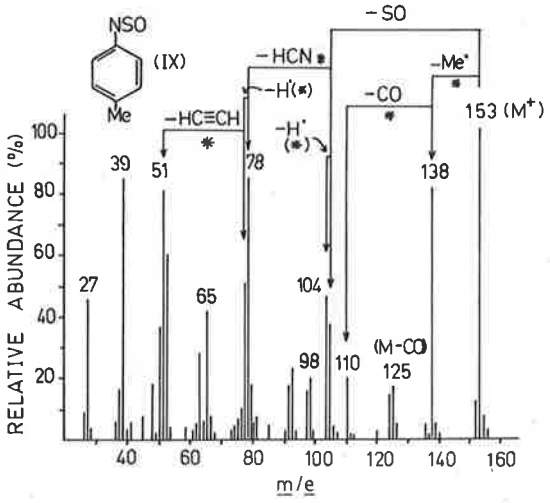


FIG. 4.

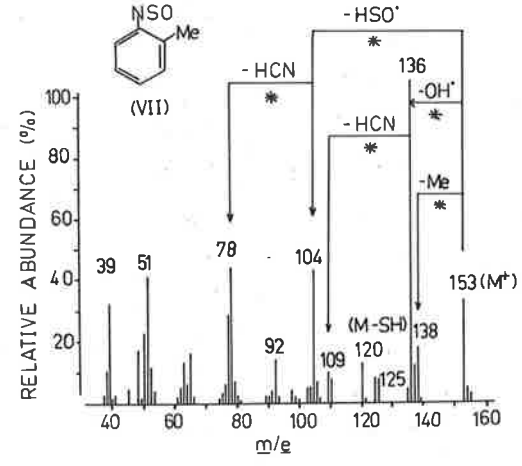
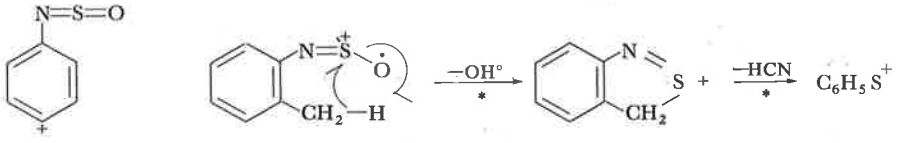


FIG. 5.



i, *m/e* 138 VII *k*, *m/e* 136 *m/e* 109

Although the spectrum (Fig. 5) of 2-methylsulphinylaniline (VII) retains the features of those of the other methyl isomers, an additional process is observed. Here, a specific "ortho-effect"[18] enables the immediate detection of the *ortho* methyl substituent. Loss of an hydroxyl radical from the molecular ion produces the base peak of the spectrum (possibly *k*, *m/e* 136) which fragments further by loss of HCN to an ion

[18] F. W. McLafferty in *Mass Spectrometry of Organic Ions* p. 337. Academic Press, N.Y. (1963).

$C_6H_5S^+$ (*m/e* 109). An M^+—$SH^\bullet$ ion (*m/e* 120 is also a feature of this spectrum. The genesis of this rearrangement process (which is substantiated by a metastable ion at *m/e* 94·1) is not clear, but it is an "ortho-effect", as analogous processes are not observed in the mass spectra of other sulphinylanilines.

An M—CO rearrangement ion (*m/e* 125, 8% of the base peak) is still observed in the spectrum (Fig. 5) of 2-methylsulphinylaniline (VII) even though the spectrum exhibits a large "ortho-effect". If both the 2 and 6 positions in sulphinylaniline were blocked by methyl substituents, an M—CO ion should still be observed in the mass spectrum provided that the rationalization in Scheme 1 is valid, and that the rearrangement process is not swamped by an enhanced "ortho-effect". The rationalization assumes that the oxygen is attached to C-1 and that the SN group migrates to either of the electron deficient ortho positions. The mass spectrum (Table 1) of 2,6-dimethylsulphinylaniline (XV) does contain a small M—CO ion (*m/e* 139, 5% of the base peak). This observation is consistent with, but does not prove the mechanism outlined in Scheme 1.

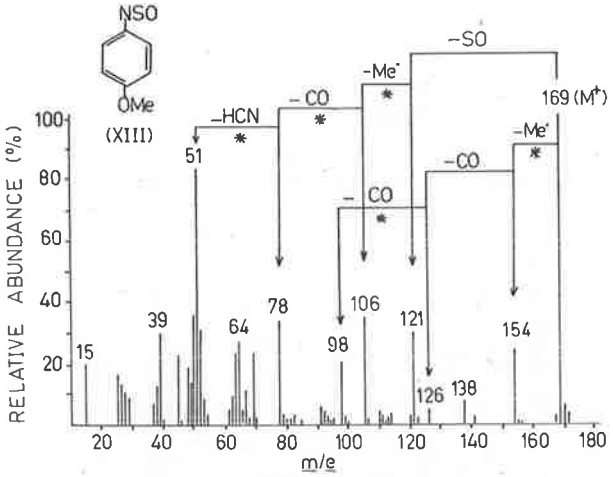


FIG. 6.

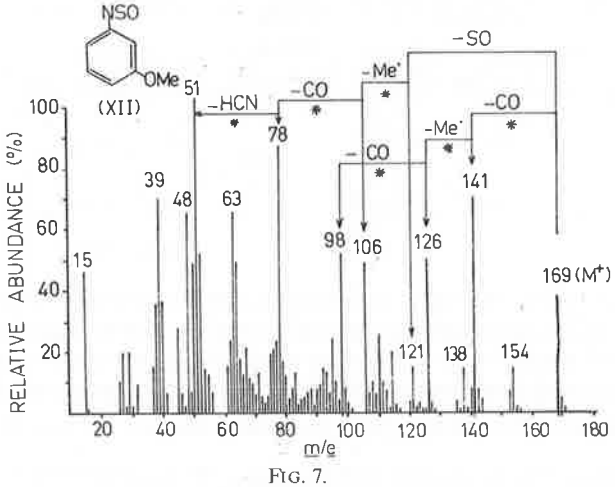


FIG. 7.

The mass spectra (Fig. 6–8) of the three methoxysulphinylanilines X, XII and XIII are very different from one another. The difference between the mass spectra (Figs. 6 and 7) of the 4-methoxy and 3-methoxy derivatives XIII and XII, is explained by the observation[3] that skeletal rearrangement processes become more prominent when simple reactions (e.g. the formation of M^+—Me$^\bullet$ or M^+—MeO$^\bullet$ fragments) are not particularly favourable. Consequently, substituent orientation plays a large part in the relative occurrence of skeletal rearrangement ions in the spectra of XII and XIII. In the spectrum (Fig. 6) of the *p*-isomer XIII, the simple processes M^+—Me$^\bullet$ (to *m/e* 154) and M^+—MeO$^\bullet$ (to *m/e* 138) predominate, whilst the M—CO rearrangement ion (*m/e* 141) constitutes only 3% of the base peak. When the methoxy substituent is *meta*, the processes M—Me$^\bullet$ and M—MeO$^\bullet$ will not be as favored,[3,16] therefore the rearrangement process (M—CO) may predominate. The M—CO ion in the spectrum (Fig. 7) of XII is now 72% of the base peak. Further fragmentation processes are outlined in Figs. 6 and 7; high resolution data is summarized in Table 2.

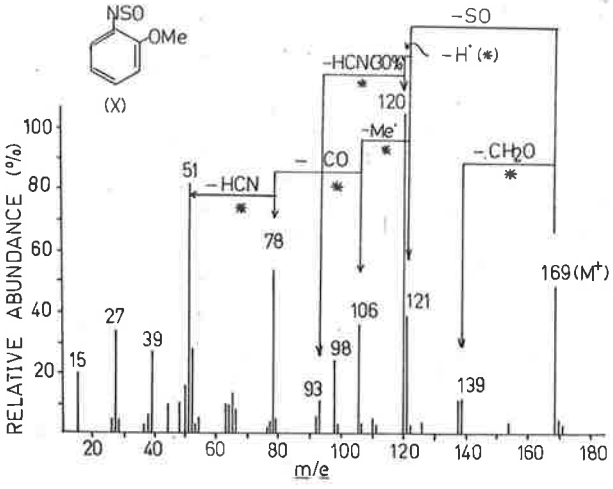
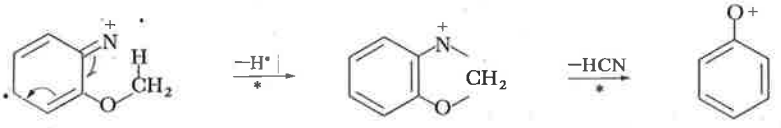


FIG. 8.

When the methoxyl substituent occupies the ortho position, as in X, the fragmentation (Fig. 8) takes a different course. The M^+—SO ion (*l*, *m/e* 121, cf. Process 1 in Scheme 1) may now lose a hydrogen atom to yield an ion *m/e* 120, which fragments further by loss of HCN possibly to *n*, *m/e* 93. Further fragmentations are illustrated in Fig. 8, and the spectrum (Table 1) of the d_3 derivative (XI) supports the above fragmentation schemes. It is therefore possible to identify all three methoxysulphinylanilines by mass spectrometry.



l, *m/e* 121 *m*, *m/e* 120 *n*, *m/e* 93

The mass spectrum (Table 1) of XIV exhibits *m/e* 48 (SO) as the base peak, and shows two separate decomposition patterns viz. M^+—SO—SO—HCN—HCN and M^+—SO—CO—HCN. Again large rearrangement ions are observed;

the M^+—SO—CO ion (*m/e* 124) constitutes 55% of the base peak. A very different situation is observed when the sulphinyl group is not directly attached to the aromatic ring. The spectrum (Table 1) of XV is a very simple one. No rearrangement ions are observed, instead the fragmentation proceeds by the process M^+— HSO—N_2—HC ≡ CH.

A series of other sulphinylamines were also investigated (e.g. nitrosulphinylanilines and aliphatic sulphinylamines) but because of their facile decomposition to the corresponding amines, their mass spectra contained peaks due to the fragmentation of the amine. Consequently they are not reported. This is a serious problem with all sulphinylamines and all spectra reported were determined with carefully purified samples.

The results presented in this paper illustrate that aromatic sulphinylamines decompose characteristically by well defined skeletal reorganisation on electron impact. This conclusion limits both the *a priori* prediction of fragmentation modes and the application of the element mapping technique[19, 20, 21] to this class of compound.

EXPERIMENTAL

All spectra were measured with a Hitachi–Perkin Elmer R.M.U. 6D mass spectrometer operating at 75 eV, and with the inlet system at approximately 100°. High resolution measurements were performed with an A.E.I. MS 9 mass spectrometer using a resolution of 14,000 (10% valley definition). Heptacosafluorotributylamine provided the reference masses and all exact mass measurements were correct to within 15 ppm.

Previously published procedures were used for the preparation of I[22], II[23], III[22], IV[22], VI[23], VII[22], VIII[23], IX[22], X[23], XII[24], XIII[25], XIV[23], XVI[26]. V was prepared from methyl anthranilate by the usual method.[27] Yield 77%. Bp. 149–150°C/12 mm Hg. n_D^{25} = 1·5844 (Anal. Rec.: C, 48·86; H, 3·54; N, 7·16; S, 16·64. Calc.: C, 48·88; H, 3·63; N, 7·12; S 16·59%.) XV was prepared as above.[27] Yield 84%, b.p. 102°C/11 mm Hg. n_D^{25} = 1·5778 (Anal.: Rec. C, 57·82; H, 5·52; N, 8·39; S, 19·29. Calc.: C, 57·48; H, 5·43; N, 8.38; S, 19·15%.) XI was prepared from *ortho*-nitrophenol by alkylation (diazomethane + D_2O)[28], reduction of the nitroanisole to *ortho*-anisidine followed by the treatment with thionylchloride.[27]

Acknowledgements—A grant (to S.-O.L.) from Statens Almindelige Videnskabsfond, and the award of an Elsie Ballot Fellowship (to R.G.C.) are gratefully acknowledged.

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[20] K. Biemann, P. Bommer and D. M. Desiderio, *Tetrahedron Letters* 1725 (1964).
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THE MASS SPECTRA OF ACRIDONES*

By J. H. Bowie,† R. G. Cooks,‡ R. H. Prager,† and H. M. Thredgold†

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Summary

The mass spectra of 34 acridones have been determined and interpreted with the aid of both high-resolution measurements and deuterium labelling studies. The spectra contain pronounced molecular ions and are free of skeletal rearrangement fragments. The fragmentation patterns are dependent on the nature and position of substituents, and therefore mass spectrometry can be a useful aid to structure determination in this class of naturally occurring compounds.

Although the mass spectra of several furoquinoline alkaloids[1] and of acridine[2a] have been described, no study of acridones has been reported.

The mass spectra of the acridone derivatives (I)–(XXXIV) are reported in Figures 1–9 and Table 1. Exact mass measurements (Table 2) confirm the composition of many ions in the spectra. Structures written for fragment ions serve the important purpose of relating fragmentation processes to the structure of the molecule in the ground state. These structures are nominal only, as it has been recently suggested that neither the benzene[3] nor the furan[4] molecular ions have the structure of the intact molecules. The presence of an asterisk in either the text or a figure denotes the presence of an appropriate metastable ion for the process indicated.

The mass spectrum (Table 1) of acridone (I) is unexceptional and is summarized in Scheme 1. Exact mass measurements establish the composition of the major ions. Loss of carbon monoxide from the molecular ion produces an ion (*m/e* 167) represented as the carbazole radical ion *a*, which may fragment further[2b] by loss of HCN and a hydrogen radical to *b* (*m/e* 139). The mass spectrum (Fig. 1 and Scheme 1) of *N*-methylacridone (II) fragments by either of the processes $M^+ - Me\cdot - CO - HCN$ (to *b*, *m/e* 139) or $M^+ - CHO\cdot - CH_2N\cdot$ (to the biphenylene radical ion *e*, *m/e* 152).

* This paper constitutes Part X in the series "Electron Impact Studies", Part IX, Bowie, J. H., Cooks, R. G., Lawesson, S.-O., and Schroll, G., *Tetrahedron*, in press, and Part II in the series "Acridone Studies", Part I, Prager, R. H., and Thredgold, H. M., *Tetrahedron Lett.*, 1966, 4909.

† Organic Chemistry Department, University of Adelaide.

‡ University Chemical Laboratory, Lensfield Road, Cambridge, England.

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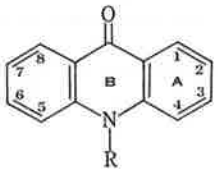
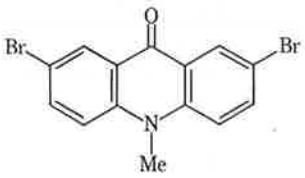


(I) R = H
(II) R = Me



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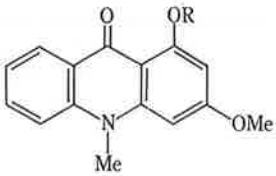
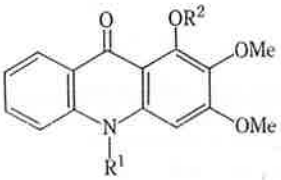
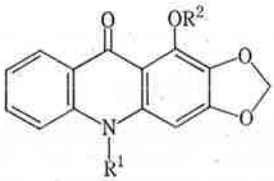


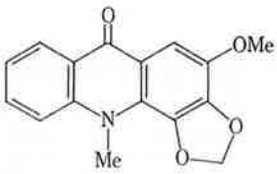
(IV) R = H
(V) R = Me
(VI) R = Et



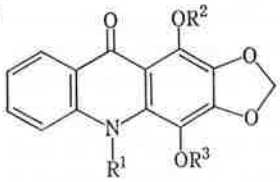
	R^1	R^2
(VII)	H	H
(VIII)	Me	H
(IX)	Me	Et



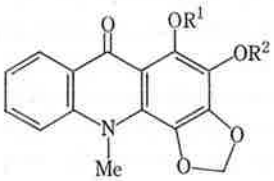
	R^1	R^2
(X)	Me	H
(XI)	Me	Me



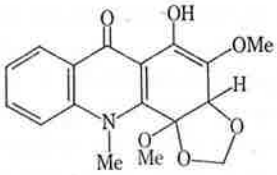
(XII)



	R^1	R^2	R^3
(XIII)	H	H	Me
(XIV)	Me	H	Me
(XV)	Me	D	Me
(XVI)	H	Me	Me
(XVII)	Me	Me	Me
(XVIII)	Me	Et	Me



	R^1	R^2
(XIX)	H	Me
(XX)	Me	Me
(XXI)	Et	Me



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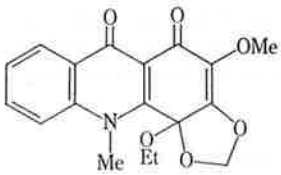

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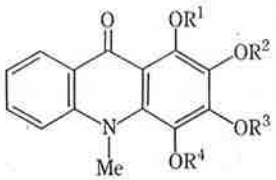
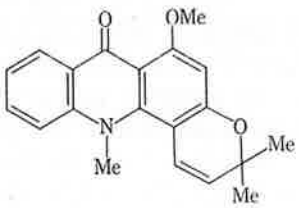
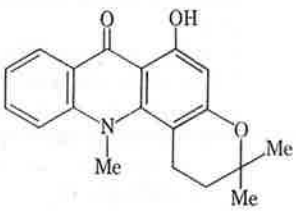


	R^1	R^2	R^3	R^4
(XXIV)	H	Me	Me	H
(XXV)	H	Me	Me	Me
(XXVI)	Me	H	Me	Me
(XXVII)	Me	Me	Me	H
(XXVIII)	Me	Me	Me	Me
(XXIX)	Me	CD_3	Me	Me
(XXX)	Me	Me	Me	CD_3
(XXXI)	Et	Me	Me	Me
(XXXII)	Me	Me	Me	Et



(XXXIII)



(XXXIV)

TABLE 1

MASS SPECTRA OF ACRIDONE DERIVATIVES (I)–(XXXIV)

For compounds marked [a], all peaks greater than 5% of the base peak were recorded; for components marked [b], 10%. For compound (XXX), because of the complexity of its spectrum, only peaks greater than 20% of the base peak were recorded

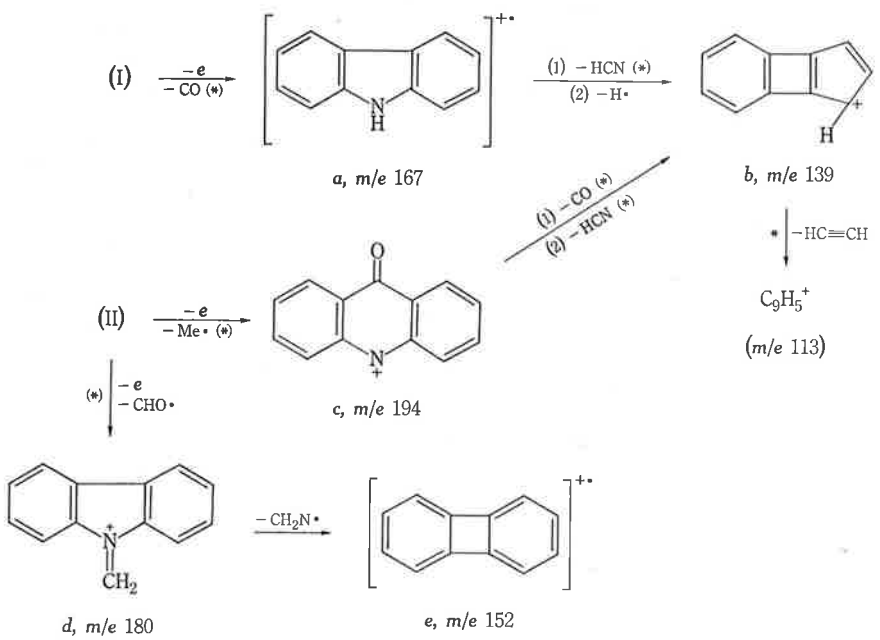
(I)[a]	*m/e*	83·5	113	115	139	140	166	167	168	195(M)	196				
	I (%)	9	8	7	19	18	24	53	6	100	19				
(III)[b]	*m/e*	151	152	153	164	165	169	178	179	180	207	243	245	271	
	I (%)	24	33	14	58	32	20	37	41	15	12	18	19	19	
	m/e	273	285	286	287	288	289	322	324	326	350	352	354	365	
	I (%)	19	16	83	29	82	15	10	15	10	15	27	16	54	
	m/e	366	367	368	369	370									
	I (%)	14	100	16	41	6									
(IV)[a]	*m/e*	77	128	140	154	168	169	182	183	184	199	200	212	225	226
	I (%)	11	6	6	9	6	8	12	9	13	11	8	19	30	54
	m/e	227	254	255(M)	256										
	I (%)	19	20	100	29										
(V)[a]	*m/e*	140	155	168	183	196	198	211	226	254	255	269(M)	270		
	I (%)	6	6	6	14	23	7	18	24	56	8	100	19		
(VII)[b]	*m/e*	77	101	102	128	129	130	140	156	157	185	186	198	199	
	I (%)	18	16	22	22	39	20	11	16	20	65	11	14	11	
	m/e	212	228	229	242	256	257	271(M)							
	I (%)	11	100	17	18	78	14	34							
(VIII)[a]	*m/e*	77	115	128	142	143	170	171	184	199	200	212	226	242	243
	I (%)	15	13	8	8	11	18	17	6	39	8	9	7	59	13
	m/e	256	270	271	284	285(M)	286								
	I (%)	14	100	23	23	74	16								
(IX)[a]	*m/e*	77	115	128	154	170	171	183	184	198	213	226	240	241	242
	I (%)	10	10	9	7	12	8	8	9	6	8	18	8	8	28
	m/e	253	254	255	268	269	270	280	284	296	298	299	300		
	I (%)	26	8	34	9	8	24	20	20	11	100	26	20		
	m/e	313(M)	314												
	I (%)	37	14												
(X)[b]	*m/e*	77	89	102	103	113	114	115	126	127	128	140	154	155	182
	I (%)	37	16	14	15	21	15	14	21	35	18	32	50	14	42
	m/e	183	184	185	199	211	212	213	240	241	269(M)	270			
	I (%)	67	21	16	12	32	60	17	34	14	100	27			
(XIV)[a]	*m/e*	77	115	158	170	198	226	228	254	255	256	284	285		
	I (%)	10	12	24	7	5	6	8	34	8	9	100	20		
	m/e	299(M)	300												
	I (%)	59	13												
(XV)[b]	*m/e*	77	158	159	253	254	255	284	285	286	299	300	301 ($d_0 = 41\%$,		
	I (%)	16	18	25	16	26	11	73	100	20	40	64	12 $d_1 = 59\%$)		

TABLE 1 (*Continued*)

(XVI)[b]	*m/e*	50	51	63	75	76	77	81	83	113	114	115	116	127	128	130
	I (%)	18	14	14	15	33	20	14	25	19	30	50	12	45	35	22
	m/e	139	140	143	154	155	168	170	171	182	183	198	210	211		
	I (%)	22	34	17	19	14	17	31	32	27	19	30	44	22		
	m/e	212	224	225	226	227	228	238	239	240	253	254	255	256		
	I (%)	16	37	15	24	15	32	78	23	17	18	58	28	100		
	m/e	257	266	270	271	284	285	299(M)	300							
	I (%)	18	29	15	30	96	17	90	22							
(XVII)[b]	*m/e*	76	77	102	114	127	128	129	130	140	141	142	154	169	182	
	I (%)	15	22	15	16	15	15	16	14	12	14	12	14	20	12	
	m/e	184	197	212	224	225	238	240	252	253	255	268	269	270		
	I (%)	11	12	16	25	11	12	20	70	16	28	32	16	100		
	m/e	271	280	285	298	313(M)	314									
	I (%)	22	46	32	52	100	28									
(XVIII)[b]	*m/e*	77	102	114	115	127	128	129	130	141	154	158	169	170	182	
	I (%)	18	15	16	18	13	13	12	20	14	14	40	13	17	12	
	m/e	226	238	240	254	255	268	269	270	283	284	285	294	295		
	I (%)	10	12	12	53	17	53	17	57	20	78	17	100	24		
	m/e	310	312	313	327(M)	328										
	I (%)	36	88	18	83	22										
(XX)[b]	*m/e*	77	102	114	129	159	169	197	212	225	238	254	268	270	271	
	I (%)	12	7	7	6	14	9	7	6	6	9	13	12	80	17	
	m/e	280	284	298	299	313(M)	314									
	I (%)	12	16	100	24	78	15									
(XXI)[b]	*m/e*	77	102	114	115	130	158	169	170	240	254	268	270	284	285	
	I (%)	15	12	12	14	13	24	23	24	11	32	16	65	68	13	
	m/e	294	310	312	313	327(M)	328									
	I (%)	21	22	100	19	62	14									
(XXII)[b]	*m/e*	77	130	158	159	170	186	226	228	242	243	254	258	284	285	
	I (%)	20	18	34	22	15	22	11	11	12	25	43	28	100	19	
	m/e	286	299	300	301	331(M)										
	I (%)	61	84	20	30	11										
(XXIII)[b]	*m/e*	77	104	115	130	158	159	226	228	243	254	258	270	284	285	
	I (%)	22	28	16	14	40	20	10	18	23	42	30	12	100	18	
	m/e	286	287	299	300	315	343(M)									
	I (%)	86	12	84	25	11	2									
(XXIV)[b]	*m/e*	77	89	103	115	130	131	144	158	159	228	242	243	258	268	
	I (%)	17	16	10	20	17	20	17	31	31	11	12	38	22	14	
	m/e	271	286	287	301(M)	302										
	I (%)	18	100	25	70	16										
(XXV)[a]	*m/e*	77	115	130	158	186	214	228	229	242	256	257	270	285	300	
	I (%)	10	7	8	38	8	6	17	8	24	8	8	8	8	100	
	m/e	301	315(M)	316												
	I (%)	20	43	12												

TABLE 1 (*Continued*)

(XXVI)[b]	*m/e*	158	228	242	256	257	270	272	284	285	287	288	289	300
	I (%)	51	19	36	14	48	15	20	93	20	11	12	14	100
	m/e	301	315(M)	316										
	I (%)	31	94	24										
(XXVII)[b]	*m/e*	77	158	228	242	257	258	270	272	282	286	300	301	
	I (%)	13	30	15	25	70	14	15	32	16	11	100	25	
	m/e	315(M)	316											
	I (%)	59	15											
(XXX)	*m/e*	228	254	255	256	257	258	270	271	283	284	285	286	298
	I (%)	50	29	40	70	32	22	60	40	27	34	21	22	30
	m/e	299	314	315	316	317	318	330	331	332				(d_1 = 25, d_2 = 37,
	I (%)	21	100	68	74	98	26	20	30	24				d_3 = 38%)
(XXXI)[b]	*m/e*	158	228	240	242	256	270	284	285	286	300	301	310	326
	I (%)	26	22	11	27	22	22	22	16	46	55	12	11	20
	m/e	328	329	343(M)	344									
	I (%)	100	22	51	11									
(XXXIII)[a]	*m/e*	63	77	116·5	160·5	204	209	248	263	264	265	276	277	291
	I (%)	7	6	11	7	7	9	10	12	30	12	12	10	11
	m/e	292	293	306	307	321(M)	322							
	I (%)	30	10	100	26	68	21							
(XXXIV)[b]	*m/e*	77	154	196	212	213	225	226	241	242	254	255	309(M)	310
	I (%)	12	12	14	13	14	45	17	100	25	44	11	100	23



Scheme 1

The spectrum (Table 1) of the dibromoacridone (VI) retains some of the features of the spectrum of *N*-methylacridone. The major fragmentation follows the pathway $M^+ - Br\cdot - Me\cdot - CO - Br\cdot$, while the biphenylene radical ion *e*, *m/e* 152 (33% of the base peak) is formed by the scheme $M^+ - Br\cdot - Br\cdot - CO - HCN$.

TABLE 2

EXACT MASS MEASUREMENTS IN THE SPECTRA OF COMPOUNDS (I–XXXIV)

Compound	*m/e*	Composition
(I)	167	$C_{12}H_9N$
	139	$C_{11}H_7$
(II)	194	$C_{13}H_8NO$
	180	$C_{13}H_{10}N$
	166	$C_{12}H_8N$
	152	$C_{12}H_8$
	140	$C_{10}H_6N$
(VI)	266	$C_{17}H_{16}NO_2$
	240	$C_{15}H_{14}NO_2$
	226	$C_{14}H_{12}NO_2$
	210	$C_{13}H_8NO_2$ (60%)
		$C_{14}H_{12}NO$ (40%)
	196	$C_{13}H_{10}NO$
	183	$C_{12}H_9NO$
	168	$C_{12}H_{10}N$
(IX)	284	$C_{16}H_{14}NO_4$
	270	$C_{15}H_{12}NO_4$
	255	$C_{15}H_{13}NO_3$
	253	$C_{15}H_{11}NO_3$ (60%)
		$C_{16}H_{15}NO_2$ (40%)
	242	$C_{14}H_{12}NO_3$
	226	$C_{13}H_8NO_3$ (50%)
		$C_{14}H_{12}NO_2$ (50%)
	198	$C_{13}H_{12}NO$ (50%)
		$C_{12}H_8NO_2$ (50%)
	170	$C_{11}H_8NO$
(XI)	240	$C_{14}H_{10}NO_3$
	237	$C_{15}H_{11}NO_2$
	224	$C_{14}H_{10}NO_2$
	212	$C_{13}H_{10}NO_2$
	196	$C_{13}H_{10}NO$ (95%)
		$C_{12}H_8NO_2$ (5%)
	182	$C_{12}H_8NO$
	154	$C_{11}H_8N$
	127	$C_{10}H_7$ (60%)
		C_9H_5N (40%)
(XIII)	144	C_9H_6NO
	128	C_9H_6N
(XIV)	158	$C_{10}H_8NO$
(XVIII)	294	$C_{17}H_{12}NO_4$
	284	$C_{15}H_{10}NO_5$ (80%)
		$C_{16}H_{14}NO_4$ (20%)
	270	$C_{15}H_{12}NO_4$
	268	$C_{15}H_{10}NO_4$
(XXIV)	268	$C_{15}H_{10}NO_4$
	258	$C_{14}H_{12}NO_4$
	144	$C_6H_8O_4$
(XXXI)	326	$C_{19}H_{20}NO_4$
	310	$C_{18}H_{16}NO_4$
	300	$C_{16}H_{14}NO_5$ (85%)
		$C_{17}H_{18}NO_4$ (15%)
	270	$C_{15}H_{12}NO_4$ (90%)
		$C_{14}H_8NO_5$ (10%)
	256	$C_{14}H_{10}NO_4$ (80%)
		$C_{15}H_{14}NO_3$ (20%)
	242	$C_{13}H_8NO_4$ (80%)
		$C_{14}H_{12}NO_3$ (20%)
	228	$C_{13}H_{10}NO_3$
(XXXII)	314	$C_{17}H_{16}NO_5$
	300	$C_{16}H_{14}NO_5$ (60%)
		$C_{17}H_{18}NO_4$ (40%)
	298	$C_{16}H_{12}NO_5$
	296	$C_{17}H_{14}NO_4$
	284	$C_{16}H_{14}NO_4$ (40%)
		$C_{15}H_{10}NO_5$ (60%)
	270	$C_{15}H_{12}NO_4$ (95%)
		$C_{14}H_8NO_5$ (5%)
	256	$C_{15}H_{14}NO_3$ (20%)
		$C_{14}H_{10}NO_4$ (80%)
	242	$C_{14}H_{12}NO_3$ (60%)
		$C_{13}H_8NO_4$ (40%)
	228	$C_{13}H_{10}NO_3$
(XXXIV)	254	$C_{15}H_{10}NO_3$
	241	$C_{14}H_{11}NO_3$
	225	$C_{14}H_{11}NO_2$

Acridones containing oxygenated substituents behave characteristically upon electron impact. Compounds containing either C2 or C4 substituents decompose simply by fragmentations which proceed through either of these substituents.

Fig. 1

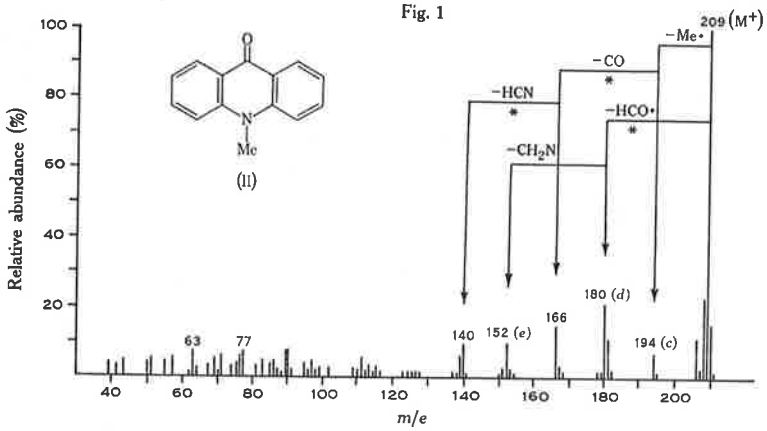
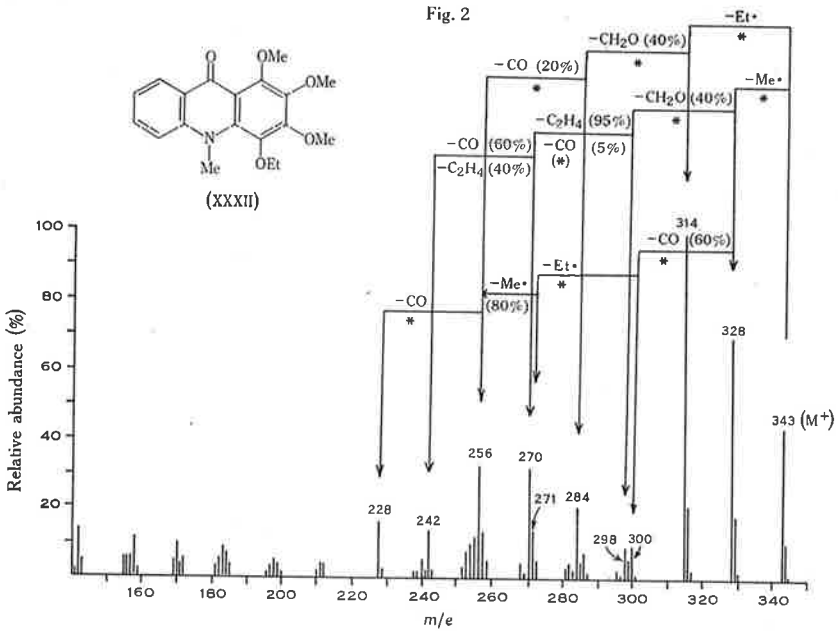


Fig. 2



The fragmentations occur by concerted processes which specifically involve the nitrogen atom. If 2- and 4-alkoxyl substituents are absent, the fragmentations are complex and non-specific. This feature has been investigated by studying the fragmentation modes of various compounds labelled in different positions with either ethoxyl or OCD_3 groups. During the course of this investigation, it became apparent

that if an hydroxyl substituent at C1 was converted into the 1-ethyl ether, the presence of this substituent could be unequivocally detected by a specific "*ortho*-effect" (see McLafferty[5]) involving the adjacent carbonal group. Finally, the spectrum of an alkoxy *N*-methylacridone differs from that of the corresponding alkoxy

Fig. 3

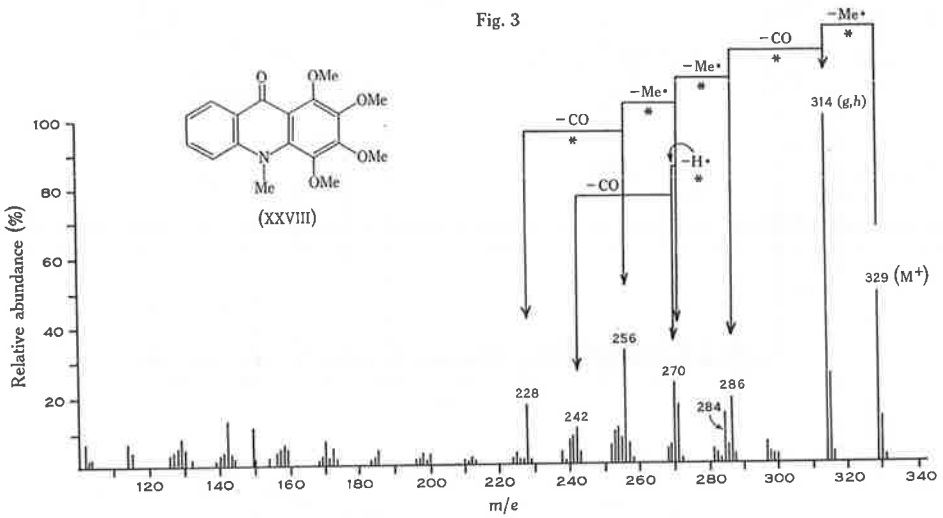
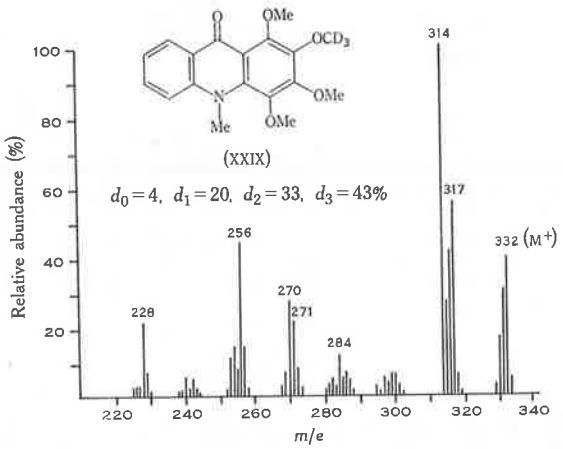


Fig. 4



acridone in being completely shifted by *m/e* 14 to higher mass values. These observations are of considerable use for the structure elucidation of acridones and they are illustrated by a consideration of the mass spectra of the substituted acridones (IV)–(XXXII).

[5] McLafferty, F. W., in "Mass Spectrometry of Organic Ions." p. 337. (Academic Press: New York 1963.)

In order to rationalize the fragmentation processes of alkoxyacridones, it is convenient to start with a discussion of the 1,2,3,4-tetrasubstituted derivatives (XXIV–XXXII) because of the information available from labelling studies. The overall fragmentations of these compounds are complex; nevertheless those processes which originate from the molecular ions give considerable insight into the orientation of substituents. The spectra of (XXIV), (XXV), (XXVI), (XXVII), (XXX), and (XXXI) are recorded in Table 1, while those of (XXVIII), (XXIX), and (XXXII) are illustrated in Figures 2–4. Specific features of these spectra are summarized in Table 3. It can be seen that $M^+-Me\cdot$ ions are the base peaks of

Table 3

RELATIVE ABUNDANCE OF IONS IN THE SPECTRA OF COMPOUNDS (XXIV–XXXII)

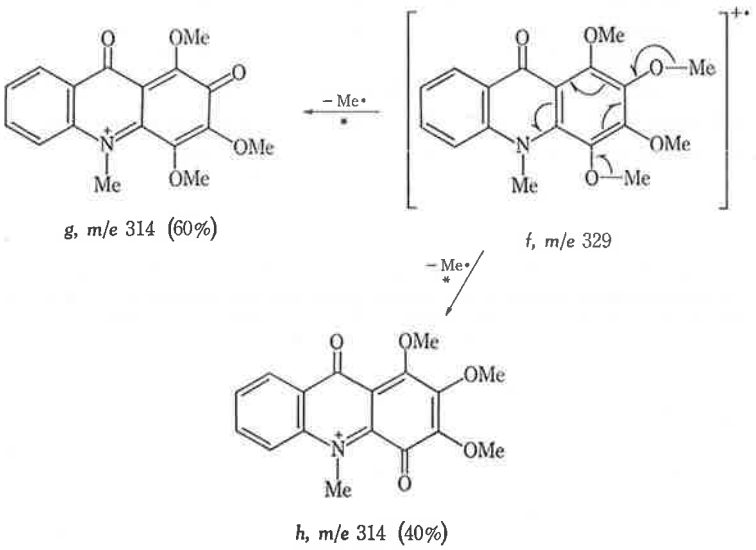
Compound	$M^+-Me\cdot$	$M^+-CD_3\cdot$	$M^+-Et\cdot$	Compound	$M^+-Me\cdot$	$M^+-CD_3\cdot$	$M^+-Et\cdot$
(XXIV)	100	—	—	(XXIX)	40	60	—
(XXV)	100	—	—	(XXX)	60	40	—
(XXVI)	100	—	—	(XXXI)	100	—	0
(XXVII)	100	—	—	(XXXII)	70	—	100
(XXVIII)	100	—	—				

the spectra of all compounds containing only methoxyl groups (and for those which in addition contain hydroxyl substituents). When a 1-ethoxyl substituent is present (as in XXXI), the spectrum (Tables 1 and 2) is extremely complex, and no ion corresponding to the process $M^+-Et\cdot$ is observed. However, when a 4-ethoxyl group is present (XXXII; Fig. 2 and Table 2), the $M^+-Et\cdot$ cation is the base peak of the spectrum, indicating a large contribution to the total ion current due to the general fragmentation from the 4-substituent. It seems reasonable (see above) that fragmentations may proceed by concerted mechanisms via the 2- and 4-substituents. To establish this point the labelled methyl ethers (XXIX) and (XXX) were synthesized (cf.[6]) and their spectra determined. The mass spectra (Figs. 3 and 4; Table 1) of melicopicine (XXVIII) and of compounds (XXIX) and (XXX) establish that 60% of the $M^+-Me\cdot$ cation originates by the loss of a methyl radical from the 2-methoxyl group, while 40% is produced by fragmentation of the 4-methoxyl substituent. In addition, all fragment ions below *m/e* 271 in the spectrum (Fig. 4) of (XXIX) have lost the label (i.e. after the loss of the second methyl radical). This establishes fragmentations through the substituents at C 2 and C 4 (see Scheme 2). Similar effects have recently been observed in the spectra of coumarins,[7] flavones,[8] and spermatheridine alkaloids.[9]

The spectra of the naturally occurring acridones (and their derivatives) which contain methylenedioxy groups illustrate the features described above.

[6] Van der Merwe, K. J., Steyne, P. S., and Eggers, S. H., *Tetrahedron Lett.*, 1964, 3923.
[7] Shapiro, R. H., and Djerassi, C., *J. org. Chem.*, 1965, **30**, 955.
[8] Bowie, J. H., and Cameron, D. W., *Aust. J. Chem.*, 1966, **19**, 1627.
[9] Bick, I. R. C., Bowie, J. H., and Douglas, G. K., *Aust. J. Chem.*, in press.

The mass spectra of evoxanthine (XI) and (XII) are illustrated in Figures 5 and 6. Compound (XII) behaves simply on electron impact, fragmenting initially through the 2-methoxyl substituent probably to *i* (*m/e* 240) and then by the processes indicated



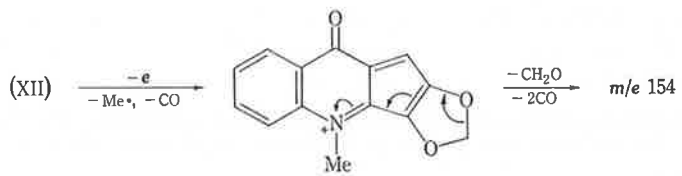
g, *m/e* 314 (60%)

f, *m/e* 329

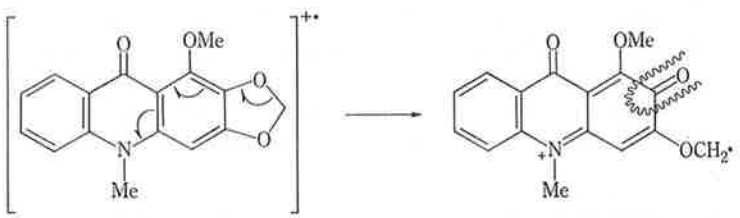
h, *m/e* 314 (40%)

Scheme 2

in Figure 5 and Scheme 3. Evoxanthine (XI) exhibits a very complex spectrum (Fig. 6), and it is suggested that the M^+—CO ion originates by decomposition of



i, *m/e* 240



j, *m/e* 283

k, *m/e* 283

Scheme 3

the methylenedioxy group ($j \rightarrow k$) and that the acridone carbonyl group is probably lost last. Attempts to confirm this suggestion by ^{18}O labelling were unsuccessful, as no exchange of the carbonyl oxygen could be detected with $^{18}OD_2$ in dioxan

alone or in the presence of acid, or in pyridine with $^{18}OD^-$. The absence of any nucleophilic additions to the carbonyl group will be reported on in a subsequent communication. The spectrum (Table 1) of norevoxanthine (X) is similar to that of evoxanthine, exhibiting analogous fragmentation processes.

Fig. 5

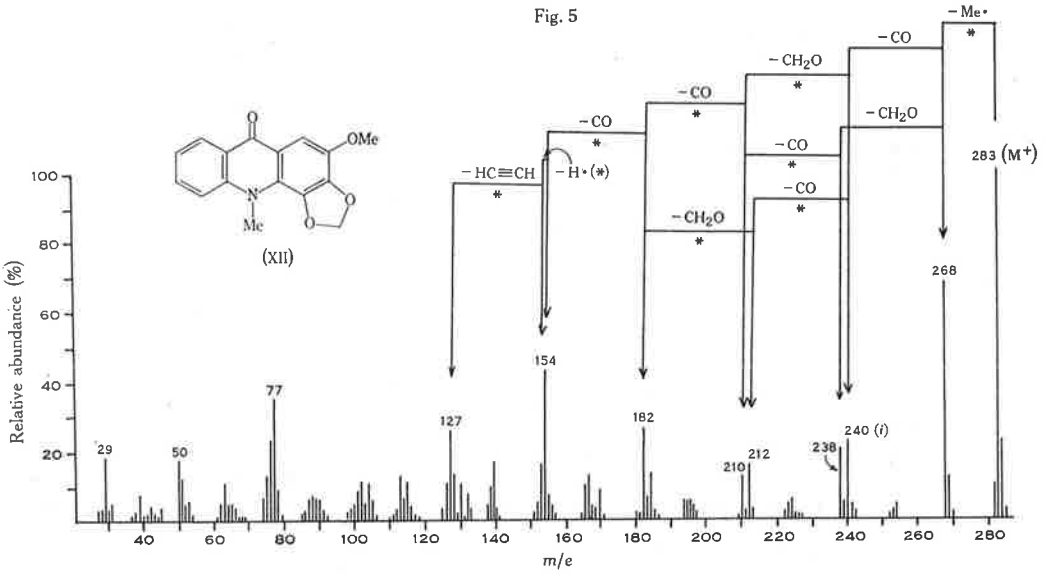
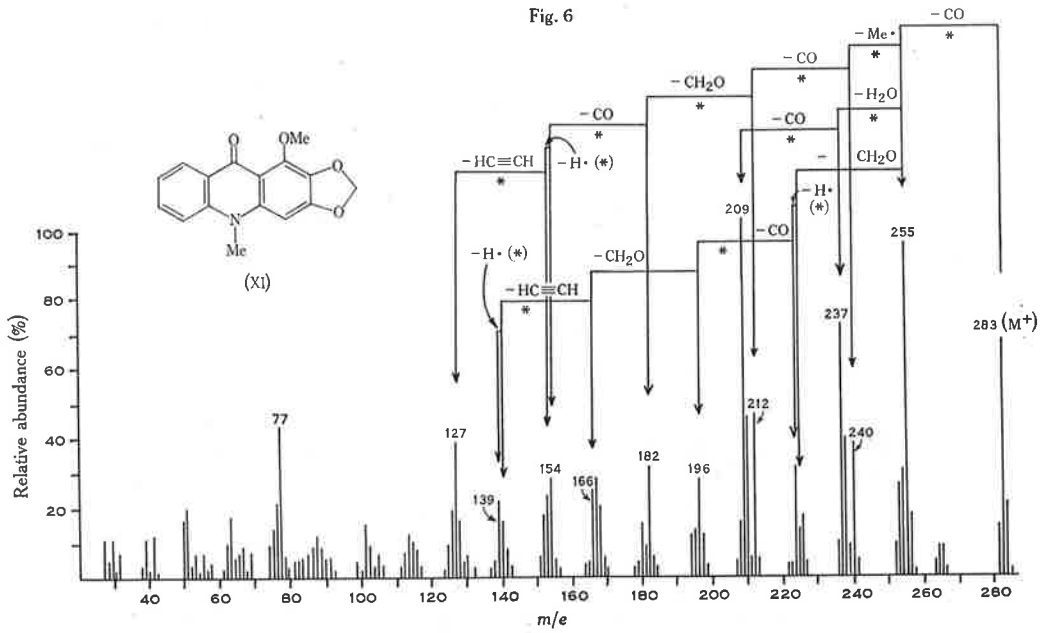


Fig. 6



The mass spectra (Tables 1 and 2; Figs. 7 and 8) of compounds (XIII–XXI) illustrate the applicability of *a priori* prediction of the fragmentation modes for

this class of compound. The isomeric pairs (XIV) and (XIX), melicopidine (XVII) and melicopine (XX), and (XVIII) and (XXI) exhibit very similar spectra. The only difference in the spectra (Table 1) of (XVII) and (XX), and of (XVIII) and

Fig. 7

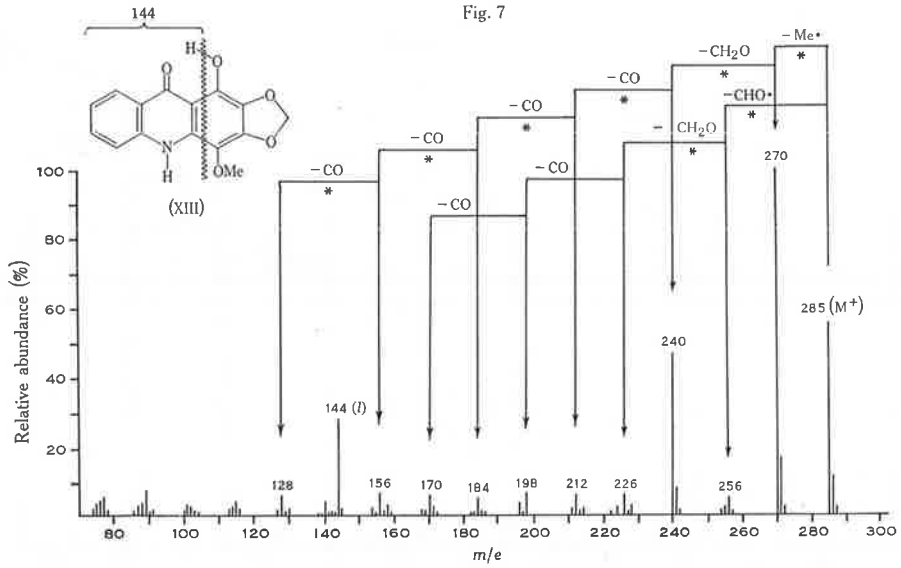
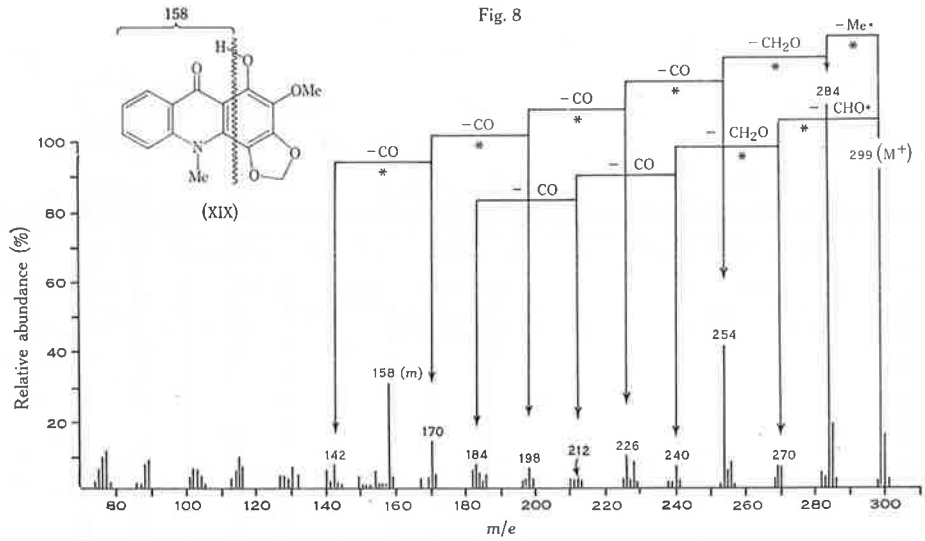


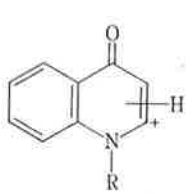
Fig. 8



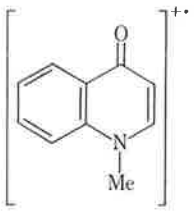
(XXI) lies in the differing relative abundances of the M^+—Me·—H_2O cations. Such ions do not appear to be of diagnostic value.

An additional feature of 1,2,3,4-tetrasubstituted acridones is that the compounds having either hydroxyl groups (XIII, XIV, XIX, XXII, XXIV, XXV, XXVI, and XXVII) or ethoxyl substituents (XVIII, XXI, XXIII, XXXI, and XXXII)

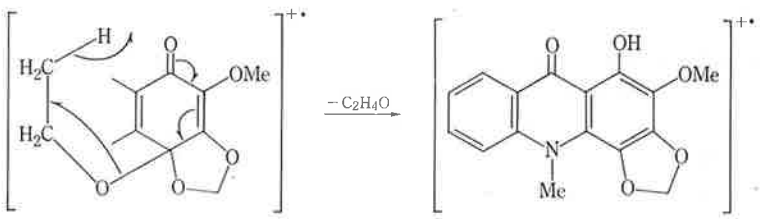
(which may fragment by elision of ethylene to give the corresponding phenol radical ion), exhibit the prominent ions (25–50% of the base peak) *l* (*m/e* 144) and *m* (*m/e* 158) in the spectra of acridones and *N*-methylacridones respectively. On the other hand, these ions are either absent or very small in the spectra of those compounds containing only methoxyl and/or methylenedioxy groups. Although there is no firm evidence to suggest the origin of these ions, hydrogen transfer from the hydroxyl group [as proved by the spectrum of (XV)] to ring B, is a prerequisite for their formation. Indeed, the spectrum of (XXIV) (which contains two hydroxyl groups) exhibits *m* (*m/e* 158, 31% of the base peak), and *n* (*m/e* 159, 31% of the base peak) which have resulted from one and two hydrogen transfers respectively. The presence of such ions in the spectrum of an acridone indicates 1,2,3,4-tetrasubstitution and may be used to determine the substituent on nitrogen, and to detect the number of hydroxyl groups (or potential hydroxyl radical ion producers, e.g., ethoxyl and probably acetoxyl groups) on ring A.



l, *m/e* 144 (R = H)
m, *m/e* 158 (R = Me)



n, *m/e* 159



o, *m/e* 343 *m/e* 299

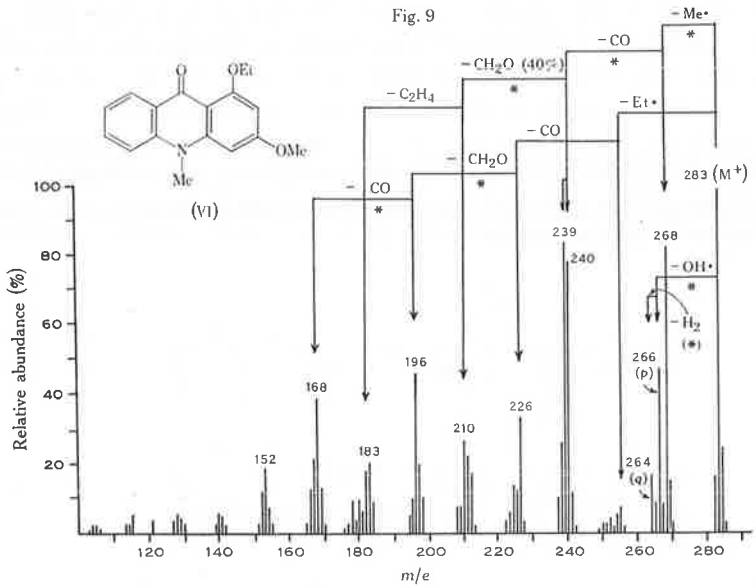
The mass spectra (Table 1) of xanthoxoline (VII) and of the other 1,2,3-oxygenated acridones are unexceptional. However, the spectra (Table 1) of the two ketals (XXII) and (XXIII) show some interesting features. Compound (XXII), on electron impact, loses methanol from its molecular ion to produce the normelicopine radical ion (*m/e* 299), which fragments as described earlier (Fig. 8). The mass spectrum of (XXIII) affords verification of the structure of this compound, as the major fragmentation involves the elision of C_2H_4O from the molecular ion with concomitant hydrogen rearrangement, probably by a concerted mechanism (see *o*), to again furnish the normelicopine radical ion. The spectrum (Table 1) of acronycine (XXXIII) can be likened to that of 2,2-dimethylchromene,[10,11] while the spectrum (Table 1) of (XXXIV) may be explained by reference to the mass

[10] Barnes, C. S., and Occolowitz, J. L., *Aust. J. Chem.*, 1964, **17**, 975.
[11] Willhalm, B., Thomas, A. F., and Gantschi, F., *Tetrahedron*, 1964, **20**, 1185.

spectra of chromans[11] and flavans.[12] The compositions of many ions in these spectra are recorded in Table 2.

The mass spectra (Tables 1 and 2; Fig. 9) of the 1,3-disubstituted acridones (IV–VI) reflect the complexity of fragmentation modes when an acridone lacks either a C2 or C4 substituent. In the spectrum (Fig. 9) of 1-ethoxy-3-methoxy-

Fig. 9



N-methylacridone (VI), complex decomposition patterns can be seen to originate from either the ethoxyl or methoxyl groups.

Further examination of the spectrum (Fig. 9) of (VI) shows the presence of the process $M^+ - OH\cdot - H_2$ to give an ion *m/e* 264. Comparison of the spectra of all other 1-ethoxyacridones shows this to be a general process, not observed in

TABLE 4

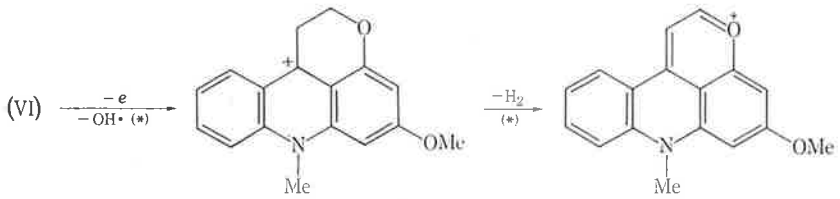
RELATIVE ABUNDANCES (%) OF $M^+ - OH\cdot$ IONS IN THE SPECTRA OF ETHOXYACRIDONES

Compound	$M^+ - OH\cdot$	$M^+ - OH\cdot - H_2$	Compound	$M^+ - OH\cdot$	$M^+ - OH\cdot - H_2$
(VI)	50	18	(XXI)	22	1
(IX)	11	2	(XXXI)	20	2
(XVIII)	36	3	(XXXII)	—	—

either the spectrum of a 4-ethoxyacridone (Tables 1 and 4) or in those of other acridones studied. The compositions of these ions have been established in the spectra of (VI) and (XXXI). This process may be plausibly represented (e.g. in the case of (VI)) by the bond-forming process (VI) $\rightarrow p \rightarrow q$ (Scheme 4). Electron impact processes involving loss of hydroxy radicals and water from compounds containing ethoxyl groups adjacent to carbonyl functions will be reported in a future publication.

[12] Pelter, A., Stainton, P., and Barber, M., *J. heterocyclic Chem.*, 1965, **2**, 262.

In summary, mass spectrometry provides valuable information regarding the type of substituents at the 1,2 and 4 positions of the acridone nucleus, and in some cases, allows the determination of the substituent on nitrogen. This technique, in



p, *m/e* 266 *q*, *m/e* 264

Scheme 4

conjugation with other physical methods, should prove of considerable value in the structure elucidation of acridones.

Experimental

All mass spectra were determined with a Hitachi Perkin–Elmer RMU 6D mass spectrometer operating at 75 eV and with a source and inlet temperature of approximately 200°. Exact mass measurements were determined with an A.E.I. MS9 mass spectrometer with a resolution of 14000 (10% valley definition) using heptacosafluorotributylamine to provide reference masses. All measurements were correct to within 15 p.p.m.

Compounds (V), (XVII), (XX), (XXVIII), and (XXXIII) were isolated from *Acronychia baueri*, and compounds (IV), (XIV), (XIX), and (XXV) derived from them.[13] Compounds (VII), (XI), and (XVI) were isolated from *Evodia xanthoxyloides* and compounds (VIII), (X), and (XIII) derived from them.[14] Compound (III) was prepared by the method of Acheson,[15] (XXII) and (XXIII) by that of Prager and Thredgold.[16] Compounds (VI), m.p. 134°; (IX), m.p. 132°; (XVIII), m.p. 95–96°; (XXI), m.p. 153–154°; and (XXXI) (non-crystalline gum[17]) were prepared by ethylating the corresponding 1-hydroxy compound with ethyl iodide in the presence of silver oxide. Compounds (XXIX) and (XXX) were prepared from melicopidine and melicopine respectively by opening the methylenedioxy group with sodium methoxide to give (XXVI) and (XXVII),[17] and methylating with deuterodiazomethane in dioxan/ether.[6] Compound (XXXII) was prepared by ethylation of (XXVII) with ethyl iodide.[17] Compound (XXXIV), m.p. 214–216°, was prepared by hydrogenation of noracronycine, a method found superior to that of Brown *et al.*[18] The spectrum of (XV) was obtained by introducing (XIV) directly into the source with deuterium oxide.[19]

Acknowledgments

One of us (R.G.C.) is grateful for the award of an Elsie Ballot Fellowship.

The Hitachi Perkin–Elmer RMU 6-D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

[13] Lahey, F. N., and Thomas, W. C., *Aust. J. scient. Res.* A, 1949, **2**, 423.
[14] Hughes, G. K., Neill, K. G., and Ritchie, E., *Aust. J. scient. Res.* A, 1952, **5**, 401.
[15] Acheson, R. M., and Robinson, M. J., *J. chem. Soc.*, 1953, 232.
[16] Prager, R. H., and Thredgold, H. M., *Tetrahedron Lett.*, 1966, 4909.
[17] Crow, W. D., and Price, J. R., *Aust. J. scient. Res.* A, 1949, **2**, 255.
[18] Brown, R. D., Drummond, L. J., Lahey, F. N., and Thomas, W. C., *Aust. J. scient. Res.* A, 1949, **2**, 622.
[19] Shannon, J. S., *Aust. J. Chem.*, 1962, **15**, 265.

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ELECTRON IMPACT STUDIES

XI.* MASS SPECTRA OF AROMATIC AZOXY COMPOUNDS. SKELETAL REARRANGEMENT UPON ELECTRON IMPACT

By J. H. Bowie,† R. G. Cooks,‡ and G. E. Lewis†

[*Manuscript received January* 25, 1967]

Summary

The mass spectra of 15 aromatic azoxy compounds are reported and discussed. The spectra exhibit pronounced molecular ions, and fragmentation modes which are produced by both simple cleavage and complex skeletal reorganization processes.

This paper is concerned with the interpretation of the mass spectra (Figs. 1–11) of the azoxy compounds (I–XV). Although the compositions of many ions have been established by exact mass measurements (Table 1), the structures of these are generally not known. Nominal structures have been written, however, in order that the fragmentation processes may be related to (or rationalized with) the structures of the intact molecule. The presence of a metastable ion for a process (indicated either in the text or a figure) is depicted by an asterisk.

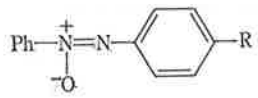
The purpose of this investigation was to study the basic fragmentation processes of substituted azoxy compounds, and to investigate the nature and genesis of any skeletal rearrangement ions. The study was prompted by our knowledge of the skeletal rearrangements of azobenzenes on electron impact,[1] and of the photochemical behaviour of azoxybenzenes.[2]

Aromatic azoxy compounds fragment in a characteristic manner on electron impact. In general, although the position of substituents on the aromatic rings can only be determined when a specific "proximity effect" operates between the substituent (e.g. α-2-methyl) and the azoxy-oxygen atom, the position of the N-oxide link can always be determined. All the azoxy compounds studied exhibit skeletal rearrangement ions in their spectra, and four distinct rearrangement processes operate.

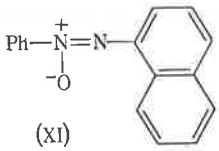
The mass spectra (Figs. 1–4) of azoxybenzene (I) and of compounds (X), (XII), and (XIV) illustrate the characteristic fragmentation processes which are

* Part X, *Aust. J. Chem.*, 1967, **20**, 1179.
† Department of Organic Chemistry, University of Adelaide.
‡ University Chemical Laboratory, Lensfield Road, Cambridge, England.

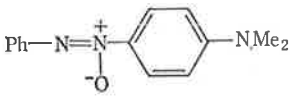
[1] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *J. chem. Soc.* B, in press.
[2] Lewis, G. E., and Reiss, J. A., *Aust. J. Chem.*, 1966, **19**, 1887, and references therein.



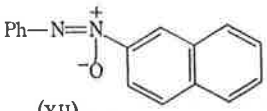
(I) R = H (III) R = NO_2
(II) R = CO_2Et (IV) R = NMe_2



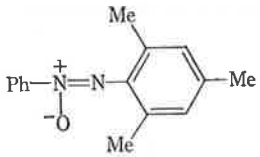
(XI)



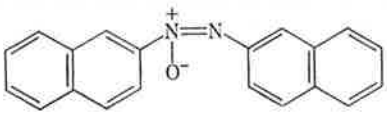
(V)



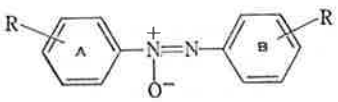
(XII)



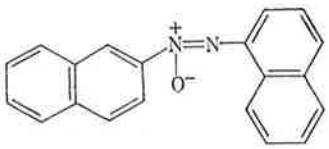
(VI)



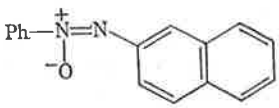
(XIII)



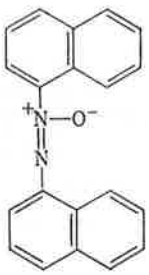
(VII) R = *o*-Me
(VIII) R = *m*-Me
(IX) R = *p*-Me



(XIV)

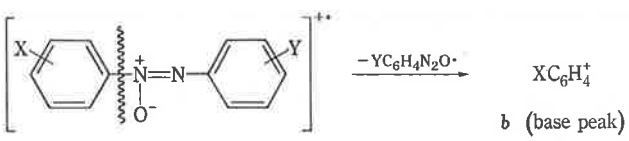


(X)



(XV)

common to the majority of aromatic azoxy compounds. The base peaks of these spectra are produced by C–N cleavage α to the *N*-oxide group (see $a \rightarrow b$), e.g. to give $C_6H_5^+$ (*m/e* 77) in the spectrum of (X) and $C_{10}H_7^+$ (*m/e* 127) in the spectrum of (XII). This is a general feature of the spectra examined (except in that of the



a *b* (base peak)

TABLE 1

IONS OF CONFIRMED COMPOSITION IN THE MASS SPECTRA OF COMPOUNDS (I–XV)

Compound	*m/e*	Composition	Compound	*m/e*	Composition
(I)	182	$C_{12}H_{10}N_2$	(V)	213	$C_{13}H_{15}N_3$
	170	$C_{11}H_{10}N_2$		196	$C_{13}H_{12}N_2$
	169	$C_{11}H_9N_2$		184	$C_{13}H_{14}N$
	152	$C_{12}H_8$		167	$C_{12}H_9N$
	142	$C_{11}H_{10}$		162	$C_9H_{10}N_2O$
				150	$C_8H_{10}N_2O$
(II)	242	$C_{14}H_{14}N_2O_2$ (70%)		147	$C_9H_{11}N_2$
		$C_{13}H_{10}N_2O_3$ (30%)		134	$C_8H_{10}N_2$
	225	$C_{13}H_9N_2O_2$		120	$C_8H_{10}N$
	213	$C_{14}H_{13}O_2$ (20%)		106	C_7H_8N
		$C_{12}H_9N_2O_2$ (80%)		105	C_7H_7N (60%)
	197	$C_{12}H_9N_2O$			$C_6H_5N_2$ (40%)
	179	$C_{14}H_{11}$	(VI)	208	$C_{14}H_{12}N_2$
	178	$C_{14}H_{10}$		197	$C_{13}H_{13}N_2$
	169	$C_{11}H_9N_2$		132	$C_9H_{10}N$
	149	$C_9H_9O_2$		118	C_8H_8N
	141	$C_{11}H_9$		91	C_7H_7
(III)	168	$C_{11}H_8N_2$	(VII)	211	$C_{13}H_{11}N_2O$
	141	$C_{11}H_9$		209	$C_{14}H_{13}N_2$
	139	$C_{11}H_7$		198	$C_{14}H_{14}O$
	127	$C_{10}H_7$		194	$C_{13}H_{10}N_2$
	126	$C_{10}H_6$		183	$C_{12}H_{11}N_2$
	122	$C_6H_4NO_2$		165	$C_{13}H_9$
	107	C_6H_5NO (90%)		155	$C_{12}H_{11}$
		C_8H_{11} (10%)		104	C_7H_6N
	105	$C_6H_5N_2$	(X)	220	$C_{15}H_{12}N_2$
				191	$C_{15}H_{11}$
				105	$C_6H_5N_2$
			(XII)	220	$C_{15}H_{12}N_2$
				219	$C_{15}H_{11}N_2$
				191	$C_{15}H_{11}$
				155	$C_{10}H_7N_2$
				141	$C_{10}H_7N$
				114	C_9H_6
			(XIV)	270	$C_{19}H_{14}N_2$
				252	$C_{20}H_{12}$
				241	$C_{19}H_{13}$

TABLE 2

RELATIVE ABUNDANCE OF CATIONS PRODUCED BY C–N CLEAVAGE

Compound	(II)	(III)	(IV)	(V)	(VI)	(X)	(XII)
m/e (%)	77 (100)	77 (100)	77 (47)	120 (100)	77 (100)	77 (100)	127 (100)
m/e (%)	149 (34)	122 (6)	120 (20)	77 (64)	119 (11)	127 (23)	77 (27)

dimethylaminoazoxybenzene (IV), see below) and may be used to ascertain the position of the *N*-oxide group (see Table 2 and Figs. 1–11). Other fragmentations which occur by normal cleavages are unexceptional, and are indicated in Figures 1–4. The spectra of (X) and (XI) are almost identical, as are those of (XIII–XV).

Fig. 1

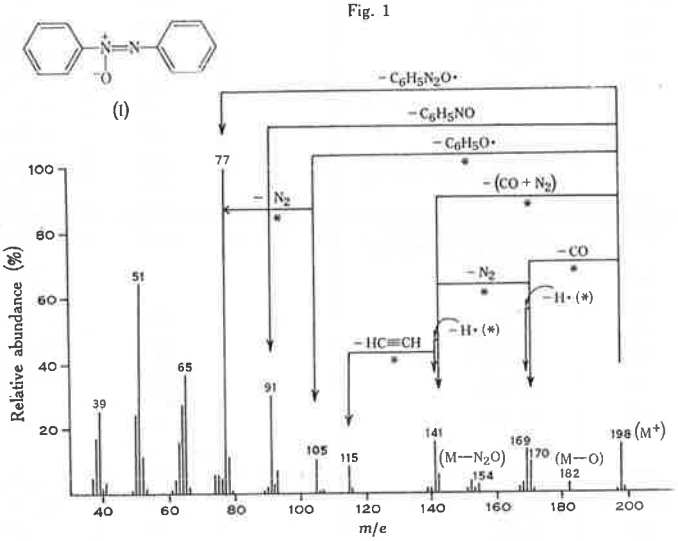
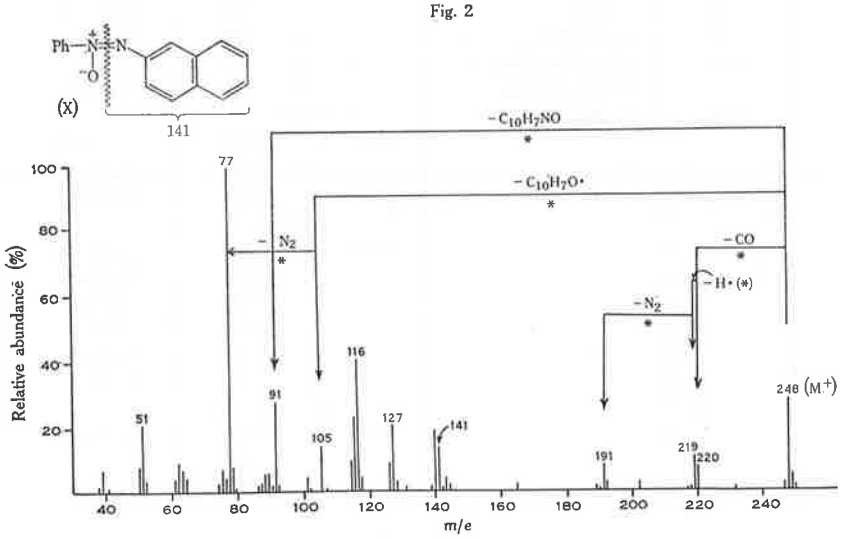


Fig. 2



It is appropriate to consider the skeletal rearrangements in the spectra of compounds (I), (X), (XII), and (XIV), because they are generally more obvious in these spectra than in those of the substituted derivatives, which may fragment additionally through the various substituents. Four skeletal reorganization processes are exhibited in Figures 1–4.

Process 1. $M^+—N_2O$. This is a process of the type $ABC \rightarrow AC+B$ to furnish diaryl radical ions. Such processes have been previously noted in the spectra of

Fig. 3

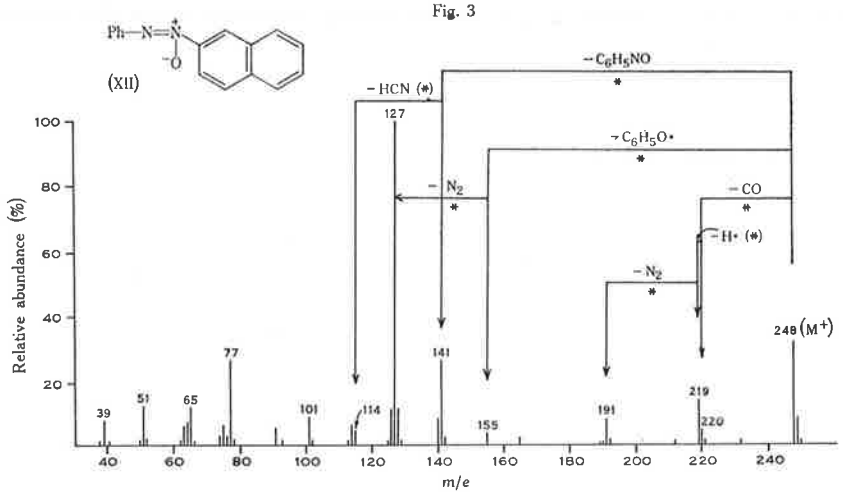
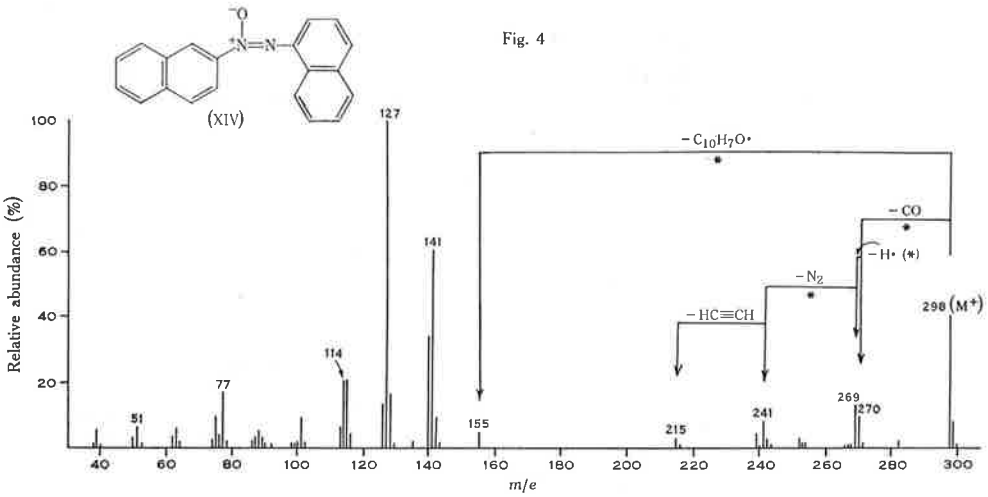


Fig. 4



diaryl sulphides,[3] disulphides,[4] sulphones,[5–8] sulphoxides,[7] and azobenzenes.[1] Such ions, when observed, are generally small in the spectra of aromatic azoxy compounds (Figs. 1 and 4).

[3] Bowie, J. H., Lawesson, S.-O., Madsen, J. Ø., Nolde, C., and Williams, D. H., *J. chem. Soc.* B, 1966, 951.

[4] Bowie, J. H., Lawesson, S.-O., Madsen, J. Ø., Nolde, C., Schroll, G., and Williams, D. H., *J. chem. Soc.* B, 1966, 946.

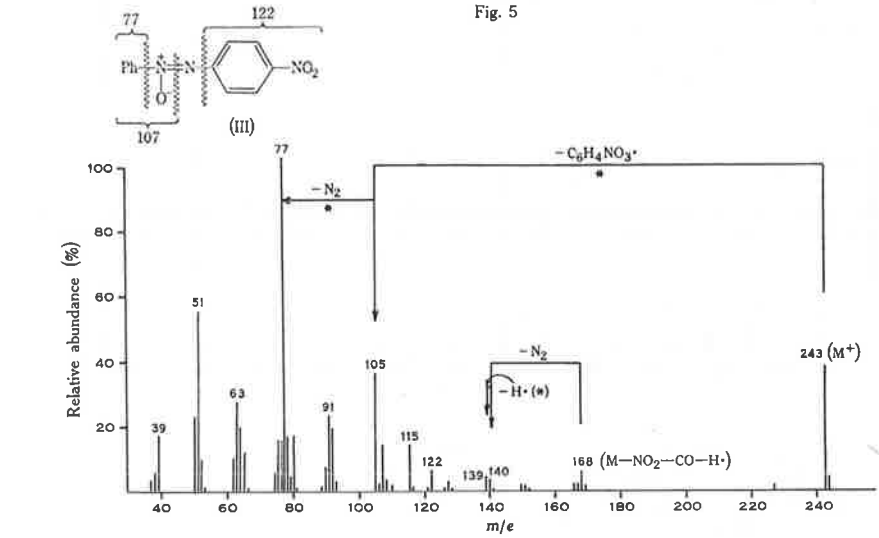
[5] Meyerson, S., Drews, H., and Fields, E. K., *Analyt. Chem.*, 1964, **36**, 1294.

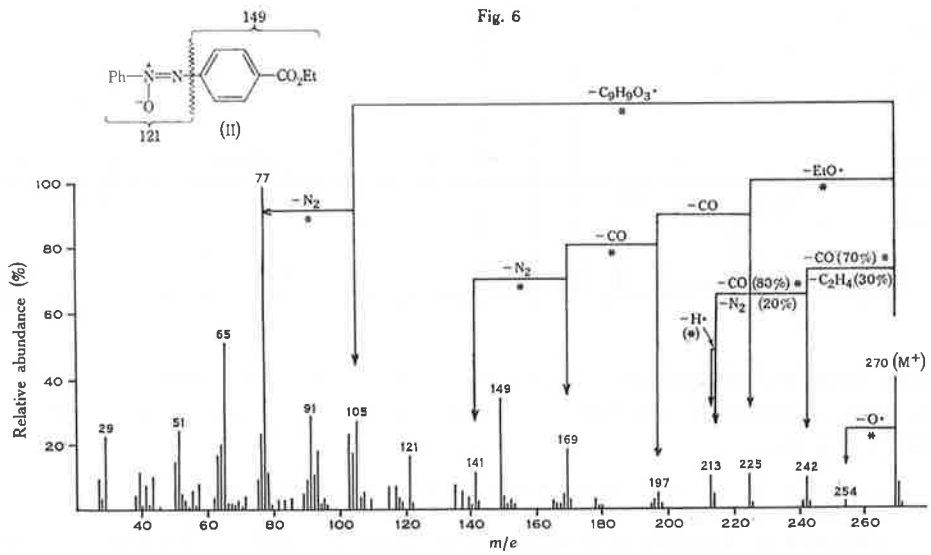
[6] Bowie, J. H., Williams, D. H., Lawesson, S.-O., Madsen, J. Ø., Nolde, C., and Schroll, G., *Tetrahedron Lett.*, 1965, 4377.

[7] Bowie, J. H., Williams, D. H., Lawesson, S.-O., Madsen, J. Ø., Nolde, C., and Schroll, G., *Tetrahedron*, 1966, **22**, 3515.

[8] Fields, E. K., and Meyerson, S., *J. Am. chem. Soc.*, 1966, **88**, 2836.

Process 2. $M^+-CO-N_2-H\cdot$. This process can either occur in successive steps (each step substantiated by a metastable ion) or by the concerted elimination $M^+-(CO+N_2)-H\cdot$. Similar processes are noted in all spectra, but may be modified by additional fragmentation through the substituent in the spectra of the substituted compounds (II–IX).





Process 3. The spectra of (X) and (XII) exhibit the fragmentations $M^+-C_{10}H_7O\cdot$ (to *m/e* 105 in X) and $M^+-C_6H_5O\cdot$ (to *m/e* 155 in XII). This process, e.g. in the case of (X), demands an oxygen migration to the naphthalene ring, and is a process noted in the majority of spectra, but is notably absent in that of (VI) (which contains two *ortho* methyl groups in ring B).

Fig. 7

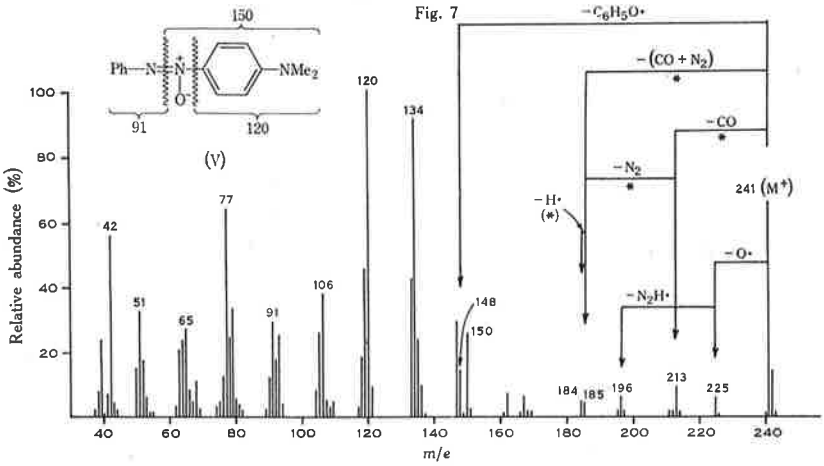


Fig. 8

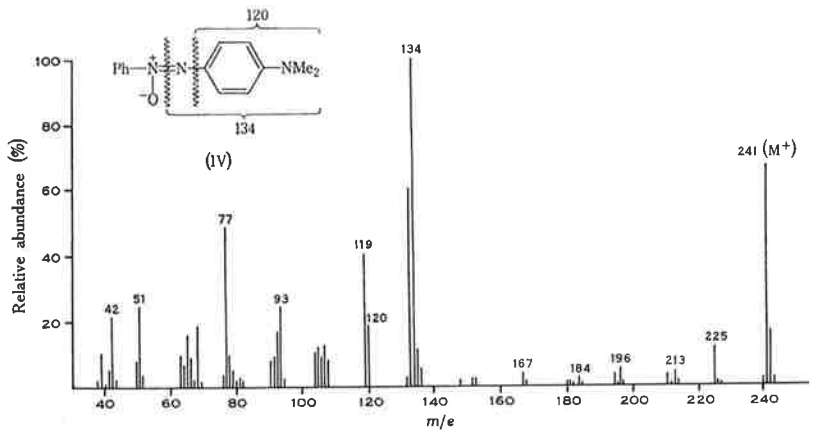
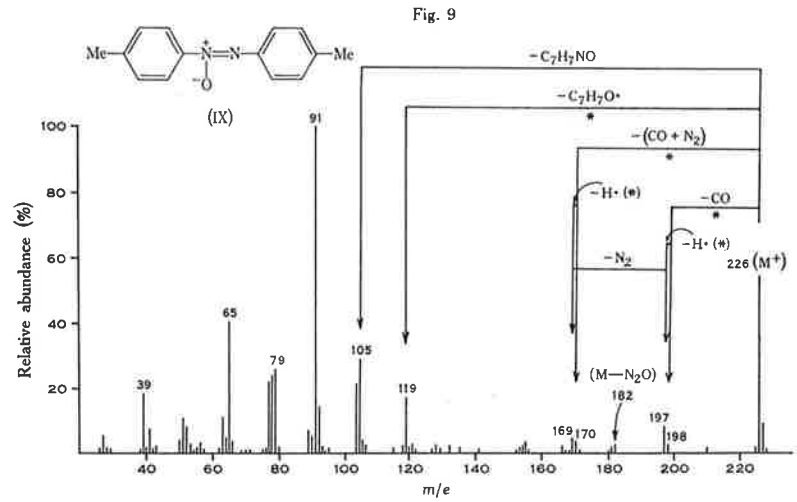


Fig. 9



Process 4. The spectra of (X) and (XII) exhibit the fragmentations $M^+ - C_{10}H_7NO\cdot$ (to *m/e* 91 in X) and $M^+ - C_6H_5NO\cdot$ (to *m/e* 141 in XII). This process is restricted to the azoxy compounds (I), (V), and (X–XV).

Fig. 10

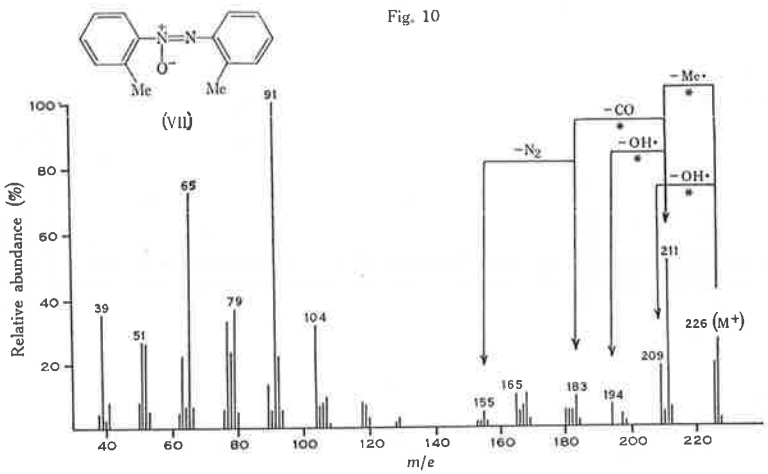
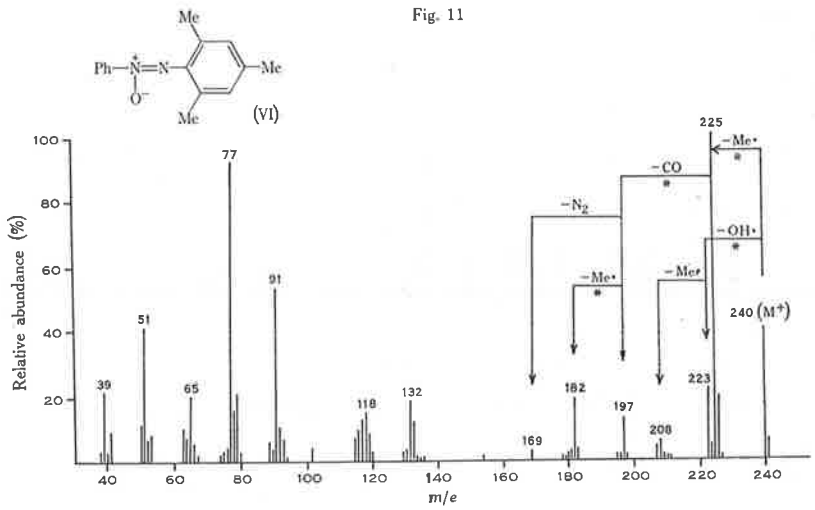


Fig. 11

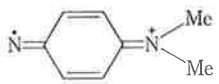


The rearrangement processes of the substituted azoxybenzenes follow the general processes 2 and 3 and specific modes have been briefly mentioned in a previous communication[9] (see also Figs. 5–11). A general discussion of the simple cleavages of the monosubstituted derivatives (II–V) is not necessary here, as a compendium of the mass spectra of substituted benzenes is available.[10] Before leaving a discussion of monosubstituted azoxybenzenes, it is important to note that although the

[9] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *Chem. Commun.*, 1967, 284.

[10] Djerassi, C., Budzikiewicz, H., and Williams, D. H., "Interpretation of Mass Spectra of Organic Compounds." (Holden Day: San Francisco 1964.)

dimethylamino derivative (V) obeys the general rule that the base peak of the spectrum is produced by α-cleavage to the *N*-oxide group (i.e. to *m/e* 120, Fig. 7), its isomer (IV) does not. In this case (Fig. 8), although *m/e* 77 carries more of the total ion current than *m/e* 120 (Table 2), the base peak of the spectrum is produced by N–N cleavage to form *m/e* 134, presumably due to the stability of this ion (represented as *c*). This does not affect the determination of the *N*-oxide position, which may still be ascertained from the relative intensities of *m/e* 77 and 120.



c, *m/e* 134

It is necessary that an attempt should be made to rationalize the rearrangement processes 2–4. Although such a rationale is of necessity a speculative one, it is supported (in a negative sense) by the known fragmentations of azobenzenes,[1] and is analogous to the proposed mechanisms for the photochemical rearrangements of azoxybenzenes.[2] It is proposed (Scheme 1) for the general case *a*, that partial rearrangement of the molecular ion involves oxygen migration to afford a cyclized ion *e* (similar processes have been noted in the spectra of diaryl sulphones[7]). It is clear that the *o*-hydroxyazobenzene radical ion (*f*) is not the intermediate which is responsible for process 2 in the spectrum of azoxybenzene, as the skeletal rearrangement process exhibited by the *o*-hydroxyazobenzene molecular ion[1] is $M^+—N_2—CO—H\cdot$ and not $M^+—CO—N_2—H\cdot$ (for azoxybenzene), i.e. *e* will not form *f*. The ion *e* may explain process 2 ($e \rightarrow g$) and process 3 ($e \rightarrow h$). Process 4 could be initiated from *e*, but may be more plausibly explained by the ion *k* (i.e. $k \rightarrow l$), which could equally be responsible for process 3. It is important to note that even though the proposed genesis of such ions is speculative, their presence limits both the *a priori* prediction of fragmentation modes, and the application of the "element mapping" technique[11–13] to this class of compound.

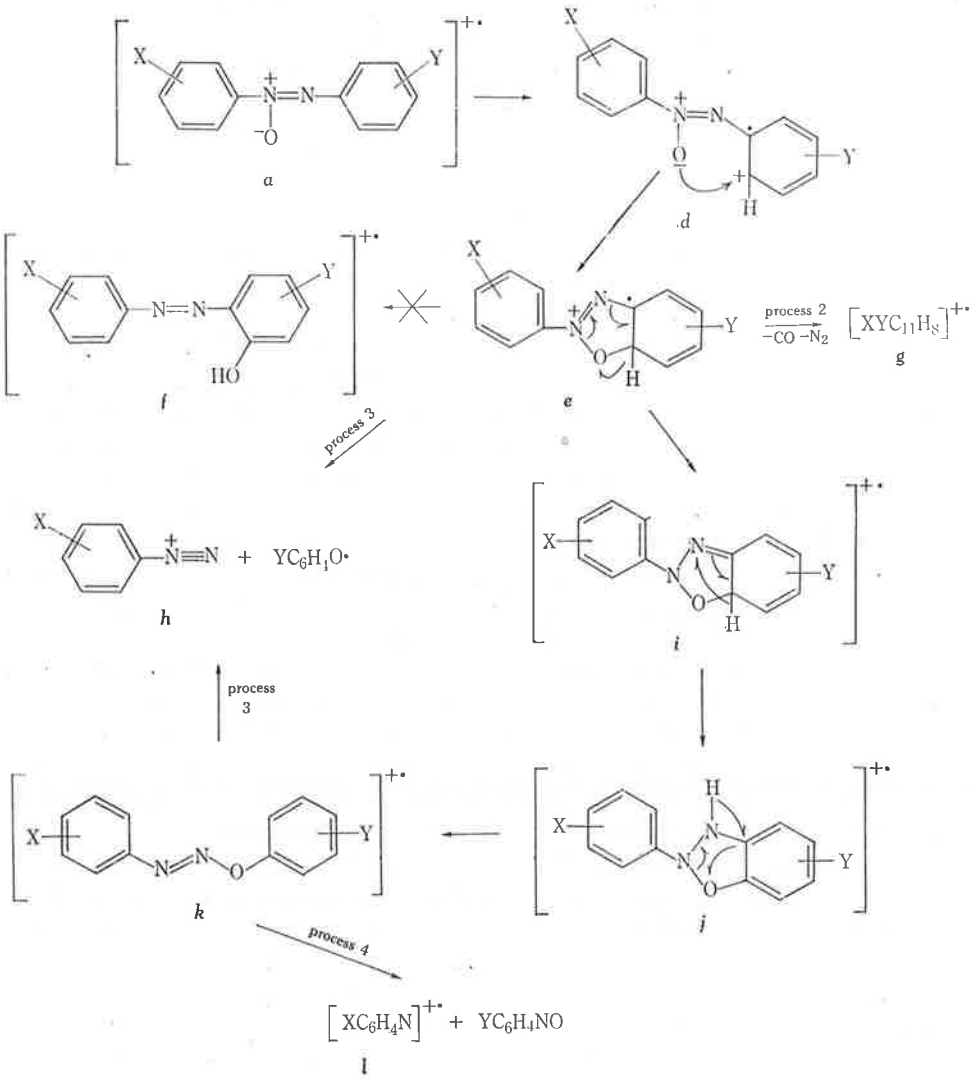
The mass spectra of the dimethylazoxybenzenes (VII–IX) show some interesting features. The mass spectrum (Fig. 9) of 4,4′-dimethylazoxybenzene (IX) (which is very similar to that of 3,3′-dimethylazoxybenzene (VIII)) shows fragmentation modes which are analogous to azoxybenzene itself. 2,2′-Dimethylazoxybenzene (VII) fragments in an entirely different manner (Fig. 10) on electron impact, exhibiting a large $M^+—Me\cdot$ ion (*m/e* 211). Such behaviour is not observed in the spectra of the isomeric azotoluenes,[1] and consequently it must be due to a "proximity effect", operating between the *ortho* methyl substituent and the oxygen of the azoxy link. This process is so pronounced that the skeletal rearrangement process 2 for this compound is $M^+—Me\cdot—CO—N_2$. A pronounced $M^+—OH\cdot$ ion (*m/e* 209) is also observed in this spectrum (Fig. 10) but not in those of the other isomers.

[11] Biemann, K., *Pure appl. Chem.*, 1964, **9**, 95.

[12] Biemann, K., Bommer, P., and Desiderio, D. M., *Tetrahedron Lett.*, 1964, 1725.

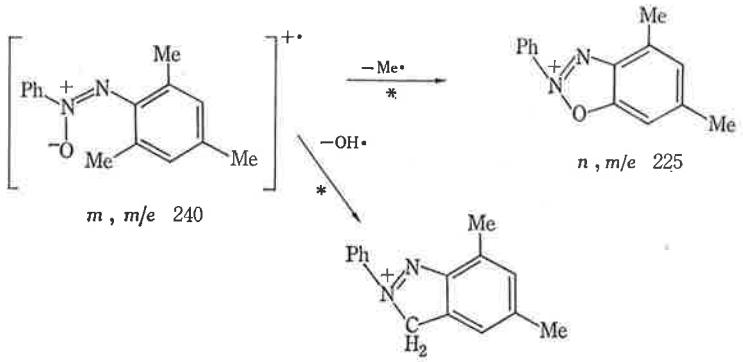
[13] Biemann, K., Bommer, P., Desiderio, D. M., and McMurray, W. J., in "Advances in Mass Spectrometry." Vol. 3, pp. 639–53. (Ed. W. L. Mead.) (Institute of Petroleum: London 1966.)

In the spectrum (Fig. 11) of (VI) (in which the A ring is unsubstituted and the B ring has the two *ortho* positions occupied by methyl substituents), the $M^+-Me\cdot$ (base peak) and $M^+-OH\cdot$ ions are even more pronounced than they are in Figure 10. This indicates that these processes are due to interaction between oxygen and the



Scheme 1

ortho methyl substituents on the aromatic ring furthest from the NO group, and they may be explained by processes $m \rightarrow n$ and $m \rightarrow o$ (for VI). The ion *n* (*m/e* 225 may now fragment by successive losses of CO and N_2 (cf. Scheme 1, process 2). The presence of this "proximity effect" allows the determination of the α-2-methyl substituent in an azoxybenzene.



m, *m/e* 240 *n*, *m/e* 225 *o*, *m/e* 223

Experimental

All mass spectra were measured with an Hitachi Perkin–Elmer RMU 6D mass spectrometer operating at 75 eV, with the source and inlet system at *c.* 180°. The spectra of (IV) and (V) were additionally determined directly at 80° in order to prove that no thermal migration of oxygen was taking place. The "heated" and "direct" spectra were identical. Exact mass measurements were determined with an A.E.I. MS9 mass spectrometer using a resolution of *c.* 14000 (10% valley definition) with heptacosafluorotributylamine providing the reference masses. All exact mass measurements were correct to 15 p.p.m.

All the compounds employed were prepared by reported procedures, as indicated: (I),[14] (II),[15] (III),[16] (IV–V),[17] (VI),[2] (VII–IX),[18] and (X–XV).[19]

Acknowledgments

One of us (R.G.C.) gratefully acknowledges the award of an Elsie Ballot Fellowship. The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

[14] Badger, G. M., Buttery, R. G., and Lewis, G. E., *J. chem. Soc.*, 1953, 2143.
[15] Badger, G. M., and Lewis, G. E., *J. chem. Soc.*, 1953, 2147.
[16] Werner, A., and Stiasny, E., *Ber. dt. chem. Ges.*, 1899, **32**, 3256.
[17] Anderson, W., *J. chem. Soc.*, 1952, 1722.
[18] Sayigh, A. A., *J. org. Chem.*, 1960, **25**, 1707.
[19] Badger, G. M., and Lewis, G. E., *J. chem. Soc.*, 1953, 2151.

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ELECTRON IMPACT STUDIES

XII.* MASS SPECTRA OF SUBSTITUTED IMIDAZOLES

By J. H. Bowie,† R. G. Cooks,‡ S.-O. Lawesson,§ and G. Schroll§

[*Manuscript received February* 9, 1967]

Summary

The mass spectra of 37 imidazoles are reported and discussed. The spectra exhibit pronounced molecular ions and characteristic fragmentation patterns. The fragmentation modes have been substantiated by deuterium labelling, exact mass measurements, and appropriate metastable ions. Skeletal rearrangement fragments are rare in these spectra; consequently mass spectrometry is useful for structure elucidation of imidazoles.

The mass spectra of imidazoylquinoline alkaloids have recently been investigated,[1] but no survey of simple imidazoles has been reported. This paper is concerned with the mass spectra of the imidazoles (I–XXXVII), which are recorded in Table 1 and Figures 1–8. Exact mass measurements are listed in Table 2. The presence of an appropriate metastable ion for a process is indicated by an asterisk. Although the structures of fragment ions are not known, nominal structures have been written to rationalize the fragmentation processes with the structure of the intact molecule.

The mass spectra (Figs. 1–3) of imidazole (I) and the alkylimidazoles (IV, VI, VIII, and XXVIII) are relatively simple, and an examination of the spectra of the deuterium-labelled derivatives (II, III, V, VII, XXIX, and XXX) has aided the rationalization of fragmentation modes.

The mass spectra of imidazole (I) and the two labelled imidazoles (II and III) are recorded in Figure 1 and Table 1. Imidazole (I), on electron impact, undergoes the decompositions outlined in Scheme 1 and Figure 1, with the ultimate formation of the aziridine cation (*c*, *m/e* 40).

The major problem, arising from the loss of HCN from the molecular ions of both imidazole (I) and the substituted imidazoles, concerns the pathways followed in these eliminations. The spectra of 1-*d*-imidazole (II) and 1,2-d_2-imidazole (III)

* Part XI, *Aust. J. Chem.*, 1967, **20**, 1601.
† Department of Organic Chemistry, University of Adelaide.
‡ University Chemical Laboratory, Lensfield Road, Cambridge, England.
§ Department of Organic Chemistry, Aarhus University, Aarhus C, Denmark.

[1] Joynt, V. P., Arndt, R. R., Jordaan, A., Biemann, K., and Occolowitz, J. L., *J. chem. Soc.* B, 1966, 980.

TABLE 1

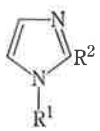
MASS SPECTRA OF SUBSTITUTED IMIDAZOLES

All peaks greater than 5% of the base peak (100%) (and peaks due to skeletal rearrangement ions and molecular ions which are less than this value) are recorded. Because of the large M − 1 and M − 2 peaks in the spectra of (III), (VII), and (XXIX) the isotopic purities cannot be determined

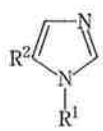
(III)	*m/e*	28	29	30	38	39	40	41	42	43	67	68	69	70	71			
	I (%)	6	23	24	14	15	40	81	62	14	6	62	100	57	15			
(VII)	*m/e*	40	41	42	43	54	55	56	81	82	83	84						
	I (%)	7	17	22	21	37	22	7	25	86	100	11						
(IX)	*m/e*	65	91	92	158(M)	159												
	I (%)	10	100	7	58	8												
(X)	*m/e*	65	91	92	172(M)	173												
	I (%)	8	100	8	47	6												
(XI)	*m/e*	39	40	41	42	67	68	69	95	96(M)	97							
	I (%)	6	27	45	10	15	58	5	6	100	7							
(XIII)	*m/e*	51	65	91	92	130	157	158	186(M)	187								
	I (%)	5	14	100	8	5	75	12	43	5								
(XIV)	*m/e*	40	41	42	47	68	69	95	96	97	98	124	125	126	170(M)			
	I (%)	6	13	14	10	36	19	7	10	100	7	9	45	21	2			
(XV)	*m/e*	41	42	47	56	81	82	83	110	111	112	139	140	184(M)				
	I (%)	6	16	6	6	12	15	7	29	100	6	39	19	3				
(XVI)	*m/e*	36	40	41	42	43	44	53	54	55	57	67	68	69	70	71	80	81
	I (%)	12	12	32	20	13	14	17	8	13	13	13	10	26	10	6	7	21
	m/e	95	96	97	98(M)	99												
	I (%)	8	5	78	100	9												
(XVII)	*m/e*	40	41	42	43	44	52	54	55	56	81	82	83	95	96	110	111	
	I (%)	15	15	40	52	18	9	34	18	16	38	49	15	25	13	100	50	
	m/e	112(M)	113															
	I (%)	61	5															
(XVIII)	*m/e*	65	91	92	97	157	186	188(M)										
	I (%)	10	100	12	10	15	8	22										
(XIX)	*m/e*	36	38	39	40	41	42	44	45	47	67	68	94	95	112(M)	113		
	I (%)	16	7	7	32	52	6	60	9	8	25	76	33	13	100	7		
(XXI)	*m/e*	41	43	44	47	65	91	92	157	158	159	201	202(M)					
	I (%)	6	11	13	11	16	100	8	8	55	8	4	4					
(XXIII)	*m/e*	27	28	39	51	65	77	89	91	92	95	106	129	130	155	156		
	I (%)	10	20	6	5	10	5	5	100	9	5	18	5	5	5	17		
	m/e	157	183	184	201(M)	202												
	I (%)	12	7	29	100	13												

TABLE 1 (*Continued*)

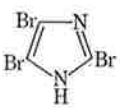
(XXVII)	*m/e*	36	41	47	54	55	56	69	72	81	82	86	109	113	114	115	116
	I (%)	12	7	7	6	13	9	10	30	16	11	6	18	31	80	7	5
	m/e	127	141	142	186(M)	187	188										
	I (%)	8	8	4	100	10	5										
(XXIX)	*m/e*	27	28	29	39	40	41	42	43	51	52	53	54	55	56	81	82
	I (%)	28	74	52	7	10	18	20	9	9	17	14	66	55	16	43	100
	m/e	83	84														
	I (%)	88	22														
(XXXI)	*m/e*	40	41	42	53	54	69	70	81	95	97	98(M)	99				
	I (%)	11	9	31	9	11	30	10	25	6	100	75	5				
(XXXII)	*m/e*	36	39	40	41	67	68	94	95	112(M)	113						
	I (%)	7	7	32	8	37	16	36	24	100	5						
(XXXIV)	*m/e*	40	65	67	68	93	94	95	159	187(M)	188						
	I (%)	5	5	5	9	100	8	48	2	54	6						
(XXXV)	*m/e*	25	27	28	38	39	40	42	51	67	79	81	91	92	93	94	119
	I (%)	6	8	57	18	25	82	9	6	37	5	5	7	18	8	18	13
	m/e	121	146(M)	147	148(M)	149											
	I (%)	13	100	12	95	10											
(XXXVII)	*m/e*	39	51	63	77	82·5	83	89	90	95·5	108	109	109·5	110	165		
	I (%)	10	10	15	11	18	13	30	6	9	7	7	23	15	41		
	m/e	166	219	220(M)	221												
	I (%)	7	76	100	15												



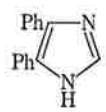
(I) – (XXVII)



(XXVIII) – (XXXV)

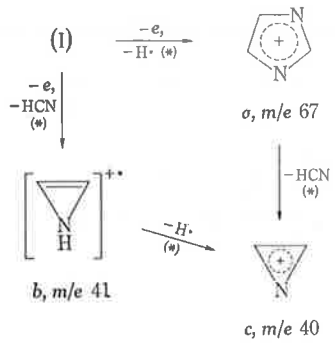


(XXXVI)



(XXXVII)

	R^1	R^2		R^1	R^2		R^1	R^2
(I)	H	H	(XIV)	H	$CH(OEt)_2$	(XXVIII)	H	Me
(II)	D	H	(XV)	Me	$CH(OEt)_2$	(XXIX)	D	Me
(III)	D	D	(XVI)	H	CH_2OH	(XXX)	Me	D
(IV)	Me	H	(XVII)	Me	CH_2OH	(XXXI)	H	CH_2OH
(V)	Me	D	(XVIII)	$PhCH_2$	CH_2OH	(XXXII)	H	CO_2H
(VI)	H	Me	(XIX)	H	CO_2H	(XXXIII)	H	CO_2Me
(VII)	D	Me	(XX)	D	CO_2D	(XXXIV)	H	CONHPh
(VIII)	Me	Me	(XXI)	$PhCH_2$	CO_2H	(XXXV)	H	Br
(IX)	$PhCH_2$	H	(XXII)	H	CO_2Me			
(X)	$PhCH_2$	Me	(XXIII)	$PhCH_2$	$CONH_2$			
(XI)	H	CHO	(XXIV)	$PhCH_2$	CONHPh			
(XII)	Me	CHO	(XXV)	H	SH			
(XIII)	$PhCH_2$	CHO	(XXVI)	Me	SH			
			(XXVII)	Me	SCO_2Et			



Scheme 1

Fig. 1

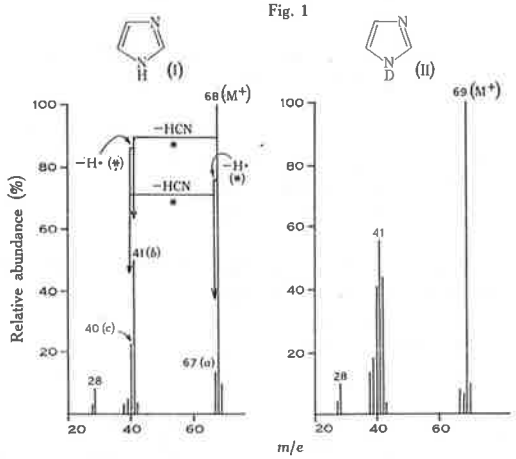
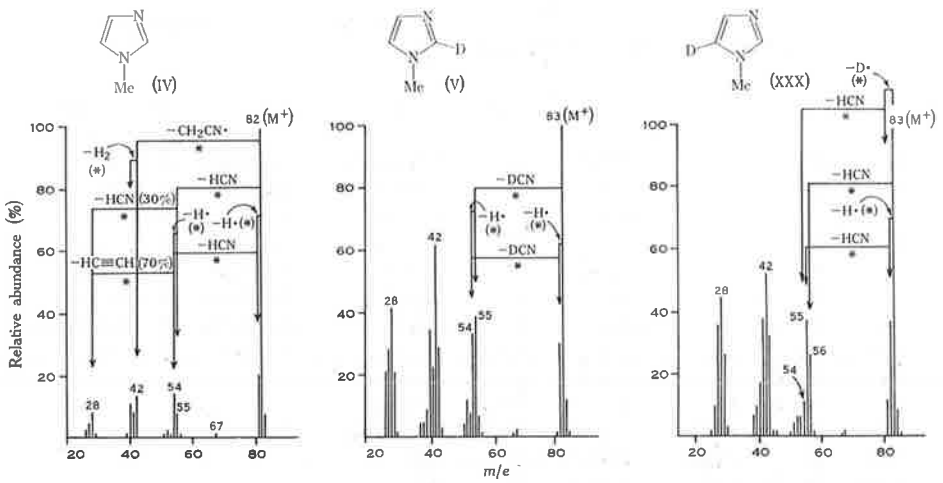


Fig. 2



clearly show loss of HCN and DCN from the various molecular ions, which means that the loss of HCN from the imidazole molecular ion does not occur by a specific process.

TABLE 2
IONS OF KNOWN COMPOSITION IN THE SPECTRA OF (I–XXXVII)

Compound	*m/e*	Composition
(I)	41	C_2H_3N
	40	C_2H_2N
(IV)	55	C_3H_5N
	54	C_3H_4N
	42	C_2H_4N
	41	C_2H_3N
	28	CHN (70%)
		C_2H_4 (30%)
(VI)	55	C_3H_5N
	54	C_3H_4N
	42	C_2H_4N
	41	C_2H_3N
	28	CHN (80%)
		C_2H_4 (20%)
(XII)	82	$C_4H_6N_2$
	81	$C_4H_5N_2$
	56	$C_2H_4N_2$
	42	C_2H_4N
	41	C_2H_3N
(XVI)	70	C_3H_4NO
	69	$C_3H_5N_2$
(XIX)	68	$C_3H_4N_2$ (90%)
		C_3H_2NO (10%)
	67	$C_3H_3N_2$ (50%)
		C_3HNO (50%)
(XXII)	96	$C_4H_4N_2O$
	95	$C_4H_3N_2O$
	69	$C_3H_5N_2$
	68	$C_3H_4N_2$ (90%)
		C_3H_2NO (10%)
(XXIII)	184	$C_{11}H_8N_2O$
	156	$C_{10}H_8N_2$
	130	C_9H_8N
	129	C_9H_7N
	106	C_7H_8N
(XXIV)	260	$C_{17}H_{12}N_2O$
	249	$C_{16}H_{15}N_3$
	182	$C_{13}H_{12}N$
(XXVI)	81	$C_4H_5N_2$
	72	C_2H_2NS
(XXVII)	142	$C_6H_{10}N_2S$
	127	$C_5H_7N_2S$
	114	$C_4H_6N_2S$
	113	$C_4H_5N_2S$
	81	$C_4H_5N_2$
	72	C_2H_2NS
(XXVIII)	28	CHN (70%)
		C_2H_4 (30%)
(XXXII)	68	$C_3H_4N_2$ (70%)
		C_3H_2NO (30%)
	67	$C_3H_3N_3$ (45%)
		C_3HNO (55%)
(XXXIII)	95	$C_4H_3N_2O$
	94	$C_4H_2N_2O$
	68	$C_3H_4N_2$ (50%)
		C_3H_2NO (50%)
	67	$C_3H_3N_2$ (50%)
		C_3HNO (50%)
(XXXIV)	159	$C_9H_9N_3$
	95	$C_4H_3N_2O$
	93	C_5H_7N
(XXXVI)	275	C_2NBr_3
	277	
	279	
	281	
(XXXVII)	165	$C_{13}H_9$
	89	C_7H_5

The substitution pattern of an imidazole greatly affects the elimination of HCN. Comparison of the spectra (Fig. 2) of 1-methyl-, 2-*d*-1-methyl-, and 5-*d*-1-methylimidazole (IV, V, and XXX) shows specific loss of HCN from the 2,3-positions

(see A), while the spectra (Fig. 3 and Table 1) of 2-methyl-, and 1-*d*-2-methylimidazole (VI and VII) show the loss of HCN to originate either from the 1,5- or 3,4-positions. The latter possibility seems unlikely, as other imidazoles do not eliminate HCN from the 3,4-position (see (B)). The spectra (Fig. 3 and Table 1) of 4(5)-methyl-, and 1-*d*-4(5)-methylimidazole (XXVIII and XXIX) indicate loss of HCN from only the

Fig. 3

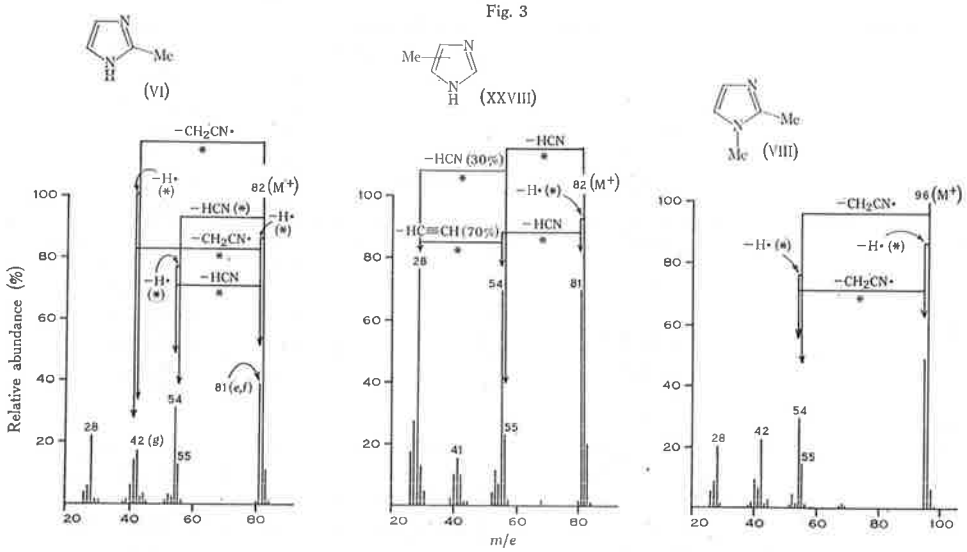
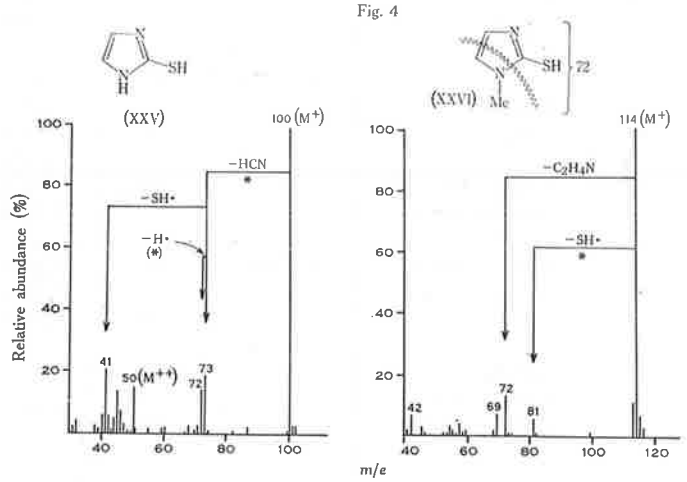
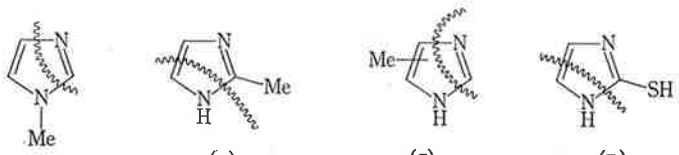


Fig. 4



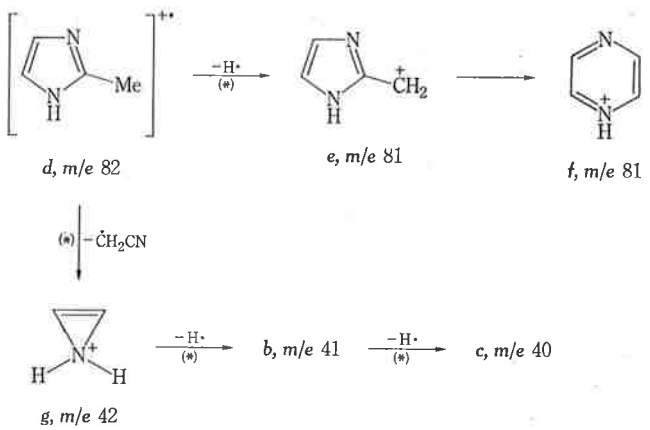
2,3-positions (C), while that (Fig. 3) of 1,2-dimethylimidazole (VIII) shows a negligible loss of HCN from the molecular ion, supporting the general observation that HCN is not lost from the 3,4-positions. 1-Methyl-2-mercaptoimidazole (XXVI) also does not eliminate HCN from its molecular ion, whereas 2-mercaptoimidazole (XXV) does (see Fig. 4), showing that this elimination probably originates from the 1,5-positions (D). The extremes to which an imidazole will go to eliminate HCN are

illustrated by the spectrum (Fig. 5) of 2,4,5-tribromoimidazole (XXXVI), where the M—HCN ion (40% of the base peak) requires a bromine migration for its formation.



(A) (B) (C) (D)

There are certain other aspects of the spectra of the methylimidazoles which need clarification. The processes ($M-CH_2CN\cdot$) and [($M-H\cdot$)$-CH_2CN\cdot$] are favoured in the spectra of 1- and 2-methylimidazole (IV and VI), but not in that of 4(5)-methylimidazole (XXVIII). Although the spectrum of 1-*d*-2-methylimidazole (VII) shows the loss to originate from the 2,3-positions, those (Fig. 2) of the labelled 1-methylimidazoles do not give an absolute answer, but it is apparent that both C2 and C5 are involved in this process, as some deuterium is lost from both these positions during the elimination.



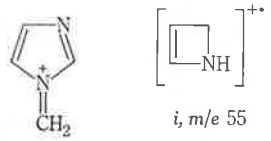
d, *m/e* 82 *e*, *m/e* 81 *f*, *m/e* 81

g, *m/e* 42 *b*, *m/e* 41 *c*, *m/e* 40

Scheme 2

Although it is reasonable that the $M-H\cdot$ ion (*e*; *m/e* 81) in the spectrum of (VI) arises by loss of a $H\cdot$ radical from the methyl group (to form *f*, *m/e* 81) (Scheme 2) the situation is more complex in the case of 1-methylimidazole (IV). Although no loss of deuterium occurs in the spectrum of 2-*d*-1-methylimidazole, that of 5-*d*-1-methylimidazole shows a 38% (of the base peak) $M-H\cdot$ ion and a 12% $M-D\cdot$ ion (i.e. a 76% relative loss of $H\cdot$ and a 24% loss of $D\cdot$). This shows that even though the favoured species *h* (*m/e* 81) is formed, a substantial amount of the M—1 ion originates by loss of a hydrogen radical from C5. Another process noted in the spectra of the three monomethylimidazoles, and especially in that (Table 1) of 4(5)-bromoimidazole (XXXV), is M—HCN—HCN to furnish either the ethylene or the bromoethylene radical ion. For 1-methylimidazole, this means that the methyl-

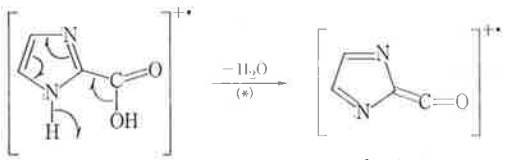
aziridine radical ion (*m/e* 55) formed by loss of HCN from the molecular ion, must either undergo methyl migration, or more probably rearrange to the species *i* (*m/e* 55) before loss of the second HCN occurs.



h, *m/e* 81 *i*, *m/e* 55 *j*, *m/e* 165

The spectra (Table 1) of the *N*-benzylimidazoles (IX and X) are unexceptional, and merely show fragmentation to the tropylium cation (*m/e* 91). The mass spectrum of 4,5-diphenylimidazole (XXXVII) shows a remarkable one-step elimination from the molecular ion to form the fluorene cation *j*, *m/e* 165. This feature may be used to detect the presence of the 4,5-diphenyl substitution pattern in this, and other heterocyclic systems, and is to be the subject of a future publication.

Formyl (XI–XIII), carboxyl (XIX and XXXII), and methoxycarbonyl (XXII and XXXIII) substituents are often eliminated with concomitant hydrogen rearrangement to give the corresponding imidazole radical ions. This is especially noticeable in the spectra (Table 1 and Fig. 6) of the formylimidazoles, and the spectrum (Fig. 6) of 2-formyl-1-methylimidazole (XII) illustrates this feature.



k, *m/e* 112 *l*, *m/e* 94

After initial loss of carbon monoxide, the spectrum is very similar to that (Fig. 2) of 1-methylimidazole. The spectra (Tables 1 and 2) of 2- and 4(5)-formylimidazole and of the 2- and 4(5)-imidazole carboxylic acids are very similar, and it is not possible to distinguish between these types of compounds by mass spectrometry. The spectra (Table 1) of the two isomeric carboxylic acids (XIX and XXXII) exhibit large M—H_2O ions, and the spectrum of the labelled (XX) shows this process to occur by the concerted elimination $k \rightarrow l$. The spectra (Fig. 7) of the two isomeric methoxycarbonylimidazoles are strikingly different, allowing the differentiation of these compounds. 2-Methoxycarbonylimidazole (XXII) fragments primarily by elimination of the ester group with hydrogen rearrangement to give the imidazole radical ion (*m/e* 68, base peak). This elimination is not favoured in the spectrum of 4(5)-methoxycarbonylimidazole where the imidazole radical ion (*m/e* 68) constitutes only 6% of the base peak. Instead, the process M—MeO· (to *m/e* 95, base peak) is preponderant, and other processes are indicated in Figure 7. The acetals (XIV) and (XV) fragment by the process M—EtO· —C_2H_4 to their respective protonated formylimidazole cations, which fragment analogously to the corresponding formylimidazoles.

Fig. 5

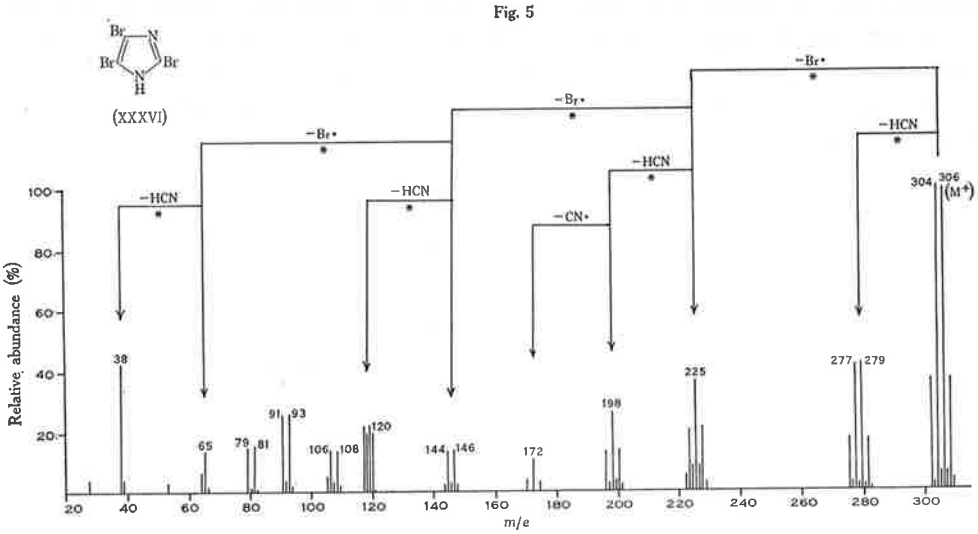
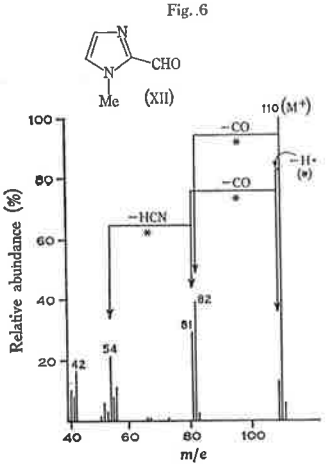
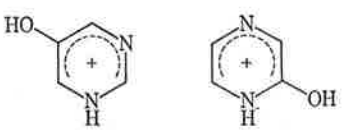


Fig. 6

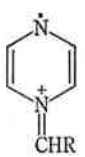


The 2- and 4(5)-hydroxymethylimidazoles (XVI and XXXI) cannot be distinguished by mass spectrometry. Their spectra (Table 1) exhibit pronounced loss of a hydrogen radical from the molecular ions. As these M−1 ions do not undergo the fragmentations of the corresponding formylimidazole molecular ions, it is reasonable to represent their structures as *m* (for XVI) and *n* (for XXXI)



m, *m/e* 97

n, *m/e* 97



o, *m/e* 110, R = H (XVII)

p, *m/e* 186, R = Ph (XVIII)

respectively (cf. benzyl alcohol[2]). Other processes observed in these spectra are M—CHO· and M—OH·. In marked contrast to the spectra of (XVI) and (XXXI), those of 1-methyl- and 1-benzyl-2-hydroxymethylimidazoles (XVII and XVIII) exhibit pronounced M—2 peaks (see Table 1) which may be represented as the ions *o* and *p*.

Fig. 7

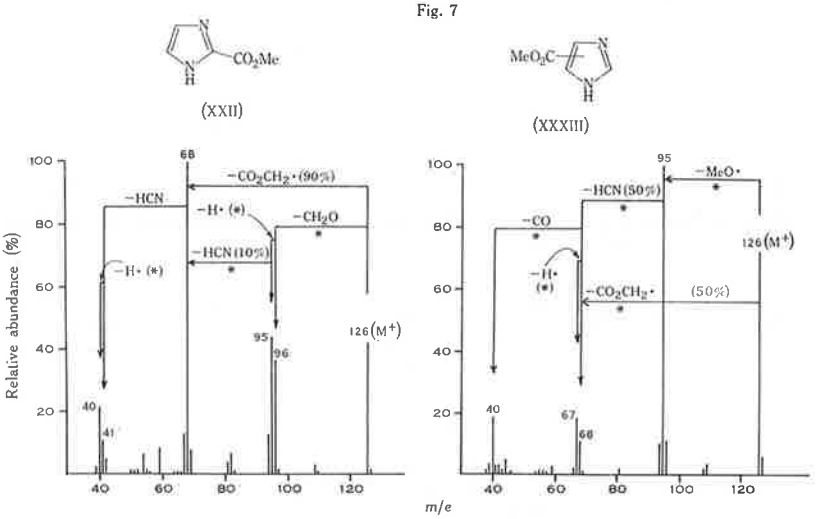
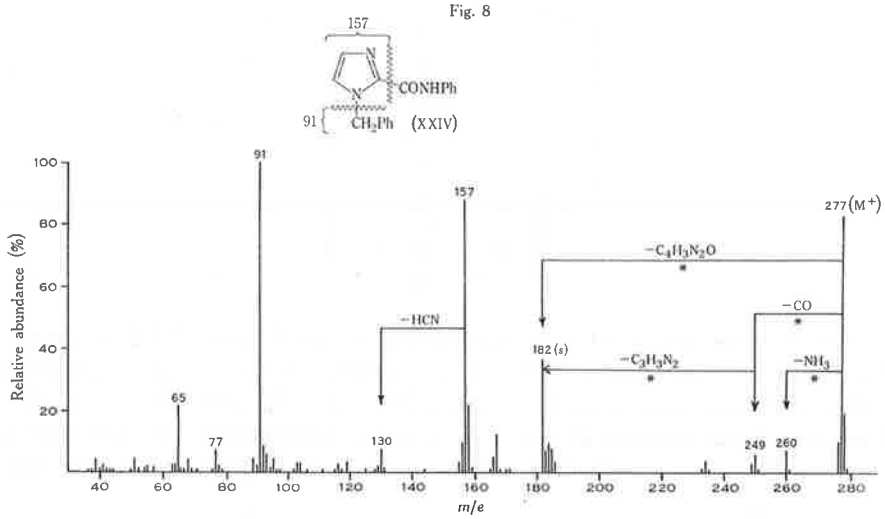


Fig. 8

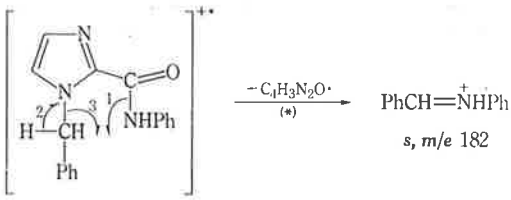


Finally, four of the compounds studied exhibit skeletal rearrangement ions in their spectra. One of these, 2,4,5-tribromoimidazole, has been discussed above, while the other three (XXIV, XXVII, and XXXIV) have been briefly mentioned[3]

[2] Meyerson, S., Rylander, P. N., Eliel, E. L., and McCollum, J. D., *J. Am. chem. Soc.*, 1959, **81**, 2606; 1961, **83**, 2481.

[3] Bowie, J. H., Cooks, R. G., Lawesson, S.-O., Jakobsen, P., and Schroll, G., *Chem. Commun.*, 1966, 539.

in a previous communication. These involve loss of either CO or CO_2, and such processes are currently exciting much interest (for a compendium see ref.[4]). Apart from the skeletal rearrangement ions in the spectra (Table 1) of (XXVII) and (XXXIV), other fragmentations are unexceptional. The mass spectrum of 2-anilido-1-benzylimidazole (XXIV) is illustrated in Figure 8. Three rearrangement processes are noted in this spectrum, i.e. M—CO, M—NH_3, and M—$C_4H_3N_2O$. The latter rearrangement is one of the most complicated skeletal rearrangements yet documented, as it involves the concerted formation of an ion represented as *s*, possibly by the process $r \rightarrow s$. The first stage of this rearrangement probably involves the migration of the PhNH moiety as the M—CO ion also fragments to *s*.



r, *m/e* 277 *s*, *m/e* 182

In summary, mass spectrometry is of considerable use in the structure determination of imidazoles, and may be used to determine the type and position of various substituents. Skeletal rearrangement ions are rare in the spectra of simple imidazoles, and consequently the *a priori* prediction of fragmentation modes is applicable to this class of compound.

Experimental

All mass spectra (except those mentioned below) were measured with an A.E.I. MS9 mass spectrometer operating at 70 eV, and with the source and inlet system between 150 and 180°. The spectra of compounds (XIX), (XXI), (XXIV), (XXVII), and (XXXIV) were measured by the direct inlet procedure with a source temperature of *c.* 100°. Exact mass measurements were determined with a resolution of 14000 (10% valley definition) using heptacosafluorotributylamine to provide reference masses. All measurements were correct to within 15 p.p.m.

The purity of all compounds was routinely checked by gas chromatography and n.m.r. spectroscopy. Compounds (I), (XXVI), and (XXXVII) were purified commercial samples. The following compounds were prepared by reported procedures: (IV),[5] (VI),[6] (VIII),[7] (IX),[6] (X),[6] (XI),[8] (XIII),[8] (XIV),[8] (XV),[8] (XVI),[6] (XVII),[9] (XVIII),[6] (XIX),[6] (XXI),[6] (XXIII),[9] (XXIV),[10] (XXVIII),[11] (XXXI),[12] (XXXII),[13] (XXXIV),[14] (XXXV),[15] and (XXXVI).[15]

[4] Brown, P., and Djerassi, C., *Angew. Chem.*, in press.
[5] Wohl, A., and Marckwald, W., *Ber. dt. chem. Ges.*, 1889, **21**, 1353.
[6] Jones, R. G., *J. Am. chem. Soc.*, 1949, **71**, 383.
[7] Sonn, A., Hotes, E., and Sieg, H., *Ber. dt. chem. Ges.*, 1924, **57**, 953.
[8] Iversen, P., and Lund, H., *Acta chem. scand.*, in press.
[9] Shirley, D. A., and Alley, P. W., *J. Am. chem. Soc.*, 1957, **79**, 4922.
[10] Iverson, P., and Lund, H., *Acta chem. scand.*, 1966, **20**, 2649.
[11] Huchel, W., Datow, J., and Simmersbach, E., *Z. phys. Chem.* A, 1940, **186**, 159.
[12] Pyman, F. L., *J. chem. Soc.*, 1911, **99**, 668.
[13] Pyman, F. L., *J. chem. Soc.*, 1916, **109**, 186.
[14] Forgher, R. G., and Pyman, F. L., *J. chem. Soc.*, 1919, **115**, 217.
[15] Balaban, I. E., and Pyman, F. L., *J. chem. Soc.*, 1922, **121**, 947.

Compound (XXXIII) was prepared by esterification of (XXXII).[16] The spectra of (VII) and (XX) were obtained by introducing (VI) and (XIX) into the source with deuterium oxide,[17] while that of (II) was obtained by subtracting the spectrum of (I) from that of partially labelled (II). The labelled compounds (II) and (XXIX) were prepared by stirring a benzene solution of (I) and (XXVIII) respectively with an excess of D_2O.

1,2-d_2*-Imidazole* (*III*)

Imidazole (10 g, 0·15 moles) in deuterium oxide (25 g, 1·25 moles) was heated under reflux for 17 hr. The n.m.r. spectrum of the labelled imidazole indicated an 84% exchange of the 1-proton and an 87% exchange of the 2-proton (relative to the signal from the 4,5-protons).

*2-*d*-1-Methylimidazole*

This compound (IV) was prepared by metalation of 1-methylimidazole with n-butyllithium at −60° for 2 hr, followed by treatment with deuterium oxide; b.p. 82°/12 mm.

*5-*d*-1-Methylimidazole* (*XXX*)

5-Bromo-1-methylimidazole was treated with n-butyllithium at −35° for 4 min, and then treated with deuterium oxide. B.p. 84–85°/14 mm.

Acknowledgments

One of us (R.G.C.) gratefully acknowledges the award of an Elsie Ballot Fellowship. A grant (to S.-O.L.) from Statens Almindelige Videnskabsfond is gratefully acknowledged. Dr P. Iverson generously provided some of the samples.

[16] Lawesson, S.-O., unpublished data.

[17] Shannon, J. S., *Aust. J. Chem.*, 1962, **15**, 265.

Reprinted from CHEMICAL COMMUNICATIONS, 1967, page 284.

Skeletal Rearrangement Processes of Aromatic Azoxy-compounds on Electron Impact

By J. H. BOWIE and G. E. LEWIS

(*Department of Organic Chemistry, The University of Adelaide, South Australia*)

and R. G. COOKS

(*University Chemical Laboratory, Lensfield Road, Cambridge*)

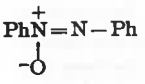
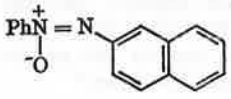
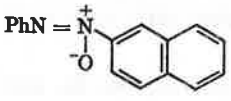
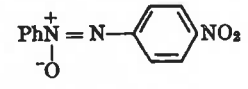
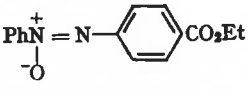
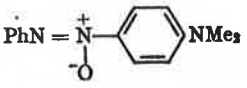
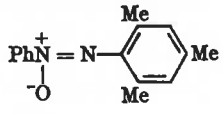
AROMATIC azoxy-compounds have been found to exhibit prominent skeletal rearrangement ions in their mass spectra. Seven examples are summarised in the Table. An asterisk denotes the presence of a metastable ion for the process indicated, and the compositions of all ions have been established by exact mass measurements.

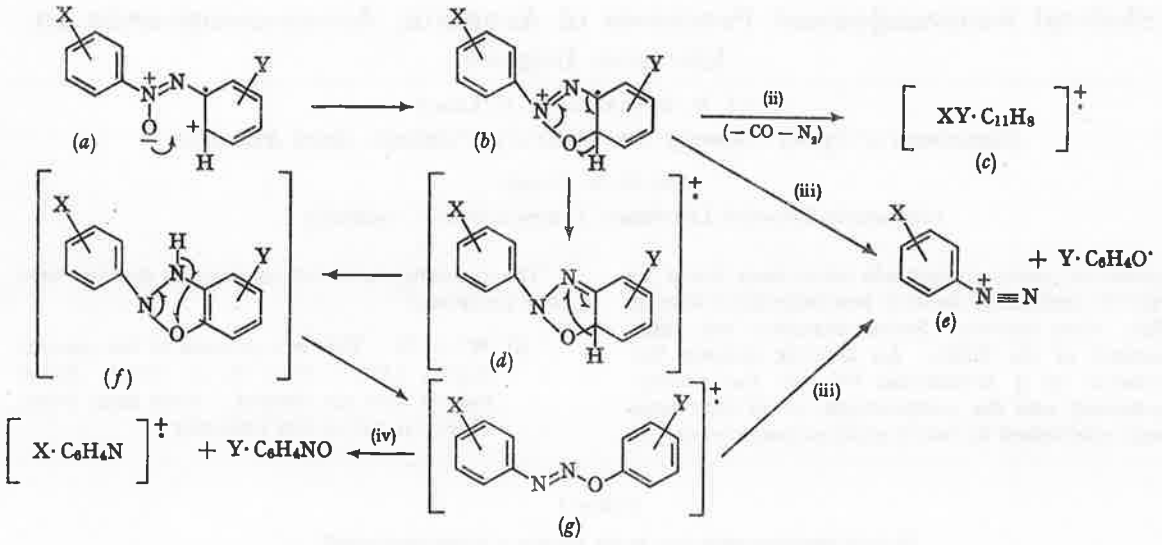
The rearrangement modes may be divided into four processes:

(i) M^+–N_2O. This is a process of the general type[1], ABC → AC + B, in which diaryl radical ions are formed. Such ions, when observed, are of low intensity;

TABLE 1

Skeletal rearrangement ions in the spectra of azoxy-compounds

Compound	Process	Final ion	Relative abundance of final ion (%)
	$M-N_2O-H_2$	152	4
	$M-\overset{*}{CO}-\overset{*}{N_2}-\overset{*}{H}\cdot$ $M-\overset{*}{(CO+N_2)}-\overset{*}{H}\cdot$	141	16
	$M-\overset{*}{CO}-\overset{*}{H}\cdot-\overset{*}{N_2}$	191	9
	$M-\overset{*}{C_{10}H_7N}\cdot$	105	13
	$M-\overset{*}{C_{10}H_7NO}$	91	28
	$M-\overset{*}{CO}-\overset{*}{H}\cdot-\overset{*}{N_2}$	191	9
	$M-\overset{*}{C_6H_5O}\cdot$	155	4
	$M-\overset{*}{C_6H_5NO}$	141	26
	$M-\overset{*}{C_6H_4NO_2}$	105	36
	$M-\overset{*}{EtO}-\overset{*}{CO}-\overset{*}{CO}-N_2$	141	10
	$M-\overset{*}{CO}-\overset{*}{N_2}-\overset{*}{H}\cdot$	213	2
	$M-\overset{*}{CO}-\overset{*}{N_2}-\overset{*}{H}\cdot$ $M-\overset{*}{(CO+N_2)}-\overset{*}{H}\cdot$	184	4
	$M-\overset{*}{C_6H_5O}\cdot$	148	12
	$M-\overset{*}{C_6H_5NO}$	134	92
	$M-\overset{*}{Me}-CO-N_2$	169	3



(ii) M^+–CO–N_2 or M^+–(CO + N_2). This process which may occur in either successive steps or in a concerted manner is observed in most spectra. The process is modified by the presence of substituents on either aromatic ring (see the Table);

(iii) M^+–Y·C_6H_4O· (see *a*). This process is not observed in all spectra;

(iv) M^+–Y·C_6H_4·NO· (see *a*). This process likewise is not observed in all spectra.

The above scheme is postulated to explain the rearrangement processes. It should be noted that the *o*-hydroxyazobenzene radical ion is not the intermediate in the rearrangement process of azoxybenzene, as its rearrangement process[2] is M^+–N_2–CO–H· (not M^+–CO–N_2–H· as in the case of azoxybenzene). The oxygen migration to form the cyclised intermediate *b*, is similar to the behaviour of aryl sulphones on electron impact,[1] and the mechanism suggested for the formation of *g* is very similar to that suggested to explain the photochemical rearrangement of azoxybenzenes.[3]

(*Received, January 26th*, 1967; *Com.* 076.)

[1] J. H. Bowie, D. H. Williams, S. O.Lawesson, J. Ø. Madsen, C. Nolde, and G. Schroll, *Tetrahedron*, **1966**, **22**, 3515 and references therein.
[2] J. H. Bowie, R. G. Cooks, and G. E. Lewis, *J. Chem. Soc.* (*B*), in the press.
[3] G. E. Lewis and J. A. Reiss, *Austral. J. Chem.*, **1966**, **19**, 1887.

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Skeletal Rearrangement of Mercapto-esters upon Electron Impact[1]

By J. H. BOWIE,

(*Department of Organic Chemistry, University of Adelaide, South Australia*)

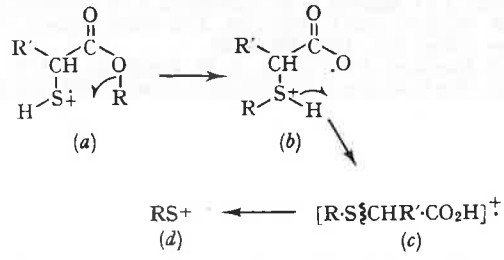
and S.-O. LAWESSON, F. DUSS, and P. MADSEN

(*Department of Organic Chemistry, University of Aarhus, Aarhus C, Denmark*)

and R. G. COOKS

(*University Chemical Laboratory, Lensfield Road, Cambridge, England*)

SKELETAL-REARRANGEMENT ions have been observed previously in the mass spectra of a variety of sulphur compounds.[2] We report the general occurrence of RS^+ ions (*d*) in the spectra of a series of mercapto-esters. When the substituent attached to sulphur is hydrogen, the rearranged ions are produced in a one-step process from the molecular ion (Table). The composition of all rearranged ions have been established by exact mass measurements. In general, RS^+ ions are more prominent in those spectra where R is able to stabilise the cation (*e.g.*, allyl and benzyl). It is important to note that when the substituent attached to sulphur is acetyl, no evidence is available to indicate that the rearranged ion is



TABLE

Compound	Rearranged ion (RS^+) (m/e)	Relative abundance of RS^+ (%)	Metastable ion for process $M \rightarrow RS^+$ Calc.	Found
$HS{\cdot}CH_2{\cdot}CO_2R$				
R = Et	61	3	31·0	—
= Pr^n	75	12	42·0	42·0
= Pr^i	75	12	42·0	42·0
= Bu^n	89	13	53·5	53·4
= Bu^s	89	17	53·5	53·6
= iso-C_5H_{11}	103	6	65·4	65·4
= Cyclohexyl	115	12	76·8	77·0
= CH_2Ph	123	28	83·2	83·1
$HS{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2{\cdot}CH_2Ph$	123	16	77·2	77·3
$HS{\cdot}CHMe{\cdot}CO_2R$				
R = Pr^i	75	16	38·0	38·0
= allyl	73	66	36·5	36·4
= CH_2Ph	123	46	77·2	—
$Me{\cdot}CH(S{\cdot}CO{\cdot}Me){\cdot}CO_2Pr^i$	75	3	29·6	—
$MeCH(S{\cdot}COMe){\cdot}CO_2{\cdot}CH_2Ph$	123	12	60·9	—

produced in a one-step process. A possible mechanism (for the general case *a*, $a \rightarrow d$) is suggested to explain this rearrangement process. This process limits both the prediction of fragmentation modes and the application of the 'element-mapping' technique[3] for this class of compound.

(*Received, February 13th*, 1967; *Com.* 140.)

[1] Previous paper in this series, J. H. Bowie, R. G. Cooks, and G. E. Lewis, *Chem. Comm.*, 1966, 284

[2] J. H. Bowie, F. C. V. Larsson, G. Schroll, S.-O. Lawesson, and R. G. Cooks, *Tetrahedron*, in the press; J. H. Bowie, D. H. Williams, S.-O. Lawesson, J. Ø. Madsen, C. Nolde, and G. Schroll, *Tetrahedron*, 1966, **22**, 3515, and references therein; J. O. Madsen, S.-Ø. Lawesson, A. M. Duffield, and C. Djerassi, *J. Org. Chem.*, in the press; E. Bach, A. Kjær, R. H. Shapiro, and C. Djerassi, *Acta Chem. Scand.*, 1965, **19**, 2438; J. B. Thomson, P. Brown, and C. Djerassi, *J. Amer. Chem. Soc.*, 1966, **88**, 4049.

[3] K. Biemann, P. Bommer, D. M. Desiderio, and W. J. McMurray in "Advances in Mass Spectrometry," ed. W. L. Mead, The Institute of Petroleum, London, 1966, Vol. 3, pp. 639–653.

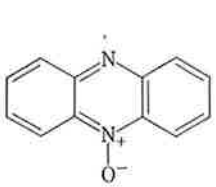
Short Communication reprinted from the
AUSTRALIAN JOURNAL OF CHEMISTRY

ELECTRON IMPACT STUDIES*

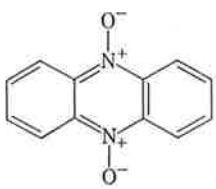
XV.† SKELETAL REARRANGEMENT FRAGMENTS IN THE MASS SPECTRA OF AROMATIC *N*-OXIDES

By J. H. Bowie,‡ R. G. Cooks,§ N. C. Jamieson,‡ and G. E. Lewis‡

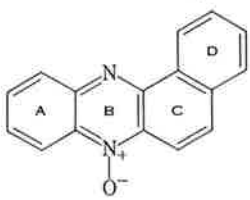
The mass spectra of quinoline *N*-oxides,[1] pyridine *N*-oxides,[2] and Δ^1-pyrroline *N*-oxides[2] have been reported. Although M—O ions are of diagnostic value in some of the spectra,[1,2] no skeletal rearrangement ions have been reported.



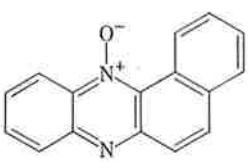
(I)



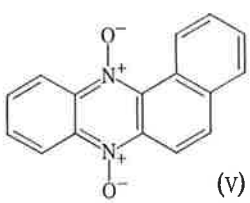
(II)



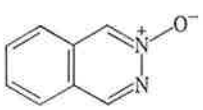
(III)



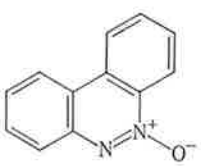
(IV)



(V)



(VI)



(VII)

* Manuscript received March 14, 1967.
† Part XIV, *Chem. Commun.*, 1967, 346.
‡ Department of Organic Chemistry, University of Adelaide, S.A. 5001.
§ University Chemical Laboratory, Lensfield Road, Cambridge, U.K.
[1] Bryce, T. A., and Maxwell, J. R., *Chem. Commun.*, 1965, 206.
[2] Grigg, R., and Odell, B. G., *J. chem. Soc.* B, 1966, 218.

Because of current interest in these laboratories[3] and elsewhere[4] in the photochemical rearrangements of aromatic *N*-oxides, and also because of the recently observed skeletal rearrangement processes which occur in the mass spectra of

Fig. 1

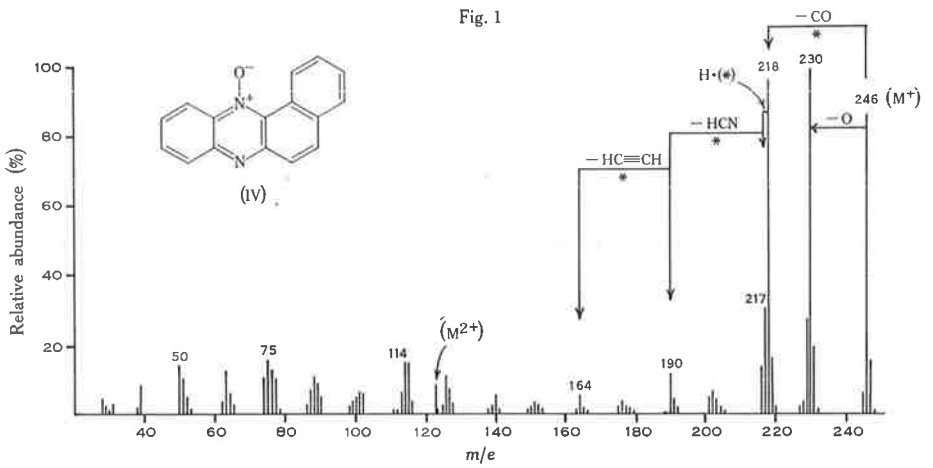
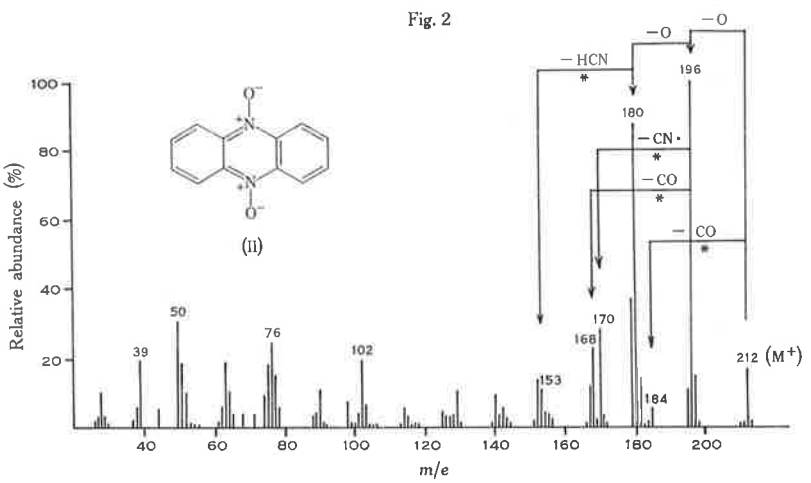


Fig. 2



azoxybenzenes,[5,6] we have determined the mass spectra of the following seven aromatic *N*-oxides (I–VII). The spectra are recorded in Figures 1 and 2 and Table 1, and the exact mass measurements are listed in Table 2. An asterisk represents the presence of a metastable peak for the process indicated.

[3] Lewis, G. E., unpublished data.
[4] Buchardt, O., *Tetrahedron Lett.*, 1966, 6221.
[5] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *Chem. Commun.*, 1967, 284.
[6] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *Aust. J. Chem.*, 1967, **20**, 1601.

The mass spectra of the phenazine *N*-oxides (I, II) and the benzo[*a*]phenazine *N*-oxides (III–V), apart from the normal loss of oxygen from the molecular ion (to form the corresponding phenazine or benzo[*a*]phenazine radical ions), exhibit

TABLE 1

MASS SPECTRA OF COMPOUNDS (I), (III), (V–VIII)

All peaks greater than 5% of the base peak (100%) are recorded

(I)	*m/e*	39	50	51	52	63	64	74	75	76	77	90	98	102	114	125	129
	I (%)	13	23	18	8	14	8	8	15	17	13	8	7	14	6	6	6
	m/e	140	141	142	152	153	167	168	170	179	180	181	195	196(M)			
	I (%)	8	7	7	11	8	6	15	30	30	72	7	15	100			
	m/e	197															
	I (%)	18															
(III)	*m/e*	50	51	63	75	76	77	102	114	115	116	123	126	175	176	190	
	I (%)	10	8	8	11	10	8	8	8	6	10	9	8	6	6	7	
	m/e	201	202	217	218	220	229	230	231	245	246(M)	247					
	I (%)	7	7	14	20	18	24	62	11	8	100	20					
(V)	*m/e*	39	50	51	63	74	75	76	77	101	102	113	114	115	123	127	128
	I (%)	11	14	12	14	10	13	16	12	9	9	7	11	13	10	10	9
	m/e	140	151	152	175	176	190	201	202	217	218	220	229	230	231		
	I (%)	6	6	6	6	7	10	7	8	18	38	16	19	84	15		
	m/e	234	245	246	247	262(M)											
	I (%)	5	7	100	19	7											
(VI)	*m/e*	37	38	39	50	51	52	62	63	64	75	76	77	88	89	90	91	102
	I (%)	8	14	30	27	14	6	16	54	20	10	13	13	7	100	44	7	9
	m/e	103	116	117	130	146(M)	147											
	I (%)	10	44	6	15	94	10											
(VII)	*m/e*	39	50	51	62	63	64	74	75	76	77	78	86	87	88	89	98	99
	I (%)	27	18	18	17	33	9	26	25	18	9	9	13	19	10	10	13	9
	m/e	100	113	114	115	126	139	140	141	150	151	152	164	166	167			
	I (%)	9	20	17	17	17	41	50	9	18	20	27	10	48	10			
	m/e	180	196(M)	197														
	I (%)	12	100	19														
(VIII)	*m/e*	39	50	51	62	63	64	75	76	77	114	140	141	142	167	168	169	
	I (%)	15	12	8	8	20	9	8	13	10	8	12	7	6	13	31	7	
	m/e	195	196(M)	197														
	I (%)	6	100	16														

pronounced M—CO ions, and in addition, the spectra of the two di-*N*-oxides (II and V) contain prominent M—O—CO ions (Figs. 1 and 2). The relative abundances of the skeletal rearrangement fragments are summarized in Table 3. *N*-Oxides of heterocyclic compounds containing adjacent nitrogen atoms, e.g. phthalazine *N*-oxide (VI) and benzo[*c*]cinnoline *N*-oxide (VII), would not be expected to exhibit skeletal rearrangement ions in their mass spectra because of the simple fragmentation

processes which may operate in these cases. Both (VI) and (VII) decompose by the simple scheme M—NO·—HCN, and no skeletal rearrangement fragments are observed (see Table 1).

TABLE 2

COMPOSITION OF SOME IONS IN THE SPECTRA OF (I–VIII)

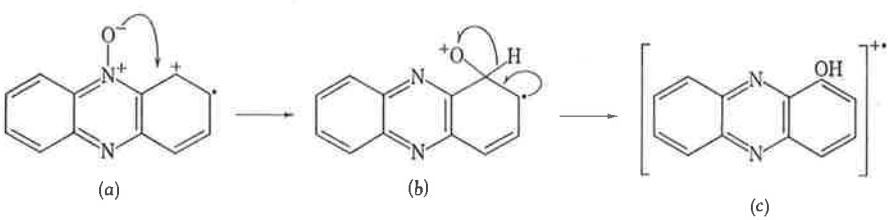
Compound	*m/e*	Composition	Compound	*m/e*	Composition
(I)	180	$C_{12}H_8N_2$	(V)	218	$C_{15}H_{10}N_2$
	170	$C_{11}H_8NO$			
	168	$C_{11}H_8N_2$	(VI)	103	C_7H_5N
				102	C_7H_4N (50%)
(II)	184	$C_{11}H_8N_2O$			C_8H_6 (50%)
	168	$C_{11}H_8N_2$		90	C_7H_6 (80%)
					C_6H_4N (20%)
(III)	220	$C_{15}H_{10}NO$		89	C_7H_5
	218	$C_{15}H_{10}N_2$			
			(VIII)	168	$C_{11}H_8N_2$
(IV)	218	$C_{15}H_{10}N_2$			
	190	$C_{14}H_8N$			

TABLE 3

SKELETAL REARRANGEMENT IONS IN THE MASS SPECTRA OF (I–V)

Compound	(I)	(II)	(III)	(IV)	(V)
M—CO (% of base peak)	15	5	20	98	0
M—O—CO (%)	—	23	—	—	38

It is of interest to consider the genesis and structure of the rearrangement ions. The rearrangement process (M—CO) demands oxygen migration to carbon, possibly to form the corresponding 1-hydroxyphenazine radical ion ($a \rightarrow c$). A sample of



1-hydroxyphenazine could not be obtained, but 2-hydroxyphenazine (VIII) (which should have a very similar spectrum) was available, and its mass spectrum (Table 1) was found to exhibit the fragmentation pattern M—CO—H·—HCN—HC≡CH. This process is identical with the skeletal rearrangement processes in the spectra of (I–V) (cf. especially Fig. 1). Additional support is forthcoming from the spectra of (III) and (IV). Compound (IV), which has the *N*-oxide linkage next to the D ring ion, should have a much larger peak due to the rearrangement ion than should (III)

because of the proximity effect. The relative abundances of the M—CO ions in the spectra of (III) and (IV) are 20 and 98% respectively.

Experimental

All mass spectra were measured with an Hitachi Perkin–Elmer RMU 6D mass spectrometer operating at 75 eV, and with the source and inlet system at 200°. Exact mass measurements were performed with an A.E.I. MS9 mass spectrometer with a resolution of 14,000 (10% valley definition) using heptacosafluorotributylamine to provide reference masses.

The *N*-oxides were prepared by known chemical procedures, and the observed melting points were in agreement with the literature values, according to the following references: (I), (III), (IV), and (V);[7] (II);[8] (VI);[9] (VII).[10]

Acknowledgments

An Elsie Ballot Fellowship (to R.G.C.) is gratefully acknowledged. We thank Dr H. J. Rodda for a sample of phthalazine *N*-oxide. The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

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THE MASS SPECTRA OF SUBSTITUTED IMIDES[1]

SKELETAL REARRANGEMENTS ON ELECTRON IMPACT

C. NOLDE and S.-O. LAWESSON

Department of Organic Chemistry, Aarhus University, Aarhus C., Denmark

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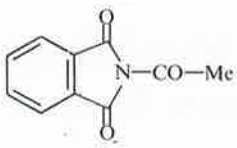
OXFORD NEW YORK LONDON PARIS

$R \cdot CO \cdot N(R') \cdot CO \cdot R''$

	R	R′	R″
I	Me	H	Me
II	Me	Me	Me
III	CD_3	Me	CD_3
IV	Me	nPr	Me
V	Me	nBu	Me
VI	CD_3	nBu	CD_3
VII	Me	isoBu	Me
VIII	Me	secBu	Me
IX	Me	allyl	Me
X	Me	Ph	Me
XI	Me	CH_2Ph	Me
XII	Me	H	Et
XIII	Me	H	Ph
XIV	Ph	H	Ph
XV	Ph	Ph	Ph
XVI	Ph	CH_2Ph	Ph

$MeCO \cdot NH \cdot CO \cdot NH \cdot CO \cdot Me$

XVII



XVIII

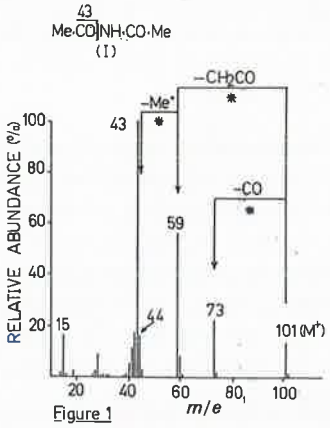


Figure 1

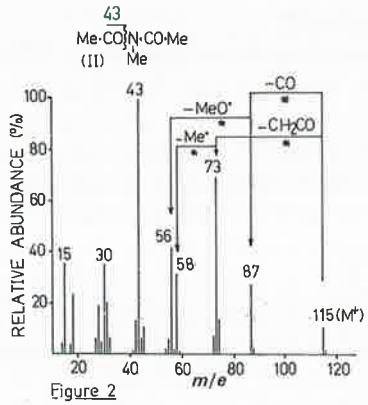


Figure 2

TABLE 1*. MASS SPECTRA OF COMPOUNDS IV, VII–XI, XIII–XVII

IV *m/e*	15	26	27	28	29	30	39	40	41	42	43	44	54	55	56	58	73	77	83	84
I(%)	40	8	43	24	28	22	21	7	23	46	100	10	7	6	10	10	4	17	6	6
	86	100	101	102	114	115	128	143(M)												
	8	6	3	2	3	3	8	3												
VII *m/e*	15	27	28	29	30	39	41	42	43	55	56	57	58	60	72	73	84	100	102	
I(%)	21	14	8	14	87	10	20	10	100	8	9	6	10	16	82	15	38	11	36	
	103	114	115	142	157(M)															
	3	9	5	3	2															
VIII *m/e*	15	27	28	29	39	40	41	42	43	44	45	55	56	57	58	60	72	84	86	87
I(%)	24	20	15	41	20	14	78	20	100	76	10	15	20	18	20	20	10	16	44	7
	97	100	102	114	128	142	157(M)													
	7	7	22	9	9	2	1													
IX *m/e*	15	27	28	39	41	42	43	54	56	57	98	99	113	141(M)						
I(%)	16	10	12	22	15	18	100	7	26	15	5	8	2	1						
X *m/e*	43	51	65	66	77	93	94	117	135	136	177(M)									
I(%)	23	5	5	4	15	100	6	10	66	6	5									
XI *m/e*	39	42	50	51	63	65	77	78	79	89	90	91	92	104	106	107	131	148	149	
I(%)	11	5	6	15	7	18	20	8	25	6	5	34	6	6	100	16	3	38	20	
	191(M)																			
	17																			
XIII *m/e*	38	39	42	43	50	51	74	75	76	77	78	104	105	106	134	135	146			
I(%)	4	6	5	43	16	38	6	6	13	64	11	10	100	10	6	10	2			
	163(M)	164																		
	40	8																		
XIV *m/e*	39	50	51	76	77	78	94	104	105	106	148	197	225(M)	226						
I(%)	4	10	30	6	65	6	3	5	100	9	2	10	38	8						
XV *m/e*	39	50	51	65	76	77	78	105	106	197	198	273	301(M)							
I(%)	10	6	23	9	3	63	6	100	8	48	10	3	1							
XVI *m/e*	39	50	51	65	76	77	78	79	91	104	105	106	210	211	212	315(M)				
I(%)	8	8	26	10	5	64	8	6	16	8	90	32	35	100	18	1				
XVII *m/e*	28	40	41	42	43	44	59	70	85	102	129									
I(%)	16	6	13	25	100	40	60	34	16	2	2									

* All ions greater than 2% of the base peak (arbitrarily 100%) are recorded. Several molecular ions which are less than this value are also recorded.

TABLE 2. EXACT MASS MEASUREMENTS IN THE MASS SPECTRA OF I–XVIII

Compound	*m/e*	Composition
I	73	C_3H_7NO
	44	CH_2NO
	43	C_2H_3O
	42	C_2H_4N
II	87	C_4H_9NO
	73	C_3H_7NO
	58	C_2H_4NO
	56	C_3H_6N
	43	C_2H_3O
	31	CH_5N
	30	CH_4N
IV	115	$C_6H_{13}NO$ (70%) $C_5H_9NO_2$ (30%)
	114	$C_5H_8NO_2$
	102	$C_4H_8NO_2$ (60%) $C_5H_{12}NO$ (40%)
	101	$C_5H_{11}NO$ (95%) $C_4H_7NO_2$ (5%)
	100	$C_5H_{10}NO$
	86	C_4H_8NO (55%) $C_3H_4NO_2$ (45%)
	83	C_5H_9N
	84	C_4H_6NO
	72	C_3H_6NO
	58	C_3H_8N
	56	C_3H_6N (60%) C_2H_2NO (40%)
	43	C_2H_3O (90%) C_3H_7 (10%)
V	128	$C_6H_{10}NO_2$
	115	$C_6H_{13}NO$ (90%) $C_5H_9NO_2$ (10%)
	114	$C_6H_{12}NO$ (85%) $C_5H_8NO_2$ (15%)
	102	$C_4H_8NO_2$
	100	$C_5H_{10}NO$
	87	C_4H_9NO
	86	C_4H_8NO (65%) $C_3H_4NO_2$ (35%)
	84	C_4H_6NO
	73	C_3H_7NO
	72	C_3H_6NO (80%) $C_4H_{10}N$ (20%)
	60	C_2H_6NO (80%) $C_2H_4O_2$ (20%)
	43	C_2H_3O (95%) C_3H_7 (5%)
	30	CH_4N
VII	115	$C_6H_{13}NO$
	114	$C_6H_{12}NO$ (50%) $C_5H_8NO_2$ (50%)
	102	$C_4H_8NO_2$
	100	$C_5H_{10}NO$
	84	C_4H_6NO

TABLE 2.—*continued*

Compound	*m/e*	Composition
VII (*continued*)	72	C_3H_6NO (90%) $C_4H_{10}N$ (10%)
	60	C_2H_6NO (80%) $C_2H_4O_2$ (20%)
	43	C_2H_3O (90%) C_3H_7 (10%)
	30	CH_4N
VIII	128	$C_6H_{10}NO_2$
	97	$C_6H_{11}N$
	86	C_4H_8NO
IX	113	$C_6H_{13}NO$
	99	C_5H_9NO
	98	C_5H_8NO
	57	C_3H_7N
	56	C_3H_6N
	43	C_2H_3O
X	135	C_8H_9NO
	117	C_8H_7N
	93	C_6H_7N
XI	131	C_9H_9N
XII	87	C_4H_9NO
	73	C_3H_7NO
	60	C_2H_6NO
	57	C_3H_5O
	43	C_2H_3O
XIII	135	C_8H_9NO
	134	C_8H_8NO
XIV	197	$C_{13}H_{11}NO$
	94	C_6H_6O
XV	273	$C_{19}H_{15}NO$
XVI	211	$C_{14}H_{13}NO$
XVIII	148	$C_8H_6NO_2$
	147	$C_8H_5NO_2$
	105	C_7H_5O
	104	C_7H_4O
	103	C_7H_5N
	90	C_6H_4N

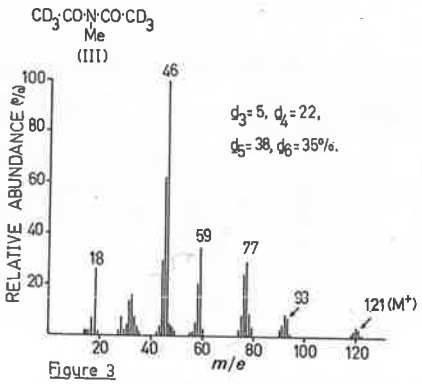


Figure 3

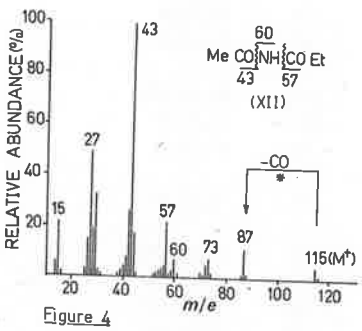


Figure 4

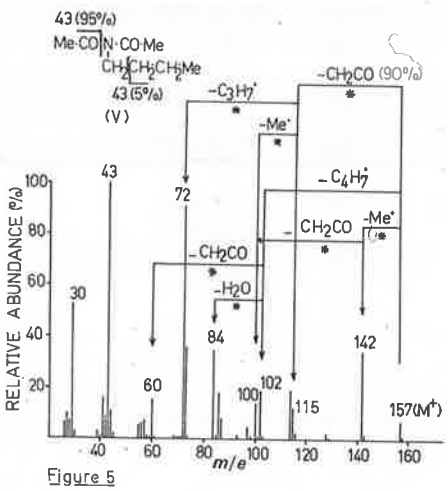


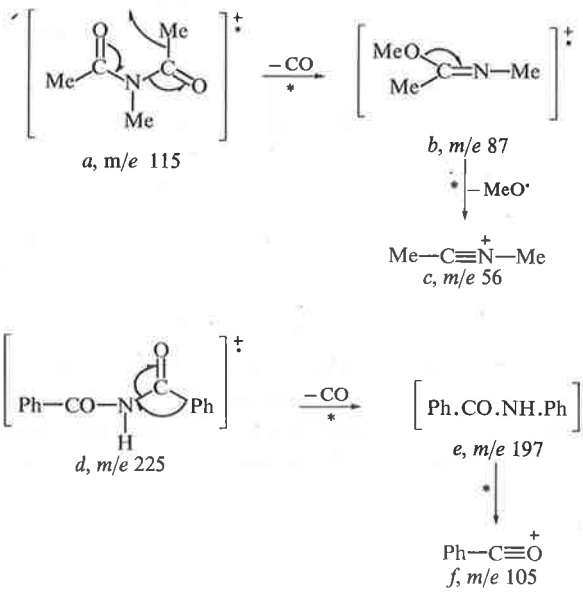
Figure 5

TABLE 3. RELATIVE ABUNDANCE (%) OF M^+—CO IONS IN THE SPECTRA OF I–XVI

Compound	I	II	IV	V	VII	VIII	IX	X	XI	XII	XIII	XIV	XV	XVI
M^+—CO	24	28	2	—	—	—	3	—	—	13	11	10	3	—

It is possible to follow the decomposition of the skeletal rearrangement ion in the spectrum (Fig. 2) of II, and therefore to determine the site of migration of the Me group. The interpretation has been aided by the spectrum (Fig. 3) of the d_6 derivative III. The rearrangement process M^+—CO—MeO· is substantiated by metastable ions, and indicates Me migration to oxygen, possibly by the process $a \rightarrow c$. A similar process is observed in the mass spectrum (Fig. 1) of diacetamide I, but here, loss of MeO· from the M^+—CO species is not substantiated by a metastable peak. It is reasonable to assume that oxygen is the migration site of the rearrangement process (M^+—CO) in the mass spectra of those imides where R and R″ = Me or Et, even though it cannot be proven in the majority of cases.

A different situation is observed in the mass spectrum (Table 1) of XIV, where the M^+—CO ion (*e*, *m/e* 197) decomposes by loss of PhNH· (substantiated by a metastable ion at *m/e* 56·0) to the benzoyl cation (*f*, *m/e* 105), indicating phenyl migration to nitrogen ($d \rightarrow e \rightarrow f$).



a, m/*e* 115 *b*, *m/e* 87 −MeO· *c*, *m/e* 56 *d*, *m/e* 225 *e*, *m/e* 197 *f*, *m/e* 105

It has been shown (*vide supra*) that imides, on electron impact, may lose CO with concomitant rearrangement of the incipient radical either to oxygen (R = R″ = Me) or nitrogen (R = R″ = Ph). The presence of such processes limits both *a priori* predictions of fragmentation modes and the application of the "element mapping" technique[25–27] to this class of compound.

The normal decomposition modes of I–XVII are unexceptional, and specific examples are summarized in Figs. 1–6. Some of the general features may be illustrated

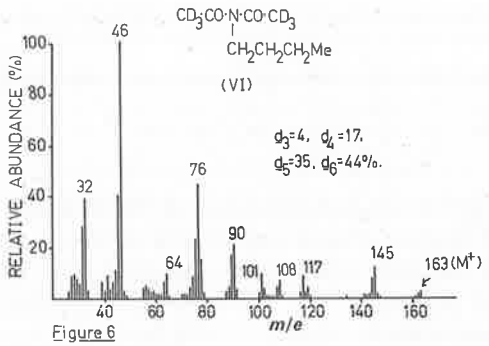


Figure 6

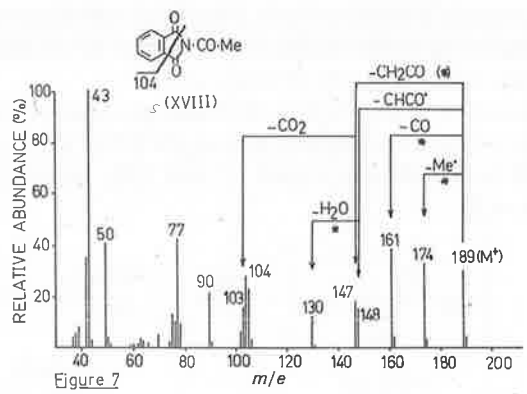
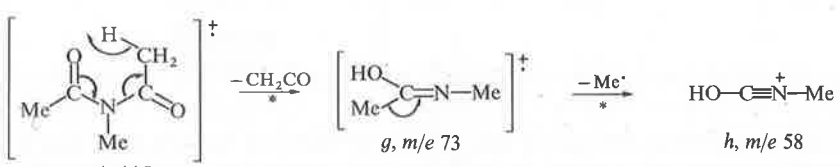


Figure 7

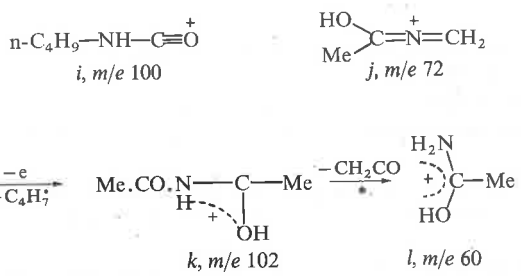
by a consideration of the spectra of II and V (Figs. 2 and 5) and of their d_6 derivatives III and VI (Figs. 3 and 6). The base peak of the spectrum of II is the acetyl cation (*m/e* 43) as is the case with the N-substituted imides II–IX. The other major process in the spectrum of II is M^+—CH_2CO—Me·. The Me radical lost in this process is that adjacent to the carbonyl group (Fig. 3), and as there is no evidence to suggest that the M^+—CH_2CO ion (*m/e* 73) decomposes by loss of MeNH· to the acetyl cation (*m/e* 43), we have a marginal preference for hydrogen rearrangement to oxygen (i.e. $a \rightarrow g \rightarrow h$) which is analogous to the behaviour of β-diketones.[9]



a, *m/e* 115 *g*, *m/e* 73 *h*, *m/e* 58

The spectra of the propyl and butylimides (IV–VIII) are complex, and extensive high resolution measurements (Table 2) were necessary for their interpretation. The mass spectrum (Fig. 5) of the n-butyl derivative V, illustrates this feature. Three major fragmentation processes operate, *viz.* (A) M^+—Me·—CH_2CO (to *m/e* 100), (B)

M^+—CH_2CO—C_3H_7· and other combinations (to *m/e* 72), and (C) M^+—C_4H_7·—CH_2CO (to *m/e* 60). Other variations of these modes are outlined in Figs. 5 and 6. The Me radical lost in process A is that adjacent to carbonyl (Fig. 6), and consequently *m/e* 100 is best represented as *i*. If the loss of ketene in process B proceeds *via* a favoured 6-membered transition state (McLafferty rearrangement),[28,29] then *m/e* 72 may be represented as *j*. The M^+—C_4H_7· ion (*m/e* 102) occurs to the extent of 18–36% of the base peak (*m/e* 43) in the spectra of the three butyl isomers V, VII and VIII, whereas the corresponding M^+—C_3H_5· ion (*m/e* 102) constitutes only 1% in that of the n-propyl compound IV. Such processes do not occur in the spectra of substituted β-diketones,[9] but are observed in those of alkylbarbiturates.[30] Process C may then be represented by the Scheme V → *k* → *l*. The sec-butyl derivative VIII may be distinguished from the n- and iso-butyl compounds V and VII, by the presence of a prominent M^+—Et· cation (10% of the base peak) in the spectrum of VIII.



Finally, it is of interest to consider the spectrum (Fig. 7) of N-acetylphthalimide (XVIII). Many of the fragmentation modes in this spectrum are unexceptional and are indicated in Fig. 7. However, the remarkable loss of CO_2 from phthalimides on electron impact[3,4] is also observed in this spectrum, viz. the process M^+—CH_2CO—CO_2 to *m/e* 103 ($C_7H_5N^+$) (Fig. 7). This certainly means that the M^+—CH_2CO ion (*m/e* 148) has the structure of the phthalimide radical ion, i.e. in this case, elision of ketene has occurred with concomitant hydrogen rearrangement to nitrogen.

EXPERIMENTAL

All mass spectra (except that of XIV) were determined with an Hitachi Perkin–Elmer R.M.U. 6D mass spectrometer with a source and inlet temp of approximately 150°. Compound XIV (which decomposed under the above conditions) was determined by the direct insertion technique at 60°. Exact mass measurements were determined with an A.E.I. MS 9 mass spectrometer using a resolution of 14,000 (10% valley definition) and heptacosafluorotributylamine provided the reference masses. All measurements were correct to within 15 ppm.

The purity of all samples was routinely checked by VPC and NMR spectroscopy. Compound II was a purified commercial sample. The following compounds were prepared by reported procedures: I,[31] V,[32] IX,[33] X,[34] XI,[35] XII,[36] XIII,[36] XIV,[37] XV,[33] XVI,[38] XVII[39] and XVIII.[40]

Compounds IV, VII and VIII were prepared by the following general synthesis.

The amine (0·25 mole) was added dropwise over a period of 30 min to Ac_2O (250 ml), keeping the temp below 5°. The reaction mixture was then heated under reflux for 1 hr, whereafter the apparatus was arranged for distillation. Over a period of 10–20 hr a mixture of AcOH–Ac_2O was distilled off through a

15 × 0·6 cm packed column at atm press. The various products were obtained (in almost quantitative yield) by vacuum distillation, and were further purified by preparative VPC. Their purity was checked by NMR spectroscopy.[41]

Compound	B.p.		%C	%H	%N
IV	84°/10 mm	Found	58·62	9·22	10·04
		Calc.	58·72	9·15	9·78
VII	87°/10 mm	Found	61·55	9·93	
		Calc.	61·12	9·62	—
VIII	86°/12 mm	Found	61·23	9·71	9·08
		Calc.	61·12	9·62	8·91

Labelled samples

(a) *Compound* III. $MeNH_2$. HCl (1·0 g) and Ac_2O-d_6 (3·0 ml) were refluxed for $3\frac{1}{2}$ hr. The pure product was obtained by preparative VPC.

(b) *Compound* VI. n-Butylamine (0·9 ml) was slowly dropped onto a mixture of Mg turnings (300 mg) and Ac_2O-d_6 (2·24 g). After heating under reflux for $3\frac{1}{2}$ hr, the product was obtained by preparative VPC.

Acknowledgements—A grant (to S.-O.L.) from Statens Almindelige Videnskabsfond, and the award (to R.G.C.) of an Elsie Ballot Fellowship are gratefully acknowledged. Thanks are expressed to Dr. I. Wadsö for some samples.

The Hitachi Perkin–Elmer R.M.U. 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

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THE MASS SPECTRA OF [18]ANNULENE DERIVATIVES. SKELETAL REARRANGEMENT UPON ELECTRON IMPACT*

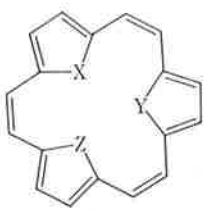
By G. M. Badger,† J. H. Bowie,† J. A. Elix,† G. E. Lewis,† and U. P. Singh†

[*Manuscript received May* 8, 1967]

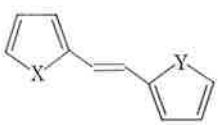
Summary

The mass spectra of a series of [18]annulene derivatives are reported and discussed. The majority of fragmentation modes exhibited in these spectra are produced by well-defined skeletal reorganization. In the case of one compound, all the observed fragmentations occur as the result of skeletal rearrangement processes. This appears to be the first reported example of such a phenomenon.

The mass spectra of the [18]annulene derivatives (I–V) are recorded in Figures 1,3,4,7, and 8. The 1,2-diarylethylenes (VI–VIII) have been synthesized in order that their spectra (Figs. 2, 5, and 6) may be compared with those of the annulenes. The composition of ions determined by exact mass measurements in the spectra of (III) and (V) are listed in Table 1, and the presence of a metastable peak for a particular process is indicated by an asterisk. Although the structures of fragment ions are not known, nominal structures have been drawn in order that fragmentation modes may be correlated with the structures of the molecules in the ground state.



	X	Y	Z
(I)	O	O	O
(II)	O	O	S
(III)	O	S	S
(IV)	S	S	S
(V)	S	S	NH



	X	Y
(VI)	O	O
(VII)	O	S
(VIII)	S	S

A priori predictions of the fragmentation modes in the mass spectrum of the trioxide (I) might suggest the possibility of a pronounced molecular ion (because of the inherent stability of the annulene system) and either M—HC≡CH ions (which would, however, involve unfavourable vinylic cleavage) or M—O ions (although furans do not generally lose oxygen from their molecular ions[1,2]). It is known[3] that

* This paper constitutes Part XVII in the series "Electron Impact Studies." Part XVI, S.-O. Lawesson, C. Nolde, J. H. Bowie, and R. G. Cooks, *Tetrahedron*, in press.

† Department of Organic Chemistry, University of Adelaide, S.A. 5001.

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Fig. 1

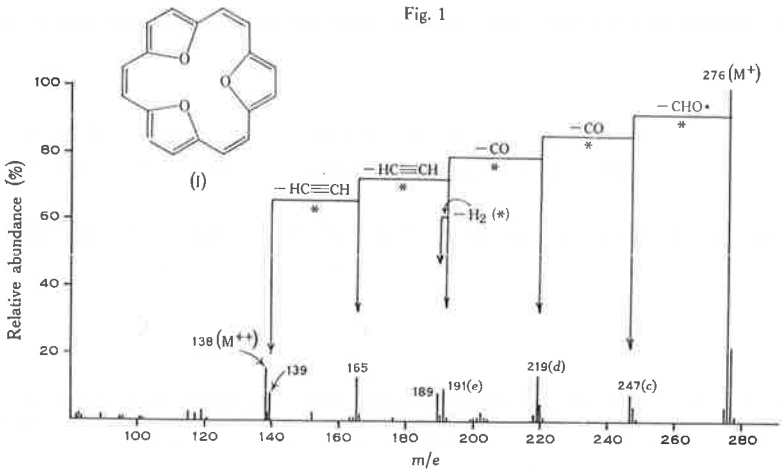


Fig. 2

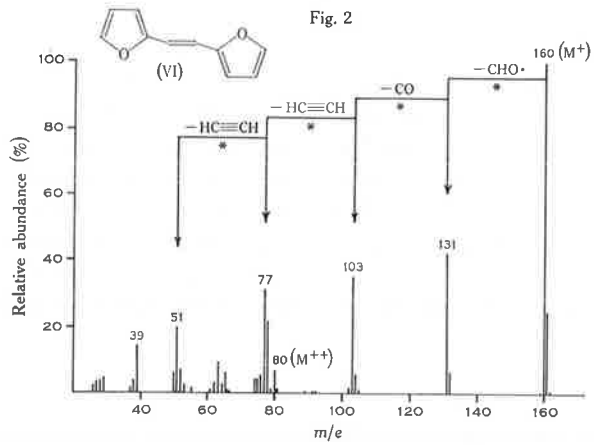
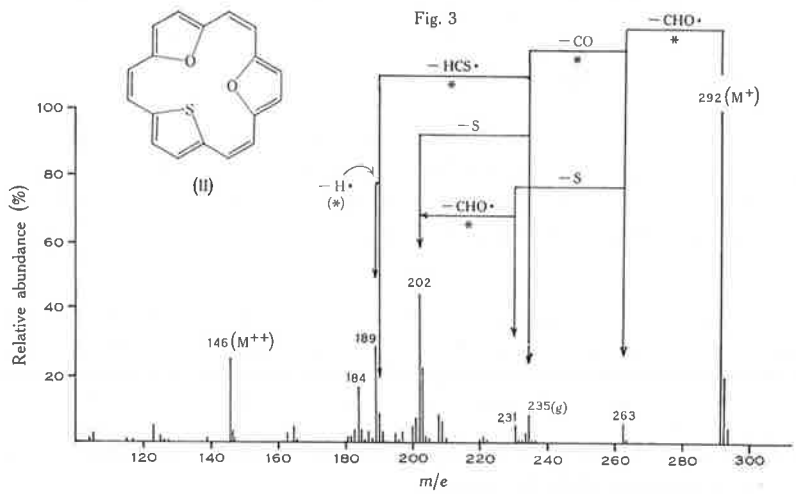
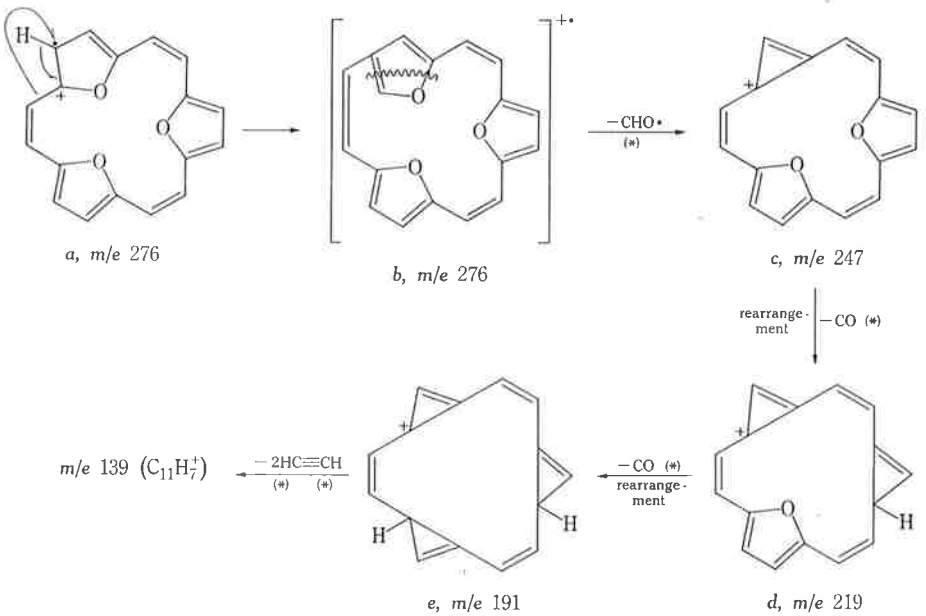


Fig. 3



skeletal rearrangement processes occur when normal fragmentations are energetically unfavourable, and when there are sites of unsaturation in the vicinity of bond cleavage. It is also important to note that 2,5-diphenylthiophen,[4] 2,5-diphenylfuran,[5] and 2,5-diphenylpyrrole[5] have skeletal rearrangement ions in their spectra due to the processes M—CHS· (4% of the base peak), M—CHO· (10%), and M—H_3CN· (4%) respectively. The presence of such ions requires phenyl migration from C2 to C3 on electron impact. It would therefore seem reasonable that the mass spectrum of (I) should contain skeletal rearrangement ions.



Scheme 1

The mass spectrum of (I) is illustrated in Figure 1. The molecular ion is the base peak of the spectrum [as is the case for all the annulene derivatives (I–V)] and it can be seen that the entire fragmentation proceeds via skeletal rearrangement ions; viz. M—CHO·—CO—CO—HC≡CH—HC≡CH. This should be compared with the similar spectrum (Fig. 2) of 1,2-di(2-furyl)ethylene (VI) which exhibits the normal scheme M—CHO·—CO—HC≡CH—HC≡CH. An explanation of the spectrum of (I) is summarized in Scheme 1. In order that the process M—CHO· may occur, the substituent attached to the 2-position of one of the furan nuclei must migrate to the 3-position with concomitant counter migration of the hydrogen from the 3-position to the 2-position ($a \rightarrow b$). It is possible that the aryl group may migrate to either the 3, 4, or 5 positions, but we favour migration to C3 from a knowledge[4,5] of the skeletal rearrangement processes that are observed in the spectra of heterocyclic systems containing 2,5-diaryl substituents. The subsequent losses of carbon monoxide

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require similar 2,3-migrations (without hydrogen migration) to furnish *e* (*m/e* 191) which then fragments by successive losses of acetylene to produce ultimately *m/e* 139 ($C_{11}H_7^+$). Another feature of the spectrum (and of those of other annulenes) is the presence of a prominent M^{++} ion, a further illustration of the stability of the [18]-annulene system.

The mass spectra (Figs. 3 and 4) of the dioxide sulphide (II) and the disulphide oxide (III) are similar to that (Fig. 1) of the trioxide (I) and should be compared with the spectra (Fig. 5 and 6) of 1-(2-furyl)-2-(2-thienyl)ethylene (VII) and 1,2-di(2-thienyl)-ethylene (VIII), which show fragmentations that produce the indene cation (*m/e* 115),

TABLE 1

COMPOSITION OF SOME IONS IN THE SPECTRA OF (III) AND (V)

Compound (III)		Compound (V)	
m/e	Composition	*m/e*	Composition
308	$C_{18}H_{12}S_2O$	307	$C_{18}H_{13}S_2N$
279	$C_{17}H_{11}S_2$	274	$C_{18}H_{12}SN$
275	$C_{18}H_{11}SO$	260	$C_{17}H_{10}SN$
274	$C_{18}H_{10}SO$	247	$C_{17}H_{11}S$
263	$C_{17}H_{11}SO$	241	$C_{18}H_{11}N$
247	$C_{17}H_{11}S$	215	$C_{16}H_9N$
245	$C_{17}H_9S$	214	$C_{16}H_8N$
221	$C_{15}H_9S$		
215	$C_{17}H_{11}$		
202	$C_{16}H_{10}$		

by the respective processes M—CHO·—S (Fig. 5) and M—HCS·—S (Fig. 6). The spectra of both [18]annulene derivatives exhibit the initial loss of a formyl radical from the molecular ion (cf. $a \rightarrow b$), and (II) shows the fragmentation modes M—CHO·—S—CHO· (to *m/e* 202) and M—CHO·—CO—HCS·—H· (to *m/e* 189). Loss of sulphur from the molecular ions of arylthiophens (to form the corresponding aryl-cyclobutadiene ion radical) has been observed previously.[4] The loss of a thioformyl radical from the molecular ion of a 2,5-disubstituted thiophen requires a 2,3-migration (in this case $f \rightarrow g$). Skeletal rearrangement processes of this type have been reported,[4] and have photochemical analogies.[6,7] The fragmentations in the spectrum of the disulphide oxide (III) are analogous, and are summarized in Figure 4. The compositions of the major ions in the spectrum of (III) have been substantiated by exact mass measurements (Table 1).

The spectra (Figs. 7 and 8) of the trisulphide (IV) and the imino disulphide (V) exhibit skeletal rearrangement ions in their spectra, even though these compounds may fragment by the normal loss of sulphur from the thiophen units.[4] Rearrangement ions in the spectrum of (IV) involve loss of the thioformyl radical, while those of the imino disulphide (V) involve loss of both the thioformyl radical and hydrogen cyanide. Both these processes involve 2,3-migrations of the type discussed above,

[6] Wynberg, H., and van Driel, H., *J. Am. chem. Soc.*, 1965, **87**, 3999.

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Fig. 4

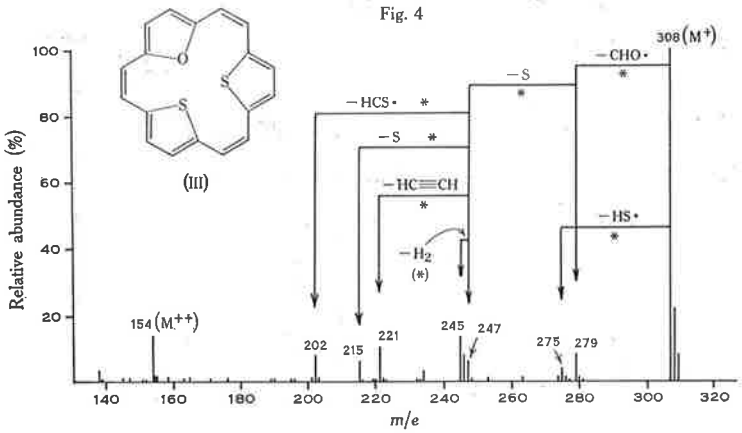


Fig. 5

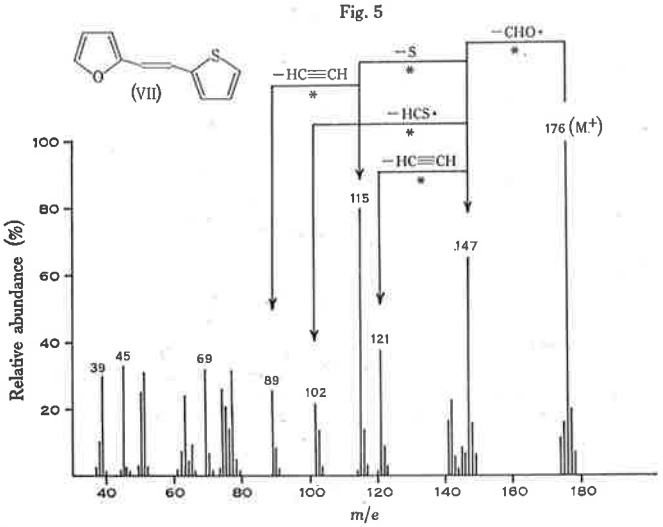


Fig. 6

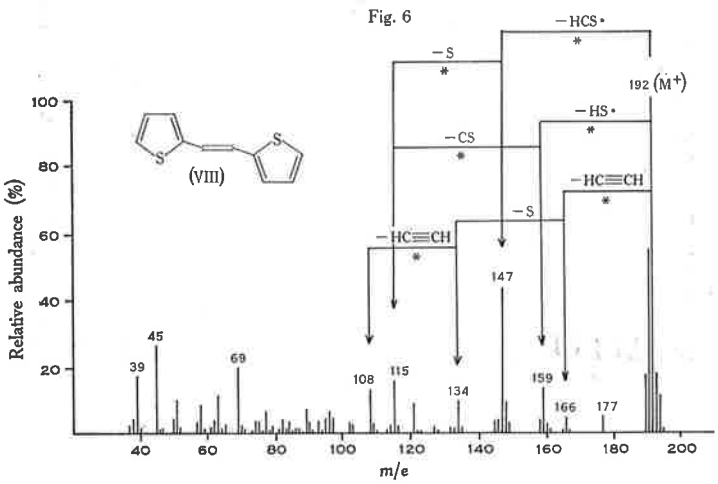


Fig. 7

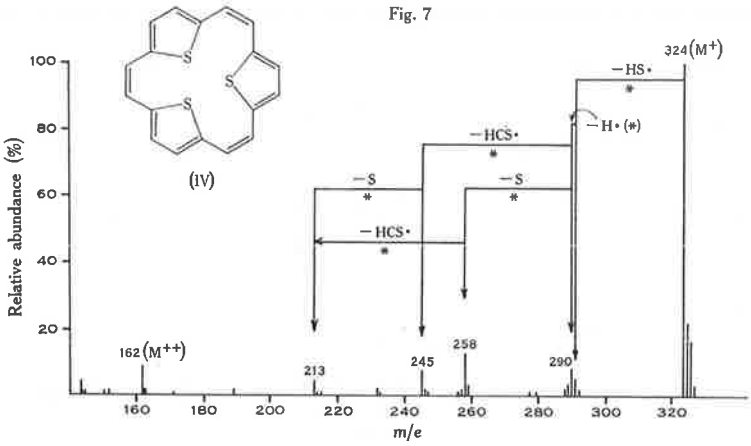


Fig. 8

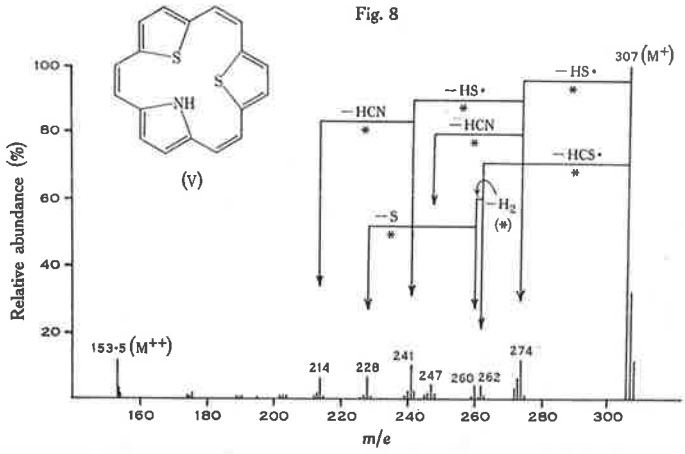
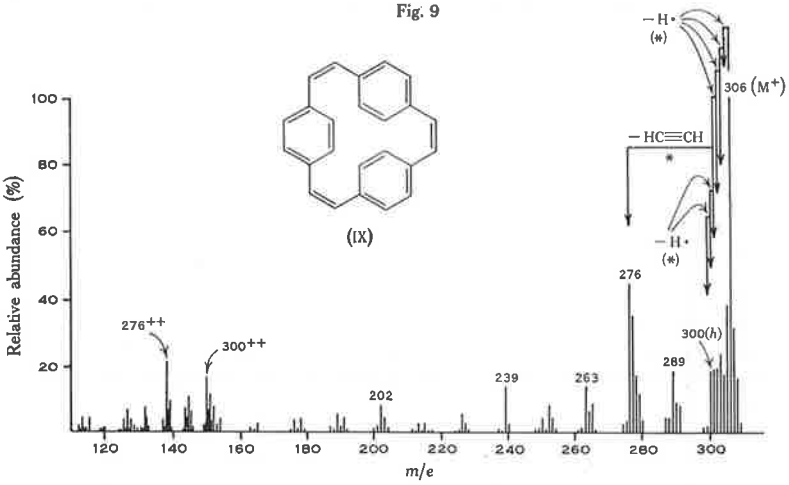
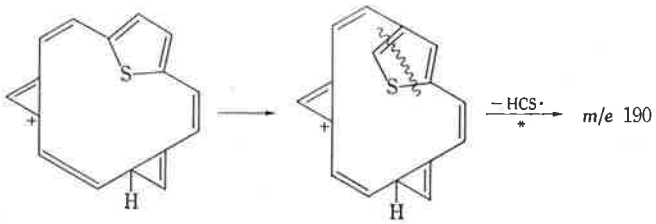


Fig. 9

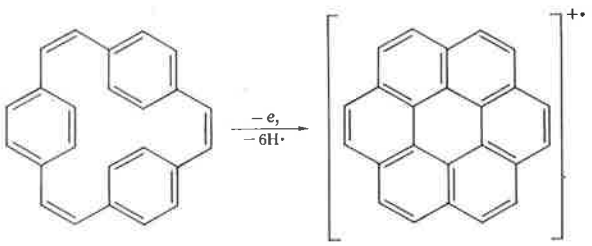


and it is of interest to note that fragmentation of the pyrrole ring occurs after the thiophen system has been disrupted.



f, *m/e* 235 *g*, *m/e* 235

In marked contrast to the annulene derivatives (I–V) (which fragment through the heteroatom by characteristic skeletal reorganization), the triene (IX)[8] on electron impact (Fig. 9) simply loses six hydrogen atoms from the molecular ion to furnish the coronene radical ion (*h*, *m/e* 300). Another fragmentation is loss of acetylene from an M—4 ion to form *m/e* 276, which might be represented as the benzo[*ghi*]perylene radical ion.



(IX) *h*, *m/e* 300

In summary, the stability of the [18]annulenes derivatives (I–V) is illustrated by the large number of skeletal rearrangement ions which are observed in their mass spectra. The presence of these ions limits the use of both the "element mapping" technique,[9] and the application of *a priori* prediction of simple fragmentation modes for this class of compound.

Experimental

All mass spectra were measured with a Hitachi Perkin–Elmer RMU 6D mass spectrometer operating at 75 eV. Samples were introduced directly using a source and sample heater temperature between 200 and 250°. Exact mass measurements were measured with an A.E.I. MS9 mass spectrometer with a resolution of 14000 (10% valley definition) using heptacosafluorotributylamine to provide reference masses. All measurements were correct to within 10 p.p.m.

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[9] Biemann, K., Bommer, P., Desiderio, D. M., and McMurray, W. J., in "Advances in Mass Spectrometry." (Ed. W. L. Mead.) Vol. 3, pp. 639–653, and references therein. (Institute of Petroleum: London 1966.)

[18]Annulene Derivatives

Samples of the [18]annulene derivatives (I–V) were available from the original syntheses, as indicated: (I),[10] (II),[11] (III),[12] (IV),[13] and (V).[14]

1,2-Diarylethylenes

The 1,2-diarylethylenes (VI–VIII) were prepared by decarboxylation of the corresponding diarylacrylic acids which were available from the above-cited syntheses.[10–13]

In each case the *cis*-diarylacrylic acid (500 mg) was heated in admixture with quinoline (5 ml) and copper chromite (200 mg) to 160–170° for 20–25 min. The reaction mixture was then cooled and treated with a slight excess of dilute hydrochloric acid; and the decarboxylated product was extracted from the acidified mixture with chloroform. After the chloroform extract had been removed it was washed successively with dilute hydrochloric acid, water, and aqueous sodium bicarbonate, following which it was dried ($CaCl_2$) and evaporated to dryness. The residual crude product was in each case purified initially by chromatography on alumina, ether being used as developer and eluent; and the product which remained after evaporation of the eluate was further purified by sublimation, or distillation, under reduced pressure (40–50°/0·1 mm).

cis-α,β-Di(2-furyl)acrylic acid[10] (500 mg) in this way gave trans-*1,2-di(2-furyl)ethylene* (VI) (190 mg; 48%) as off-white needles, m.p. 90° (Found: C, 74·7; H, 5·3. $C_{10}H_8O_2$ requires C, 75·0; H, 5·0%).

cis-α-(2-Thienyl)-β-(2-furyl)acrylic acid[12] (500 mg) likewise gave trans-*1-(2-furyl)-2-(2-thienyl)ethylene* (VII) (135 mg; 34%) as a yellow oil, b.p. 60°/0·1 mm (Found: C, 68·3; H, 4·75. $C_{10}H_8OS$ requires C, 68·2; H, 4·6%).

cis-α,β-Di(2-thienyl)acrylic acid[13] (500 mg) yielded trans-*1,2-di(2-thienyl)ethylene* (VIII) (200 mg; 49%) as colourless needles, m.p. 132° (Found: C, 62·6; H, 4·3. $C_{10}H_8S_2$ requires C, 62·5; H, 4·2%).

trans-Configurations were assigned to all the 1,2-diarylethylenes (VI–VIII), as the ultraviolet absorption spectrum of each resembled that of *trans*-stilbene,[15] and not that of *cis*-stilbene.[15] The positions and intensities of the main absorption bands in ethanolic solutions are as follows: (VI) 320, 338 mμ (ε 34000, 25000); (VII) 332 mμ (ε 28000); (VIII) 342 mμ (ε 27000).

Acknowledgments

We are grateful to Dr R. G. Cooks for the high resolution measurements, to Professor D. J. Cram for a generous sample of the triene (IX), and to Dr J. S. Shannon for the measurement of several annulene spectra on an Atlas CH 4 mass spectrometer.

The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

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ELECTRON IMPACT STUDIES

XVIII.* MASS SPECTRA OF PYRIDAZINES, PHTHALAZINES, AND RELATED COMPOUNDS

By J. H. Bowie,† R. G. Cooks,‡ P. F. Donaghue,† J. A Halleday,† and H. J. Rodda†

[*Manuscript received April* 6, 1967]

Summary

The mass spectra of substituted pyridazines, phthalazines, and related compounds are reported and discussed. Molecular ions are a prominent feature of all the spectra, and fragmentation modes may be usefully correlated with both the type of heterocycle and its substitution pattern. Fragmentation patterns have been substantiated by extensive high resolution studies and appropriate metastable ions.

The mass spectra of imidazoles,[1] pyrimidines,[2,3] pyrazines,[4,5] benzimidazoles,[6] and purines[2,7] have been discussed, but no such survey of heterocyclic systems containing adjacent nitrogen atoms has been published.

This paper is concerned with the mass spectra (Figs. 1–12 or Table 1) of the pyridazines (I–XIII), the phthalazines (XIV–XXVI), pyrido[2,3-*d*]pyridazine (XXVII), and quinoxalino[2,3-*d*]pyridazine (XXVIII). High resolution data are summarized in Table 2, and the presence of an appropriate metastable ion for a particular process is indicated by an asterisk in the figures and the text. Although the structures of fragment ions are not known, nominal structures have been written to serve the important purpose of relating fragmentation processes to the structures of the molecules in the ground state.

Pyridazine (I) and the dichloropyridazines (II and III) behave simply on electron impact (see Figs. 1 and 2 and Table 1). The spectrum (Fig. 1) of pyridazine reveals the fragmentation modes $M-N_2-H_2$ ($I \rightarrow a \rightarrow b$) while (II) fragments by the similar process $M-N_2-Cl\cdot-H\cdot$ (Fig. 2) probably to *c* (*m/e* 84/86). This facile

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† Department of Organic Chemistry, University of Adelaide, S.A. 5001.

‡ University Chemical Laboratory, Lensfield Road, Cambridge, England.

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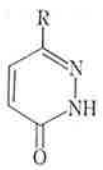
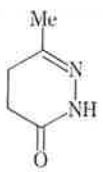
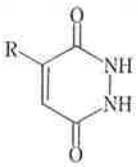
(I)-(VII)



(VIII)-(X)



(XI)



(XII), (XIII)

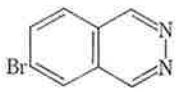
(XIV)-(XXI)

	R^1	R^2	R^3
(I)	H	H	H
(II)	Cl	H	Cl
(III)	Cl	Me	Cl
(IV)	MeO	H	H
(V)	MeO	H	Cl
(VI)	MeO	H	MeO
(VII)	Cl	H	NH_2

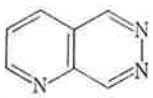
	R
(VIII)	H
(IX)	Me
(X)	Cl
(XII)	H
(XIII)	Me

	R^1	R^2
(XIV)	H	H
(XV)	Me	H
(XVI)	Cl	Me
(XVII)	Ph	H
(XVIII)	NH_2	H
(XIX)	NH_2	NH_2
(XX)	Cl	OMe
(XXI)	OEt	OEt

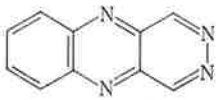
(XXII) R = H
(XXIII) R = Me
(XXIV) R = Br
(XXV) R = Ph



(XXVI)



(XXVII)



(XXVIII)

TABLE 1

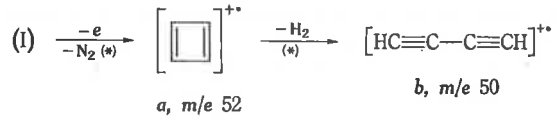
MASS SPECTRA OF PYRIDAZINES AND PHTHALAZINES

All peaks greater than 5% of the base peak (arbitrarily 100%), and certain others of diagnostic value less than 5%, are recorded

(III)	*m/e*	37	38	39	40	47	49	50	51	52	60	61	62	63	64	73	74	75	84
	I (%)	30	30	75	11	10	13	10	16	9	8	15	20	42	15	34	7	11	8
	m/e	97	99	100	101	133	135	162(M)			164(M)								
	I (%)	7	100	6	27	6	4	26			18								
(IV)	*m/e*	26	29	37	38	39	51	52	53	80	109	110(M)							
	I (%)	7	6	7	12	100	8	12	16	7	2	11							
(V)	*m/e*	15	26	29	37	38	47	50	51	52	72	73	75	79	109	115	143		
	I (%)	21	9	10	22	29	10	7	15	20	8	100	26	59	7	3	7		
	m/e	144(M)		146(M)															
	I (%)	15		6															
(VII)	*m/e*	26	27	28	37	38	39	40	41	42	51	52	54	65	66	67	72	73	
	I (%)	12	14	34	27	34	30	18	100	14	17	26	25	12	66	13	6	23	
	m/e	75	101	103	129(M)		131(M)												
	I (%)	13	76	24	34		13												

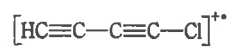
TABLE 1 (*Continued*)

(X)	*m/e*	25	27	28	35	36	37	38	39	40	41	42	43	47	49	51	52	53	67
	I (%)	30	11	20	10	12	53	87	58	14	10	12	14	22	8	25	30	10	44
	m/e	72	73	74	75	79	102	104	130(M)	132(M)									
	I (%)	15	100	29	42	7	74	24	25	6									
(XI)	*m/e*	26	27	28	29	30	37	38	39	40	41	42	43	50	51	52	53	54	
	I (%)	51	100	48	53	32	18	23	86	25	56	47	70	26	31	15	26	13	
	m/e	55	56	57	67	69	83	84	112(M)	113									
	I (%)	36	34	30	7	10	18	16	63	8									
(XIII)	*m/e*	27	37	38	39	40	41	43	53	67	68	69	96	97	98	126(M)			
	I (%)	8	15	31	100	25	15	15	8	15	23	44	17	11	6	26			
(XVI)	*m/e*	39	50	51	57	62	63	74	75	76	89	102	115	116	142	143	149		
	I (%)	9	15	14	10	8	14	9	19	11	12	18	42	17	11	22	7		
	m/e	177	178(M)	179	180(M)														
	I (%)	4	100	11	31														
(XVII)	*m/e*	50	51	75	76	77	89	151	152	176	177	178	205	206(M)	207				
	I (%)	8	10	6	17	10	8	8	5	8	5	5	100	52	7				
(XVIII)	*m/e*	28	37	38	39	50	51	52	62	63	64	74	75	76	89	90	116	117	
	I (%)	10	7	12	19	20	13	12	15	28	11	8	10	11	57	51	14	44	
	m/e	118	144	145(M)	146														
	I (%)	7	8	100	15														
(XIX)	*m/e*	38	39	49	50	51	61	62	64	73	74	75	76	77	88	101	102	103	
	I (%)	10	16	33	42	22	9	11	16	13	21	42	59	17	22	21	29	53	
	m/e	104	114	115	128	129	130	131	144	145	159	160(M)	161						
	I (%)	12	26	7	30	69	19	7	8	6	100	89	10						
(XXI)	*m/e*	26	28	50	51	75	76	77	102	103	104	105	129	130	132	133			
	I (%)	30	29	21	15	10	54	21	12	42	62	28	14	45	13	14			
	m/e	146	147	148	162	163	175	190	191	203	218(M)								
	I (%)	29	6	6	100	8	27	57	7	86	18								
(XXIII)	*m/e*	27	39	50	51	52	63	74	75	76	77	78	102	103	104	105	131		
	I (%)	9	13	26	30	9	16	15	16	18	43	13	25	59	24	10	39		
	m/e	132	160(M)	161															
	I (%)	10	100	14															
(XXIV)	*m/e*	29	39	50	51	61	62	63	74	75	76	86	87	88	89	90	91	102	
	I (%)	6	15	17	11	9	28	18	9	22	13	9	13	42	13	80	6	15	
	m/e	117	145	146	167	169	180	195	197	224(M)	225	226(M)	227						
	I (%)	37	44	5	15	15	9	6	6	100	10	97	9						
(XXV)	*m/e*	39	50	51	63	77	115	139	163	164	165	166	192	193	194	221			
	I (%)	9	8	10	10	7	6	11	15	14	36	10	5	7	6	96			
	m/e	222(M)	223																
	I (%)	100	16																
(XXVI)	*m/e*	37	38	49	50	51	62	63	73	74	75	76	100	101	102	154	156		
	I (%)	10	9	9	40	30	12	8	10	44	80	10	10	56	32	5	5		
	m/e	180	181	182	183	208(M)	209	210(M)	211										
	I (%)	5	11	5	11	100	14	97	9										



a, *m/e* 52

b, *m/e* 50



c, *m/e* 84/86

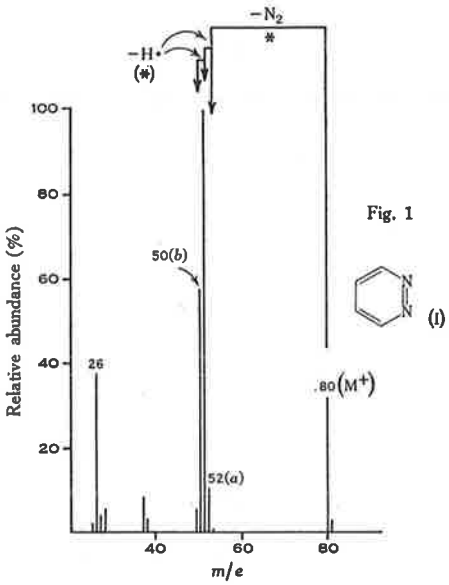


Fig. 1

(I)

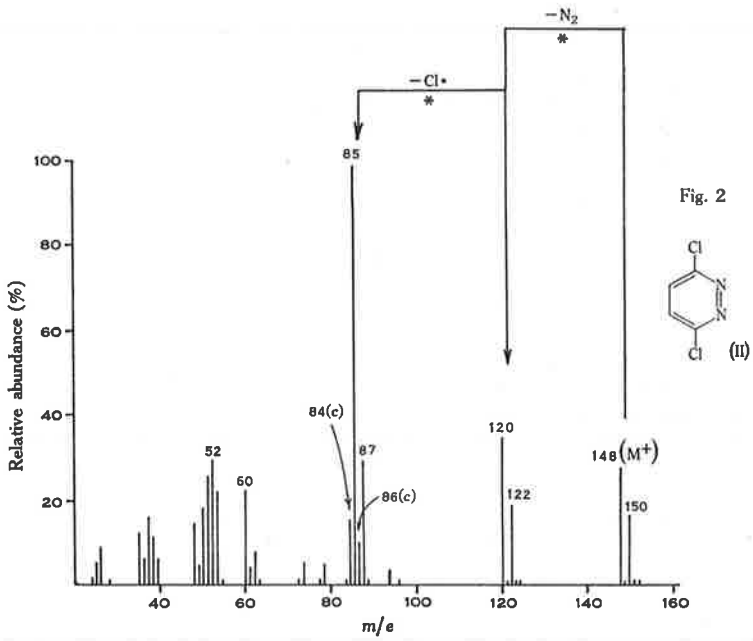
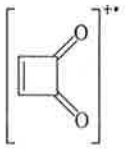


Fig. 2

(II)



d, *m/e* 82

e, *m/e* 69 (70%)

f, *m/e* 69 (30%)

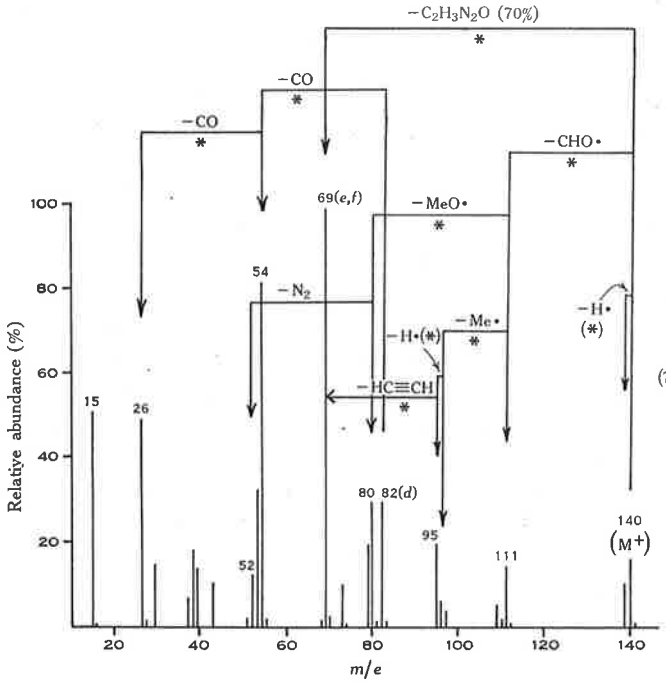
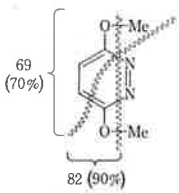


Fig. 3



(VI)

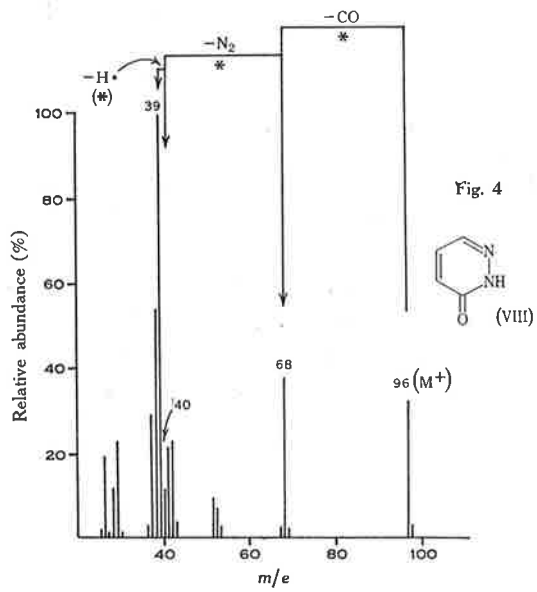


Fig. 4

(VIII)

loss of nitrogen from the molecular ion is a general feature of fragmentations of simple pyridazines which contain substituents through which fragmentation does not proceed readily, e.g. chloro, methyl, and amino (II, III, and VII). The energetically favoured loss of nitrogen from the molecular ions of simple pyridazines may be used to detect the presence of the –N=N– group (cf. the loss of HCN from the molecular ions of imidazoles[1]).

When the substituent is methoxy (e.g. (IV)–(VI)) the initial fragmentation proceeds through this substituent. This is most clearly illustrated by the spectrum (Fig. 3) of 3,6-dimethoxypyridazine, where extensive high resolution measurements (Table 2) were necessary for the interpretation. A series of major decompositions are noted in this spectrum; viz.: (1) $M-CHO\cdot-CH_3O\cdot-N_2$ (to *a*, *m/e* 52). (2) The formation of an ion *d* (90% of *m/e* 82) which fragments by successive loss of two molecules of carbon monoxide to form the acetylene radical ion. (3) The methoxycyclopropenyl cation *e* (70% of *m/e* 69 (base peak)) is produced in a one-step process from the molecular ion, while the complement (30% of *m/e* 69), represented as *f*, is produced as indicated in Figure 3.

The pyridazones (VIII–X) fragment specifically by the initial loss of carbon monoxide. The spectra (Fig. 4 and Table 1) of 3-pyridazone (VIII) and 6-chloro-3-pyridazone (X), show the decomposition modes $M-CO-N_2-H\cdot$ to give the base peaks (the cyclopropenyl cation *m/e* 39, and the chlorocyclopropenyl cation *g*, *m/e* 73/75 respectively). The spectrum (Fig. 5) of 6-methyl-3-pyridazone (IX) retains the features of that of 3-pyridazone, but in addition reveals the presence of a large $M-CHO\cdot$ ion (*m/e* 81). This is characteristic of the methyl substituent, which may facilitate the formation of the stable cation *h*. The partially reduced system in (XI) does not alter the initial fragmentation, as M—CO and $M-CHO\cdot$ ions are still observed.

g, *m/e* 73/75

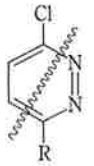
h, *m/e* 81

i, *m/e* 84

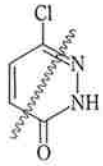
The dihydroxypyridazines (XII) and (XIII), which are predominantly in the amide form (cf.[8]), behave as expected on electron impact, and the spectrum (Fig. 6) of (XII) illustrates the general features. The process $M-N_2H_2$ produces *d* (*m/e* 82) which fragments as outlined above, while M—CO produces *i* (*m/e* 84).

Several additional salient features emerge from the spectra of pyridazines. (1) The spectra of 3-chloro derivatives of the types (A) (where R is not chloro), and (X), exhibit large peaks due to the ion *g* (base peak in the spectra of (V) and (X)). This is characteristic of monochloro substitution. It should be noted however that *g* also occurs in the spectrum of (III), but this exception is due to the additional methyl group and not the second chloro substituent. (2) Pyridazines and pyridazones with methoxy groups adjacent to nitrogen exhibit pronounced M—1 ions (see below).

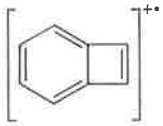
[8] Maccoll, A., *J. chem. Soc.*, 1946, 670.



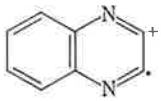
(A)



(X)



j, *m/e* 102 (50%)



k, *m/e* 128

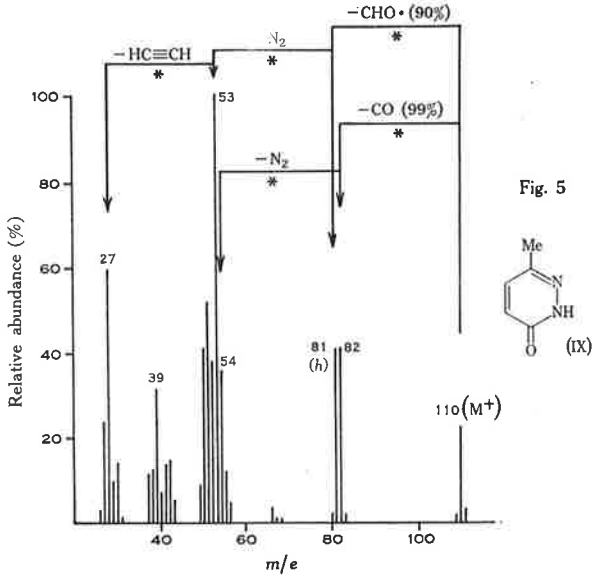


Fig. 5

(IX)

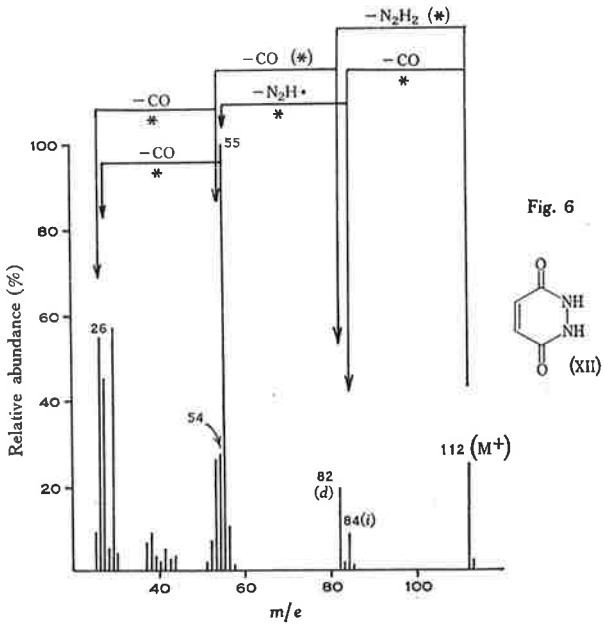


Fig. 6

(XII)

TABLE 2

COMPOSITION OF SOME IONS IN THE SPECTRA OF (I–XXVIII)

Compound	*m/e*	Composition	Compound	*m/e*	Composition
(IV)	80	$C_4H_4N_2$	(XV)	117	C_8H_7N
				116	C_8H_6N (80%)
(V)	115/117	$C_4H_4N_2Cl$			C_9H_8 (20%)
	73/75	C_3H_2Cl		115	C_9H_7
(VI)	111	$C_7H_7N_2O$	(XVI)	116	C_8H_6N
	95	$C_4H_3N_2O$		115	C_9H_7 (95%)
	82	$C_3H_2O_2$ (90%)			C_8H_6N (5%)
		C_4H_4NO (10%)			
	80	$C_4H_4N_2$ (90%)	(XVII)	178	$C_{13}H_8N$
		C_4H_3NO (10%)		177	$C_{13}H_7N$ (50%)
	69	C_4H_5O (70%)			$C_{14}H_9$ (50%)
		C_3HN_2O (30%)		176	$C_{14}H_8$
	54	C_3H_2O (90%)			
		C_3H_4N (10%)	(XVIII)	117	C_8H_7N
		C_2H_3O (55%)			
	43	CH_3N_2 (40%)	(XIX)	130	$C_8H_8N_2$
		CHNO (5%)		129	$C_8H_5N_2$
(VIII)	68	$C_3H_4N_2$	(XX)	165/167	$C_6H_6N_2Cl$
	42	C_2H_2O (70%)		129	$C_8H_5N_2$
		CH_2N_2 (30%)		125	C_7H_4Cl
(IX)	82	$C_4H_6N_2$	(XXI)	190	$C_{10}H_{10}N_2O_2$
	81	$C_4H_5N_2$ (90%)		175	$C_9H_7N_2O_2$
		C_5H_5O (10%)		162	$C_8H_6N_2O_2$
	54	C_4H_2 (70%)		146	$C_8H_6N_2O$
		C_3H_4N (30%)		130	C_8H_4NO (70%)
	53	C_4H_5			$C_8H_8N_2$ (30%)
				104	C_6H_3NO
(X)	102/104	$C_3H_3N_2Cl$	(XXII)	118	C_8H_6O (50%)
	75/73	C_3H_2Cl			$C_7H_6N_2$ (50%)
	52	C_3H_3N		117	C_8H_5O (80%)
(XI)	84	$C_4H_8N_2$			$C_7H_5N_2$ (20%)
	83	$C_4H_7N_2$		91	C_6H_5N
				90	C_7H_6
(XII)	84	$C_3H_4N_2O$		89	C_7H_5
	82	$C_4H_2O_2$			
	56	C_3H_4O	(XXIV)	195/197	C_8H_4OBr
	55	C_3H_3O		167/169	C_7H_4Br
	54	C_3H_2O		117	$C_7H_5N_2$
(XIII)	98	$C_4H_6N_2O$	(XXV)	194	$C_{13}H_{10}N_2$
	97	$C_4H_5N_2O$ (60%)		193	$C_{13}H_9N_2$ (60%)
		$C_5H_5O_2$ (40%)			$C_{14}H_9O$ (40%)
	96	$C_5H_4O_2$		192	$C_{13}H_8N_2$ (20%)
	69	C_4H_5O (95%)			$C_{14}H_8O$ (80%)
		$C_3H_5N_2$ (5%)		178	$C_{13}H_8N$ (80%)
	68	C_4H_4O			$C_{14}H_{10}$ (20%)
(XIV)	103	C_7H_5N	(XXVII)	104	$C_6H_6N_2$
	102	C_7H_4N (50%)		103	$C_6H_4N_2$ (50%)
		C_8H_6 (50%)			C_7H_5N (50%)
	75	C_6H_3 (80%)		77	C_5H_3N
		C_5HN (20%)		76	C_5H_2N (50%)
					C_7H_6 (50%)

Before discussing the spectra of substituted phthalazines, it is convenient to consider the relationship between the spectra of pyridazine (I), phthalazine (XIV), pyrido[2,3-*d*]pyridazine (XXVII), and quinoxalino[2,3-*d*]pyridazine (XXVIII).

Although no "bond fixation" would be expected in pyridazine, quantum mechanical calculations[9] have shown phthalazine to exist preferentially in the C=N form. Similar

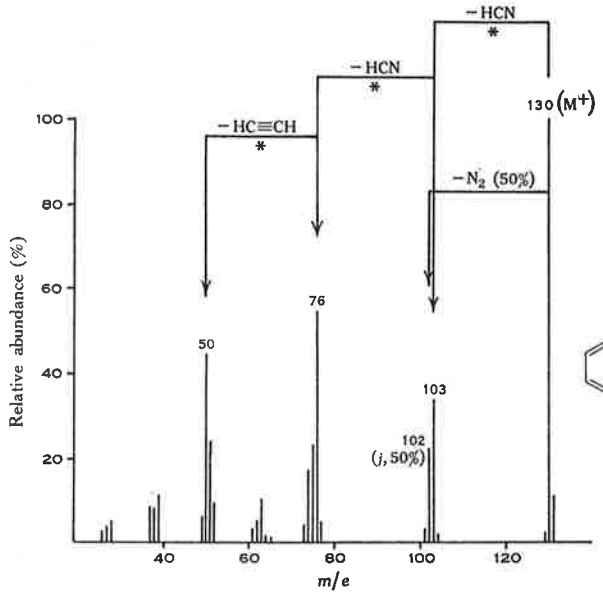
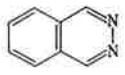


Fig. 7



(XIV)

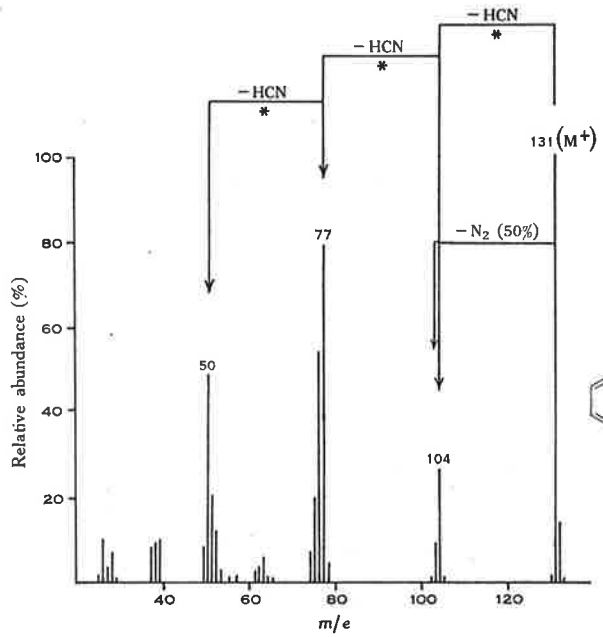
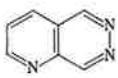


Fig. 8



(XXVII)

behaviour would be expected of (XXVII) and (XXVIII). This feature can be qualitatively correlated with the spectra (Figs. 1, 7–9) of (I), (XIV), (XXVII), and

[9] Overend, W. G., Turton, L. M., and Wiggins, L. F., *J. chem. Soc.*, 1950, 3500.

(XXVIII) where $M-N_2$ peaks would be indicative of the –N=N– grouping. No loss of HCN is seen in the spectrum of (I), while (XIV) and (XXVII) fragment mainly

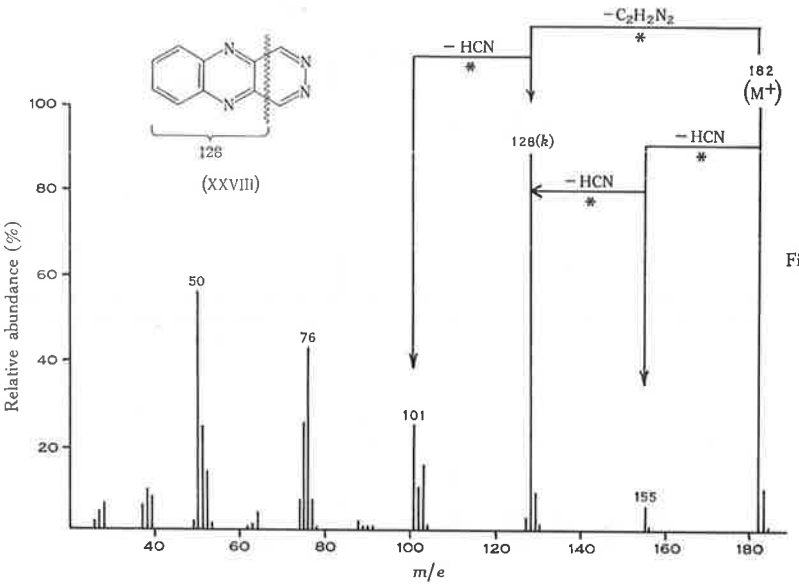


Fig. 9

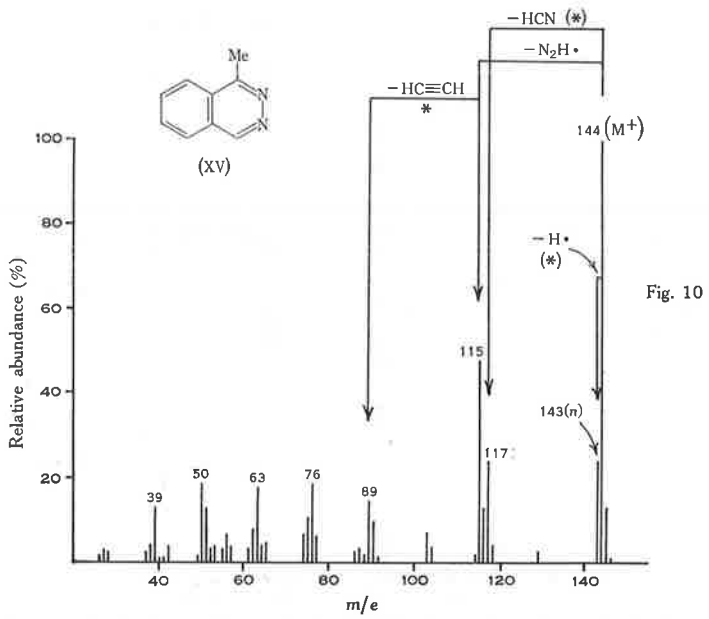


Fig. 10

by the process M—HCN, although 50% of the M—28 peaks in both Figures 7 and 8 arise by the process $M-N_2$ (e.g. to *j*, *m/e* 102, in Fig. 7). No $M-N_2$ peak is noted in the spectrum (Fig. 9) of (XXVIII). This is indicative of complete bond fixation

in the C=N form. The main process is concerted loss of two molecules of HCN to form *k* (see Fig. 9).

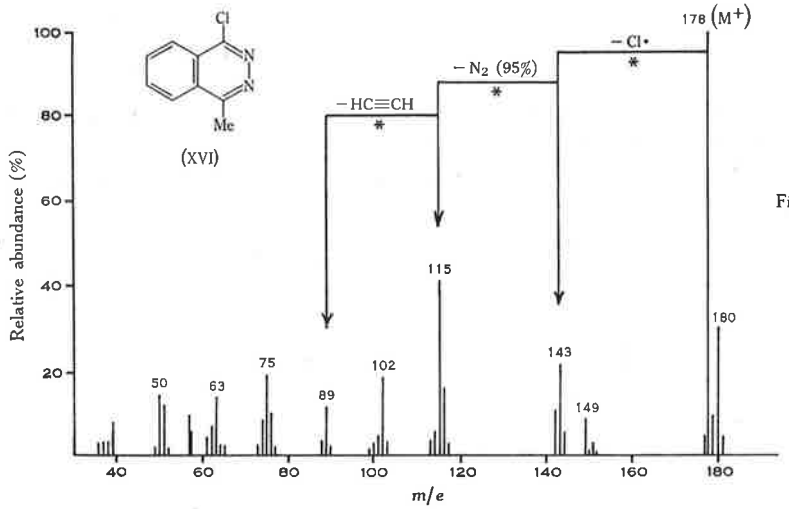


Fig. 11

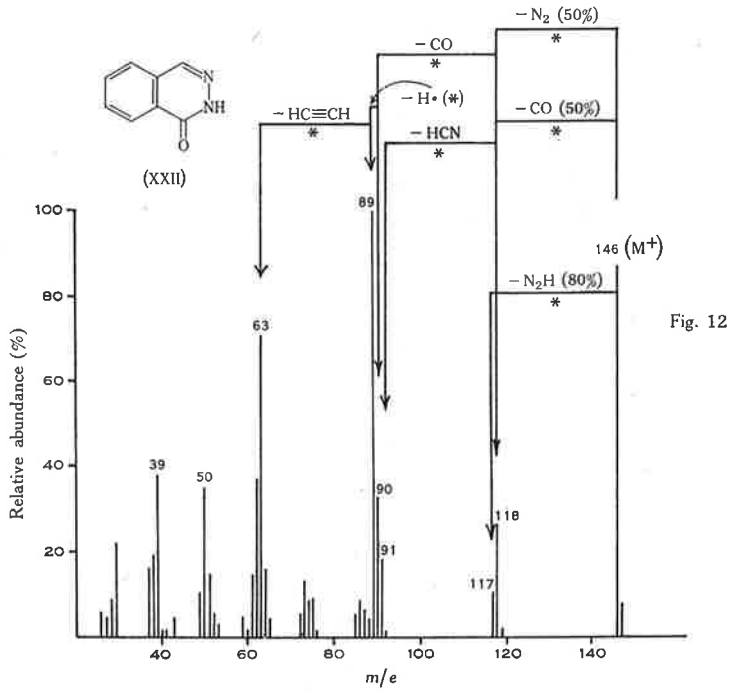


Fig. 12

It has been shown that the presence of adjacent nitrogens can be detected in the spectrum (Fig. 7) of phthalazine by the presence of an M—N_2 peak. However,

the main fragmentation scheme is M—HCN—HCN—HC≡CH (to form *b*, *m/e* 50), and this is modified in the spectrum (Table 1) of 6-bromophthalazine (XXVI) to M—HCN—HCN—Br·.

When amino, chloro, methyl, or methoxyl substituents are present at either C1 and/or C4 of the phthalazine nucleus (as in XV, XVI, XVIII, and XIX), the processes M—N_2 or M—N_2H· predominate, and M—HCN ions are either small or absent. This can be seen in the spectra (Figs. 10 and 11) of 1-methyl- (XV) and 1-chloro-4-methyl-phthalazine (XVI), where the processes M—N_2H· (Fig. 10) and M—Cl·—N_2 (Fig. 11) result in the formation of the stable indene cation (*m/e* 115). It is also of interest to compare the spectra (Table 1) of 3-chloro-6-methoxypyridazine (V) with that of 1-chloro-4-methoxyphthalazine (XX). The former fragments initially through the methoxyl group, the latter by either of the processes M—N_2

TABLE 3

RELATIVE ABUNDANCES* OF M^+ AND M–H· IONS IN THE SPECTRA OF CERTAIN PYRIDAZINES AND PHTHALAZINES

Ion	(III)	(IV)	(V)	(VI)	(IX)	(XI)	(XV)	(XVI)	(XVII)	(XIX)	(XX)	(XXI)	(XXV)
M^+	26	12	14	16	23	64	100	100	51	89	34	18	100
M—H·	9	3	7	11	2	2	25	4	100	100	25	2	96

* As per cent of base peak.

or M—Cl·. In marked contrast, the complex spectrum (Table 1) of 1,4-diethoxyphthalazine (XXI) shows almost exclusive fragmentation through the ethoxyl substituents. No loss of nitrogen [compare (VI), Fig. 3] is noted in this spectrum, and all ions above *m/e* 76 contain nitrogen (Table 2). The spectra of the phthalazones (XXII–XXV) are complex, and fragmentations may proceed by loss of either nitrogen or carbon monoxide from the molecular ions (see Fig. 12). This is quite different from the simple behaviour (Fig. 4) exhibited by 3-pyridazone on electron impact.

An important characteristic of the spectra of pyridazines and phthalazines which contain amino, methyl, phenyl, or methoxyl substituents adjacent to nitrogen, is the presence of M—H· ions. These ions are summarized in Table 3, where they are compared with the relative abundance of the molecular ions. There are four separate mechanisms for the geneses of the M–H· ions.

(1) Loss of a hydrogen radical from a methoxyl group. This occurs in the spectra of (IV–VI) and (XX), and is most marked in the spectrum (Table 1) of 1-chloro-4-methoxyphthalazine (XX). As large M—H· ions are not noted in the spectra of methoxybenzenes,[10] their formation in these spectra must be due to a specific "ortho effect"[11] operating between the methoxyl substituent and the adjacent nitrogen, e.g. to form an ion *l* (*m/e* 193/195) in the spectrum of (XX).

(2) Loss of a hydrogen atom from the phenyl group in the spectra of (XVII) and (XXV) (89% and the base peak respectively). As loss of a hydrogen radical is

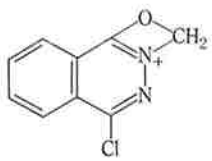
[10] Barnes, C. S., and Occolowitz, J. L., *Aust. J. Chem.*, 1963, **16**, 219.

[11] McLafferty, F. W., and Gohlke, R. S., *Analyt. Chem.*, 1959, **31**, 2079.

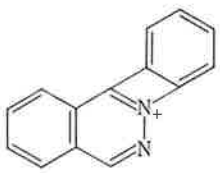
not as pronounced in the spectrum of diphenyl,[12] an "ortho effect" is again operative, for instance the M−1 ion in the spectrum of (XVII) may be represented as *m* (*m/e* 205).

(3) The loss of a hydrogen radical from methyl in the spectra of (III), (IX), (XIII), (XV), and (XXIII). This loss of a hydrogen radical from methyl with concomitant ring expansion is a characteristic fragmentation of a methyl group attached to an aromatic ring.[1,13] The structure of the M−1 ion in the spectrum (Fig. 7) of 1-methylphthalazine is probably *n* (*m/e* 143).

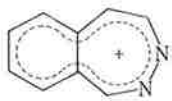
(4) Although there is no M−1 ion in the spectrum of 1-aminophthalazine, the M−1 ion in that of 1,4-diaminophthalazine represents the base peak of the spectrum. This is due to the formation of the stabilized cation *o* (*m/e* 159).



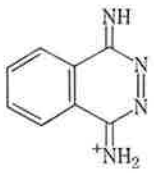
l, *m/e* 193/195



m, *m/e* 205



n, *m/e* 143



o, *m/e* 159

In summary, the mass spectra of these compounds allow the determination of both the type of heterocyclic compound, and the nature of the substituents. In certain cases, "ortho effects" allow the determination of the position of substituents (e.g. phenyl and methoxyl), and the absence of skeletal rearrangement fragments in the spectra allows mass spectrometry to be used for analytical purposes.

Experimental

All mass spectra were measured with an Hitachi Perkin–Elmer RMU 6D mass spectrometer operating at 75 eV, and with an inlet and source temperature of *c.* 150°. Exact mass measurements were determined with an A.E.I. MS9 mass spectrometer, using a resolution of 14000 (10% valley definition) with heptacosafluorotributylamine providing reference masses.

The following compounds were prepared by reported procedures: (I),[14] (II),[14] (IV),[15] (V),[16] (VI),[16] (VII),[17] (VIII),[18] (IX),[19] (X),[16] (XI),[19] (XII),[14] (XIV),[20] (XV),[21] (XVI),[21] (XVII),[22]

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[22] Lieik, A., *Ber. dt. chem. Ges.*, 1905, **38**, 3918.

(XVIII),[23] (XIX),[24] (XX),[25] (XXI),[26] (XXII),[27] (XXIII),[28] (XXIV),[29] (XXV),[22] (XXVI),[24] (XXVII),[30] and (XXVIII).[31]

Compounds (III) and (XIII) were synthesized by the general methods[14] used for (II) and (XII).

Acknowledgments

One of us (R.G.C.) is grateful for the award of an Elsie Ballot Fellowship.

The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

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F. Duus, P. Madsen, S.-O. Lawesson, J. H. Bowie and R. G. Cooks

Electron impact studies

XIX. Mass spectra of α- and β-mercaptoesters: Skeletal rearrangement upon electron impact

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Electron impact studies

XIX. Mass spectra of α- and β-mercaptoesters: Skeletal rearrangement upon electron impact

By F. DUUS, P. MADSEN, S.-O. LAWESSON J. H. BOWIE and R. G. COOKS

ABSTRACT

The mass spectra of a series of α- and β-mercaptoesters are reported and discussed. All spectra exhibit molecular ions and characteristic fragmentation modes. Skeletal rearrangement fragments, produced by C–S and in some cases by O–O bond formation, are present in the spectra of all α- and β-mercaptoesters.[1]

Because of our interest in the skeletal rearrangement processes which occur in the mass spectra of a variety of sulphur compounds [1–11], we have synthesized a series of mercaptoesters (I–XXII) and have determined their mass spectra. This paper is primarily concerned with the skeletal rearrangement fragments present in these spectra. Some of these processes have been briefly mentioned in a previous communication [12]. We wish here, to present the work in full.

$HS \cdot CH_2 \cdot COOR$

	R
I	C_2H_5
II	CD_2CH_3
III	*n*-C_3H_7
IV	*iso*-C_3H_7
V	*n*-C_4H_9
VI	*sec*-C_4H_9
VII	*iso*-C_5H_{11}
VIII	cyclohexyl
IX	$CH_2C_6H_5$
X	$CD_2C_6H_5$
XI	$CH_2CH_2OCH_3$

$CH_3 \cdot CH(SH) \cdot COOR$

	R
XII	C_2H_5
VIII	*n*-C_3H_7
XIV	*iso*-C_3H_7
XV	allyl
XVI	$CH_2C_6H_5$

$CH_3 \cdot CH(SR') \cdot COOR$

	R	R'
XVII	*iso*-C_3H_7	$COCH_3$
XVIII	$CH_2C_6H_5$	$COCH_3$
XIX	*iso*-C_3H_7	COC_6H_5
XX	$CH_2C_6H_5$	$CH_2C_6H_5$

$HS \cdot CH_2CH_2 \cdot COOR$

	R
XXI	C_2H_5
XXII	$CH_2C_6H_5$

[1] Part XVIII of this series: J. H. Bowie, R. G. Cooks, P. P. Conaghue, J. A. Halleday, and H. J. Rodda, *Aust. J. Chem.* (in press).

Table 1.[a] Mass spectra of mercaptoesters.

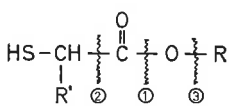
(IV)	*m/e*	27	29	39	41	42	43	45	46	47
	I(%)	39	6	15	38	13	100	19	15	59
		59	74	75	92	93	119	134(M)		
		10	12	36	28	14	5	16		
(VI)	*m/e*	27	28	29	39	41	42	43	45	46
	I(%)	34	10	95	15	83	18	23	22	13
		47	55	56	57	59	74	75	89	92
		86	10	84	100	11	10	34	17	20
		93	119	148(M)						
		20	13	3						
(VII)	*m/e*	27	29	39	41	42	43	45	46	47
	I(%)	24	36	15	34	14	100	9	11	38
		55	57	70	71	74	75	92	103	115
		23	6	37	30	8	10	11	6	7
		162(M)								
		4								
(VIII)	*m/e*	27	29	39	41	47	54	55	67	75
	I(%)	24	20	24	60	26	12	100	26	6
		81	82	83	92	93	115	174(M)		
		8	59	70	13	12	12	3		
(XI)	*m/e*	27	28	29	31	42	43	44	45	46
	I(%)	13	13	36	23	16	22	12	100	18
		47	58	59	74	75	77	118	150(M)	
		67	66	61	7	17	27	12	5	
(XII)	*m/e*	26	27	28	29	35	45	59	60	61
	I(%)	17	37	16	59	8	9	11	29	100
		88	89	134(M)						
		20	6	25						
(XIII)	*m/e*	29	30	35	39	41	43	60	61	75
	I(%)	36	12	5	8	31	74	28	100	9
		88	89	106	148(M)					
		19	10	22	13					
(XIV)	*m/e*	27	28	35	39	41	43	45	59	60
	I(%)	43	14	9	13	40	100	9	12	20
		61	62	75	88	89	106	148(M)		
		92	9	15	11	9	41	20		
(XVI)	*m/e*	27	39	51	61	65	77	91	92	107
	I(%)	12	10	9	35	12	8	100	12	6
		123	196(M)							
		46	2							
(XVII)	*m/e*	15	27	41	43	60	61	75	88	103
	I(%)	13	14	10	100	11	16	5	8	17
		106	131	148	190(M)					
		8	7	15	2					

Table 1 (*continued*)

(XVIII)	*m/e*	15	39	43	61	65	77	91	92	103
	I(%)	8	8	100	8	15	7	96	12	7
		107	123	162	195	248(M)				
		8	12	12	12	2				
(XIX)	*m/e*	27	45	51	77	105	106	193	252(M)	
	I(%)	8	12	11	29	100	10	6	3	
(XX)	*m/e*	39	45	51	65	77	91	92	107	123
	I(%)	9	11	6	18	7	100	13	15	14
		195	286(M)							
		40	2							
(XXI)	*m/e*	26	27	28	29	35	43	45	46	47
	I(%)	12	77	84	77	21	19	24	15	32
		55	59	60	61	62	73	88	89	90
		18	19	73	100	8	18	80	46	8
		106	134(M)							
		7	56							
(XXII)	*m/e*	27	39	51	61	65	77	79	91	92
	I(%)	13	11	11	8	16	10	9	100	30
		107	123	196(M)						
		6	16	3						
(XXVI)	*m/e*	27	28	29	39	41	43	45	46	47
	I(%)	57	19	86	27	96	13	50	34	85
		55	56	57	60	61	73	72	71	77
		93	92	31	20	75	15	12	11	39
		89	90	92	103	105	148(M)			
		100	8	8	9	10	54			

[a] All peaks greater than 5 % of the base peak (100 %), and skeletal rearrangement ions and molecular ions which are less than this value, are recorded.

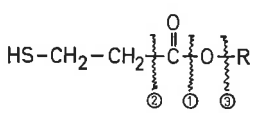
The mass spectra of I–XXII are recorded in Figs. 1–7 and Table 1. An asterisk in either the text or a figure represents the presence of an appropriate metastable ion for the process indicated. Structures drawn for fragment ions are nominal only, and are intended to relate fragmentation processes to the structures of molecules in the ground state.



A

$HS-\overset{+}{C}H_2$

a, m/e 47



B

$HS-\overset{+}{C}H-CH_3$

b, m/e 61

Table 2. Exact mass measurements in the spectra of I–XXIX.

Compound	*m/e*	composition
I	92	$C_2H_4O_2S$
	74	C_2H_2OS
	61	C_2H_5S(60 %) $C_2H_5O_2$(40 %)
III	105	$C_3H_5O_2S$
	75	C_2H_3OS(60 %) C_3H_7S(40 %)
	74	C_2H_2OS(95 %) C_3H_6S(5 %)
IV	75	C_2H_3OS(50 %) C_3H_7S(50 %)
V	119	$C_4H_7O_2S$
	105	$C_3H_5O_2S$
	92	$C_2H_4O_2S$
	89	C_4H_9S
	74	C_2H_2OS
	57	C_4H_9
	47	CH_3S
VI	93	$C_2H_5O_2S$
	92	$C_2H_4O_2S$
	89	C_4H_9S
	75	C_2H_3OS
	57	C_4H_9(80 %) C_3H_5O(20 %)
VII	144	$C_7H_{12}OS$
	115	$C_6H_{11}O_2$
	103	$C_5H_{11}S$
	92	$C_2H_4O_2S$
	70	C_5H_{10}
	55	C_4H_7
VIII	115	$C_6H_{11}S$
	93	$C_2H_5O_2S$
	92	$C_2H_4O_2S$
	83	C_6H_{11}
	82	C_6H_{10}
	67	C_5H_7
	55	C_4H_7
IX	123	C_7H_7S
XI	118	$C_4H_6O_2S$(80 %) $C_5H_{10}O_3$(20 %)
	77	C_2H_5OS
	75	C_2H_3OS(75 %) $C_2H_7O_2$(25 %)
	59	C_3H_7O
	58	C_3H_6O
XIII	75	$C_3H_7O_2$
	61	C_2H_5S
	57	C_3H_5O
XIV	75	C_3H_7S(70 %) $C_3H_7O_2$(30 %)
XV	73	C_3H_5S(95 %) $C_3H_5O_2$(5 %)
XVI	123	C_7H_7S
XVII	148	$C_6H_{12}O_2S$(95 %) $C_5H_8O_3S$(5 %)
	106	$C_3H_6O_2S$
	75	C_3H_7S
	61	C_2H_5S
XVIII	123	C_7H_7S
XXI	106	$C_3H_6O_2S$
	105	$C_3H_5O_2S$
	61	C_2H_5S
	60	C_2H_4S(90 %) $C_2H_4O_2$(10 %)
	55	C_3H_3O
XXII	123	C_7H_7S
XXVI	89	C_4H_9S
	77	C_2H_5OS
	61	C_2H_5S

The normal fragmentations of the α-mercapto- (A) and β-mercaptoesters (B) are unexceptional and are illustrated in Figs. 1–8. Three major processes are observed: (*a*) M–RO–CO or M–RCO_2 (cleaves 1 and 2 in A and B). This process, which is characteristic of esters [13], is observed in the majority of spectra. When R is a small alkyl group (<Pr), the process produces the base peak of the spectrum; viz. *a* (*m/e* 47) in A (R′ = H) and *b* (*m/e* 61) in A(R′ = Me) and B. (*b*) Cleavage 3 (in A and B) to form R^+ ions. This process (or a further fragmentation of R^+) generally produces the base peak of the spectrum when R ⩾ Et. This is most prominent when R^+ is the tropylium cation (*m/e* 91), e.g. in the spectra (Table 1 and Fig. 5) of IX, XVI and XXII. There are exceptions to this general rule, e.g. the base peak in the spectrum (Fig. 7) of the allyl ester (XV) is *b* (*m/e* 61).

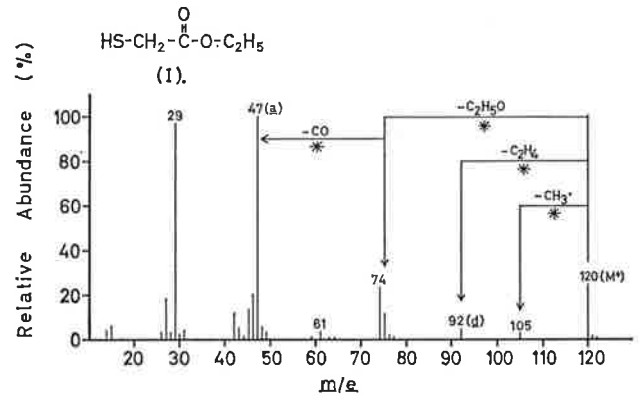


Fig. 1

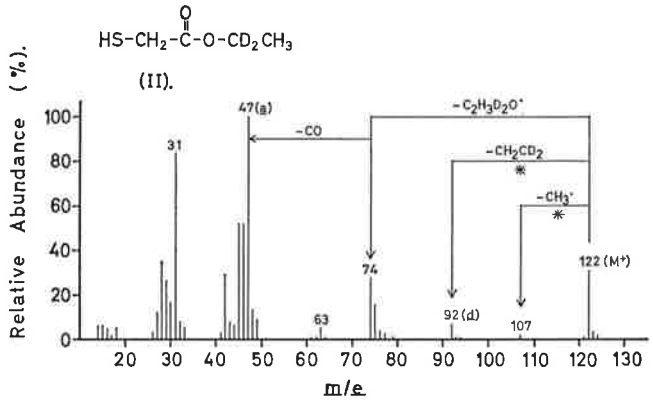


Fig. 2

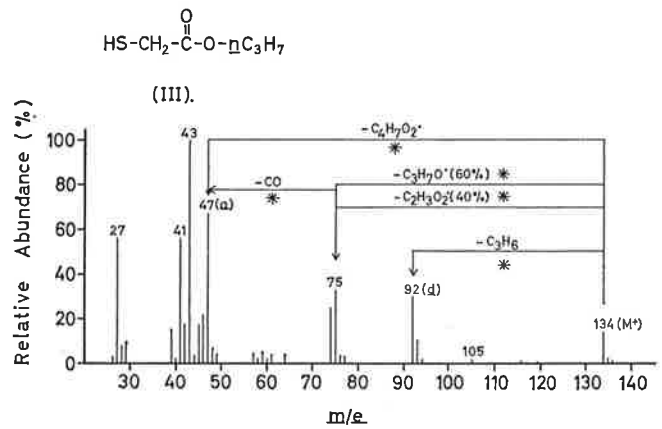


Fig. 3

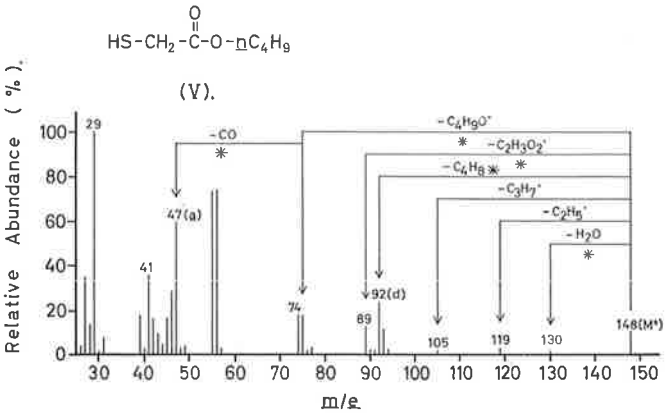


Fig. 4

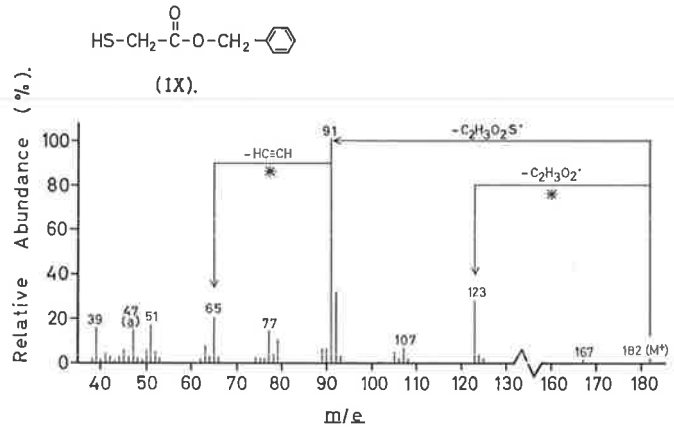


Fig. 5

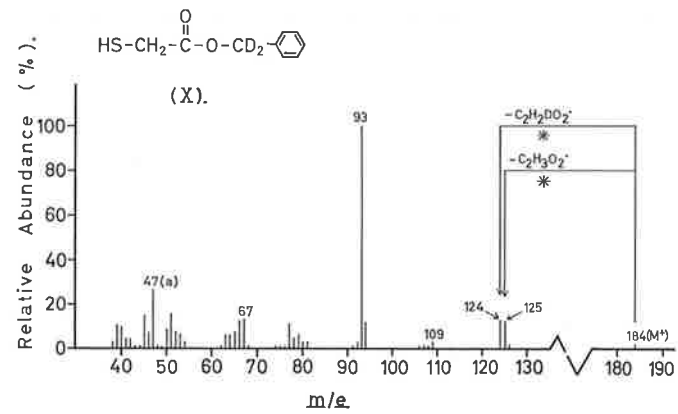


Fig. 6

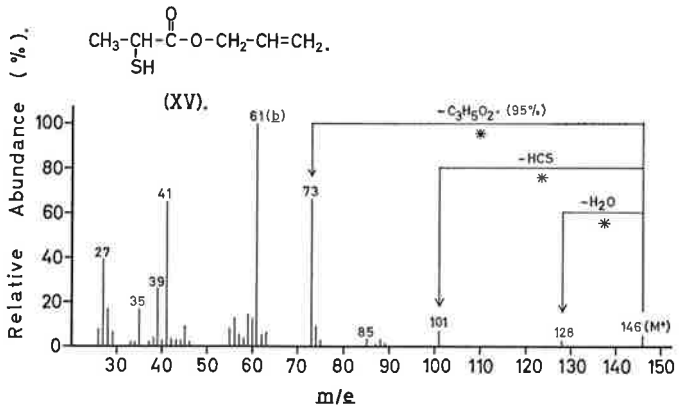


Fig. 7

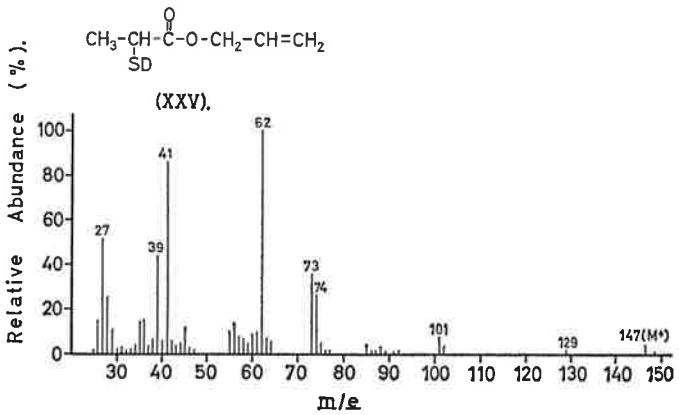
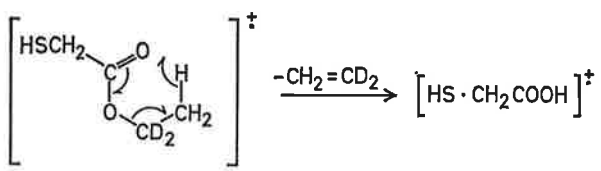


Fig. 8

(*c*) M–(R–H·) to form the corresponding mercapto acid radical ion. This is a general process in the spectra of all the alkyl mercaptoesters, but is not observed when R is allyl or benzyl. The spectrum (Fig. 2) of the labelled ethyl ester (II) shows complete loss of $\dot{C}H_2=CD_2$, indicative of fragmentation via a favoured McLafferty rearrangement $c \rightarrow d$ [14].



c, m/e 122 d, m/e 92

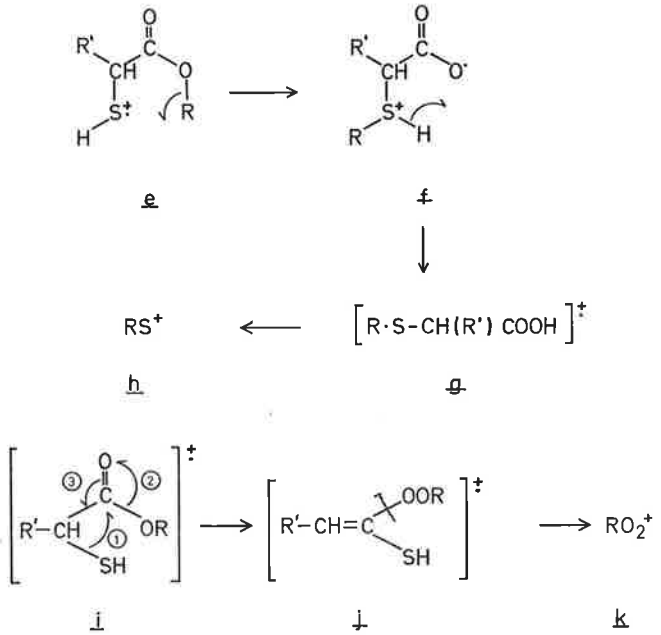
Table 3. Rearrangement ions in the spectra of mercaptoesters.

Compound	Rearrangement ion (*m/e*)	Relative abundance (% of base peak)	% of rearrangement ion		Metastable ion for rearrangement process	
			RS^+	RO_2^+	Calc.	Found
HS CH_2COOR:						
R = C_2H_5 (I)	61	5	60	40	31.0	—
n-C_3H_7 (III)	75	34	40[a]	—	42.0	42.0
iso-C_3H_7 (IV)	75	36	50[a]	—	42.0	42.0
n-C_4H_9 (V)	89	13	100	—	53.5	53.4
sec-C_4H_9 (VI)	89	17	100	—	53.5	53.6
iso-C_5H_{11} (VII)	103	6	100	—	65.4	65.4
cyclohexyl (VIII)	115	12	100	—	76.8	77.0
$CH_2C_6H_5$ (IX)	123	28	100	—	83.2	83.1
MeCH(SH)COOR:						
R = *n*-C_3H_7 (XIII)	75	8	10	90	38.0	38.0
iso-C_3H_7 (XIV)	75	16	70	30	38.0	38.0
Allyl (XV)	73	66	95	5	36.5	36.4
$CH_2C_6H_5$ (XVI)	123	46	100	—	77.2	—
XVII	75	3	100	—	29.6	—
XVIII	123	12	100	—	60.9	—
$HSCH_2CH_2COOR$:						
R = C_2H_5 (XXI)	61	100	100[b]	—	28.8	—
$CH_2C_6H_5$ (XXII)	123	16	100	—	77.2	77.3

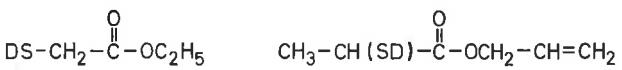
[a] The complement is made up of the normal ion $HS \cdot CH_2 \cdot C = O^+$.
[b] This ion is probably entirely produced by the normal process (*a*)—*vide supra*.

The mass spectra of all the simple mercaptoesters surprisingly exhibit RS^+ ions (where R is the ester substituent). Even more notably, when all these ions were highly resolved, certain compounds (where R is a small alkyl group, e.g. Et and Pr) were shown to exhibit RO_2^+ as well as RS^+ rearrangement ions. The relative proportions of these ions are summarised in Table 3, and in general, they are formed by a one step process from the molecular ion. RO_2^+ ions have not been noted in the spectra of simple esters, and it is reasonable to assume that they must owe their genesis to the presence of the sulphur atom. RO_2^+ ions decrease in relative abundance as the size of R increases, whereas the relative abundances of RS^+ ions show a general increase as the size of the R (alkyl) increases, and RS^+ ions are most abundant when R may stabilize the charge (e.g. $PhCH_2$ and allyl). The spectra of the acetyl mercaptoesters XVII and XVIII contain RS^+ ions (Table 3) but there is no evidence to suggest that these are produced in one step processes from the various molecular ions. When acetyl is replaced by benzoyl (e.g. XIX) no skeletal rearrangement ions are observed, presumably because of the inherent stability of the benzoyl cation (*m/e* 105).

It is of interest to attempt to rationalise these rearrangements and it is stressed that such a rationale is of necessity speculative. The following general schemes are proposed for the α-mercapto esters (the same type of process can equally hold for the β-mercaptoesters), viz. $e \rightarrow h$ (RS^+) and $i \rightarrow k$ (RO_2^+).

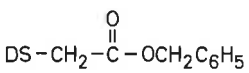


Neither of the proposed rearrangement processes involve either loss of a hydrogen atom from the alkoxyl group, or transfer of the hydrogen of the mercapto group to the alkoxyl group. In order to test these mechanisms a series of labelled derivatives have been prepared. The spectrum (Fig. 2) of the labelled ethyl ester II shows an almost complete shift of the rearrangement ion, *m/e* 61 (Fig. 1) to *m/e* 63 (Fig. 2), while the spectrum of XXIII indicates only a 5 % incorporation of deuterium into the rearrangement ions. In this case it is probably that mechanisms $e \rightarrow h$ and $i \rightarrow k$ operate.

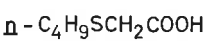


XXIII

XXV



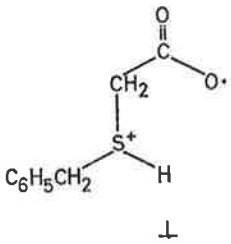
XXIV



XXVI

A different situation is observed in the spectrum of the benzyl ester (IX). The spectra (Figs. 5 and 6) of IX and X show a shift of *m/e* 123 ($PhCH_2S^+$) to *m/e* 124 (50 % relative to 125) and 125 (50 %) (at both 75 and 10 eV), while that of XXIV shows a 50 % shift of *m/e* 123 to 124. This can only mean that *l* (a specific example of *f*) may fragment by C–S cleavage with concomitant rearrangement of either the

mercapto hydrogen or a benzylic hydrogen (in the ratio 2 to 1). A similar situation is observed in the spectra (Figs. 7 and 8) of the allyl esters XV and XXV, where there is a 40 % shift of the rearrangement ion. Therefore, in these two cases, although $e \rightarrow h$ may account for a portion of the rearrangement process, the overall rearrangement is generally more complex, i.e. the process $f \rightarrow RS^+$ may proceed by several different pathways. It should be noted in this context, that the process $g \rightarrow h$ is certainly facile, as it produces the base peak ($C_4H_9S^+$, m/e 89) in the spectrum (Table 1) of XXVI.



⊥

Although the rationalisation of the rearrangement processes is speculative, the presence of such prominent rearrangement ions limits *a priori* prediction of fragmentation processes, and excludes the use of the "element mapping" technique [15] for this class of compound.

Experimental

All mass spectra were measured with an Hitachi Perkin-Elmer RMU 6D mass spectrometer with an inlet temperature of 50° and source temperature of 150°. (Elevation of the inlet temperature results in the formation of small amounts of disulphide, cf. [16].) The spectra of XXIII, XXIV and XXV were obtained by introducing I, IX and XV into the source with D_2O [17]. Fig. 8 was obtained by substracting the spectrum of XV from that of XXV ($d_0 = 27$, $d_1 = 73$ %). Exact mass measurements were carried out with an AEI MS 9 mass spectrometer using a resolution of 14.000 (10 % valley definition) and heptacosafluorotributylamine to provide reference masses. All measurements were correct to within 15 ppm.

All compounds were tested for purity by vapour phase chromatography, NMR and mass spectrometry. Compound XI were a purified commercial sample. Pre-

Table 4

Compound	Bp (°C/mm Hg)	n_D^{25}	Yield %	Calc. C	Calc. H	Calc. S	Found C	Found H	Found S
III	64/10	1.4530	84	44.77	7.52	23.86	44.45	7.71	23.73
VI	68/10	1.4492	80	48.64	8.16	21.60	48.83	7.73	21.88
XIII	65/11	1.4452	86	48.64	8.16	21.60	48.93	8.19	21.89
XV	67/10	1.4651	82	49.31	6.90	21.90	49.46	6.63	21.77
XXII	115/0.4	1.5367	74	61.21	6.17	16.31	61.38	6.04	16.46

viously published procedures were used for the preparation of I [18], IV [19], V [19], VII [19], VIII [19], IX [19], XII [20], XIV [21], XVI [21], XVII [21], XVIII [21], XIX [21], XX [21], XXI [22] and XXVI [23]. Compounds III, VI, XIII, XV and XXII were prepared by common esterifications (Table 4). The labelled compounds II and X were similarly prepared from ethyl-1,1-d_2 alcohol (Merck Sharpe and Dohme) and d_2-benzyl alcohol [24], respectively.

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A grant (to S.-O. L.) from Statens Almindelige Videnskabsfond and an Elsie Ballot Fellowship (to R. G. C.) are gratefully acknowledged. The Hitachi Perkin-Elmer RMU 6 D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

Department of Organic Chemistry, Chemical Institute, University of Aarhus, Aarhus C, Denmark (F. D., P. M. and S.-O. L.), *Department of Organic Chemistry, University of Adelaide, Adelaide, South Australia* (J. H. B.) *and University Chemical Laboratory, Lensfield Road, Cambridge, U.K.* (R. G. C.)

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Skeletal Rearrangement Processes of Organic Sulphur Compounds on Electron Impact[1]

By F. DUUS, S.-O. LAWESSON, and G. SCHROLL
(*Department of Organic Chemistry, Aarhus University, Aarhus C., Denmark*)
and J. H. BOWIE*
(*Department of Organic Chemistry, The University of Adelaide, South Australia*)
and R. G. COOKS
(*University Chemical Laboratory, Lensfield Road, Cambridge*)

ARYL SULPHONES,[2,3] sulphoxides,[2a,3] sulphides,[4] disulphides,[5] sulphinylamines,[6] sulphonylhydrazones,[7] aliphatic thioesters,[8] mercaptoesters,[9] and arylsulphonamides[10] undergo a series of skeletal

TABLE

Compound		Rearrangement process	Relative abundance of rearrangement ion (%)
$R{\cdot}CS{\cdot}CH_2{\cdot}COPh$			
(I) R = Me		M−CO	3
(II) R = Ph		M−CO	3
$R{\cdot}C_6H_4{\cdot}SO_2Cl$			
(III) R = H		$M-SO_2$	3
(IV) R = *p*-Me		$M-SO_2$	5
(V) R = *o*-NO_2		$M-SO_2$	2
		$M-SO_2-NO_2$	14
$R{\cdot}SO_2{\cdot}NHR^1$			
R	R^1		
(VI) Ph	H	$M-SO_2$	37
(VII) *p*-tolyl	H	$M-SO_2$	15
(VIII) Ph	*o*-tolyl	$M-SO_2$	3
(IX) Ph	SO_2Ph	$M-SO_2$	25
		$M-SO_2-SO_2$	3
$R{\cdot}CS{\cdot}CH_2{\cdot}CO_2R^1$		Formation of MeO^+	
R	R^1		
(X) Me	Et	MeO^+	64
(XI) Me	Pr^n	MeO^+	100
(XII) Me	Bu^n	MeO^+	38
(XIII) Ph	Et	MeO^+	82
(XIV) $MeCS{\cdot}CH(CO_2Et)_2$		MeO^+	100
(XV) $S=C(CH_2{\cdot}CO_2Et)_2$		MeO^+	100

rearrangement processes on electron impact. As a continuation we have investigated the skeletal rearrangement processes which are observed in the mass spectra of some further sulphur compounds, including sulphonyl chlorides, β-thioketo-esters, and some simple arylsulphonamides. These processes are summarised in the Table. The compositions of all rearrangement ions have been established by exact mass measurements and the presence of an appropriate metastable ion for a process is indicated by an asterisk.

The losses of carbon monoxide from the molecular ions of (I) and (II) were not expected, as the analogous β-diketones do not contain M−CO ions.[11] This is a further illustration of the role sulphur may play in rearrangement processes. The loss of SO_2 from the molecular ions of the sulphonyl chlorides (III—V) and the sulphonamides (VI—IX) exactly parallel the $M-SO_2$ processes in the spectra of aryl sulphones[2,3] and sulphonylhydrazones.[7]

The MeO^+ ions [*m/e* 31, base peak in the spectra of (XI), (XIV), and (XV)] produced by the β-thioketo-esters on electron impact, must owe their genesis to participation between the C=S and the ester groups, as similar ions are not generally observed in the spectra of β-ketoesters[8,12] (an exception is the spectrum of allyl-acetoacetate[8] where the MeO^+ peak constitutes 24% of the base peak). Labelling studies are in progress to examine the formation of the MeO^+ ion.

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[1] Part XX in the series "Electron Impact Studies". Part XIX, cf. ref. 9b.

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[5] J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, C. Nolde, G. Schroll, and D. A. Williams, *J. Chem. Soc.* (*B*), 1966, 946.

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Electron-impact Studies. Part XXI.[1] The Mass Spectra of Sulphonamides and Sulphonyl Chlorides: The Formation of C–O and C–N Bonds upon Electron Impact

By E. Dynesen, S.-O. Lawesson, and G. Schroll, Department of Organic Chemistry, Aarhus University Aarhus C, Denmark
J. H. Bowie, Department of Organic Chemistry, The University of Adelaide, South Australia
R. G. Cooks, University Chemical Laboratory, Cambridge

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Electron-impact Studies. Part XXI.[1] The Mass Spectra of Sulphonamides and Sulphonyl Chlorides: The Formation of C–O and C–N Bonds upon Electron Impact

By **E. Dynesen, S.-O. Lawesson,** and **G. Schroll,** Department of Organic Chemistry, Aarhus University Aarhus C, Denmark
J. H. Bowie, Department of Organic Chemistry, The University of Adelaide, South Australia
R. G. Cooks, University Chemical Laboratory, Cambridge

The mass spectra of a series of arenesulphonamides and some representative sulphonyl chlorides are reported and discussed. The sulphonyl chlorides and the primary arenesulphonamides have prominent rearrangement ions in their spectra owing to loss of the elements of SO_2 from the molecular ions, whereas the sulphonamido-groups of *N*-alkyl and dihydrophenanthrenesulphonamides are not involved in skeletal-rearrangement processes. Fragmentation modes have been established by high resolution measurements and metastable ions.

SKELETAL-REARRANGEMENT fragments have recently been observed in the mass spectra of sulphides,[2-4] disulphides,[2,5] sulphones,[2,6-8] sulphoxides,[2,7] sulphinylamines,[9,10] sulphonylhydrazones,[3] sulphonylureas,[11] mer-

[1] Part XX, F. Duus, S.-O. Lawesson, G. Schroll, J. H. Bowie, and R. G. Cooks, *Chem. Comm.*, 1967, 697.
[2] J. Ø. Madsen, C. Nolde, S.-O. Lawesson, G. Schroll, J. H. Bowie, and D. H. Williams, *Tetrahedron Letters*, 1965, 4377.
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[8] E. K. Fields and S. Meyerson, *J. Amer. Chem. Soc.*, 1966, **88**, 2836.
[9] B. E. Job, *Chem. Comm.*, 1967, 44.
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[11] M. F. Grostic, R. J. Wnuk, and F. A. MacKeller, *J. Amer. Chem. Soc.*, 1966, **88**, 4664.

TABLE 1*

Mass spectra of (II), (III), (VI), (IX)—(XII), (XVI), and (XVIII)

(II)	*m/e*	27	38	39	41	50	51	62	63	64
	I (%)	6	6	30	6	8	13	7	17	8
	m/e	65	77	79	89	91	92	106	107	108
	I (%)	39	9	5	12	100	9	6	23	16
	m/e	155	171(*M*)		172					
	I (%)	30	34		7					
(III)	*m/e*	27	28	29	30	39	41	43	50	51	77	78
	I (%)	11	8	6	11	6	8	6	6	28	100	13
	m/e	141	142	143	158	170	171	172	213(*M*)			
	I (%)	93	7	6	13	92	14	6	11			
(VI)	*m/e*	16	17	18	27	28	29	30	31	32		
	I (%)	8	9	11	9	53	9	7	15	11		
	m/e	36	38	39	48	50	51	52	64	65		
	I (%)	6	7	21	73	30	50	31	35	11		
	m/e	66	74	76	77	78	79	94	97	106		
	I (%)	10	9	7	8	100	14	10	6	6		
	m/e	109	110	125	142	172(*M*)						
	I (%)	11	17	14	16	Absent						
(IX)	*m/e*	36	48	165	192	194	195	273(*M*)		274		
	I (%)	7	18	8	6	100	17	33		6		
(XI)	*m/e*	139	152	153	154	165	166	178	179	180		
	I (%)	6	8	10	9	34	8	9	24	15		
	m/e	181	190	192	209	222	239	240	318(*M*)			
	I (%)	11	9	13	21	16	100	17	90			
	m/e	319	320									
	I (%)	16	6									
(XII)	*m/e*	165	166	180	193	209	239	240	318(*M*)			
	I (%)	21	10	5	19	6	100	17	52			
	m/e	319										
	I (%)	9										
(XVI)	*m/e*	27	38	39	50	51	74	77	78	112		
	I (%)	7	6	11	25	47	7	100	13	3		
	m/e	113	114	125	141	176(*M*)		178(*M*)				
	I (%)	1	1	2	40	16		6				
(XVII)	*m/e*	39	51	63	65	89	91	92	126	139		
	I (%)	14	6	10	24	8	100	13	5	3		
	m/e	155	190(*M*)		192(*M*)							
	I (%)	45	17		7							

* All peaks greater than 5% of the base peak (100%) (and skeletal rearrangement ions less than this value) are recorded. (*M*), molecular ion.

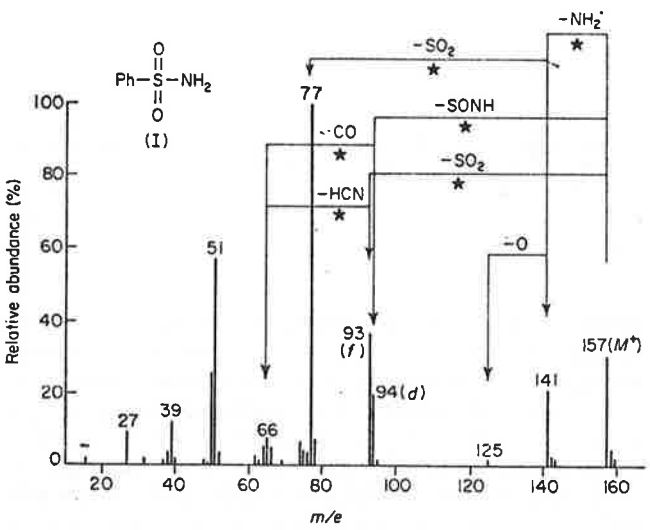


FIGURE 1

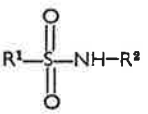
TABLE 2

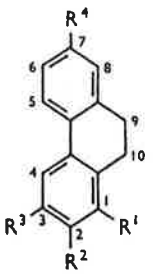
High-resolution data in the spectra of (I)—(XVIII)

Cmpd.	*m/e*	Composition	Cmpd.	*m/e*	Composition
(I)	65	C_5H_5	(XIII)	165	$C_{13}H_9$
	66	C_5H_6		180	$C_{13}H_{10}N$ (70%)
	93	C_6H_7N			$C_{12}H_8N_2$ (30%)
	94	C_6H_6O		192	$C_{14}H_{10}N$
	125	C_6H_5OS		203	$C_{14}H_7N_2$
				221	$C_{14}H_9N_2O$
(II)	107	C_7H_9N (65%)			
		C_7H_7O (35%)	(XIV)	179	$C_{14}H_{11}$
	108	C_7H_8O		181	$C_{13}H_{11}N$
	155	$C_7H_7O_2S$		192	$C_{14}H_{10}N$
				209	$C_{14}H_{11}NO$
(III)	141	$C_6H_5O_2S$		222	$C_{14}H_{10}N_2O$
	158	$C_6H_8NO_2S$			
	170	$C_7H_8NO_2S$	(XV)	193	$C_{14}H_{11}N$
(VI)	94	C_6H_6O	(XVI)	97	C_5H_5S
	97	C_5H_5S (70%)		112/114	C_6H_5Cl
		C_3H_4NS (30%)		125	C_6H_5OS
	125	C_6H_5OS			
			(XVII)	124	C_7H_8S
(VII)	168	$C_{12}H_{10}N$		125/127	C_7H_8Cl
	183	$C_{13}H_{13}N$		126/128	C_7H_7Cl
(VIII)	92	C_6H_6N	(XVIII)	111/113	C_6H_4Cl
	94	C_6H_6O		156	$C_6H_4O_3S$
	140	C_6H_6NOS		157	$C_6H_4NO_2Cl$
	141	$C_6H_5O_2S$			
	168	$C_{12}H_{10}N$			
	233	$C_{12}H_{11}NO_2S$			

captoesters,[12-14] thiuram disulphides,[15] and sulphonamides.[16] As a continuation of these studies we have investigated the skeletal-rearrangement processes which are observed in the spectra (Figures 1—9 or Table 1) of

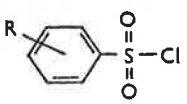
	R^1	R^2
(I)	Ph	H
(II)	*p*-tolyl	H
(III)	Ph	Bu^n
(IV)	*p*-tolyl	Bu^n
(V)	*p*-tolyl	Bu^t
(VI)	Ph	NH_2
(VII)	Ph	*o*-tolyl
(VIII)	Ph	SO_2Ph





	R^1	R^2	R^3	R^4
(IX)	H	$NH{\cdot}SO_2Me$	H	H
(X)	H	$NH{\cdot}SO_2$-*p*-tolyl	H	H
(XI)	H	$NH{\cdot}SO_2Me$	NO_2	H
(XII)	H	$NH{\cdot}SO_2Me$	H	NO_2
(XIII)	NO_2	$NH{\cdot}SO_2$-*p*-tolyl	H	H
(XIV)	H	$NH{\cdot}SO_2$-*p*-tolyl	NO_2	H
(XV)	H	$NH{\cdot}SO_2$-*p*-tolyl	H	NO_2

	R
(XVI)	H
(XVII)	*p*-Me
(XVIII)	*o*-NO_2



the sulphonamides (I)—(XV) and the sulphonyl chlorides (XVI)—(XVIII). These have been briefly mentioned.[1] The compositions of those ions determined by exact

[12] J. H. Bowie, R. G. Cooks, P. Jakobsen, S.-O. Lawesson, and G. Schroll, *Austral. J. Chem.*, 1967, **20**, 689.
[13] J. H. Bowie, S.-O. Lawesson, F. Duus, P. Madsen, and R. G. Cooks, *Chem. Comm.*, 1967, 346.
[14] F. Duus, P. Madsen, S.-O. Lawesson, J. H. Bowie, and R. G. Cooks, *Arkiv Kemi*, in press.
[15] J. Ø. Madsen, S.-O. Lawesson, A. M. Duffield, and C. Djerassi, *J. Org. Chem.*, in press.
[16] G. Spiteller and R. Kaschnitz, *Monatsh.*, 1963, **94**, 964.

mass measurements are listed in Table 2, and the presence of a metastable ion for a particular process is indicated in either the text or a Figure by an asterisk.

The mass spectra of a series of sulphonamides of the general formula (XIX) (where R = H or aryl) have been reported.[16] Prominent $M - SO_2$ peaks are noted in these spectra; *e.g.*, the $M - SO_2$ ion in the spectrum of rearrangements involving C–O bond formation (cf. ref. 7) occur.

The mass spectra (Figure 1 and Table 1) of benzenesulphonamide (I) and toluene-*p*-sulphonamide (II) exhibit the normal cleavage processes $M - NH_2^{\cdot} - SO_2$ to form, respectively, the benzene cation (*m/e* 77) and the tropylium cation (*m/e* 91), which are the base

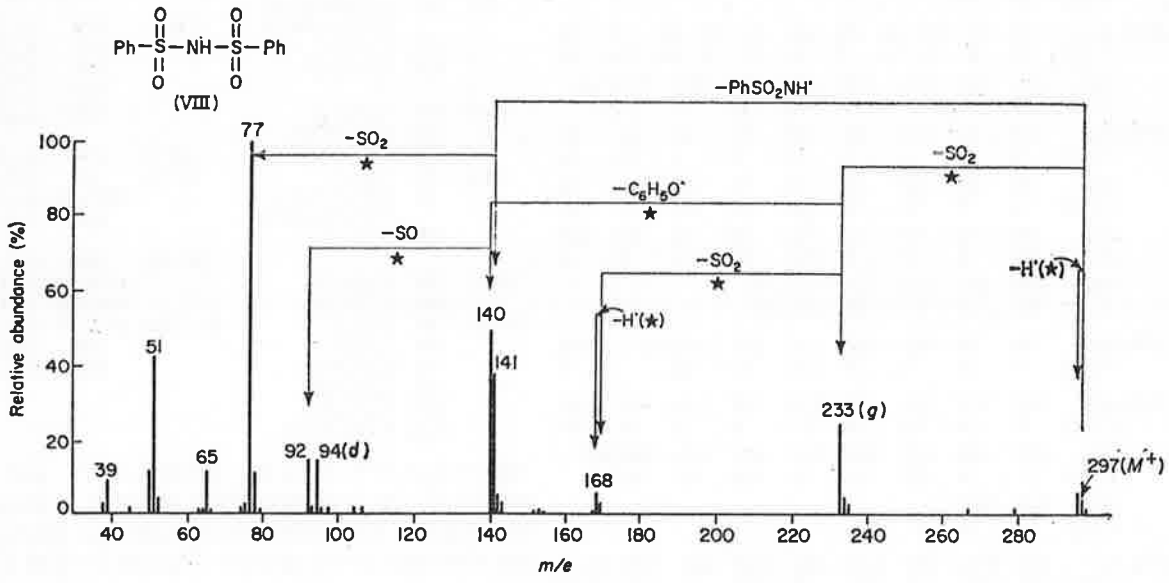


FIGURE 2

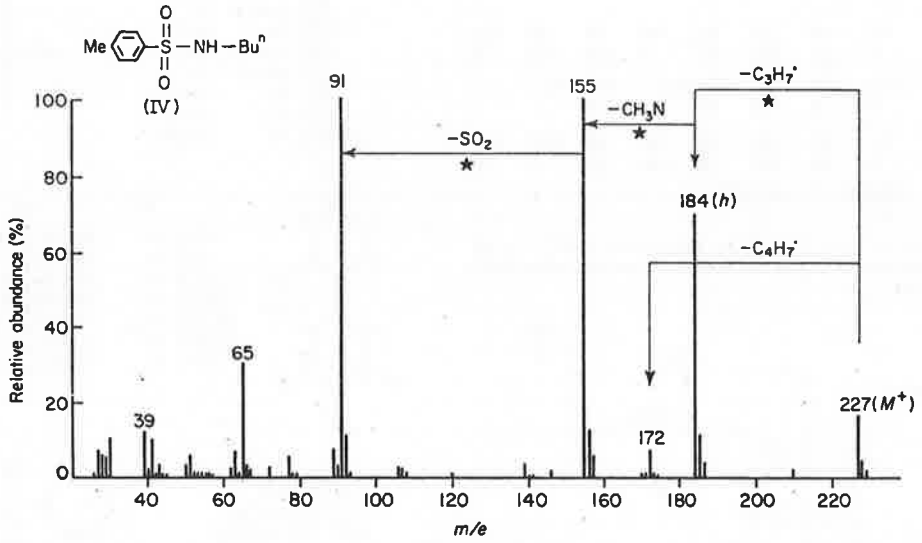
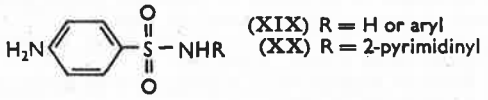


FIGURE 3

sulphadiazine (XX) is the base peak. We have determined the mass spectra of a variety of sulphonamides



(I)—(XV) in order to determine the generality of the $M - SO_2$ process, and, in addition, to ascertain whether peaks of the spectra. However, these spectra are notable for the presence of pronounced skeletal-rearrangement ions whose geneses involve the formation of C–O and C–N bonds. Two rearrangement processes occur; (*a*) $M - SO_2$ and (*b*) $M -$ SONH. Similar processes occur in the mass spectra of sulphones,[6-8] sulphoxides,[7] sulphonylhydrazones,[3] and sulphonylureas.[11] An explanation of the spectrum (Figure 1) of

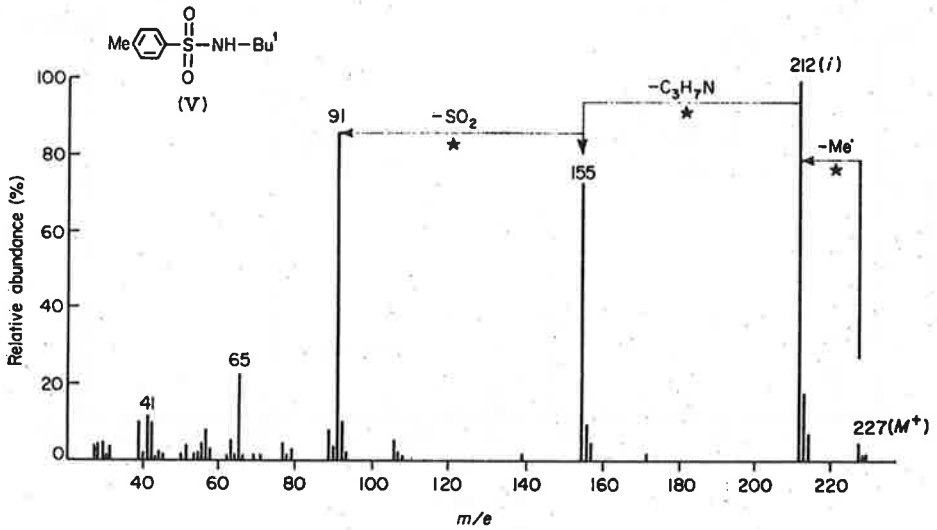


FIGURE 4

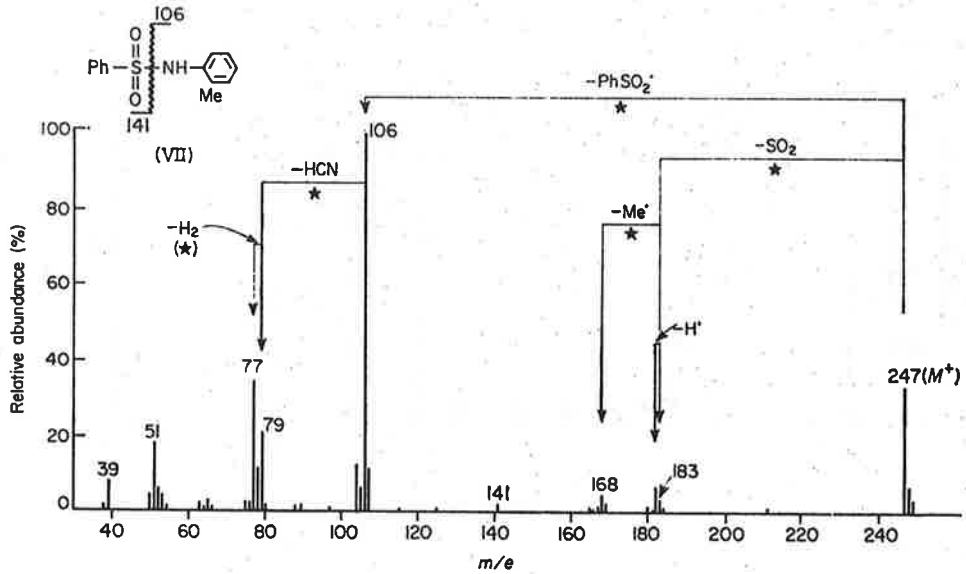


FIGURE 5

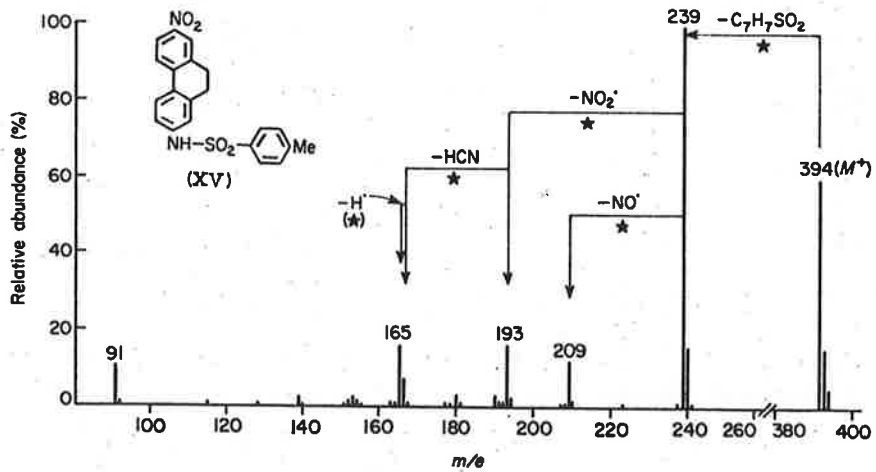


FIGURE 6

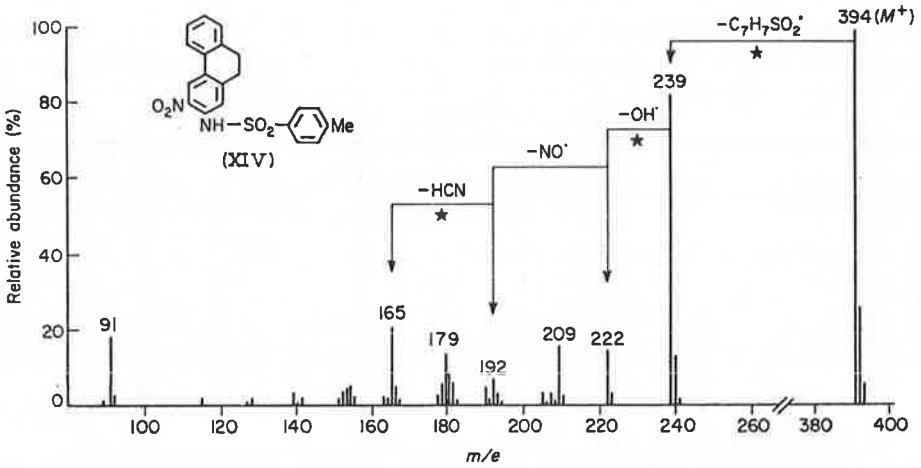


FIGURE 7

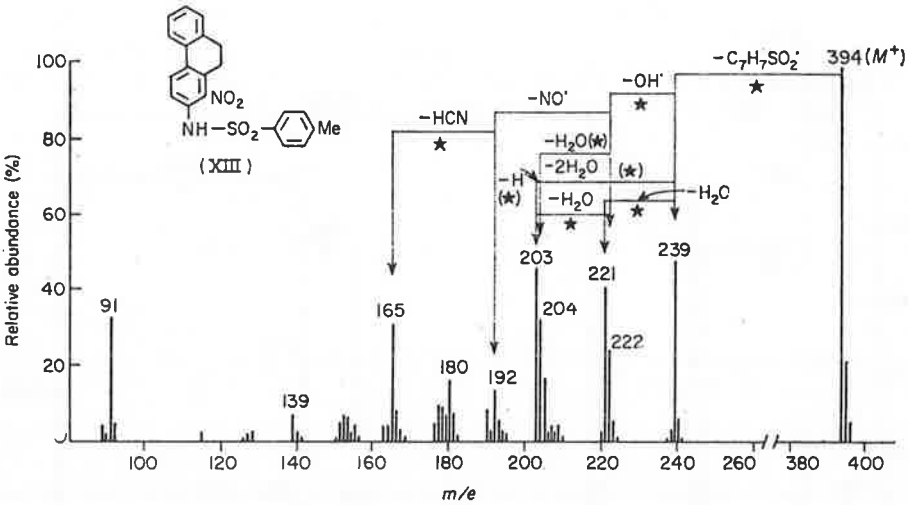


FIGURE 8

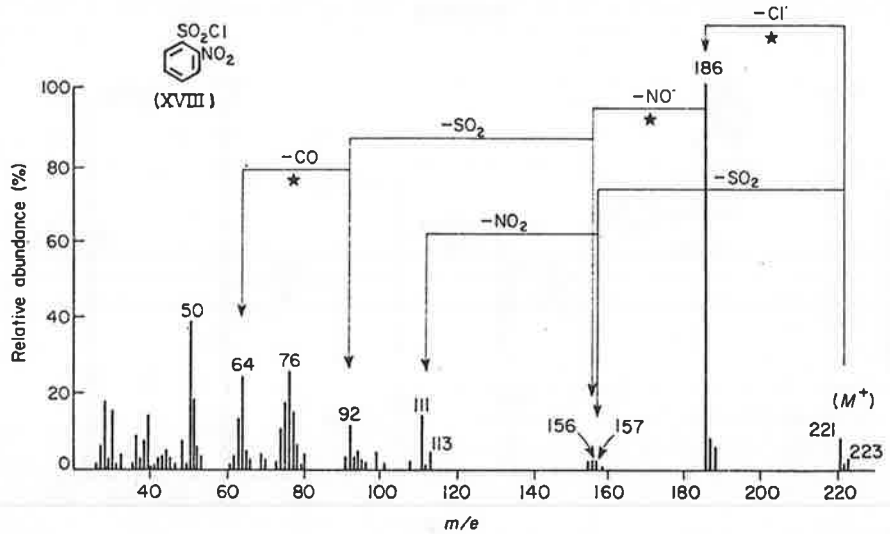
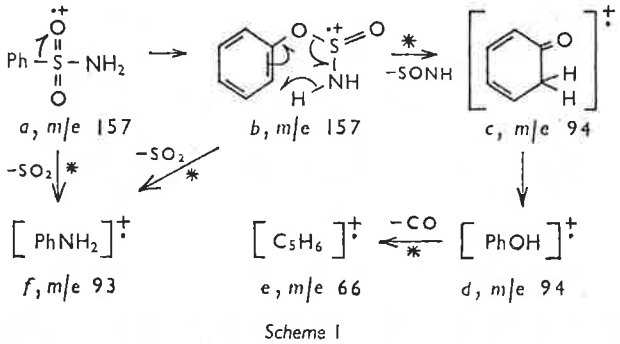


FIGURE 9

(I) is summarised in Scheme 1. A 1,2-phenyl migration from sulphur to oxygen produces *b* (*m/e* 157) which may then fragment to the phenol radical ion (*d*, 19% of the



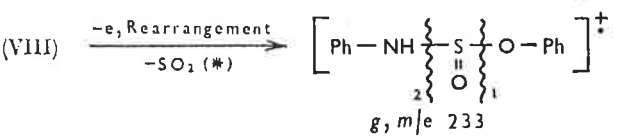
a, *m/e* 157 *b*, *m/e* 157 *c*, *m/e* 94

f, *m/e* 93 *e*, *m/e* 66 *d*, *m/e* 94

Scheme 1

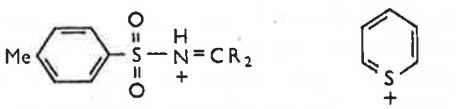
base peak). The hydrogen involved in the M — SONH process has been shown to be attached to nitrogen (from a consideration of the spectrum of [*amino*-$^2H_2$]benzenesulphonamide). It is noteworthy that corresponding ions to *b* in the spectra of sulphoxides [7] and arylsulphones [7] (where the NH_2 group is replaced by an aryl group) readily lose CO by a process analogous to that suggested to explain the elimination of the same fragment from diphenyl ether.[17] This process (M — CO) is not observed in the spectra of sulphonamides. The alternate rearrangement process (M — SO_2) can presumably be derived from either *a* or *b* to form the aniline radical ion (*f*, *m/e* 93, 37% of the base peak). The composition of the major ions in these spectra have been established by exact measurements.

The mass spectrum (Figure 2) of (VIII) also contains a series of rearrangement peaks. Apart from the normal fragmentations (outlined in Figure 2), the processes M — SO_2 — SO_2 and M — SO_2 — $C_6H_5O\cdot$ — SO operate. The losses of SO_2 are analogous to those in the spectra of the simple sulphonamides, but the second process (which is substantiated by appropriate metastable ions and high-resolution data) must occur from the rearranged M — SO_2 ion (*g*). Further cleavages occur as indicated in *g*. The phenol radical ion (*d*, *m/e* 94) is also observed in this spectrum (cf. Scheme 1).



g, *m/e* 233

The nature of the alkyl substituent in the secondary sulphonamides (III)—(V) can be determined by mass spectrometry. This can be seen from a comparison of the spectra (Figures 3 and 4) of the two butyl isomers (IV) and (V). The initial cleavage in the spectra of the n-butyl derivative (IV) is M — $C_3H_7\cdot$ and in that of the t-butyl derivative, M — Me·. This is due to β-cleavage to nitrogen to yield the stable cations *h* and *i*, respectively, which then fragment as indicated in Figures 3 and 4. This behaviour is also noted in the spectra of secondary amides.[18] No skeletal rearrangement ion is present in the spectra of the secondary sulphonamides (III)—(V). When the alkyl group is replaced by an amino-group (as in VI) the spectrum (Table 1) changes markedly.

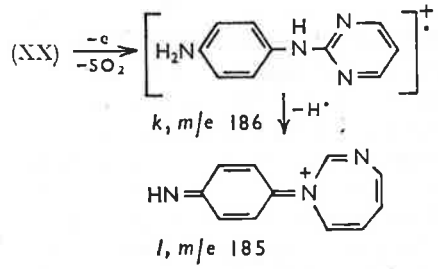


h, *m/e* 184 (IV, R = H) *j*, *m/e* 97

i, *m/e* 212 (V, R = Me)

No molecular ion is observed, and the major process is M — N_2H_2 — SO_2, to form the benzene radical ion (*m/e* 78, base peak). Prominent peaks are also present owing to charged SO and SO_2 (73 and 35% of the base peak), the thiophenol radical ion (*m/e* 110, 18%), the phenol radical ion (*d*, *m/e* 94, 10%), and the thiopyrylium cation (*j*, *m/e* 97, 7%).

Secondary sulphonamides which contain two benzenoid substituents behave simply on electron impact. The major process is N–S cleavage with the nitrogen-containing portion retaining the charge. This process is useful for analytical purposes, and is illustrated by the spectrum (Figure 5) of *N*-*o*-tolylbenzenesulphonamide (VII), where N–S cleavage produces the *o*-toluidine cation, *m/e* 106 (probably best represented as the aminotropylium cation) which is the base peak, while the benzenesulphonyl cation (*m/e* 141) has only a relative abundance of 2%. Skeletal-rearrangement ions are relatively small in this spectrum, and no fragment arising from C–O bond formation is observed. This should be contrasted with the large M — SO_2 ions occurring in the spectra of sulphadiazine (XX) and related compounds.[16] In this case, the loss has been attributed to the formation of the ion *k*, which then loses a hydrogen atom to form the stable cation *l*. This type of stabilisation should only occur when a suitable substituent is present in the A ring.



k, *m/e* 186

l, *m/e* 185

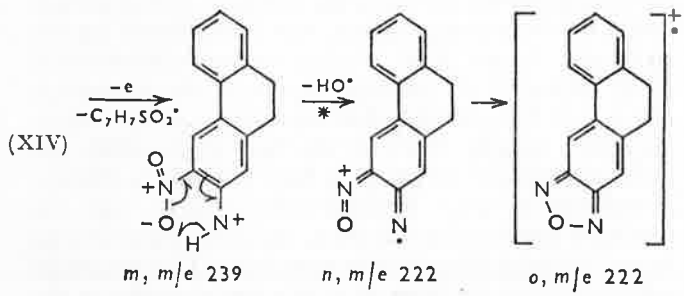
In order to determine whether '*ortho*-effects' [19] are operative in the spectra of substituted arenesulphonamides, we synthesised a series of dihydrophenanthrenesulphonamides (IX)—(XV). No rearrangement peak is

[17] J. H. Beynon, G. R. Lester, and A. E. Williams, *J. Chem. Phys.*, 1959, **63**, 1861.

[18] Z. Pelah, M. A. Kielczewski, J. M. Wilson, M. Ohashi, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 2470.

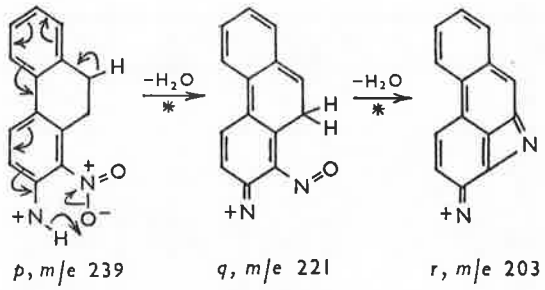
[19] F. W. McLafferty and R. S. Gohlke, *Analyt. Chem.*, 1959, **31**, 2076.

observed in these spectra. The major process of (IX) and (X) on electron impact is loss of the RSO_2 radical to give the 2-amino-9,10-dihydrophenanthrene cation (*m/e* 194) which may fragment by loss of HCN and hydrogen to yield the fluorene cation (*m/e* 165). These decomposition pathways are similar to those observed in the spectrum of 2-trifluoroacetamido-9,10-dihydrophenathrene.[20] The presence of '*ortho*-effects' can be seen by a comparison of the spectra (Figures 6—8) of the three nitro-isomers (XIII)—(XV). A large 'proximity-effect' has already been observed in the spectra of 9,10-dihydro-1-nitrophenanthrenes, where the base peak is due to an $M - OH\cdot$ ion which is produced by participation between an oxygen of the 1-nitro-group and a hydrogen at C(10).[20] It is therefore possible to equate this effect with that operating between the substituents in the spectrum of (XIV). The spectrum (Figure 6) of (XV) exhibits normal fragmentations which ultimately produce the fluorene cation (cf. reference 20). The spectrum (Figure 7) of 9,10-dihydro-3-nitro-2-*p*-toluenesulphonamidophenanthrene (XIV) shows an additional peak at *m/e* 222 ($M - C_7H_7SO_2\cdot - HO\cdot$) which is not present in that of (XV). This '*ortho*-effect' can be represented by the process *m* ⟶ *n* ⟶ *o*. An exactly similar effect is seen in the spectrum (Table 1) of (XI).



The fragmentation of 9,10-dihydro-1-nitro-2-*p*-toluenesulphonylamidophenanthrene (XIII) may be explained by the addition of the '*ortho*-effect' operating between the adjacent nitro- and NH^+ group (produced by loss of the *p*-toluenesulphonyl radical), and the 'proximity-effect' discussed above. The processes noted are $p - HO\cdot - H_2O - H\cdot$, $p - H_2O - H_2O$, and $p - 2H_2O$ (all processes substantiated by metastable ions). These can be represented by a combination of *m* ⟶ *o* and *p* ⟶ *r*. The compositions of these ions have been established by exact mass measurement. It is stressed that the structures drawn are nominal only, but serve to relate the fragmentation modes to the structure of the molecule in the ground state.

Finally, the spectra (Figure 9 and Table 1) of the sulphonyl chlorides (XVI—XVIII) also exhibit skeletal-rearrangement ions owing to the process $M - SO_2$, *viz.*, 3 and 4% of the base peaks in the spectra of (XXVI) and (XVII). The spectrum of 2-nitrobenzenesulphonyl-chloride (XVIII) (Figure 9) shows that the rearrangement process $M - SO_2 - NO_2\cdot$ produces *m/e* 111/113 ($C_6H_4Cl^+\cdot$ 12% relative abundance). No fragment ion is present



which is due to C–O bond formation, and no '*ortho*-effect' operates. The normal fragmentations are unexceptional and are summarised in Figure 9.

EXPERIMENTAL

The mass spectra of compounds (I)—(VIII) and (XVI)—(XVIII) were determined with an Hitachi Perkin-Elmer RMU 6D mass spectrometer operating at 75 ev and with an inlet and source temperature of *ca.* 150°. The spectra of (IX)—(XV) were measured by the direct-insertion technique with an A.E.I. MS 9 mass spectrometer operating at 350°. Exact mass measurement were performed with the MS 9 at a resolution of 14,000 (10% valley definition), with heptacosafluorotributylamine providing the reference masses. All measurements were correct to within 15 p.p.m.

Compounds (I), (II), (V)—(VIII), and (XVI)—(XVIII) were purified commercial samples. The compounds (III) and (IV) were synthesised by reported procedures.[21,22] The 9,10-dihydrophenanthrenesulphonamides (IX), (X), (XII), and (XIV) were prepared from the corresponding amines,[20] by reaction with the appropriate sulphonyl-chloride. The compounds (XI), (XIII), and (XIV) were prepared by nitration of the corresponding 9,10-dihydrophenanthrenesulphonamides.

TABLE 3

Analyses of compounds (IX)—(XV)

		Found (%)			Calculated (%)		
Compound	M. p.	C	H	N	C	H	N
(IX)	113—115°	66·37	5·53	5·29	65·92	5·53	5·13
(X)	204—205·5	72·52	5·37	4·08	72·19	5·48	4·01
(XI)	187—188·5	56·80	4·41	8·88	56·60	4·43	8·80
(XII)	220—222	57·08	4·18	8·89	56·60	4·43	8·80
(XIII)	153—154	64·09	4·85	7·37	63·95	4·60	7·10
(XIV)	195—196	64·24	4·77	7·37	63·95	4·60	7·10
(XV)	200—202	63·66	4·57	7·10	63·95	4·60	7·10

Some microanalyses were carried out by Mrs. B. Rusmussen of Aarhus University, and are shown in Table 3.

The award of an Elsie Ballot Fellowship (to R. G. C.) is gratefully acknowledged. The Hitachi Perkin-Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

[7/807 *Received, June 30th,* 1967]

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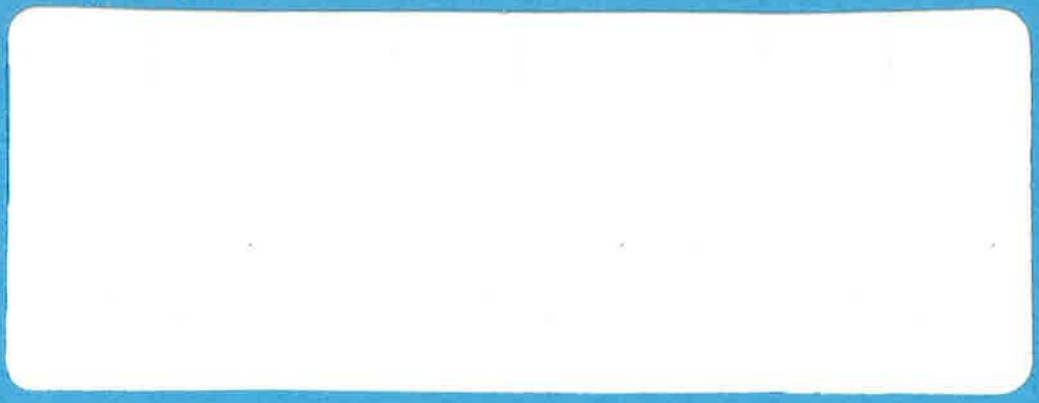

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ELECTRON IMPACT STUDIES—XXII[1]

MASS SPECTRA OF SUBSTITUTED BENZIMIDAZOLES

S.-O. LAWESSON and G. SCHROLL

J. H. BOWIE

and

R. G. COOKS

Department of Organic Chemistry, University of Aarhus, Aarhus C., Denmark

Department of Organic Chemistry, University of Adelaide, Adelaide, South Australia

University Chemical Laboratory, Lensfield Road, Cambridge, England

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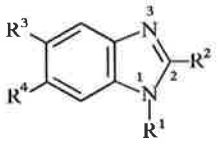
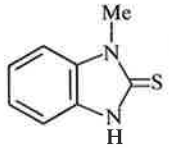
Abstract—The mass spectra of 22 benzimidazoles are reported and discussed. The basic fragmentation patterns have been substantiated by deuterium labelling, exact mass measurements and appropriate metastable ions. Skeletal rearrangement ions produced by the process M–CO are more prominent in the spectra of 2-benzoyl than 2-acetylbenzimidazoles.

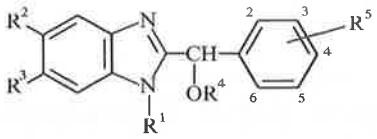
ALTHOUGH the mass spectra of imidazoles[2,3] and benzimidazolium barbiturates[4] have been discussed, no survey of the mass spectra of simple benzimidazoles has been reported. This paper is concerned with the mass spectra of the benzimidazoles (I–XXII), which are recorded in Figs 1–9 or Table 1. The compositions of ions determined by exact mass measurements are listed in Table 2. The presence of an





XXII

	R^1	R^2	R^3	R^4
I	H	H	H	H
II	D	H	H	H
III	H	Me	H	H
IV	D	Me	H	H
V	H	H	Me	Me
VI	Allyl	H	H	H
VII	H	SMe	H	H
VIII	D	SMe	H	H
IX	H	n-Pr	H	H
X	H	C_6H_5	H	H
XI	H	COMe	H	H
XII	H	COPh	H	H
XIII	H	CH(OH)Me	H	H



	R^1	R^2	R^3	R^4	R^5
XIV	H	H	H	H	H
XV	D	H	H	D	H
XVI	H	H	H	H	4-Br
XVII	D	H	H	D	4-Br
XVIII	Me	H	H	H	4-Br
XIX	H	Me	Me	H	4-Br
XX	Me	H	H	H	3-NO_2
XXI	H	Me	Me	H	3-NO_2

TABLE 1. MASS SPECTRA OF BENZIMIDAZOLES

II[a,b]	*m/e*	90	91	92	117	118	119(M)	120											
	I(%)	3	15	20	3	5	100	20											
IV[a,b,c]	*m/e*	90	93	94	104	131	132	133	134										
	I(%)	5	3	3	4	37	90	100	20										
V[a]	*m/e*	50	63	64	65	72	73	77	89	90	91	92	116	117	118	119	131	132	
	I(%)	3	6	5	7	3	3	4	4	5	22	3	5	5	10	6	66	8	
		145	146(M)	147															
		76	100	11															
VI[a]	*m/e*	41	51	52	63	65	77	90	103	104	118	129	130	131	132	156	157		
	I(%)	16	5	3	4	4	11	5	4	7	6	3	13	27	5	7	81		
		158(M)	159																
		100	12																
VIII[a,c]	*m/e*	27	39	43	44	45	63	64	77	78	90	91	92	118	119	120	122	131	132
	I(%)	4	3	3	7	3	8	5	3	3	8	7	5	16	20	6	23	57	32
		149	150	164	165	166	167												
		8	6	100	77	12	4												
XIII[d]	*m/e*	39	43	45	51	52	63	64	65	73	90	91	92	118	119	143	144	145	147
	I(%)	6	12	8	100	6	7	8	10	6	6	16	14	36	71	17	30	20	54
		162(M)	163																
		72	8																
XIV[d]	*m/e*	51	65	77	79	90	91	92	93	103	105	118	119	147	194	195	205	206	
	I(%)	6	8	23	7	6	13	9	7	8	15	33	46	22	10	18	35	80	
		207	223	224(M)	225														
		21	24	100	16														
XV[c,d]	*m/e*	39	44	51	63	64	65	77	78	79	90	91	92	103	105	106	118	119	120
	I(%)	6	7	10	7	6	8	29	9	7	8	13	11	6	20	6	23	45	28
		121	147	148	149	194	195	196	205	206	207	208	209	223	224				
		12	14	10	5	9	13	8	30	100	38	22	11	18	79				
		225	226																
		71	29																

TABLE 1—*continued*

XVII[b,c,d]	*m/e*	104	105	118	119	120	121	147	148	155	156	157	158	183	184	185
	I(%)	8	9	31	61	48	18	15	17	40	6	40	6	67	20	78
		186	187	188	189	193	194	195	200	201	202	203	205	206	207	208
		41	15	10	12	12	14	6	11	12	12	12	100	37	17	7
		272	273	274	275	284	285	286	287	288	289	300	301	302	303	304
		32	36	39	33	9	9	21	19	17	13	18	26	54	65	57
		305	306													
		45	23													
XVIII[d]	*m/e*	51	76	77	78	104	131	132	133	147	161	183	185	205	220	287	299
	I(%)	6	6	20	9	8	32	31	31	53	43	9	9	7	12	7	6
		301	315	316(M)		317	318(M)		319								
		8	27	100		43	97		16								
XIX[d]	*m/e*	77	78	91	104	131	145	146	147	155	157	175	183	185	218	219	232
	I(%)	15	6	8	6	12	12	13	36	6	6	13	10	10	8	6	10
		233	234	235	285	287	299	300	301	302	303	312	313	314	315	316	
		100	28	6	6	6	11	28	17	26	9	16	14	39	16	24	
		328	329	330(M)		331	332(M)		333								
		6	9	75		21	69		12								
XXI[d]	*m/e*	76	77	91	104	131	145	146	147	150	175	221	222	232	233	234	237
	I(%)	8	9	9	11	13	15	11	28	8	19	12	10	18	31	12	7
		249	250	251	262	265	267	281	295	296	297(M)		298				
		7	13	6	11	8	21	10	20	11	100		19				

[a] All peaks greater than 2% of the base peak (100%) are recorded.
[b] Only peaks above *m/e* 90 are recorded.
[c] Because of the M-1 and M-2 ions, the isotopic purity cannot be determined.
[d] All peaks greater than 5% of the base peak are recorded.

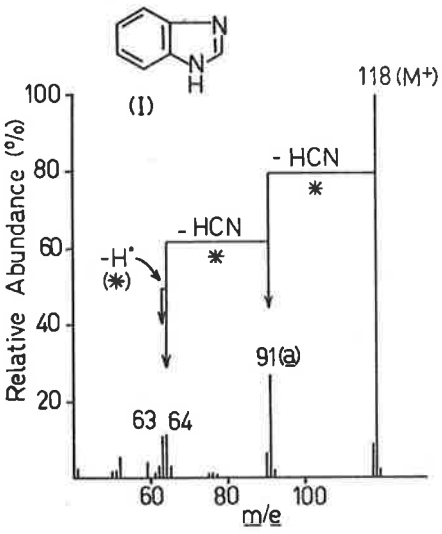


FIG. 1.

TABLE 2. COMPOSITIONS OF SOME IONS IN THE SPECTRA OF I–XX

Compound	*m/e*	Composition	Compound	*m/e*	Composition
I	63	C_5H_3	XIV	194	$C_{13}H_{10}N_2$
	64	C_5H_4		195	$C_{13}H_{11}N_2$
	91	C_6H_5N			
			XVI	205	$C_{14}H_9N_2$
V	91	C_7H_7		272/274	$C_{13}H_9N_2Br$
	118	C_8H_8N			
			XVIII	147	$C_8H_7N_2O$
VI	104	C_7H_6N		161	$C_9H_9N_2O$
	118	$C_7H_6N_2$		205	$C_{14}H_9N_2$
	131	$C_8H_7N_2$		220	$C_{15}H_{12}N_2$
				300/302	$C_{15}H_{13}N_2Br$
VII	118	$C_7H_6N_2$			
	122	C_6H_4NS	XIX	233	$C_{16}H_{13}N_2$
	131	$C_8H_7N_2$			
			XX	118	$C_7H_6N_2$
XI	117	$C_7H_5N_2$		119	$C_7H_7N_2$
	118	$C_7H_6N_2$		147	$C_8H_7N_2O$
	131	$C_8H_8N_2$		220	$C_{14}H_8N_2O$
XII	193	$C_{13}H_9N_2$	XXI	233	$C_{16}H_{13}N_2$
	194	$C_{13}H_{10}N_2$		267	$C_{15}H_{13}N_3O_2$
XIII	91	C_6H_5N	XXII	118	$C_7H_6N_2$
	92	C_6H_6N		119	$C_7H_7N_2$
	118	$C_7H_6N_2$		122	C_6H_4NS
	119	$C_7H_7N_2$			
	120	$C_7H_8N_2$			
	143	$C_9H_7N_2$			
	144	$C_9H_8N_2$			
	145	$C_9H_9N_2$			
	147	$C_8H_7N_2O$			

asterisk (*) in the text or a figure indicates that a metastable peak has been observed for the fragmentation in question.

The mass spectra (Figs 1 and 2) of benzimidazole (I) and 2-methylbenzimidazole (III) should be compared with those[3] of imidazole and 2-methylimidazole, respectively. The spectrum of benzimidazole (I) exhibits the molecular ion as the base peak, and the fragmentation process M—HCN—HCN—H· (to form $C_5H_3^+$, *m/e* 63). The initial loss of HCN probably produces *a* (*m/e* 91), and the spectrum (Table 1) of N-d_1-benzimidazole (II) shows loss of both HCN and DCN from the molecular ion, which indicates that the initial loss of HCN (Fig. 1) is non specific. This is also true of the M—HCN process in the spectrum of imidazole.[3]

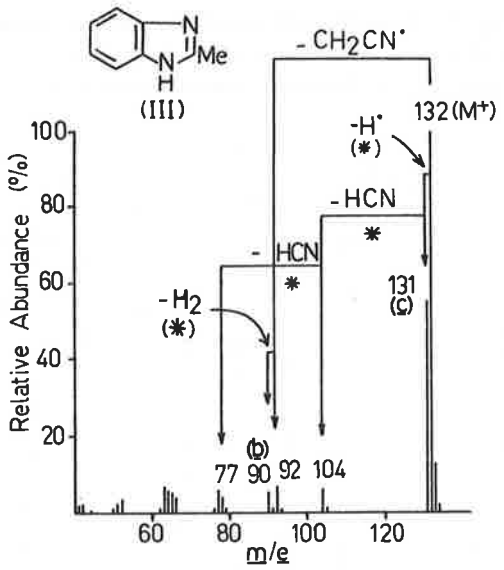
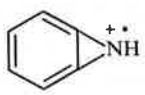
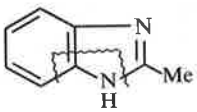


FIG. 2.

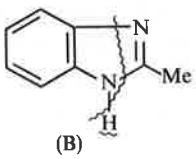
The mass spectrum (Fig. 2) of 2-methylbenzimidazole (III) exactly parallels that of 2-methylimidazole.[3] Comparison of the mass spectra of III and IV show that the M—HCN ion originates as in A (i.e. the *m/e* 104 ion in the spectrum of III remains



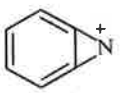
a, *m/e* 91



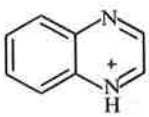
(A)



(B)



b, *m/e* 90



c, *m/e* 131

unchanged in that of IV). The M—CH_2CN· process involves the 2 and 3 positions (i.e. *m/e* 93 in III moves to 93/94 in IV), while the overall process M—CH_2CN·—H_2 (to *b*, *m/e* 90) may be explianed by the loss indicated in B (i.e. *m/e* 90 in III remains unchanged in IV). It is also probable that the M—H· ion (*m/e* 131) is formed by loss of a hydrogen atom from the Me group, with concomitant ring expansion to form the stable cation *c* (cf. Ref. 3).

The spectrum (Fig. 3) of 2-n-propylbenzimidazole (IX) shows pronounced loss of ethylene with accompanying H rearrangement to give *m/e* 132, the base peak of the spectrum. The structure of this fragment corresponds to the 2-methylbenzimidazole

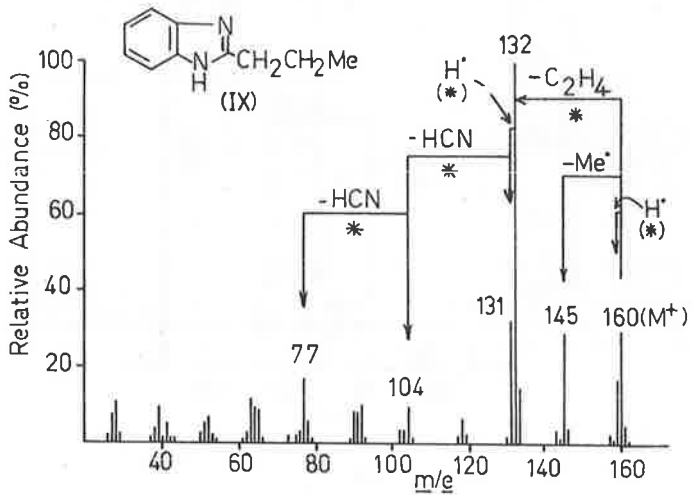
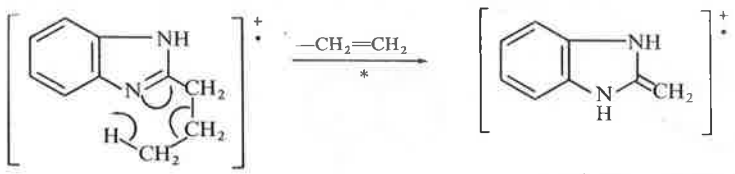


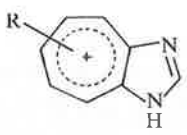
FIG. 3.

molecular ion, as the spectrum below *m/e* 132 is very similar to that (Fig. 2) of 2-methylbenzimidazole. The formation of *m/e* 132 probably proceeds by the process $d \rightarrow e$, with *e* then rearranging to the 2-methylbenzimidazole radical ion. A similar 6-membered transition state has been invoked to explain the loss of ethylene from 3-propylpyridines.[5] 2-Alkyloxazoles (where the alkyl group is greater than ethyl) also exhibit β-cleavage with hydrogen rearrangement to produce the 2-methyloxazole radical ion.[6]

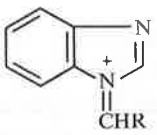


d, *m/e* 160

e, *m/e* 132



f, *m/e* 145 (R = Me)
g, *m/e* 131 (R = H)



h, *m/e* 157 (R = —CH=CH$_2$)
i, *m/e* 131 (R = H)

The spectra of V, VI and X are unexceptional. 5,6-Dimethylbenzimidazole (V), on electron impact, behaves like *o*-xylene,[7] producing prominent M—H· and M—Me· ions, which may be represented as the tropylium species *f* and *g*, respectively. The mass spectrum (Table 1) of N-allylbenzimidazole (VI) exhibits loss of both a hydrogen radical and a C_2H_3 radical from the molecular ion to form the stable cations *h* and *i*, while the molecular ion of 2-phenylbenzimidazole (X) may decompose either by loss of benzonitrile to form *a* (*m/e* 91) or by successive losses of two molecules of HCN to form *m/e* 140 ($C_{11}H_8^{+\cdot}$).

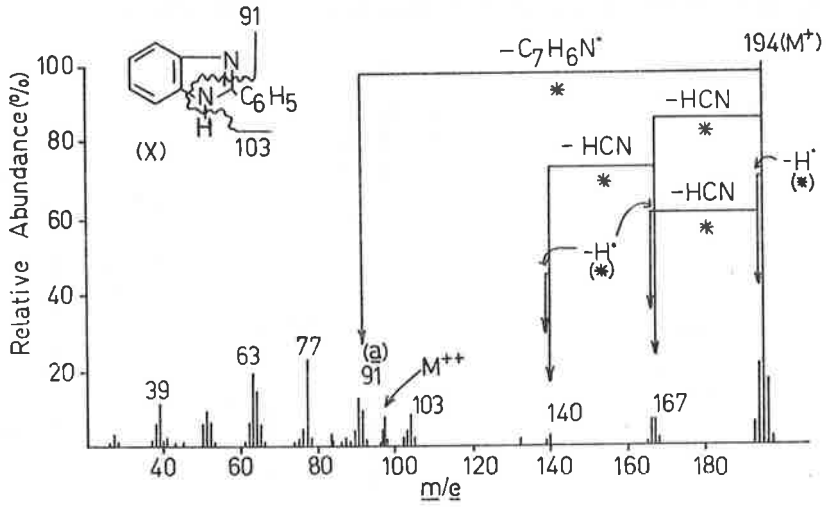
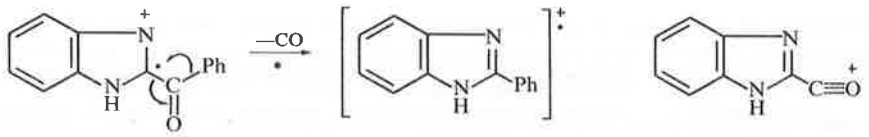


FIG. 4.

By far the most interesting features observed in the spectra (Figs 5 and 6) of the acylbenzimidazoles (XI and XII) are the pronounced skeletal rearrangement fragments which are produced by loss of carbon monoxide from the various molecular ions. Such processes are currently exciting much interest,[8] and of particular relevance are the M—CO fragments which are present in the spectra of acylthiophenes.[9] Similar processes are generally not observed in the spectra of acylbenzenes (benzophenone is an exception[10]). The M—CO fragment in the spectrum (Fig. 5) of 2-benzoylbenzimidazole is extremely pronounced (93% of the base peak), and its structure is probably that of the 2-phenylbenzimidazole radical ion (see $j \rightarrow k$), as the spectrum below *m/e* 194 is very similar to that (Fig. 4) of 2-phenylbenzimidazole, except for the presence of peaks due to the benzoyl cation (*m/e* 105) and its decomposition ions *m/e* 77 (base peak) and *m/e* 51. It is of interest to note that the expected α cleavage to carbonyl to produce the acylium cation *l* occurs only to the extent of 2% of the base peak, and that the two major processes are the formation of the skeletal rearrangement ion and the production of the benzoyl cation.



j, *m/e* 222 *k*, *m/e* 194 *l*, *m/e* 135

The skeletal rearrangement peak in the spectrum (Fig. 6) of 2-acetylbenzimidazole (XI) is not as pronounced as it is in that of XII (viz. 26% for XI, 93% for XII). The major process in this spectrum is M—CH_2CO, which forms the benzimidazole radical ion (*m/e* 118, base peak), which fragments as described above.

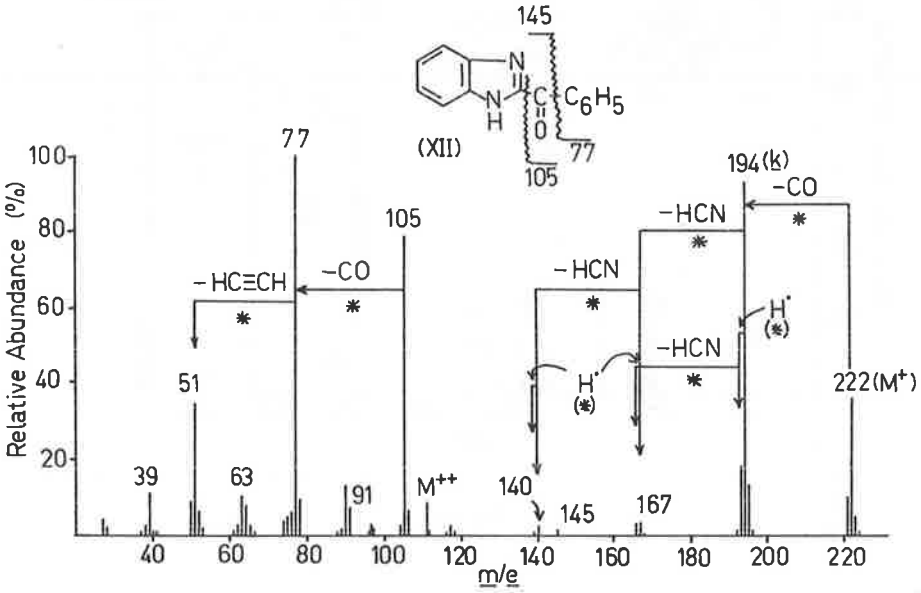


FIG. 5.

When the secondary alcohols (XIII–XXI) are introduced into the mass spectrometer through the heated inlet system, hydrogen is lost thermally, and the mass spectra obtained are those of the corresponding ketones. All these spectra contain M—CO fragments. The abundances of these ions relative to the base peaks in the spectra of the derived ketones are XIV, 100; XVI, 100; XVIII, 95; XIX, 62; XX, 43; and XXI, 92%.

The direct insertion technique was used to obtain the spectra (Figs 7 and 8 or Table 1) of the secondary alcohols XIII–XXI. Three processes are observed which are common to all spectra: (a) M—H_2—CO. The loss of hydrogen is probably thermal since no metastable ions are observed for the process M—H_2. (b) The formation of the protonated benzimidazole or N-methylbenzimidazole cation (e.g. *m* for XIV and XVI), which is formed by cleavage of the bond between C-2 and the

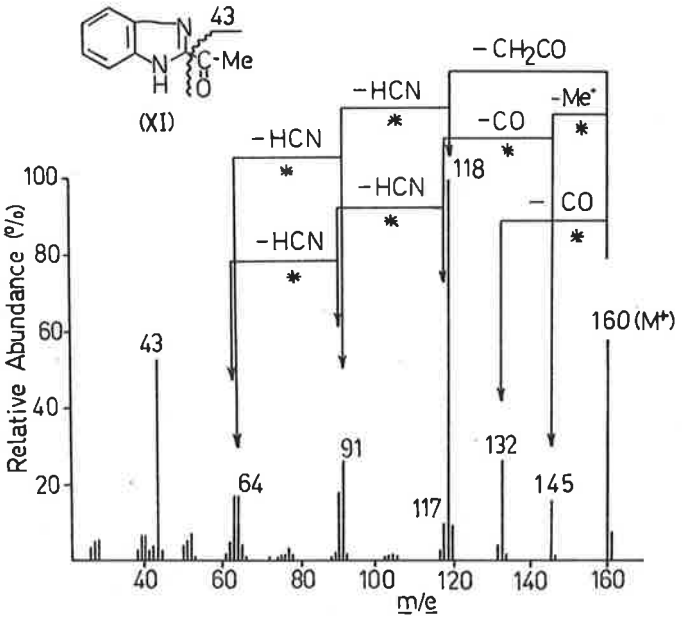

43
-Me
(XI)
-CH2CO
-HCN
-Me·
-CO
-HCN
-HCN
-HCN
-CO
118
160(M+)
Relative Abundance (%)
100
80
60
40
20
43
64
91
117
132
145
40
60
80
100
120
140
160
m/e

FIG. 6.

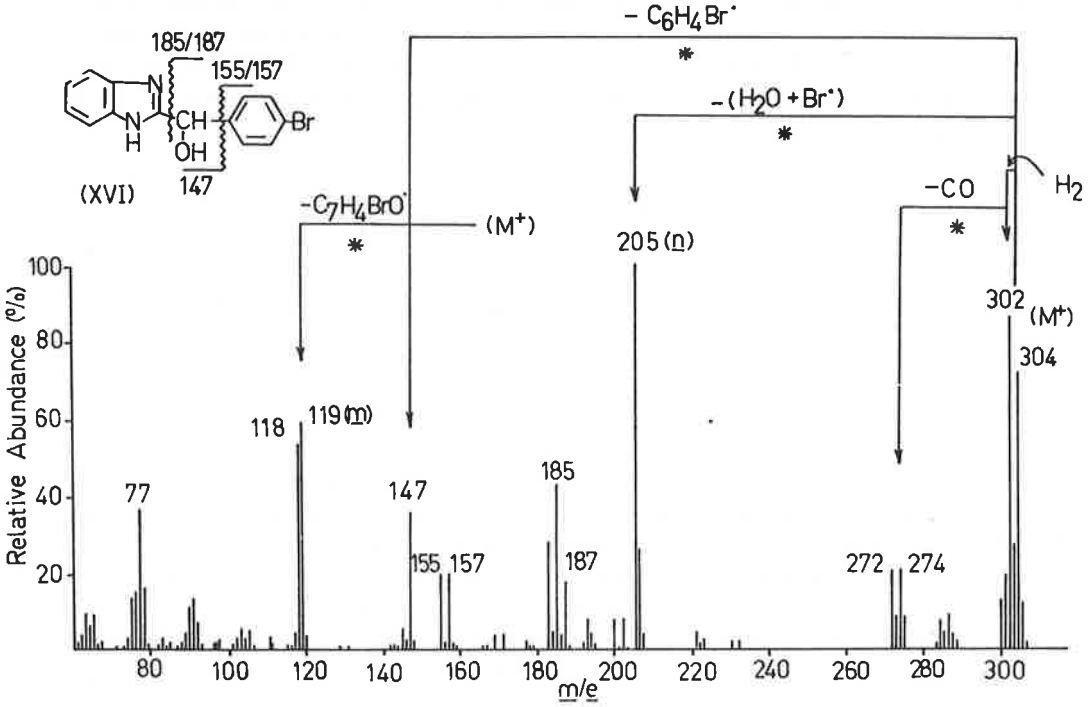

185/187
155/157
Br
CH
OH
(XVI)
147
-C6H4Br·
-(H2O+Br·)
-C7H4BrO·
(M+)
205(n)
-CO
H2
302 (M+)
304
118
119(m)
77
147
185
155
157
187
272
274
Relative Abundance (%)
100
80
60
40
20
80
100
120
140
160
180
200
220
240
260
280
300
m/e

FIG. 7.

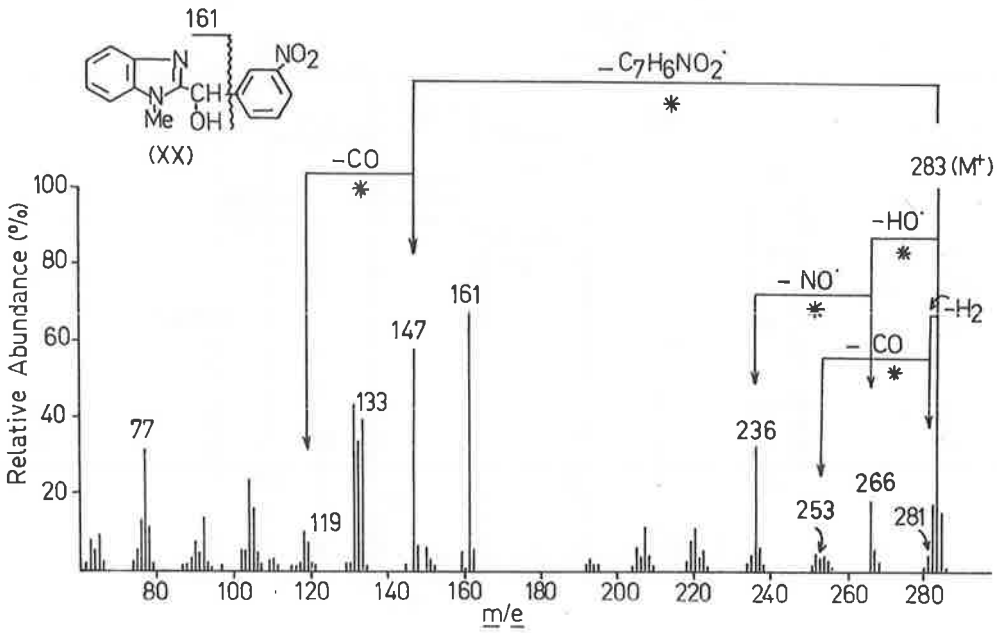
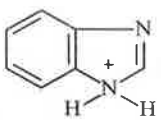
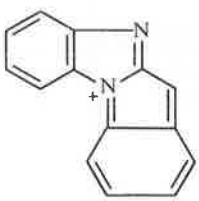


FIG. 8.

carbon bearing oxygen, with concomitant double hydrogen rearrangement. One of the migrating hydrogens is that attached to oxygen, as evidenced by the spectra (Table 1) of XV and XVII. (c) The process M—$C_6H_4R\cdot$ (R = Br or NO_2) produces an ion whose composition corresponds to the appropriate protonated formylbenzimidazole cation.



m, m/e 119



n, m/e 205

There are three further features of the spectra of the secondary alcohols (XIV–XXI) which provide information concerning the nature of the substituent on nitrogen. The spectra (Figs 7 and 8 or Table 1) of the 1-Me and 1-H benzimidazoles (XIV–XXI) show marked differences. When hydrogen is bound to nitrogen (XIV, XVI, XIX and XXI) a prominent ion (the base peak in the spectra of XVI and XIX) is produced in a one step process from the molecular ion, by combined loss of R (R = H, Br of NO_2) and water (see Fig. 7). The two hydrogens involved are those bound to nitrogen and oxygen (from the spectra of XV and XVII in Table 1). A plausible structure for this ion is *n* (*m/e* 205 in the spectrum of XV), and its presence may be used to detect

TABLE 3. MAJOR FRAGMENT IONS IN THE MASS SPECTRA OF XIV–XXI

Compound	M—H_2—CO		Protonated benzimidazole cation		M—C_6H_4R		M—(R + H_2O)		Skeletal rearrangement ion	
	m/e	(%)	*m/e*	(%)	*m/e*	(%)	*m/e*	(%)	*m/e*	(%)
XIV	196	10	119	46	147	22	205	35	—	—
XVI	272/274	20	119	60	147	34	205	100	—	—
XVIII	284/286	2	133	31	161	43	—	—	147	53
XIX	300/302	28	147	36	175	13	233	100	—	—
XX	253	3	133	38	161	65	—	—	147	57
XXI	267	21	147	28	175	19	233	31	—	—

the presence of the 1-H substituent. No corresponding ions are observed in the spectra (Fig. 8 or Table 1) of the secondary alcohols having 1-methylsubstituents (XVIII and XX).

Second, the spectra of the 1-H benzimidazoles (XIV, XVI, XIX and XXI) exhibit M—H_2O ions. This is particularly noticeable in the spectrum (Table 1) of XIV where the M—H_2O ion constitutes 80% of the base peak. The two hydrogens involved in the M—H_2O process are again those bound to nitrogen and oxygen (see the spectrum of XV, Table 1). This process is not observed in the spectra of XVIII or XX.

Third, the spectra (Fig. 8 or Table 1) of XVIII and XX exhibit an ion which is not present in those of the 1-H derivatives. This ion (produced in a one step process from the molecular ion) must be produced by a skeletal rearrangement process, as it is formally derived by α cleavage to C-2 with accompanying rearrangement of the alcoholic oxygen to the benzimidazole system. Although the structure of this ion (*m/e* 147, $C_8H_7N_2O$) is unknown, its presence allows the detection of the N-methyl substitutent.

The main features of the spectra of XIV–XXI are summarized in Table 3 and Figs 7 and 8. The spectrum (Table 1) of the substituted ethyl alcohol (XIII) is unexceptional; the major process being loss of an acetyl radical from the molecular ion to form the protonated benzimidazole cation *m*.

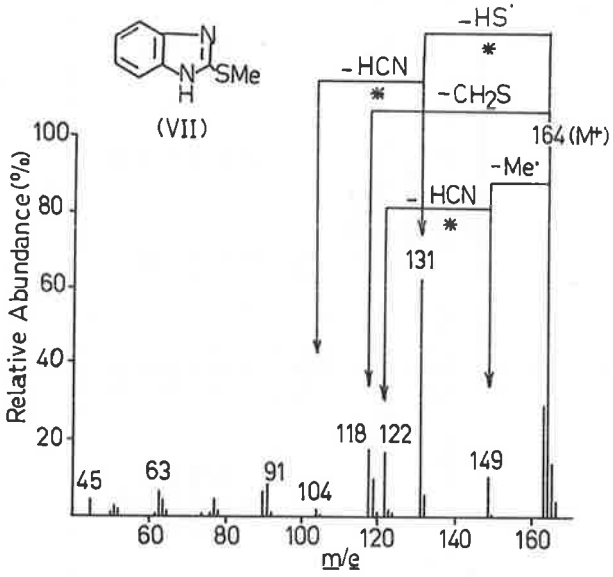
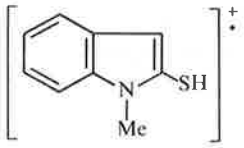


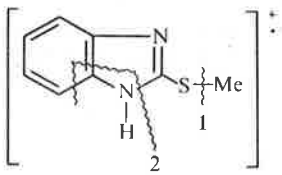
FIG. 9.

Skeletal rearrangement fragments are also observed in the spectrum (Fig. 9) of 2-thiomethylbenzimidazole (VII), where the M—SH ion (*m/e* 131) constitutes 63% of the base peak. It has been shown[11] that the M—SH process in the spectrum of thioanisole occurs from a common, rearranged molecular ion,[12] and that rearrangement processes which involve hydrogen transfers between the methyl group and the aromatic nucleus do not occur.[11] The spectra (Fig. 9, Table 1) of VII and XXII are

very similar (small differences are noted in the relative intensities of certain ions), which may indicate that they have a common molecular ion; viz. either one rearranging to the other, or with both rearranging to a common intermediate ion. The spectrum (Table 1) of 1-d_1-2-thiomethylbenzimidazole (VIII) shows that the hydrogen involved in the M—SH process is bound to carbon. The hydrogen presumably comes from the methyl group, and the rearranged molecular ion clearly cannot correspond to *o*. It is probable that the rearrangement is analogous to that observed in thioanisole.



o, *m/e* 164



p, *m/e* 164

Other processes observed in the spectrum of VII are (1) M—Me —HCN and (2) M—CH_2S. A comparison of the spectra of VII and VIII shows that process 1 occurs in a specific manner as indicated in *p* (*m/e* 122 is not shifted to *m/e* 123), while process 2 is a random one, involving loss of hydrogen attached to both carbon and nitrogen.

EXPERIMENTAL

Mass spectra were measured by the direct insertion technique with either an Hitachi Perkin–Elmer RMU 6D mass spectrometer (I–VI; IX–XII) or an A.E.I. MS9 mass spectrometer (VII, VIII and XIII–XXII) with a source temperature ca. 100°. Exact mass measurements were made with the MS9, using a resolution of 14,000 (10% valley definition) with heptacosafluorotributylamine providing reference masses. All measurements were correct to within 15 ppm.

Compounds I, III and V were purified commercial samples. The following compounds were prepared by standard procedures: VI,[13] VII,[14] IX,[15] X,[16], XI,[17] XII,[17] XIII,[18] XIV,[18] XVI,[19] XVIII,[20] XIX,[19] XX[20] and XXI.[20]

The spectra of II, IV, VIII, XV and XVII were obtained by introducing the unlabelled compounds directly into the source with D_2O.[21]

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Professor S. Siddappa generously provided samples (XIV, XVI, XVIII–XXI).

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THE MASS SPECTRA OF SOME ALKYL AND ARYL OXAZOLES[1]

J. H. BOWIE, P. F. DONAGHUE and H. J. RODDA
(Department of Organic Chemistry, the University of Adelaide, South Australia)
and
R. GRAHAM COOKS and DUDLEY H. WILLIAMS
(University Chemical Laboratory, Cambridge, U.K.)

(*Received* 23 *October* 1967)

Abstract—The mass spectra of a variety of alkyl and aryl oxazoles have been determined and the spectra analyzed with the aid of deuterium labelling and high resolution mass spectrometry. In contrast to the corresponding benzenoid compounds, the mass spectra of isomeric alkyl oxazoles are distinctive and in this respect are akin to those of the corresponding pyridines. Further analogy to the pyridines is suggested by the unfavorable nature of a carbonium ion adjacent to the 2-position and this effect may be used to locate alkyl substituents attached to the oxazole nucleus. The loss of carbon monoxide from the molecular ions of 2,5-disubstituted oxazoles probably occurs with ring opening and migration of the C-5 substituent (e.g. Br) to the C-4 position.

ALTHOUGH the behaviour of many aromatic five-membered heterocyclic ring systems upon electron impact is now fairly well documented,[2] a detailed study of the mass spectra of oxazoles has not been reported.[3] This paper deals with the mass spectra of representative alkyl-, phenyl- and alkylphenyl-oxazoles. Details of the spectra are summarized in Table 1 and Figs. 1–12.

The mass spectrum (Table 1) of oxazole (I) itself is typical of that of an unsubstituted aromatic compound insomuch as the molecular ion (*m/e* 69) constitutes the base peak. The most abundant fragment ions in the high mass region occur at M-1 (8%), M-27 (M—HCN, 13%), M-28 (M—H_2CN and/or M—CO, 21%) and M-29 (M—CHO, 37%).

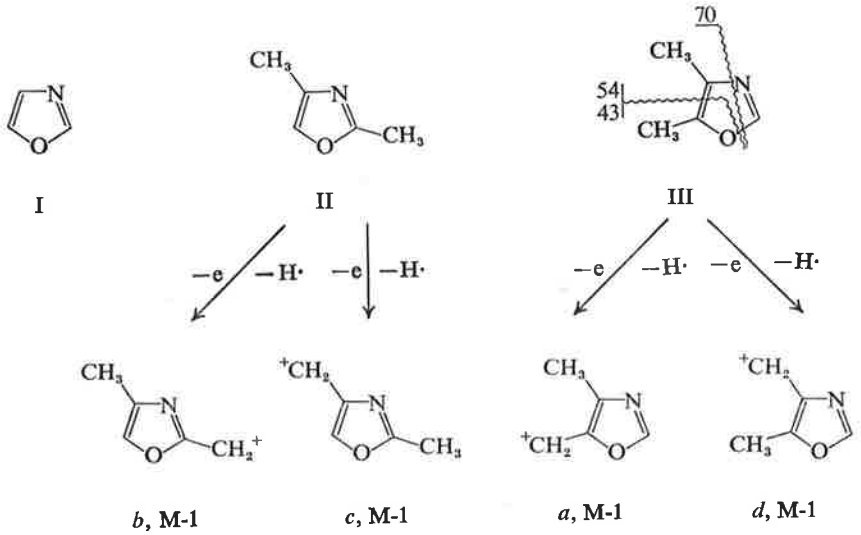
The spectra of the isomeric compounds 2,4-dimethyloxazole (II, Table 1) and 4,5-dimethyloxazole (III, Fig. 1) show characteristic differences. This behaviour is in contrast to that of the isomeric xylenes[4] and ethylmethylbenzenes,[5a] which give virtually identical spectra, but akin to that of three isomeric ethylmethylpyridines,[5a] which give distinctive spectra. Apparently, the presence of heteroatoms in the ring system prevents, or greatly retards, those processes by which the molecular ions from the isomeric xylenes, or ethylmethylbenzenes, become equivalent. The M-1 peak from III is considerably more abundant (12%) than that (2%) from II. These data parallel those for 3-ethylpyridine versus 2-ethylpyridine, the former exhibiting a much more abundant M-15 ion;[5b] the greater stability of carbonium ion *a* relative to carbonium ion *b* rationalizes the data, just as in the pyridines. Hence the M-1 peak from 2,4-dimethyloxazole (II) is probably formed largely by loss of a hydrogen atom from the 4-methyl group (see *c*) (the bond fixation within the oxazole nucleus accounts for the greater stability of *c* relative to *b*), while the M-1 peak from III will probably correspond to the formation of both *a* and *d*.

Table 1. Mass spectra of oxazoles

Compound															
I	*m/e*	38	39	40	41	42	68	69(M)	70						
	Rel. Ab.	2	4	37	21	13	8	100	4						
II	*m/e*	29	31	38	39	40	41	42	43	52	53				
	Rel. Ab.	6	27	2	4	4	9	40	4	2	2				
	m/e	54	55	56	66	68	69	96	97(M)		98				
	Rel. Ab.	5	20	8	3	34	22	2	100		6				
IV	*m/e*	26	27	28	38	39	40	41	42	43	44	53			
	Rel. Ab.	6	24	30	3	8	5	18	59	91	3	3			
	m/e	54	55	56	66	67	68	69	70	82	96	110	111(M)	11	
	Rel. Ab.	4	64	2	3	3	40	14	29	7	7	15	100		
IX	*m/e*	39	50	51	52	62	63	64	73	76	77	89	90		
	Rel. Ab.	5	4	8	2	4	8	2	3	3	6	20	38		
	m/e	103	166	117	118	145(M)		146							
	Rel. Ab.	3	9	35	3	100		11							
Xa	*m/e*	39	50	51	61	62	63	64	77	89	90	117	118		
	Rel. Ab.	8	5	6	3	9	28	8	5	60	78	5	56		
	m/e	119	145	146(M)	147										
	Rel. Ab.	4	8	100	11										
XI	*m/e*	37	38	39	41	50	51	61	62	63	64	77	88	89	116
	Rel. Ab.	6	7	23	8	12	11	8	21	42	4	8	10	100	36
	m/e	117	168	170	195	196	197	198	223(M)		224	225(M)	226		
	Rel. Ab.	6	10	9	53	6	52	5	19		2	19	2		
XIIa	*m/e*	38	39	40	41	42	43	50	51	52	53	61	62	63	
	Rel. Ab.	5	22	9	4	2	7	11	21	8	2	3	11	29	
	m/e	64	65	66	74	75	76	77	78	80	87	88	89	90	
	Rel. Ab.	19	9	8	3	4	8	16	4	4	3	3	24	54	
	m/e	91	92	103	104	105	130	131	132	133	158	159			
	Rel. Ab.	86	8	30	15	4	8	34	45	8	5	15			
	m/e	160(M)	161												
	Rel. Ab.	100	20												
XIIb	*m/e*	39	50	51	62	63	64	75	76	77	78	89	90		
	Rel. Ab.	14	9	18	12	37	12	3	6	17	4	80	98		
	m/e	103	104	105	130	131	132	133	158	159	160(M)	161			
	Rel. Ab.	36	16	10	10	27	36	4	4	16	100	15			
XIIIa	*m/e*	39	43	50	51	63	76	77	78	89	90	91	102	103	
	Rel. Ab.	5	3	9	20	8	5	42	15	7	13	50	3	19	
	m/e	104	105	119	130	131	132	133	159	160(M)	161				
	Rel. Ab.	13	20	6	11	55	17	2	11	100	12				
XIVa	*m/e*	39	43	50	51	52	61	62	63	64	75	76	77	78	
	Rel. Ab.	10	13	8	13	4	3	9	24	4	4	5	22	34	
	m/e	88	89	90	102	103	104	105	117	118	130	131			
	Rel. Ab.	3	27	7	5	35	57	12	6	7	4	15			
	m/e	132	145	159	160(M)	161									
	Rel. Ab.	2	8	7	100	12									
XV	*m/e*	39	50	51	62	63	75	76	77	78	88	89	90	91	102
	Rel. Ab.	7	3	8	3	15	2	3	21	5	2	23	10	9	2
	m/e	103	104	105	115	116	117	118	128	129	130	131	144	158	
	Rel. Ab.	48	15	7	13	6	27	7	6	2	11	6	11	100	
	m/e	159	172	173(M)	174										
	Rel. Ab.	12	7	95	15										
XVI	*m/e*	39	42	43	50	51	52	62	63	64	75	76	77	78	
	Rel. Ab.	9	6	18	6	13	3	4	11	2	2	4	21	18	
	m/e	89	90	102	103	104	105	130	131	158	172	173(M)	174		
	Rel. Ab.	10	3	3	21	62	16	7	4	6	2	100	12		

TABLE 1 (*contd.*)

Compound															
XIX	*m/e*	39	41	50	51	62	63	76	77	89	103	104	105	115	
	Rel. Ab.	18	6	4	20	4	14	5	58	12	32	16	15	7	
	m/e	116	117	118	128	131	139	144	163	164	165	166	167		
	Rel. Ab.	3	33	15	4	3	6	5	6	9	100	40	5		
	m/e	192	193	195	206	207	220	221	234	248	249(M)		250		
	Rel. Ab.	4	11	3	43	7	4	2	3	6	85		16		
XXI	*m/e*	39	41	43	51	55	62	63	76	77	83	89	91	103	104
	Rel. Ab.	11	21	5	13	15	2	10	5	58	8	11	5	77	41
	m/e	105	115	116	117	128	129	130	131	139	163	164	165	166	
	Rel. Ab.	29	7	3	8	5	6	12	4	4	5	6	73	15	
	m/e	167	193	206	207	234	235	236	248	249	250	262	263		
	Rel. Ab.	4	4	6	2	5	100	18	69	29	5	20	6		
	m/e	290	291(M)		292										
	Rel. Ab.	2	43		13										
XXII	*m/e*	39	50	51	76	77	88	89	90	105	115	139	163	164	
	Rel. Ab.	6	2	7	2	16	2	21	2	8	3	5	5	7	
	m/e	165	166	167	268	269	270	296	297(M)		298	299			
	Rel. Ab.	80	47	6	2	23	4	5	100		25	3			



Other distinctive features of the spectra of II and III include (i) the loss of a methyl radical from M^+ when the methyl groups are adjacent in III (Fig. 1), although this process is insignificant in the spectrum of II, (ii) no loss of HCN from the molecular ion of II, but loss of HCN from III to give *m/e* 70 [$C_4H_6O^+$; high resolution (h.r.)*] and (iii) an abundant *m/e* 43 ion ($CH_3C{\equiv}O^+$, h.r.) from III (Fig. 1), even though the *m/e* 43 ion from II is of very low abundance (4%). The complement to *m/e* 43 in Fig. 1 is *m/e* 54, formed exclusively by loss of C_2H_3O (h.r.) in a one-step process (metastable peak at *m/e* 30·1). In contrast, *m/e* 55 (Fig. 1) is due solely to $C_3H_3O^+$ [M—CH_4CN (h.r.) and no loss of CH_2CO].

There are differences between the spectra of 4,5-dimethyloxazole (III, Fig. 1) and 2,4,5-trimethyloxazole (IV, Table 1) which can be related to the ground state structures

* The latters 'h.r.' will be used subsequently in the paper to indicate the compositions of ions established by high resolution measurements.

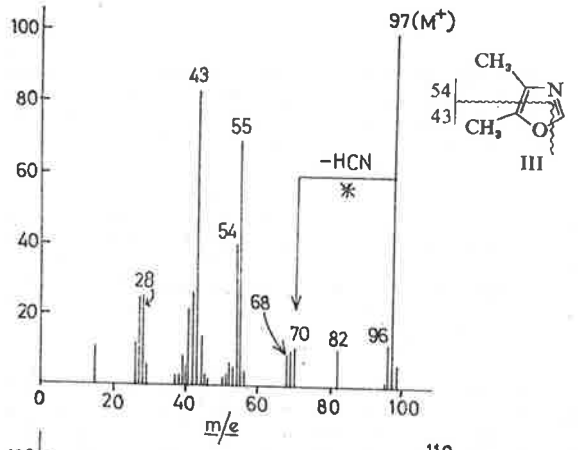


FIG. 1

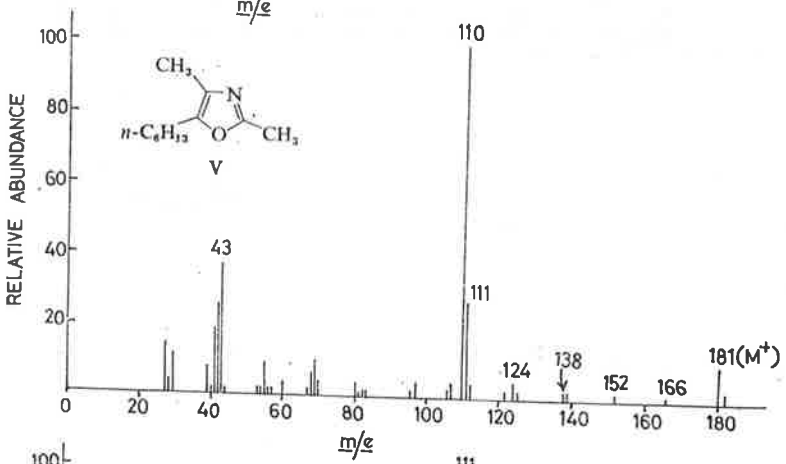


FIG. 2

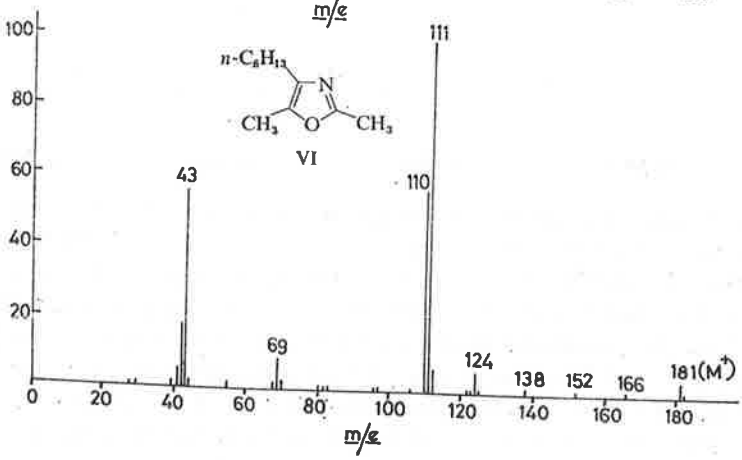


FIG. 3

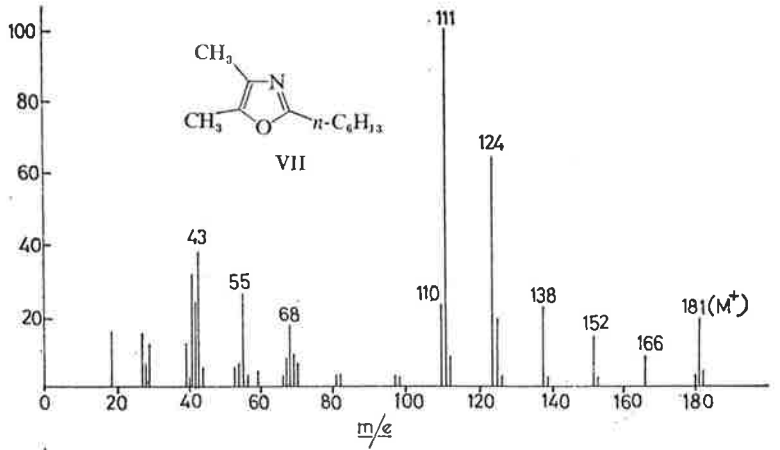


FIG. 4

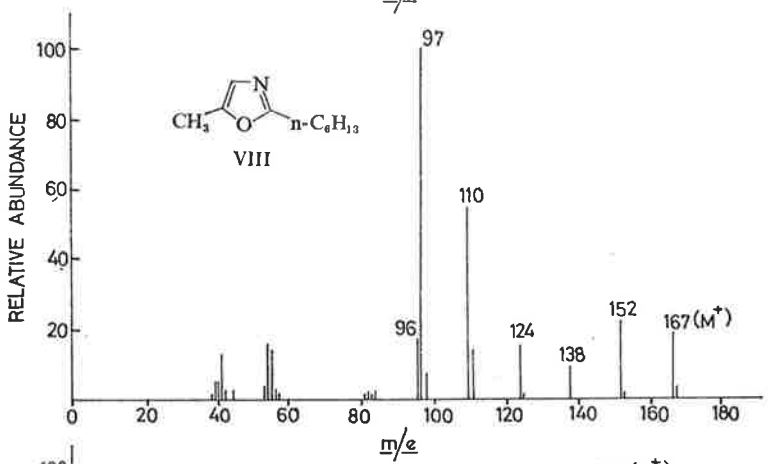


FIG. 5

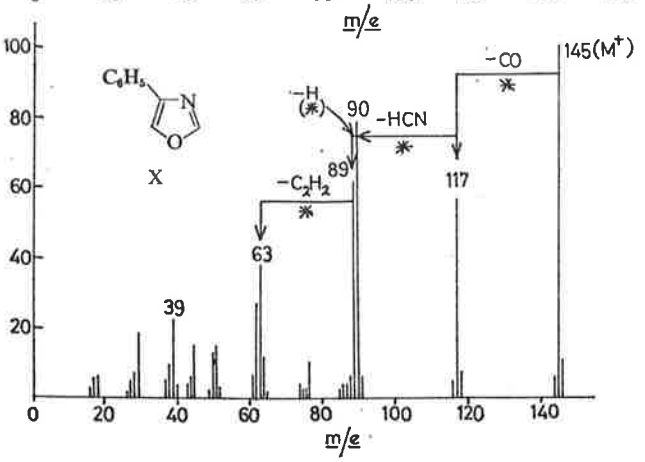


FIG. 6

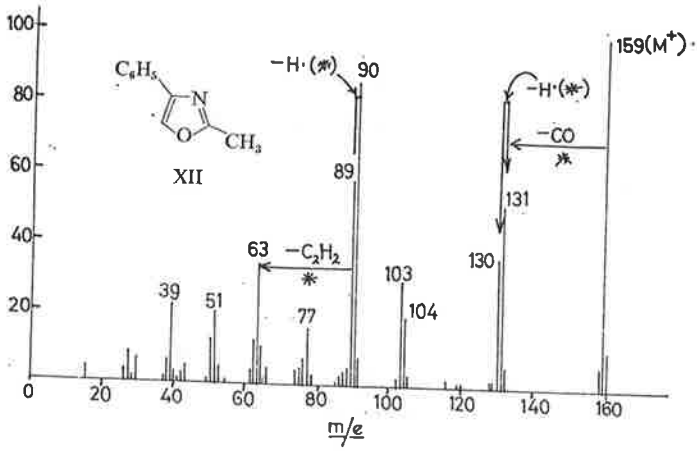


FIG. 7

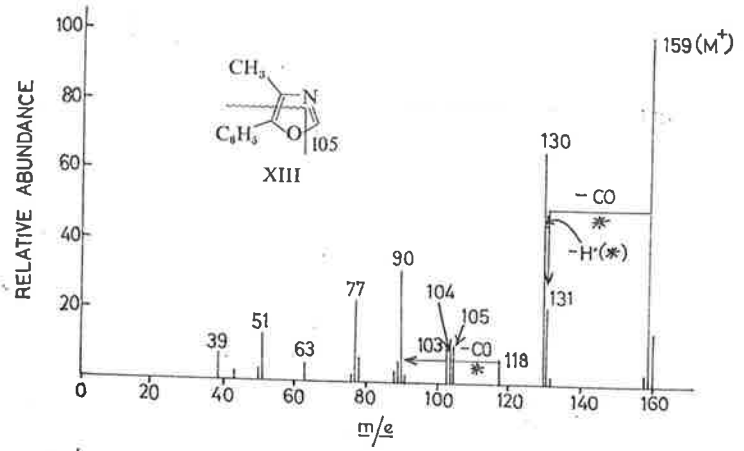


FIG. 8

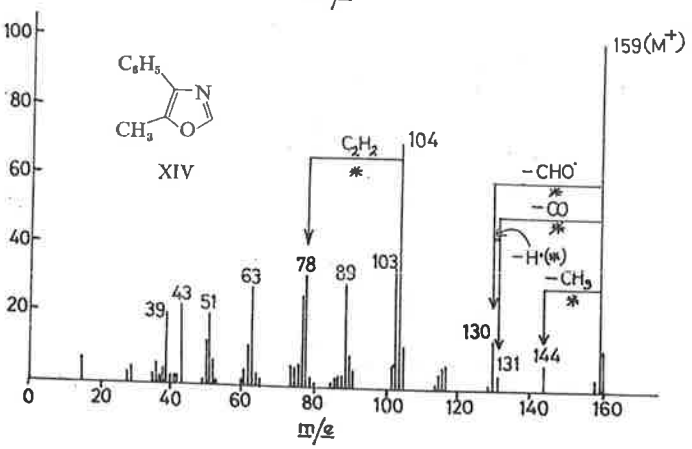
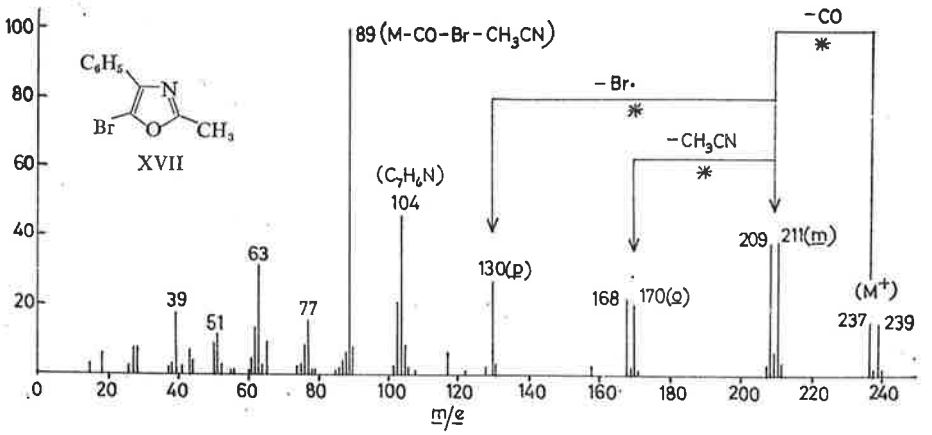
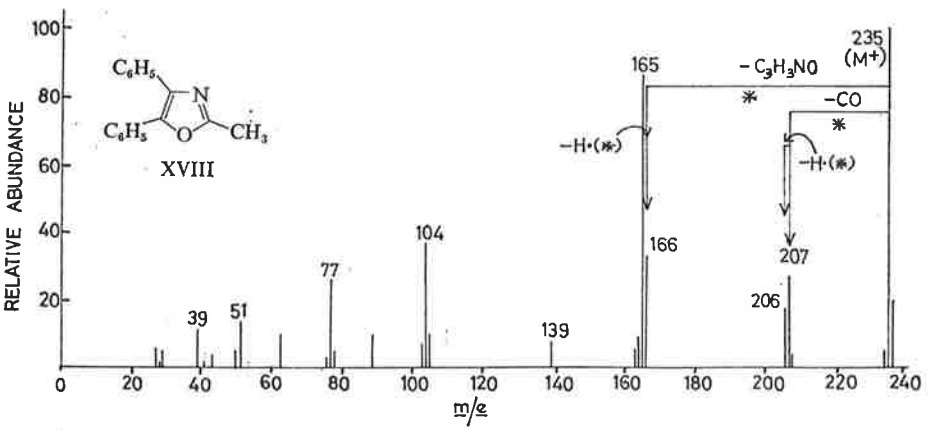


FIG. 9



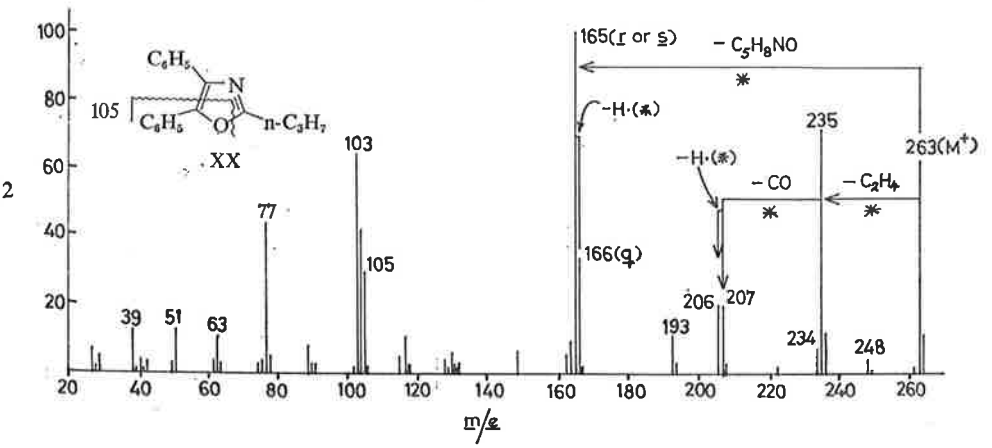
XVII

FIG. 10



XVIII

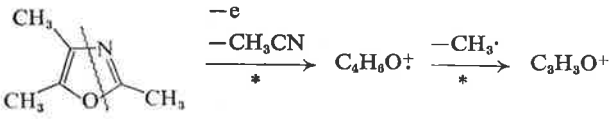
FIG. 11



XX

FIG. 12

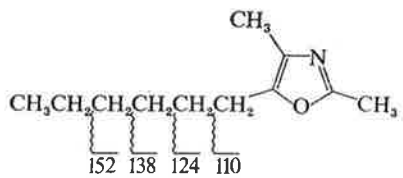
of the compounds. Thus, the M—HCN peak (*m/e* 70) of Fig. 1 is totally replaced by an M—CH_3CN peak from IV and this *m/e* 70 ion (*e*) then decomposes further by loss of a methyl radical to *m/e* 55. The one-step loss of CHO, however, from the molecular ion of IV to give *m/e* 82 ($C_5H_8N^+$, h.r.) demands a skeletal rearrangement in that form of the molecular ion undergoing this reaction, or a skeletal rearrangement



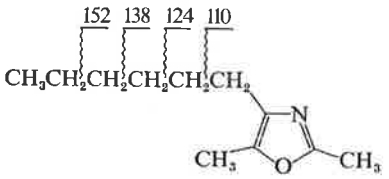
IV *e*, *m/e* 70 *m/e* 55

during the reaction leading to *m/e* 82.

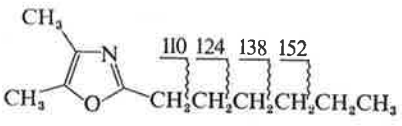
Since the only noteworthy feature of the spectra of simple methyl oxazoles is that the isomeric dimethyloxazoles II and III give different spectra, these have been dealt with rather summarily. However, since the fragmentation pattern of an aliphatic chain attached to a nitrogen heterocycle is known to vary with the site of attachment relative to the heterocyclic nitrogen atom,[5,6] the isomeric dimethyl-*n*-hexyl oxazoles V, VI and VII have been synthesized and their spectra (Figs. 2, 3 and 4) compared. 5-Methyl-2-n-hexyloxazole (VIII) was also available and its spectrum is reproduced in Fig. 5. In the spectra of the two compounds containing the *n*-hexyl chain in the 2-position (Figs. 4 and 5), the fragmentation of the side chain is very similar, and in particular the peaks due to β-cleavage (*m/e* 110 in Fig. 4 and *m/e* 96 in Fig. 5) are



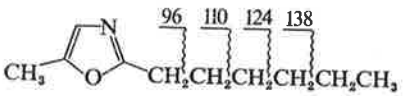
V



VI



VII



VIII

much smaller than those arising due to β-cleavage with hydrogen rearrangement (*m/e* 111 in Fig. 4 and *m/e* 97 in Fig. 5). The situation is superficially analogous (i.e. β-cleavage with hydrogen rearrangement more pronounced than simple β-cleavage) in the spectrum (Fig. 3) of 2,5-dimethyl-4-*n*-hexyloxazole (VI), but a sharp contrast is observed for the 5-*n*-hexyl isomer (Fig. 2) where β-cleavage is much more pronounced than the same process accompanied by hydrogen rearrangement [*m/e* 110 (100%, M—C_5H_{11}), *m/e* 111 (20%, M—C_5H_{10})].

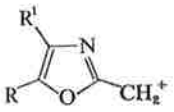
If the reasonable assumptions are made that (i) the products of the β-cleavage reactions arise predominantly from the molecular ions in one-step processes and (ii) the further decomposition reactions (if any) of these products occur at similar rates, then the ratios $[M—C_5H_{11}]/[M]$ and $[M—C_5H_{10}]/[M]$ (in terms of relative peak heights) will give the approximate relative rates of the β-cleavage processes in V–VIII.[7] The relevant data have been summarized in Table 2, which also gives data for the simple α-cleavage reaction (i.e. $[M—C_4H_9]/[M]$).

TABLE 2. APPROXIMATE RELATIVE RATES OF β-CLEAVAGE, β-CLEAVAGE WITH HYDROGEN REARRANGEMENT, AND γ-CLEAVAGE REACTIONS IN THE SPECTRA OF V–VIII*

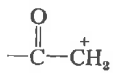
Substitution pattern	$[M—C_5H_{11}]/[M]$	$[M—C_5H_{10}]/[M]$	$[M—C_4H_9]/[M]$
2,4-Dimethyl-5-*n*-hexyl (V)	10·0	2·1	0·4
2,5-Dimethyl-4-*n*-hexyl (VI)	14·3	23·5	1·5
4,5-Dimethyl-2-*n*-hexyl (VII)	1·3	5·5	3·5
5-Methyl-2-*n*-hexyl (VIII)	1·0	5·5	3·1

* Relative peak heights are corrected for ^{13}C isotope contributions.

From the data in Table 2, it is evident that the rate of simple β-scission is much less in the 2-*n*-hexyl oxazoles VII and VIII than in the 4-*n*-hexyl-(VI) or 5-*n*-hexyl-(V) isomers. These observations again recall the relatively low abundance of the M-15 ion from 2-ethylpyridine[5b] and are compatible with the destabilization of a carbonium ion separated from a heterocyclic nitrogen atom by a double bond (*f*). This system (*f*) bears analogy to a carbonium ion adjacent to a keto group (*f'*), which is also a relatively unstable system.[5c] In contrast, when the rate of simple β-cleavage is slow, the process of γ-fission is enhanced (Table 2). Enhanced γ-cleavage reactions are also observed in the mass spectra of alkyl imines,[8] oximes,[9] semicarbazones,[10] and 2-alkylquinolines,[6] all of which contain the $—N{=}C(—)—CH_2CH_2R$ system. Allylic

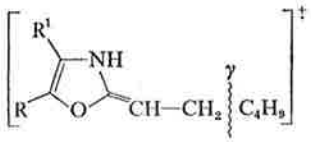


f

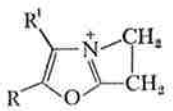


f'

cleavage in the tautomeric form *g* of the molecular ion, or formation of a cyclic ion *h* are plausible rationalizations which can account for the enhanced γ-cleavage.[11]



g

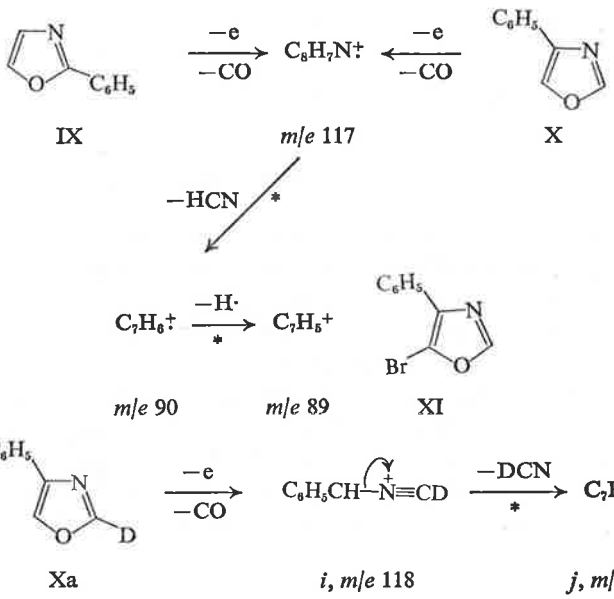


h

The reaction corresponding to β-cleavage with hydrogen rearrangement proceeds at a similar rate in the 5-hexyl compound V to the analogous reaction in *n*-butylbenzene[12] or 2-*n*-pentylfuran.[13] A significant rate enhancement is observed when

the *n*-hexyl chain is in the 2-position, and the reaction becomes very favourable when the *n*-hexyl chain is in the 4-position (Table 2 and *m/e* 111 in Fig. 3). The process of *β*-cleavage with hydrogen rearrangement is also favoured in alkylpyrazines[5d] and 2-alkylquinolines.[6]

The fragmentation reactions occurring in the isomeric phenyloxazoles, 2-phenyloxazole (IX, Table 1) and 4-phenyloxazole (X, Fig. 6) are very similar, both molecular ions sequentially eliminating CO (h.r., broad metastable peaks at *m/e* 94·5) and HCN (metastable peaks at *m/e* 69·3) to give *m/e* 90. The *m/e* 90 ion then loses a hydrogen atom to give *m/e* 89. However, the two hydrogens of the oxazole ring are predominantly not randomized in the M—CO ion from 4-phenyloxazole (X), since the M—CO ion from 2-d_1-4-phenyloxazole (Xa, Table 1) decomposes almost completely (94%)



by loss of DCN rather than by loss of HCN (4%). The M—CO ion from Xa is therefore represented as *i* (*m/e* 118), which can lose DCN to give *j* (*m/e* 90).

The introduction of a bromine atom at C-5 into 4-phenyloxazole (X) does not greatly change the fragmentation pattern, 4-phenyl-5-bromo-oxazole (XI) sequentially eliminating CO, HCN and Br (i.e. *m/e* 223/225 → 195/197 (h.r.) → 168/170 (h.r.) → 89, see Table 1). The only competing decomposition involves overall loss of COBr to give *m/e* 116.

The spectrum (Fig. 7) of 2-methyl-4-phenyloxazole (XII) has been analysed with the aid of high resolution data (Table 3) and the spectra (Table 1) of 5-d_1-2-methyl-4-phenyloxazole (XIIa) and 2-d_1-methyl-4-phenyloxazole (XIIb).

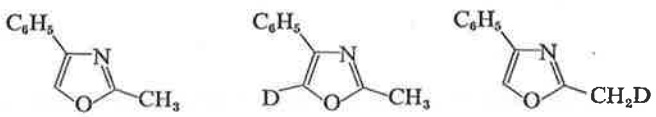
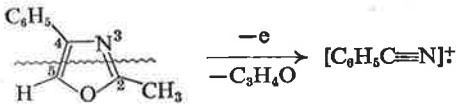


TABLE 3. COMPOSITIONS OF ABUNDANT FRAGMENT IONS IN THE SPECTRUM (Fig. 7) OF 2-METHYL-4-PHENYLOXAZOLE (XII)

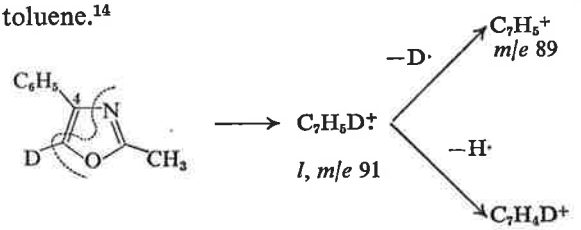
Ion (*m/e*)	Composition	Derivation
131	C_9H_9N	M—CO
130	C_9H_8N	M—CHO
104	C_7H_6N (60%)	M—C_3H_3O
	C_8H_8 (40%)	M—CO—HCN
103	C_7H_5N (95%)	M—C_3H_4O
	C_8H_7 (5%)	M—CHO—HCN
90	C_7H_6	M—CO—CH_3CN
89	C_7H_5	M—CO—CH_3CN—H

The *m/e* 131 ion of Fig. 7 is formed by loss of carbon monoxide from the molecular ion and the further loss of a hydrogen radical to *m/e* 130 involves loss of the C-5 hydrogen to the extent of less than 10% [as evidenced by the almost complete shift of *m/e* 130 to *m/e* 131 in the spectrum of XIIa (Table 1), after correction for a small amount of d_0-contaminant]. A rough calculation applied to the spectrum (Table 1) of the 2-d_1-methyl derivative (XIIb) implicates the methyl hydrogens in this reaction to the extent of approximately 60%. Although 40% of the *m/e* 104 ion formally corresponds to a fragment ion produced by sequential loss of CO and HCN, there is no metastable peak to establish the *m/e* 131 → 104 transition. The *m/e* 103 peak (Fig. 7) is formed almost exclusively by loss of C_3H_4O from the molecular ion and is not shifted in the spectra of either XIIa or XIIb. Hence the *m/e* 103 peak corresponds to ionized benzonitrile (*k*) formed by cleavage of the 2,3- and 4,5-bonds.



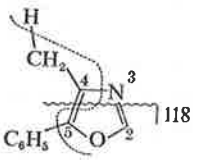
XII *k*, *m/e* 103

The large peak at *m/e* 90 (Fig. 7) is almost quantitatively shifted to *m/e* 91 in the spectrum of XIIa but very largely remains at *m/e* 90 in the spectrum of XIIb. Since *m/e* 90 arises by formal loss of CO and CH_3CN (Table 3), the C-5 deuterium of XIIa most probably migrates to C-4, or less likely, to the phenyl ring, in this reaction (XIIa → I). The ion I then decomposes by loss of a deuterium atom or a hydrogen atom, as evidenced by the only partial shift of *m/e* 89 (Fig. 7) to *m/e* 90 in the spectrum (Table 1) of XIIa. These observations again emphasize that the hydrogens of the aromatic oxazole ring are not randomized with the hydrogens of a methyl substituent for the reactions under consideration, in contrast to the almost complete randomization observed for toluene.[14]

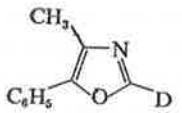


XIIa

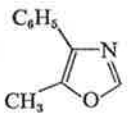
The spectra (Figs. 8 and 9) of 4-methyl-5-phenyloxazole (XIII) and 4-phenyl-5-methyloxazole (XIV) are quite different from each other (and from that of XII) and hence fragmentation does not proceed after the production of a common molecular ion. For example, *m/e* 103 from XIII is solely due to $C_8H_7^+$ (h.r., M—C_2H_2NO) [the spectrum (Table 1) of the 2-d_1-derivative XIIIa establishes the loss of the C-2 hydrogen atom in its formation, perhaps with phenyl migration as indicated by the dotted lines in XIII], while *m/e* 103 from XIV is solely due to $C_7H_5N^+$ [ionized benzonitrile]. This fragmentation also gives rise to a peak at *m/e* 103 in the spectrum of the 2-d_1-derivative XIVb (Table 1). In addition, *m/e* 104 from XIII is solely due to $C_8H_8^+$ (M—CO—HCN, h.r.), whereas the *m/e* 104 peak from XIV is solely due to $C_7H_4O^+$. The spectra of the labelled derivatives establish that the C-2 hydrogen is lost in the formation of these ions, but their origins are not simple.



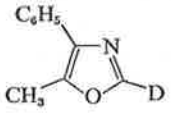
XIII



XIIIa



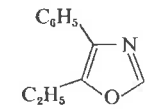
XIV



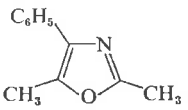
XIVa

Fragmentation of XIII also occurs via rupture of 2,3- and 4,5-bonds, but with charge retention by the oxygen-containing fragment ($C_8H_6O^+$, h.r., M—CH_3CN, *m/e* 118); the *m/e* 118 ion then decomposes by loss of carbon monoxide to *m/e* 90 (Fig. 8). As expected, the *m/e* 118 and *m/e* 90 ions of Fig. 8 are quantitatively shifted to *m/e* 119 and *m/e* 91 in the spectrum (Table 1) of XIIIa. In both spectra (Figs. 8 and 9), loss of CO from the molecular ion affords ions of mass *m/e* 131 which then undergo the pronounced loss of a hydrogen atom to *m/e* 130 (cf. also Fig. 7), although the *m/e* 130 ion is also formed in a one-step process from XIV. Surprisingly, a metastable peak at *m/e* 107·3 in the spectrum of XIVa establishes that XIVa loses CHO in the one-step process rather than CDO, this implying rearrangement in the molecular ion prior to this fragmentation. The *m/e* 105 ion from XIII (Fig. 8) is associated with the benzoyl ion ($C_6H_5C{\equiv}O^+$, h.r.).

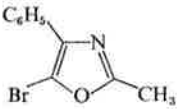
One of the most intriguing features of the spectra so far discussed is the marked tendency for many of the oxazoles (see Figs. 6–9) to eliminate carbon monoxide from the molecular ion. In the compounds hitherto described, this process has necessitated only the migration of a hydrogen atom, but it was considered of interest to study this reaction in compounds in which both positions 2 and 5 carried substituent groupings. A variety of additional oxazoles (XV–XXII) were therefore synthesized, the majority of which (XVI–XXII) carried alkyl, aryl or bromine substituents in both the 2- and 5-positions.



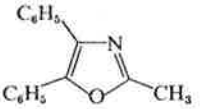
XV



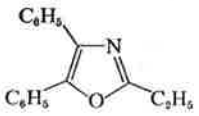
XVI



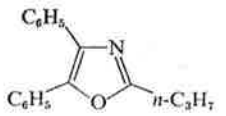
XVII



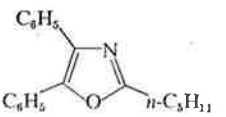
XVIII



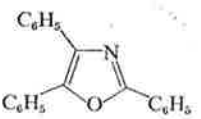
XIX



XX



XXI



XXII

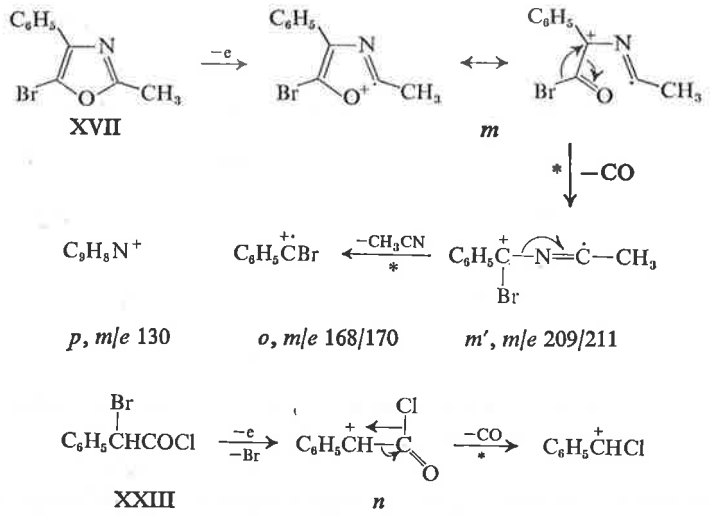
The abundances of the M-28 ions, and their compositions as established by high resolution measurements, are summarized in Table 4.

The data in Table 4 show that (i) the loss of carbon monoxide from the molecular ions of compounds containing ethyl or larger saturated alkyl substituents at C-2 or C-5 does not occur (XV, XX, XXI) or is a very minor process (XIX), (ii) when the substituents in both the 2- and 5-positions are methyl groups (XVI), no loss of CO

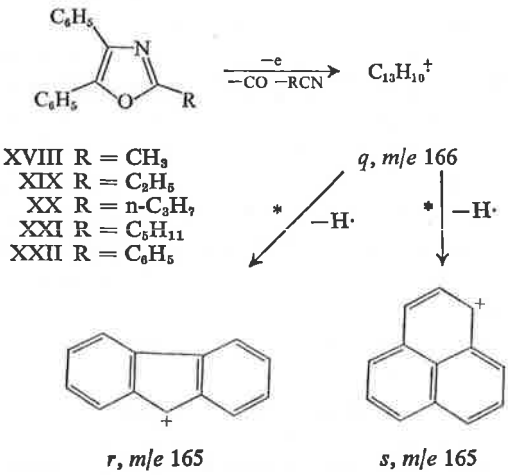
TABLE 4. ABUNDANCES AND COMPOSITIONS OF M-28 IONS FROM THE OXAZOLES XV–XXII

Compound	Rel. Ab. [M-28](%)	Composition
XV	1	M—C_2H_4
XVI	0	—
XVII	78	M—CO
XVIII	27	M—CO
XIX	2	M—CO
XX	72	M—C_2H_4
XXI	4	M—C_2H_4
XXII	23	M—CO

occurs but a metastable peak establishes the loss of ketene in a one-step process from the molecular ion to give *m/e* 131 (Table 1), (iii) if the C-5 substituent is bromine (XVII) or phenyl (XVIII, XXII) and any alkyl substituents present are not larger than methyl (XVII, XVIII), the loss of CO from the molecular ion is a prevalent process. The last point may be illustrated by reference to the spectra (Figs. 10 and 11) of 2-methyl-4-phenyl-5-bromo-oxazole (XVII) and 2-methyl-4,5-diphenyloxazole (XVIII). In the former spectrum (Fig. 10) all the peaks in the high mass region stem from the M—CO ion (*m/e* 209/211). Since the presence of methyl groups in both the 2- and 5-positions does not permit loss of CO from XVI, it must be concluded that bromine migrates prior to loss of CO from XVII and that phenyl groups migrate prior to the loss of CO from XVIII and XXII. Thus, if ionization of XVII occurs to some extent with ring opening to give *m*, then bromine migration to the carbonium ion centre with concerted loss of CO will afford *m'* (*m/e* 209/211). Such 1,2-shifts to carbonium ion centres generated upon electron impact are well established[15] (e.g. chlorine migration in the M—Br ion *n* from α-bromo-α-phenylacetyl chloride XXIII[16]). The decomposition of *m'* by loss of CH_3CN and Br, established by metastable peaks (Fig. 10), can then proceed to *o* and *p*.



Bond forming reactions also occur during the fragmentation of 4,5-diphenyloxazoles (XVIII–XXII) as evidenced by abundant ions of mass *m/e* 165 and 166 in their spectra (see Figs. 11 and 12, and Table 1). The *m/e* 165 ion ($C_{13}H_9^+$) corresponds to the base peak, or greater than 70% of the base peak abundance in all cases. Appropriate metastable peaks and low voltage spectra establish that the *m/e* 165 species are daughter ions of *m/e* 166 (*q*, $C_{13}H_{10}^{+\cdot}$), which formally originates from the two phenyl rings and one carbon atom of the oxazole nucleus.* The facile loss of a hydrogen atom is almost certainly associated with rearrangement to the fluorenyl cation *r* (*m/e* 165) or to the phenalenium cation *s* (*m/e* 165, by more extensive rearrangement). When R is ethyl or larger (XIX–XXI) fragmentation within the alkyl group may precede the formation of *m/e* 165 and 166, but in a number of the spectra metastable peaks suggest the formation of *m/e* 166 (and even *m/e* 165, see Fig. 12) from the molecular ion in a one step process. Such metastable peaks do not however exclude the operation of a two-step process.[16]



* The origin of *m/e* 165 ions in related systems will be the subject of a subsequent publication.

The analytical usefulness of the generalizations outlined in this paper are emphasized in the spectrum (Fig. 12) of 2-*n*-propyl-4,5-diphenyloxazole (XX). The large peak (*m/e* 235) due to loss of ethylene from the molecular ion, but only a small peak (*m/e* 234) due to loss of an ethyl radical, suggests the presence of a *n*-propyl substituent at C-2 (cf. Table 2), whereas the occurrence of the base peak at *m/e* 165 (*r* or *s*) is indicative of the two phenyl substituents. It is noteworthy that the M—C_2H_4 ion (*m/e* 235, Fig. 12) behaves in the same manner as the molecular ion of XVIII (Fig. 11) in sequentially eliminating CO and H to give *m/e* 207 ($C_{15}H_{13}N$, h.r.) and *m/e* 206 ($C_{15}H_{12}N$; h.r.). In an analogous manner 2-*n*-pentyl-4,5-diphenyloxazole sequentially eliminates C_4H_8, CO and H to give *m/e* 206 (Table 1). In the case of 2-ethyl-4,5-diphenyloxazole (XIX) such a sequence cannot operate, but the *m/e* 206 ion is still abundant (Table 1) and is apparently formed from the molecular ion by loss of an acetyl radical in a one-step process (metastable peak at *m/e* 170·3). Such a reaction would require extensive rearrangement in the molecular ion, and while this is not excluded, the sequential loss of CO and CH_3[16] would seem more plausible.

To summarise, the present study establishes that (i) the isomeric alkyl oxazoles studied give different spectra, in contrast to the behaviour of the simple alkyl benzenes; thus common intermediates are not generated from these isomeric alkyl oxazoles upon electron impact, (ii) deuterium atoms inserted into the oxazole nucleus, or incorporated in methyl groups attached to the oxazole nucleus, are not randomized with hydrogen atoms at other nuclear positions prior to the major fragmentation pathways, again in contrast to the simple alkyl benzenes, (iii) the position (2, 4 or 5) of an alkyl substituent (*n*-propyl or larger) is indicated by its characteristic fragmentation pattern, and (iv) the elimination of CO occurs even from the molecular ion of 2,5-disubstituted compounds, probably via ring opening to an ionized ketone and subsequent (or associated) migration of the C-5 substituent to C-4.

EXPERIMENTAL

Mass spectra were measured with an Hitachi Perkin-Elmer R.M.U. 6D mass spectrometer operating at 75 eV, with an inlet and source temperature of ca. 150°. Exact mass measurements were determined with an A.E.I. MS 9 mass spectrometer using a resolution of 15,000 (10% valley definition) with heptacosafluorotributylamine providing reference masses.

All samples (with the exception of XXII, which was recrystallized) were purified by preparative vapour phase chromatography (using a 30 ft SE 30 column) and were additionally checked by nuclear magnetic resonance spectroscopy.

The following compounds were synthesized by reported procedures: III,[17] IV,[17] X,[18] XII,[17] XIII,[18] XIV,[18] XV,[18] XVI,[17] XVIII,[19] XX,[17] XXI,[20] and XXII.[19]

3-*Hydroxybutan-2-one heptoate*. Potassium heptoate (39 g) was added to 3-bromobutan-2-one (34·5 g) in ethanol (150 ml) containing 2 drops of concentrated sulphuric acid, and the mixture stirred and heated under reflux for eight hours. Removal of the solvent under reduced pressure gave a yellow oil, which was distilled *in vacuo* to give 3-hydroxybutan-2-one heptoate (17 g, 37%), b.p. 126–128°/12 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{20}O_3$: C, 65·95; H, 10·05. Found: C, 65·6; H, 10·0%.)

2-*n-Hexyl*-4,5-*dimethyloxazole* (VII). 3-Hydroxybutan-2-one heptoate (17 g) and ammonium acetate (43 g) in glacial acetic acid (120 ml) were heated under reflux for two hours. The cooled solution was poured onto ice (200 g) and extracted with ether (4 × 100 ml). The ethereal extract was washed with aqueous sodium hydrogen carbonate and water, and dried (Na_2SO_4). After removal of the ether, the residual oil was distilled *in vacuo* to give 2-*n*-hexyl-4,5-dimethyloxazole (7·55 g, 48%), b.p. 91–92°/4·5 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{19}NO$. C, 72·9; H, 10·5; N, 7·7: Found: C, 72·9; H, 10·5; N, 7·6%.)

2-Hydroxynonan-3-one. To a stirred solution of n-hexyl lithium [from lithium (14 g) and n-hexylbromide (165 g)] in ether (500 ml) at −10° under nitrogen, was added a solution of lactic acid (20 g) in ether (100 ml) over a period of thirty minutes. The temperature was kept below −5° during the addition, then the mixture was stirred at 0° for three hours, allowed to rise to room temperature and stirred for an additional five hours. The solution was cooled to 0°, decomposed with water, and the ethereal layer separated. The ether layer was washed with aqueous sodium hydroxide (10%), dilute hydrochloric acid (2%), water, and then dried (Na_2SO_4). Removal of the ether under reduced pressure gave a yellow oil, which on distillation *in vacuo* gave 2-hydroxynonan-3-one (3·7 g, 12%), b.p. 85–87°/3·8 mm Hg. This compound was characterized as the acetate (prepared by treatment of the keto alcohol with acetic anhydride in pyridine), b.p. 96–97°/9 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{20}O_3$: C, 65·95; H, 10·05. Found: C, 66·35; H, 10·0%.)

4-n-Hexyl-2,5-dimethyloxazole (VI). 2-Hydroxynonan-3-one (5·3 g) acetyl chloride (7 ml) and pyridine (1·5 ml) were treated under reflux for thirty minutes. The solution was cooled, dry benzene (25 ml) added, the solvent removed under reduced pressure, and the crude ester remaining together with ammonium acetate (20 g) was dissolved in glacial acetic acid (70 ml) and heated under reflux for 1·5 hours. After cooling, the solution was poured onto ice (300 g), extracted with ether (2 × 100 ml), and the extract washed with aqueous sodium carbonate, water, and then dried (Na_2SO_4). Removal of the ether and distillation of the remaining oil *in vacuo* gave 4-*n*-hexyl-2,5-dimethyloxazole (2·8 g, 46%), b.p. 70–76°/2·6 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{19}NO$: C, 72·9; H, 10·5; N, 7·7. Found: C, 72·7; H, 10·4; N, 8·2%.)

5-n-Hexyl-2,4-dimethyloxazole (V). Prepared as for VI. 3-Hydroxynonan-2-one[25] (6·0 g) gave 5-n-hexyl-2,4-dimethyloxazole (1·7 g, 23%), b.p. 79–80°/4 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{19}NO$: C, 72·9; H, 10·5; N, 7·7. Found: C, 72·85; H, 10·4; N, 8·1%.)

5-Bromo-4-phenyloxazole (XI). To a stirred solution of 4-phenyloxazole[22] (14·5 g) in carbon tetrachloride (100 ml) containing dibenzoylperoxide (10 mg) was added N-bromosuccinimide (17·8 g) over a period of 2 hours at room temperature. The reaction mixture was stirred for a further two hours, filtered, the solvent removed, and the oil remaining was sublimed at 80°/0·05 mm Hg, giving 5-bromo-4-phenyloxazole (19·3 g, 86%), m.p. 44–45°. (*Anal.*: Calcd. for C_9H_6NOBr: C, 48·25; H, 2·7; N, 6·25; Br, 35·6. Found: C, 48·4; H, 3·0; N, 6·1; Br. 35·3%.) Treatment of 5-bromo-4-phenyloxazole with methyl magnesium iodide quantitatively produced 5-methyl-4-phenyloxazole (XIV) identical with an authentic specimen (V.P.C. and infrared spectrum).

5-Bromo-2-methyl-4-phenyloxazole (XVII). Prepared as for XI. 2-Methyl-4-phenyloxazole (6·4 g) gave 5-bromo-2-methyl-4-phenyloxazole (7·8 g, 83%) as a colourless solid, m.p. 54–56°, after sublimation (90°/0·1 mm Hg.). (*Anal.*: Calcd. for $C_{10}H_8NOBr$: C, 50·65; H, 3·4; N, 5·9; Br, 33·6. Found: C, 50·9; H, 3·65; N, 5·5; Br, 32·3%.) The NMR spectrum lacks the singlet at $\delta = 7{\cdot}67$ ppm indicative of the 5-H of the oxazole system.[22]

2-n-Pentyl-4,5-diphenyloxazole (XXI). A solution of benzoin hexoate (50 g) and ammonium acetate (62 g) in glacial acetic acid (150 ml) was heated under reflux for two hours. The solution was cooled, poured onto ice (300 g) and extracted with ether (4 × 100 ml). The ethereal extract was washed with aqueous sodium carbonate (10%), water, and dried (Na_2SO_4). After removal of the ether, the residual oil was distilled *in vacuo* to yield 2-*n*-pentyl-4,5-diphenyloxazole (28·6 g, 64%), b.p. 177–178°/0·6 mm Hg. (*Anal.*: Calcd. for $C_{20}H_{21}NO$: C, 82·6; H, 7·2; N, 4·8. Found: C, 82·2; H, 7·3; N, 5·0%.)

Isotopically labelled compounds

All labelled compounds were produced in high yield and purified by preparative vapour phase chromatography.

2-d_1-4-Phenyloxazole (Xa). 4-Phenyloxazole (0·29 g) was treated with *n*-butyl lithium [prepared from *n*-butyl bromide (0·68 g) and lithium (0·086 g) in ether (30 ml)] at −65° for two hours. Addition of deuterium oxide (5 ml) gave 2-d_1-4-phenyloxazole, b.p. 89-90°/4 mm.

5-d_1-2-Methyl-4-phenyloxazole (XIIa). 5-Bromo-2-methyl-4-phenyloxazole (0·48 g) was treated with *n*-butyl lithium [as for (Xa)] at −65° for ten minutes. Addition of deuterium oxide (5 ml) gave 5-d_1-2-methyl-4-phenyloxazole, m.p. 54–56°.

2-(d_1-Methyl)-4-phenyloxazole (XIIb). 2-Methyl-4-phenyloxazole (0·32 g) in ether (30 ml) was added to a stirred solution of *n*-butyl lithium [as for (Xa)] at −65°. Stirring was continued (at −65°) for 2·5 hours, then deuterium oxide (5 ml) added, yielding 2-(d_1-methyl)-4-phenyloxazole,

m.p. 54–56°. The NMR spectrum showed that all deuterium was incorporated into the methyl group.

2-*d*$_1$-4-*Methyl*-5-*phenyloxazole* (XIIIa). As for Xa. 4-Methyl-5-phenyloxazole (0·32 g) gave 2-d$_1$-4-methyl-5-phenyloxazole, b.p. 107–108°/3 mm Hg.

2-*d*$_1$-5-*Methyl*-4-*phenyloxazole* (XIVa). As for Xa. 5-Methyl-4-phenyloxazole (0·32 g) gave 2-d$_1$-5-methyl-4-phenyloxazole, b.p. 87–88°/0·05 mm Hg.

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Manuscripts should be typed in double line spacing on paper wider than 8½ inches and not deeper than 12 inches. Margins of at least 1½ inches must be left at the top, bottom and left-hand side of each page. The first page should also bear the name and full address of one author to whom the page proofs will be despatched in due course. All manuscripts should be submitted in triplicate, and in addition, a set of copies or prints of the diagrams must be attached to each copy of the manuscript. This will enable papers to be sent to two referees simultaneously and so assist rapid publication.

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References

References will be cited in the text by superior numbers and listed at the end of the article. They should be in the following form:

1. R. L. Baird and A. Aboderin, *J. Am. Chem. Soc.* **86**, 252 (1964).
2. H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds*, Holden-Day, San Francisco (1964).

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BENZO[*c*]CINNOLINE DERIVATIVES

IV.† SUBSTITUENT EFFECTS IN THE MASS SPECTRA OF SUBSTITUTED BENZO[*c*]CINNOLINES

By J. H. Bowie,‡ G. E. Lewis,‡ and J. A. Reiss‡

[*Manuscript received October* 16, 1967]

Summary

The mass spectra of a series of benzo[*c*]cinnoline derivatives are reported and discussed. The spectra are useful for analytical purposes, as all compounds give pronounced molecular ions, and the fragmentation processes generally occur without skeletal-rearrangement. Many benzo[*c*]cinnolines which are substituted in the 4-position may be differentiated from other isomers by the presence of "proximity-effects" in their mass spectra.

It has recently been shown,[1] that specific "ortho-effects"[2] operate between certain substituents (e.g. OMe, Me, and Ph) and the adjacent –N=N– moiety in the spectra of 3-substituted pyridazines and 1-substituted phthalazines. A series of benzo[*c*]cinnolines[3–8] has now been examined as a logical extension of this work; and the present paper deals with the behaviour of such compounds upon electron impact.

The spectra of the benzo[*c*]cinnolines (I–XXVI) are recorded in Figures 1–13 or Table 1, except that the spectra of (II), (V), (IX), (XVIII), and (XXI) are essentially similar to (III), (IV), (VIII), (XVII), and (XX), respectively, and are therefore not separately recorded. The compositions of ions determined by high-resolution measurements are listed in Table 2. The presence of an appropriate metastable ion for a process is depicted (in the text or a figure) by an asterisk.

† Part III, *Aust. J. Chem.*, 1968, **21**, 1097. This paper also constitutes Part XXIV in the series "Electron Impact Studies." Part XXIII, Bowie, J. H., Donaghue, P. F., Rodda, H. J., Cooks, R. G., and Williams, D. H., *Org. Mass Spectrometry*, in press.

‡ Department of Organic Chemistry, University of Adelaide, S.A. 5000.

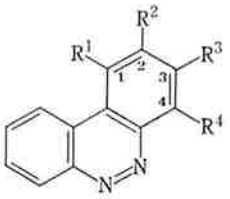
[1] Bowie, J. H., Cooks, R. G., Donaghue, P. F., Halleday, J. A., and Rodda, H. J., *Aust. J. Chem.*, 1967, **20**, 2677.
[2] McLafferty, F. W., and Gohlke, R. S., *Analyt. Chem.*, 1959, **31**, 2079.
[3] Lewis, G. E., and Reiss, J. A., *Aust. J. Chem.*, 1968, **21**, 1097.
[4] Badger, G. M., Drewer, R. J., and Lewis, G. E., *Aust. J. Chem.*, 1963, **16**, 1042.
[5] Badger, G. M., Joshua, C. P., and Lewis, G. E., *Aust. J. Chem.*, 1965, **18**, 1639.
[6] Lewis, G. E., and Reiss, J. A., *Aust. J. Chem.*, 1967, **20**, 2217.
[7] Badger, G. M., Drewer, R. J., and Lewis, G. E., *Aust. J. Chem.*, 1964, **17**, 1036.
[8] Lewis, G. E., and Reiss, J. A., *Aust. J. Chem.*, 1968, **21**, 1043.

TABLE 1

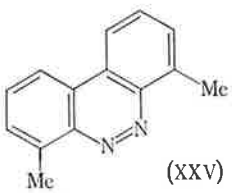
MASS SPECTRA OF (I), (III), (IV), (VI), (VII), (XX), (XXII), AND (XXV)

All peaks greater than 5% of the base peak (100%) are recorded

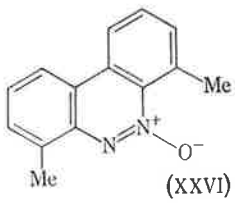
(I)	*m/e*	39	50	51	63	74	75	76	87	98	99	102	126	150	151	152	153
	I (%)	7	10	6	15	11	11	13	8	5	6	6	9	11	42	100	14
	m/e	180(M)	181														
	I (%)	67	11														
(III)	*m/e*	39	50	51	62	63	69·5	74	75	81·5	82	82·5	87	89	97	115	
	I (%)	10	8	9	7	15	12	8	9	8	14	18	7	6	6	9	
	m/e	139	163	164	165	166	167	194(M)	195								
	I (%)	19	18	18	100	43	6	93	16								
(IV)	*m/e*	50	51	62	63	74	75	75·5	76	77	80	86	87	93	94	98	99	100
	I (%)	8	8	12	8	16	36	14	8	6	6	7	8	18	6	10	12	5
	m/e	101	125	149	150	151	152	186	187	188	214(M)	215	216(M)	217				
	I (%)	5	11	7	51	80	12	79	13	27	100	16	35	6				
(VI)	*m/e*	39	51	63	69·5	70·5	76	83·5	89	113	115	139	140	141	165			
	I (%)	7	6	10	8	8	6	16	8	6	6	50	22	6	10			
	m/e	166	167	168	195(M)	196												
	I (%)	27	48	6	100	16												
(VII)	*m/e*	39	42	44	50	51	52	62	63	75	76	77	78	86	87	88	89	98
	I (%)	24	26	7	7	22	6	14	29	24	30	19	14	13	22	10	11	13
	m/e	99	100	102	113	125	126	127	138	139	150	151	152	153	164			
	I (%)	15	7	7	11	9	19	11	8	23	42	62	100	32	17			
	m/e	165	166	167	178	179	180	181	193	194	195	208	222	223(M)				
	I (%)	24	11	11	18	30	61	10	28	23	19	6	13	77				
	m/e	224																
	I (%)	12																
(XX)	*m/e*	50	51	62	63	74	75	75·5	76	77	89·5	98	99	125	150	151		
	I (%)	8	11	8	8	13	30	30	15	13	7	7	8	8	42	92		
	m/e	152	165	179	180	207	238(M)	239										
	I (%)	20	6	77	13	10	100	19										
(XXII)	*m/e*	51	63	74	75	75·5	98	99	125	139	150	151	152	179	180	181		
	I (%)	7	6	8	17	14	6	6	6	10	27	55	18	8	100	17		
	m/e	207	238(M)	239														
	I (%)	9	26	6														
(XXV)	*m/e*	39	51	63	76	88	89	104	139	151	152	163	164	165	166	176		
	I (%)	8	7	11	17	6	11	7	6	7	15	7	6	53	8	8		
	m/e	177	178	179	180	207	208(M)	209										
	I (%)	7	30	25	28	9	200	18										



	R^1	R^2	R^3	R^4		R^1	R^2	R^3	R^4
(I)	H	H	H	H	(XIII)	H	OMe	H	H
(II)	H	Me	H	H	(XIV)	H	H	H	OMe
(III)	H	H	H	Me	(XV)	H	OEt	H	H
(IV)	H	Cl	H	H	(XVI)	H	H	H	OEt
(V)	H	H	H	Cl	(XVII)	H	CO_2H	H	H
(VI)	H	NH_2	H	H	(XVIII)	H	H	CO_2H	H
(VII)	NMe_2	H	H	H	(XIX)	H	H	H	CO_2H
(VIII)	H	NMe_2	H	H	(XX)	H	CO_2Me	H	H
(IX)	H	H	NMe_2	H	(XXI)	H	H	CO_2Me	H
(X)	H	H	H	NMe_2	(XXII)	H	H	H	CO_2Me
(XI)	H	NEt_2	H	H	(XXIII)	H	CO_2Et	H	H
(XII)	H	H	H	NEt_2	(XXIV)	H	H	H	CO_2Et



(XXV)



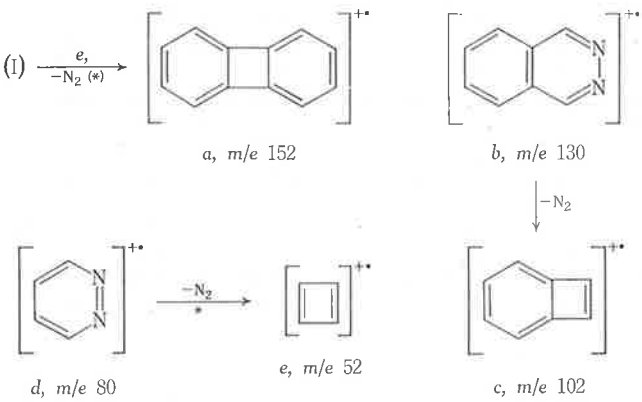
(XXVI)

TABLE 2

COMPOSITIONS OF SOME IONS IN THE SPECTRA OF (I–XXVI)

Compound	*m/e*	Composition
(X)	194	$C_{14}H_{12}N$
	180	$C_{12}H_8N_2$ (45%) $C_{13}H_{10}N$ (55%)
	179	$C_{12}H_7N_2$ (40%) $C_{13}H_9N$ (60%)
(XI)	208	$C_{13}H_{10}N_3$
	180	$C_{13}H_{10}N$
	179	$C_{13}H_9N$
	178	$C_{13}H_8N$
(XII)	222	$C_{14}H_{12}N_3$
	180	$C_{12}H_8N_2$
(XIII)	181	$C_{12}H_9N_2$
(XV)	196	$C_{12}H_8N_2O$
	168	$C_{12}H_8O$
(XVI)	196	$C_{12}H_8N_2O$
	180	$C_{12}H_8N_2$
	168	$C_{12}H_8O$
(XXIII)	224	$C_{13}H_8N_2O_2$
	196	$C_{13}H_8O_2$
	179	$C_{12}H_7N_2$ (65%) $C_{13}H_7O$ (35%)
(XXV)	196	$C_{13}H_{12}N_2$

Benzo[*c*]cinnoline (I) fragments by loss of nitrogen from the molecular ion (*m/e* 180) to produce the stable diphenylene radical ion [*a*, *m/e* 152 (base peak)]. In comparison, the production of *c* (*m/e* 102) from the phthalazine molecular ion (*b*) is a minor process (the major fragmentation being M−HCN−HCN),[1] and loss of nitrogen from the pyridazine molecular ion (*d*) produces the cyclobutadiene radical ion *e* (11% of the base peak), which readily loses a hydrogen atom to form $C_4H_3^+$ (*m/e* 51).[1,9] Cyclobutadiene and substituted cyclobutadiene radical ions are also common fragments in the spectra of a variety of quinones.[10–13]

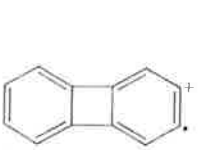


Loss of nitrogen from either the molecular ion or a fragment ion is a feature of all spectra, and is therefore indicative of the presence of the –N=N– group. In the spectra of the 1-, 2-, or 3-substituted benzo[*c*]cinnolines, the $M-N_2$ process precedes fragmentation through Me, Cl, NH_2, NMe_2, or CO_2H substituents, but when the substituent is MeO, EtO, NEt_2, CO_2Me, or CO_2Et, fragmentation through the substituent occurs before the loss of nitrogen. A detailed discussion of the normal fragmentations of these substituents when attached to an aromatic ring is not necessary here, as a compendium of such processes is available.[14] The various fragmentations are also outlined in Figures 1, 3, 5, 7, 9, and 11.

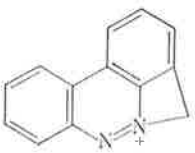
The spectra of 4-substituted benzo[*c*]cinnolines are entirely different from those of their 1-, 2-, or 3-isomers when the substituent is NR_2 (R = Me or Et), OR (R = Me or Et), or COOR (R = H, Me, or Et). These differences are due to "proximity-effects" (analogous to "ortho-effects", except that the interacting groups are not *ortho* to each other) which operate by specific interaction between the various substituents and the –N=N– grouping. Interaction between the 4-chloro group and the

[9] Benn, M. H., Sorensen, T. S., and Hogg, A. M., *Chem. Commun.*, 1967, 573.
[10] Beynon, J. H., and Williams, A. E., *Appl. Spectrosc.*, 1960, **14**, 156.
[11] Bowie, J. H., Cameron, D. W., Giles, R. G. F., and Williams, D. H., *J. chem. Soc.* (*B*), 1966, 335.
[12] Bowie, J. H., Cameron, D. W., and Williams, D. H., *J. Am. chem. Soc.*, 1965, **87**, 5094.
[13] Di Mari, S. J., Supple, J. H., and Rapoport, H., *J. Am. chem. Soc.*, 1966, **88**, 1226.
[14] Budzikiewicz, H., Djerassi, C., and Williams, D. H., "Mass Spectrometry of Organic Compounds." (Holden-Day: San Francisco 1967.)

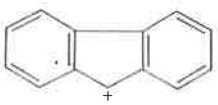
adjacent nitrogen would not be expected (cf.[15]) as the process M—Cl· would not form a particularly stable cation. The spectra (Table 1) of 2- and 4-chlorobenzo[*c*]cinnoline (IV and V) are very similar. The fragmentation process M—N_2—Cl·—H·, produces an ion most plausibly represented as *f* (*m/e* 150). The spectra (Table 1) of 2- and 4-methylbenzo[*c*]cinnoline (II and III) are also very similar. This result was not expected, as M—H· ions are a feature of the spectra of 3-methylpyridazine and 1-methylphthalazines,[1] and the formation of *g* (*m/e* 193) was predicted. The absence of this ion may be attributed to the formation of the very stable fluorene cation [*h*, *m/e* 165 (base peak)] by the process M—N_2—H·.



f, *m/e* 150



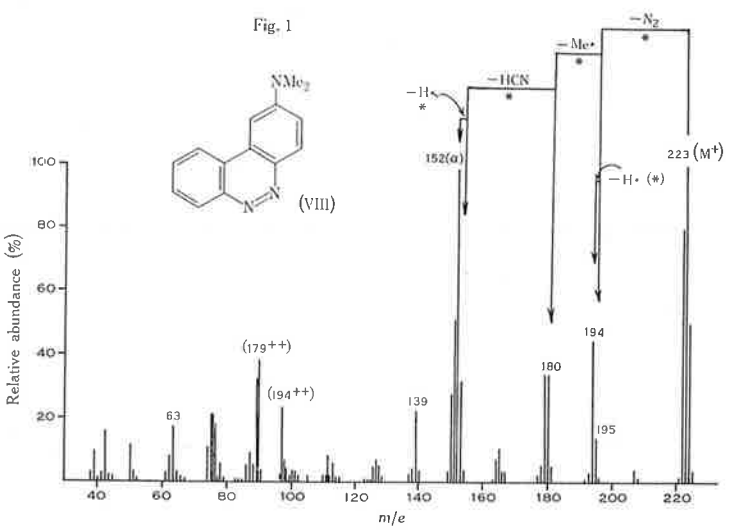
g, *m/e* 193



h, *m/e* 165

Three different types of "proximity-effect" are observed in the spectra of benzo[*c*]cinnolines substituted at the 4-position. The first can be seen in the spectra (Figs. 1–4 or Table 1) of the isomeric dimethylamino- (VII–X) and diethylamino-benzo[*c*]cinnolines (XI and XII). The spectra of 1-, 2-, and 3-dimethylaminobenzo[*c*]-

Fig. 1

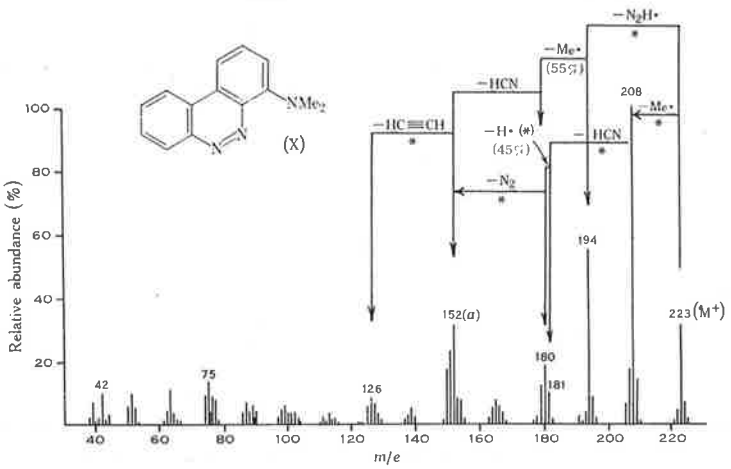


cinnoline (VII–IX) (apart from differences in the relative abundances of ions) are essentially similar. The biphenylene radical ion (*a*) is the base peak of each spectrum; and it is produced by the process M—N_2—Me·—HCN—H· (see Fig. 1). This process is also noted in the spectrum of the 4-isomer (X) although more pronounced processes

[15] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *J. chem. Soc.* (*B*), 1967, 621.

are indicated in Figure 2. The base peak of this spectrum is now produced by the process M—Me·. The differences between the spectra (Figs. 3 and 4) of 2- and 4-diethylaminobenzo[*c*]cinnoline (XI and XII) are even more striking. The major

Fig. 2



process (M—Me· —C_2H_4—N_2—H· —HCN) in the spectrum (Fig. 3) of the 2-isomer is completely absent in that (Fig. 4) of the 4-isomer. The base peak of the latter is produced by loss of an ethyl radical from the molecular ion to form *m/e* 222, which then decomposes to the biphenylene radical ion (*a*) by successive loss of Me·, HCN, and N_2.

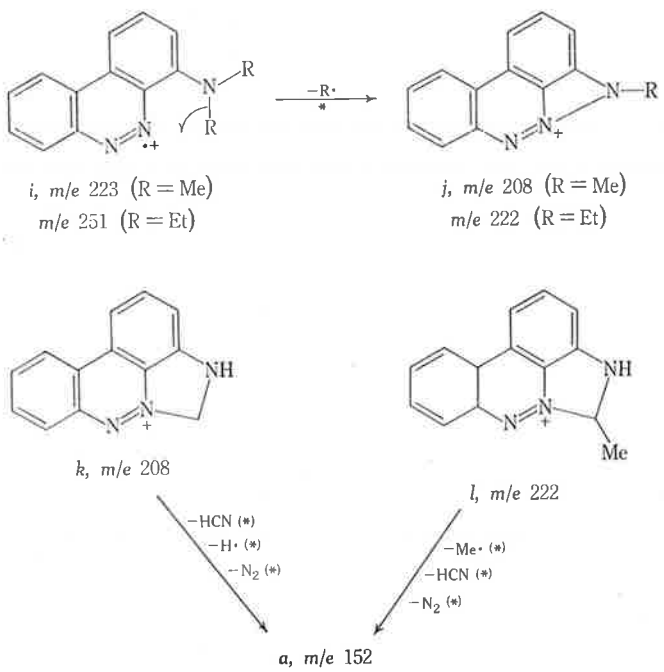


Fig. 3

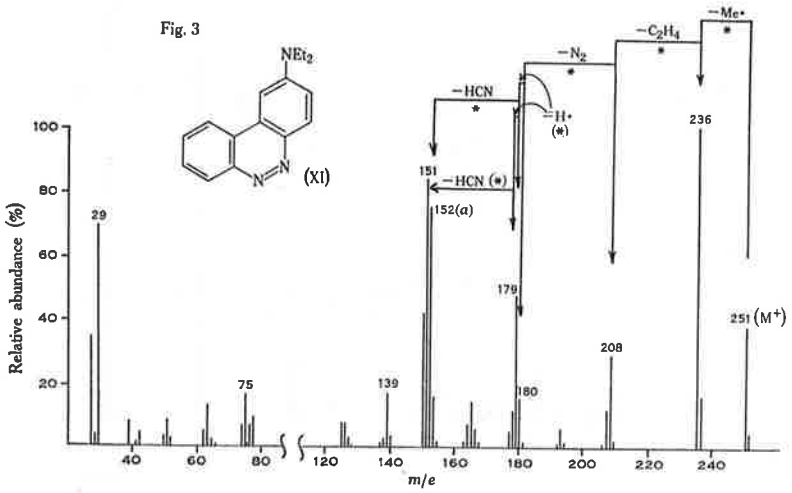


Fig. 4

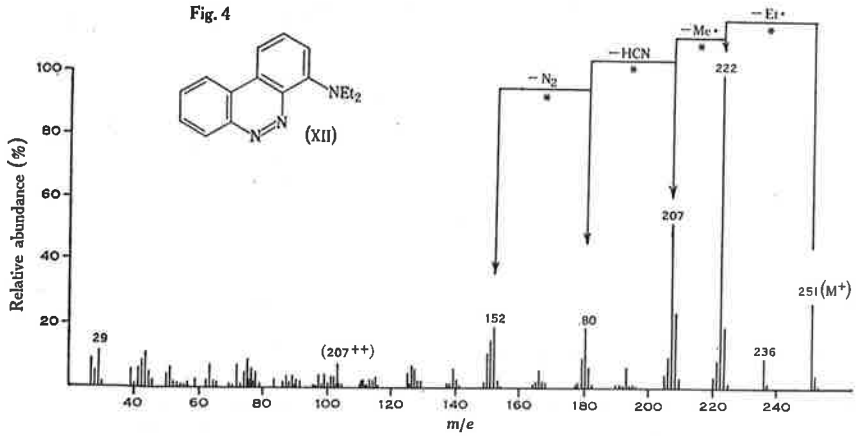


Fig. 5

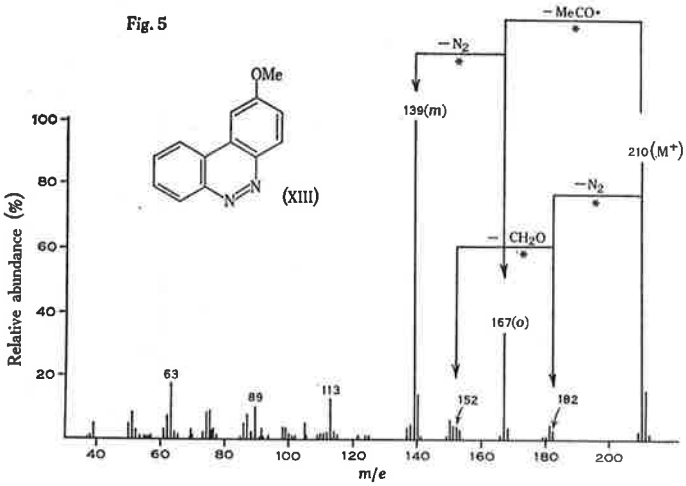


Fig. 6

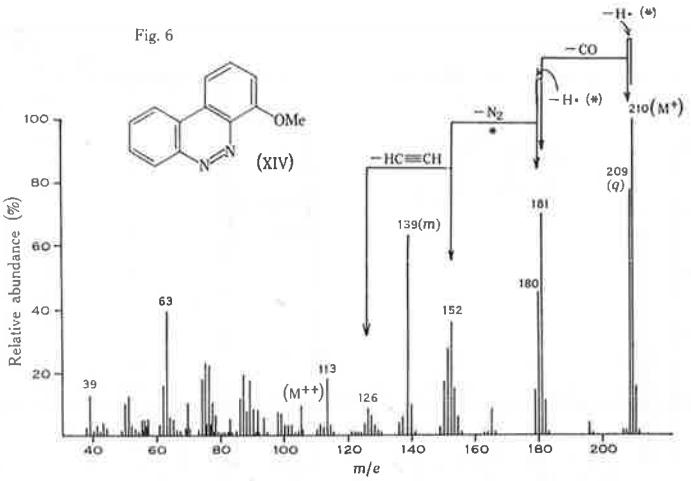


Fig. 7

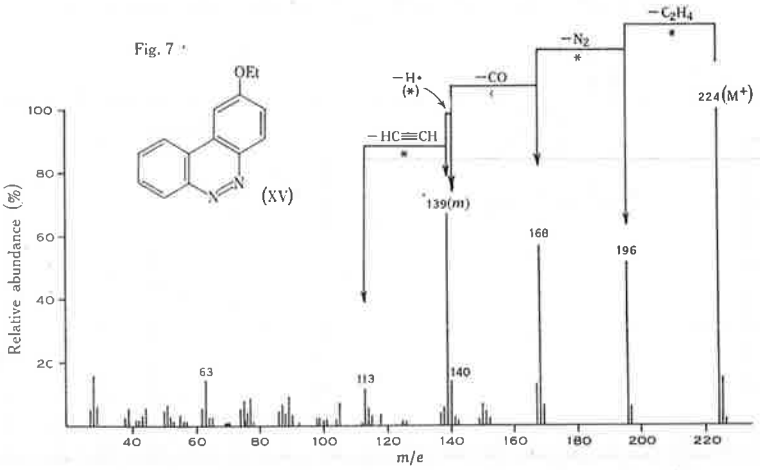
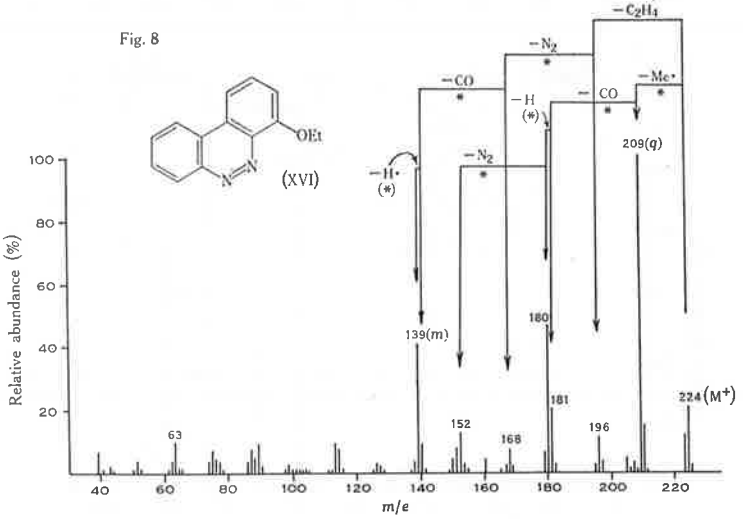
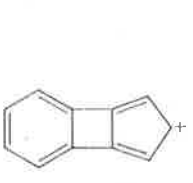


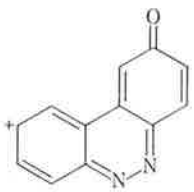
Fig. 8



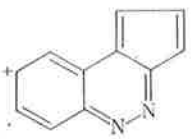
There are two ways of rationalizing this behaviour. Loss of either a methyl radical [from (X)] or an ethyl radical [from (XII)] may form the stable cations *j*. This involves the formation of a four-membered ring. Alternatively hydrogen-transfer to nitrogen followed by ring closure may form *k* [from (X)] or *l* [from (XII)]. Although formation of the five-membered ring system is analogous to the behaviour of 4-alkoxybenzo[*c*]cinnolines on electron impact, there is no way of distinguishing between the two alternative structures, as either may decompose further to the biphenylene radical ion (either $i \rightarrow a$ or k and $l \rightarrow a$) by the processes outlined in Figures 2 and 4.



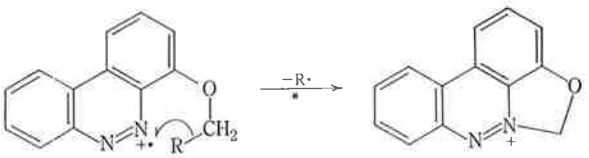
m, *m/e* 139



n, *m/e* 195



o, *m/e* 167



p, *m/e* 210 (R = H)
m/e 224 (R = Me)

q, *m/e* 209

The second "proximity-effect" can be seen from a comparison of the spectra (Figs. 5–8) of the alkoxybenzo[*c*]cinnolines (XIII–XVI). 2-Methoxybenzo[*c*]cinnoline (XIII) fragments by the process M—MeCO· —N_2 to form *m*, *m/e* 139 (base peak). The process M—43 is noted in the spectra of aromatic methoxy compounds when the normal process (M—Me· —CO) is energetically unfavourable. This may be because of the instability of the M—15 species,[16,17] or when loss of an acetyl radical produces an exceptionally stable cation.[18] In this case (XIII) the M—43 ion may arise by a combination of both effects, as the M—15 ion *n* (which is not observed in Fig. 5) would not be particularly unstable, and the M—43 ion (e.g. *o*) is not very stable, as it readily decomposes (by loss of nitrogen) to form *m*. These processes are not observed in the spectrum (Fig. 6) of the 4-methoxy isomer (XIV). Instead, the fragmentation scheme M—H· —CO—H· —N_2 (to *a*) is observed. 2-Ethoxybenzo[*c*]cinnoline (XV) fragments by the scheme M—C_2H_4—N_2—CO, as indicated in Figure 7. Although this process is also noted in the spectrum (Fig. 8) of the 4-isomer (XVI), the major breakdown occurs through the M—Me· species (*m/e* 209, base peak). The processes

[16] Bowie, J. H., and Cameron, D. W., *Aust. J. Chem.*, 1966, **19**, 1627.
[17] Clugston, D. M., and MacLean, D. B., *Can. J. Chem.*, 1966, **44**, 781.
[18] Barnes, C. S., Collins, D. J., Hobbs, J. J., Mortimer, P. I., and Sasse, W. H. F., *Aust. J. Chem.*, 1967, **20**, 699.

occurring in the mass spectra of the 4-alkoxy derivatives may be explained by β-cleavage to oxygen and concomitant C–N bond formation to give the stable cation *q* (*m/e* 209). This species then fragments to the biphenylene radical ion (*a*) as indicated in Figs. 6 and 8.

Fig. 9

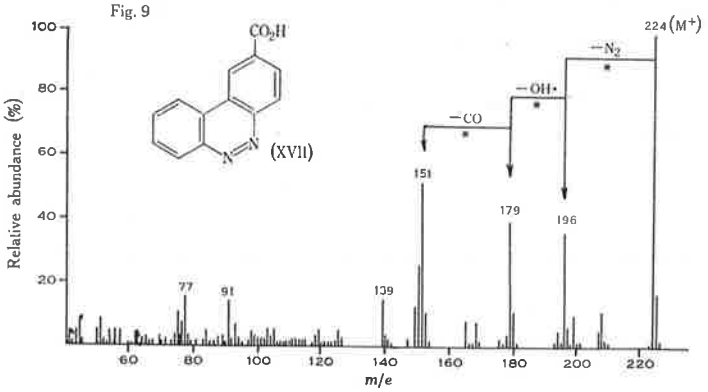


Fig. 10

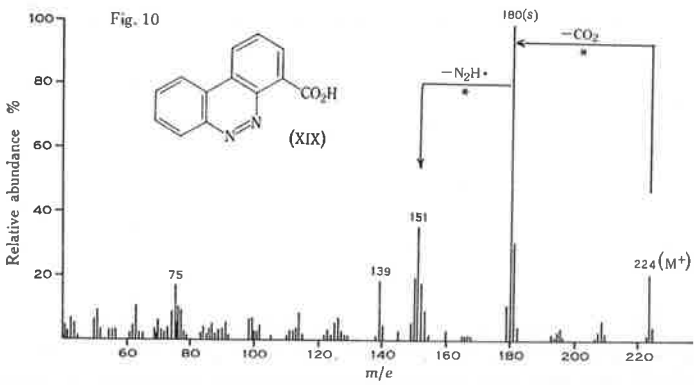
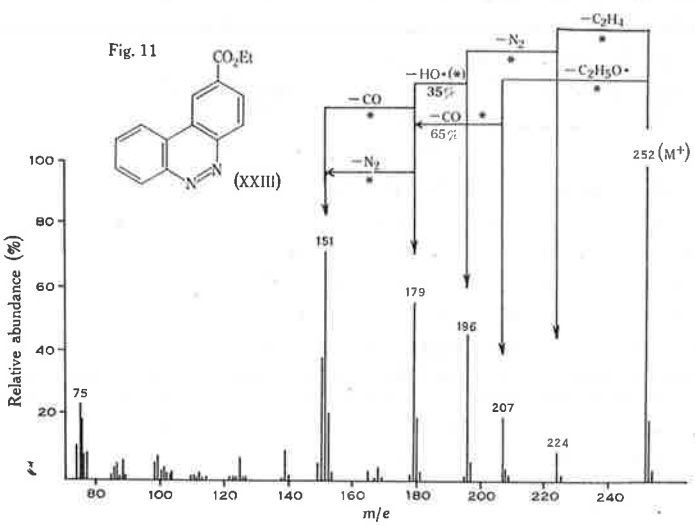
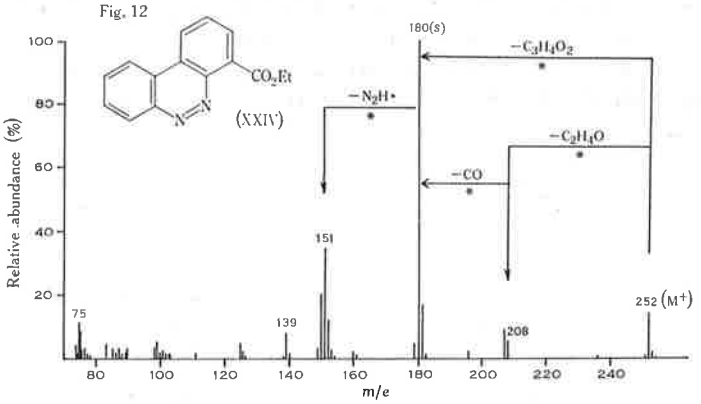


Fig. 11

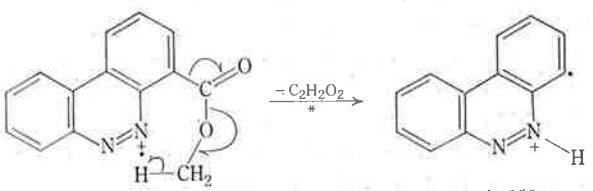


The third "proximity-effect" operates in the spectra of 4-carboxy-, methoxycarbonyl-, and ethoxycarbonyl-benzo[c]cinnoline. Again, the spectra of the 2- and 4-isomers are entirely different (see Figs. 9–12). 2- and 3-Carboxybenzo[c]cinnoline

Fig. 12



(XVII and XVIII) fragment by the scheme $M-N_2-OH\cdot-CO$ (to *m/e* 151, $C_{12}H_7^+$) while 4-carboxybenzo[c]cinnoline (XIX) loses carbon dioxide from its molecular ion to form the base peak of the spectrum [(XIX) does not decarboxylate thermally below 250°]. An exactly similar situation occurs when the substituent is methoxycarbonyl. Although 2- and 3-methoxycarbonylbenzo[c]cinnoline (XX and XXI) fragment by the normal process $M-MeO\cdot-CO-N_2$ (Table 1), the 4-isomer fragments by loss of the ester group with hydrogen rearrangement to again give *m/e* 180 (base peak). The spectrum (Fig. 11) of 2-ethoxycarbonylbenzo[c]cinnoline (XXIII) is quite complex. Processes observed are: (*a*) $M-EtO\cdot-CO-N_2$ [analogous to (XX) and (XXI)] and (*b*) $M-C_2H_4$ to form the 2-carboxybenzo[c]cinnoline molecular ion, (*m/e* 224), which decomposes as indicated in Figure 9. The 4-ethoxycarbonyl derivative (XXIV) behaves analogously to (XIX) and (XXII). Loss of the ester group with hydrogen rearrangement gives the base peak of the spectrum.

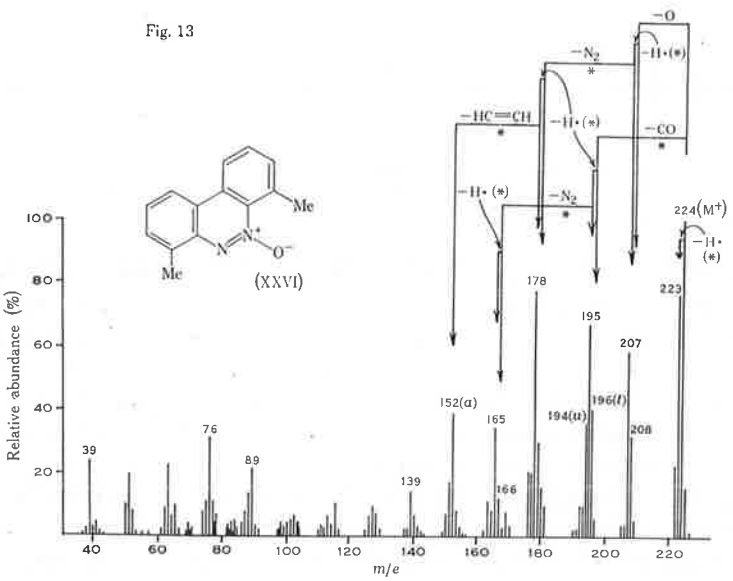


r, *m/e* 238 *s*, *m/e* 180

The hydrogen rearrangement in all three cases produces the same ion, *m/e* 180. This ion is either the benzo[c]cinnoline molecular ion or one of isomeric structure. Comparison of the decomposition of *m/e* 180 and the benzo[c]cinnoline molecular ion (Table 1) show the two fragmentations to be quite different, viz. *m/e* $180-N_2H$ (to *m/e* 151) is observed in the spectra of (XIX), (XXII), and (XXIV), while $M-N_2$ occurs in the spectrum of (I). Even when the energy of the electron beam is lowered

to 15 eV, the process $M-N_2$ is still pronounced in the spectrum of (I). Consequently, it seems plausible that *m/e* 180 in the spectra of (XIX), (XXII), and (XXIV) is best represented as *s*. This ion probably decomposes by loss of $N_2H\cdot$ before rearrangement to the benzo[*c*]cinnoline molecular ion occurs. The elimination of CO_2, $C_2H_2O_2$, or $C_3H_4O_2$ [in the spectra of (XIX), (XXII), and (XXIV) respectively] with accompanying hydrogen rearrangement to nitrogen, is not necessarily a concerted process (e.g. $r \rightarrow s$), and apart from the observation that an ionized nitrogen is available to accept the hydrogen atom, no concrete proposal can be advanced to rationalize this characteristic fragmentation.

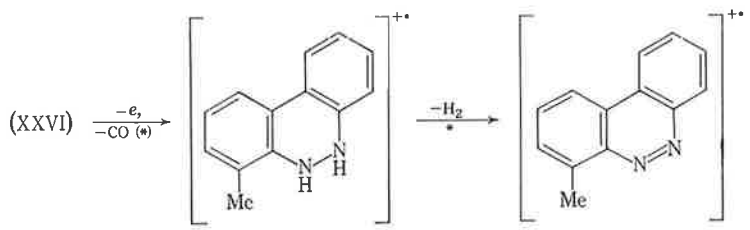
Fig. 13



It has recently been shown that skeletal-rearrangement fragments are present in the spectra of azoxybenzenes,[19,20] and phenazine *N*-oxides,[21] but absent in the mass spectrum of benzo[*c*]cinnoline *N*-oxide.[21] The spectrum (Fig. 13) of 4,7-dimethylbenzo[*c*]cinnoline *N*-oxide (XXVI) is notable for the presence of fragmentations involving the initial formation of an M—CO ion. As no similar loss is noted in the spectrum of benzo[*c*]cinnoline *N*-oxide, this skeletal-rearrangement probably involves the 4-methyl group. Loss of carbon monoxide involves a complex triple hydrogen rearrangement, possibly to form an ion *t* (*m/e* 196) which may either decompose by loss of a hydrogen radical to the protonated 4-methylbenzo[*c*]cinnoline cation (*m/e* 195), or by loss of hydrogen to form the 4-methylbenzo[*c*]cinnoline molecular ion (*u*) which may decompose by loss of nitrogen and a hydrogen radical to form the fluorene cation (*h*, *m/e* 165). The presence of these processes again illustrates the complex

[19] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *Chem. Commun.*, 1967, 284.
[20] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *Aust. J. Chem.*, 1967, **20**, 1601.
[21] Bowie, J. H., Cooks, R. G., Jamieson, N. C., and Lewis, G. E., *Aust. J. Chem.*, 1967, **20**, 2545.

skeletal reorganization that can occur when aromatic *N*-oxides are subjected to electron impact.



t, *m/e* 196 *u*, *m/e* 194

Experimental

All mass spectra were measured with an Hitachi Perkin–Elmer RMU 6D double-focusing mass spectrometer operating at 75 eV, with the source and inlet temperatures at *c.* 200°. The spectra of (XVII–XIX) were determined by the direct insertion technique with the source at *c.* 150°. Exact mass measurements were carried out at a resolution of 8,000 using heptacosafluorotributylamine to provide reference masses.

The benzo[*c*]cinnolines examined have been reported in other publications, as indicated: (I–III), (XXV), and (XXVI);[4] (IV), (V), and (XVII–XXI);[7] (VI);[5] (VII–XI);[6] (XII);[8] (XIII–XVI) and (XXII–XXIV).[3]

Acknowledgments

One of us (J.A.R.) gratefully acknowledges the award of a Commonwealth Postgraduate Scholarship. Our sincere thanks are expressed to Mr Derek Cobb for skilful assistance in obtaining some of the spectra. The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

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Studies on enethiols

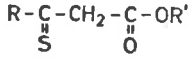
II. Mass spectra of β-thioketoesters

By F. DUUS, S.-O. LAWESSON, J. H. BOWIE and R. G. COOKS

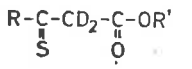
ABSTRACT

The fragmentation patterns observed in the mass spectra of β-thioketoesters have been studied with the aid of deuterium labelling studies and high resolution data. The spectra are significantly different from those of β-ketoesters, in that concerted hydrogen rearrangement (via a six or four membered transition state) in the enethiol form of the molecular ion produces an alcohol radical ion.

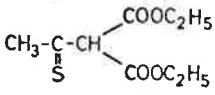
As a continuation[1] of our studies of the mass spectra of sulphur compounds [1] we have synthesized a series of β-thioketoesters (I–XV) and have determined their mass spectra (Figs. 1–13). This paper is primarily concerned with a comparison of the fragmentation modes exhibited by β-ketoesters [2–4] and β-thioketoesters upon electron impact. High resolution data are summarised in Table 1. The presence of a metastable ion for a process is indicated in the text and figures by an asterisk.



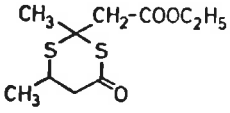
	R	R'
I	CH_3	C_2H_5
II	CH_3	CD_2CH_3
III	CH_3	CH_2CD_3
IV	CH_3	$n\text{-}C_3H_7$
V	CH_3	$n\text{-}C_4H_9$
VI	CH_3	$CH_2\text{-}C_6H_5$
VII	C_6H_5	C_2H_5
VIII	$C_2H_5OCOCH_2$	C_2H_5



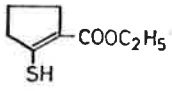
	R	R'
IX	CH_3	C_2H_5
X	C_6H_5	C_2H_5



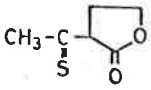
XI



XII



XIII R=H
XIV R=D



XV

[1] Part I: see ref. [18]. This paper is also considered as Part XXV in the series Electron Impact Studies. For Part XXIV, see J. H. Bowie, G. E. Lewis, and J. A. Reiss, *Austral. J. Chem.* (in press).

Table 1. Composition of some ions in the spectra of I–XV.

Compound	*m/e*	Composition
I	31	CH_3O
	59	C_2H_3S
	60	C_3H_8O (40 %)
		Isotope (60 %)
	72	C_3H_4S
	73	C_3H_5S (50 %)
		$C_3H_5O_2$ (25 %)
		C_4H_9O (5 %)
	74	C_2H_6S
	100	C_4H_4OS
	101	C_4H_5OS
	102	C_4H_6OS (50 %)
		Isotopes (50 %)
II	31	CH_3O
	32	$C_2H_4D_2$ (85 %)
		CH_2DO (7 %)
		S (8 %)
III	31	CH_3O (35 %)
		$C_2H_3D_2$ (65 %)
	32	$C_2H_4D_2$ (70 %)
		CH_2DO (15 %)
		S (15 %)
	33	CHD_2O
IV	59	C_2H_3S (70 %)
		C_3H_7O (30 %)
V	73	C_3H_5S (85 %)
		C_4H_9O (15 %)
VII	31	CH_3O
	90	C_7H_6
	91	C_7H_7
	102	C_8H_6
	103	C_8H_7
	134	C_8H_6S
	135	C_8H_7S
	136	C_8H_8S
VIII	85	C_3HOS (85 %)
		$C_4H_5O_2$ (15 %)
	88	C_3H_4OS (50 %)
		$C_4H_8O_2$ (50 %)
	98	C_4H_2OS
	100	C_4H_4OS
	116	$C_4H_4O_2S$
	127	$C_5H_3O_2S$
	144	$C_6H_8O_2S$ (70 %)
		$C_5H_4O_3S$ (30 %)
	172	$C_7H_8O_3S$
XI	31	CH_3O
	85	$C_4H_5O_2$ (40 %)
		C_3HOS (40 %)
		C_4H_5S (20 %)
	100	C_4H_4OS
	116	$C_4H_4O_2S$
	126	$C_5H_2O_4$
	144	$C_6H_8O_2S$ (60 %)
	146	$C_6H_{10}O_2S$
	172	$C_7H_8O_3S$
XII	146	$C_6H_{10}O_2S$
	203	$C_6H_{11}O_2S_2$
	218	$C_9H_{14}S_2O_2$
XV	53	C_4H_5
	59	C_2H_3S
	65	C_5H_5
	67	C_4H_3O
	69	C_3HS (90 %)
		C_4H_5O (10 %)
	71	C_3H_3S
	85	C_4H_5S
	98	C_5H_6S
	99	C_5H_7S
	115	C_5H_7OS

The major processes in the spectrum [2] of ethyl acetoacetate are M–CO (6 % of the base peak, skeletal-rearrangement process-loss from the ketone moiety), M–CH_2CO (21 %), M–EtO$^{\cdot}$ (19 %), M–EtOH (29 %), and the formation of the acetyl cation (*m/e* 43, base peak). The spectrum (Fig. 1) of ethyl thioacetoacetate is strikingly different from that of ethyl acetoacetate. The processes M–CH_2CS and M–CS (analogous to M–CH_2CO and M–CO, respectively) are not observed, the Me–C≡S$^+$ species constitutes only 69 % of the base peak (cf. Me–C≡O$^+$– base peak), and the base peak of the spectrum is produced by the process M–EtOH. In addition, a pronounced ion at *m/e* 31 (MeO$^+$) is observed. Other processes are outlined in Fig. 1.

Pronounced M–R′OH ions are observed in the spectra of the esters (I–VIII), (XI), and (XIII), this process producing the base peak in the spectra of I–III, V, and XIII. Prominent MeO$^+$ ions are observed in the spectra of I–V, VII, VIII, XI, and XIII, and this peak is the base peak in the spectra of IV, VIII, and XI. The latter process

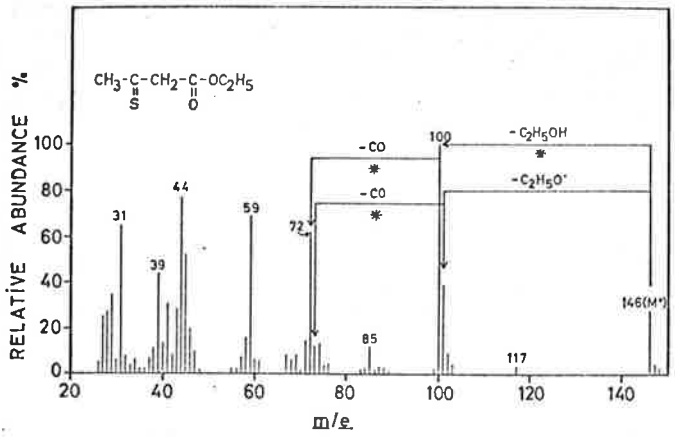
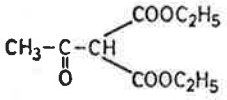


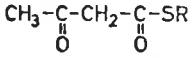
Fig. 1.

has been briefly mentioned in a previous communication [6]. The relative abundances of M–R′OH and m/e 31 ions are summarised in Table 2.

In general, m/e 31 peaks are either small or absent in the spectra of β-ketoesters [2, 5]. There are several exceptions to this general rule; viz. allyl acetoacetate (MeO^+ = 24 %) [4], t-butyl acetoacetate (30 %) [5], XVI (21 %) [5], and several other compounds having more than one ester group [5]. The M–EtOH process and the production of the MeO^+ ion in the spectra of β-thioketoesters may be plausibly explained by either of the concerted processes $a \rightarrow c + d$ or $b \rightarrow c + d$. It has been suggested [4] that the formation of the thiol radical ion in the spectra of esters of the general formula XVII possibly proceeds via a four membered transition state (cf. $b \rightarrow c + d$), but as β-thioketoesters to great extent exist on the thiol form [18], there may be a significant contribution from the process $a \rightarrow c + d$. The relative formation of b and c will depend on their stability; e.g. the allyl alcohol and t-butanol radical ions will be more stable than the ethyl alcohol radical ion (see above). The formation of the ethanol, propanol, butanol, and benzyl alcohol radical ions would account for the formation of



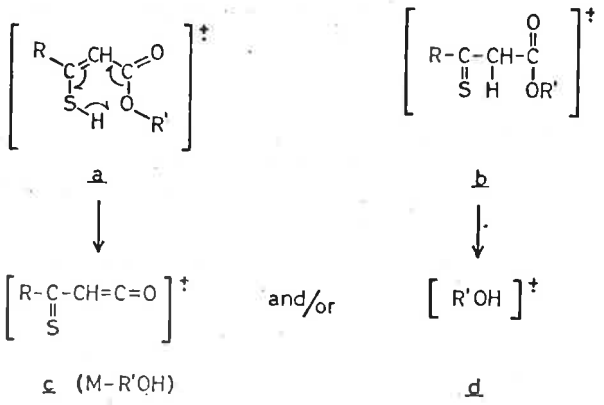
XVI



XVII

Table 2. Relative abundances of M–R′OH and MeO^+ ions in the spectra of I, IV–VIII, XI, and XIII.

Compound	I	IV	V	VI	VII	VIII	XI	XIII
M-R′OH (%)	100	96	100	39	69	18	28	100
MeO^+ (%)	64	100	39	8	82	100	100	40



the MeO^+ ions [7, 8, 9] in the spectra (Figs. 1–9 and 12) of I–VIII, XI, and XIII. The spectra of the appropriate alcohol radical ion can clearly be seen in Figs. 1–9 (especially Fig. 6). It is also noteworthy that the major fragmentation in the spectrum (Fig. 10) of XVIII involves the formation of the *iso*propyl mercaptan radical ion (*m/e* 76).

Deuterium labelling studies have indicated that both processes (M–EtOH and the production of *m/e* 31) arise solely by the processes *a* or $b \rightarrow c+d$ in the spectra of VII and XIII; viz. compounds X and XIV (produced by introducing VII and XIII directly into the source with deuterium oxide [10] show almost quantitative M–EtOD and CH_2DO^+ (*m/e* 32) peaks. The spectrum (Fig. 12) of XIII should be compared with that [2] of 2-ethoxycarbonylcyclopentanone, which fragments both by loss of ethanol, and by loss of the ester group with concomitant hydrogen rearrangement (to form the cyclopentanone molecular ion [11]). The thio analogue XIII (present mainly in the enethiol form) fragments specifically by the process $e \rightarrow g$, and this process is directly comparable with the "ortho-effects" [12] operative in the spectra of anthranilates [13], salicylates [14], and *o*-carboxythiophenols [15].

The mass spectrum of IX shows only an 80 % shift of *m/e* $31 \rightarrow 32$, indicating that

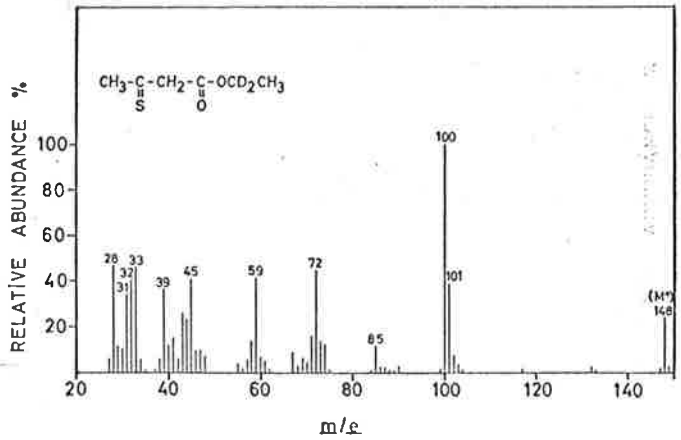


Fig. 2.

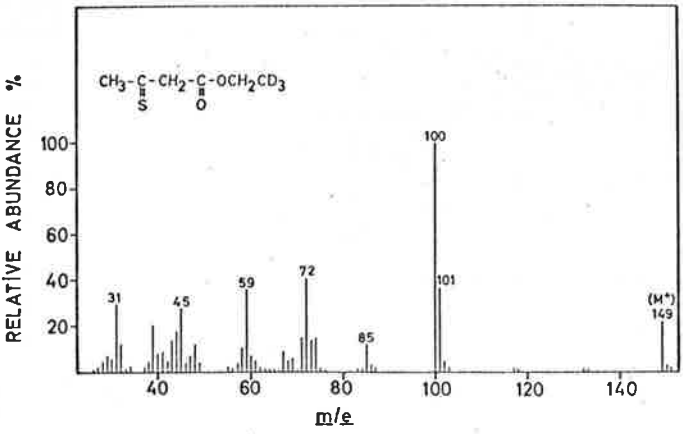
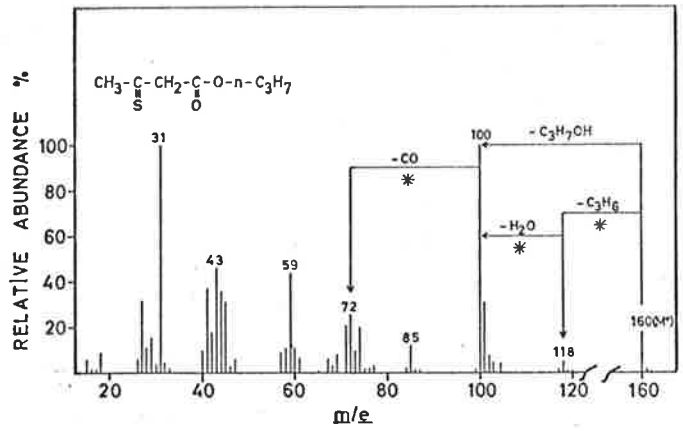


Fig. 3.



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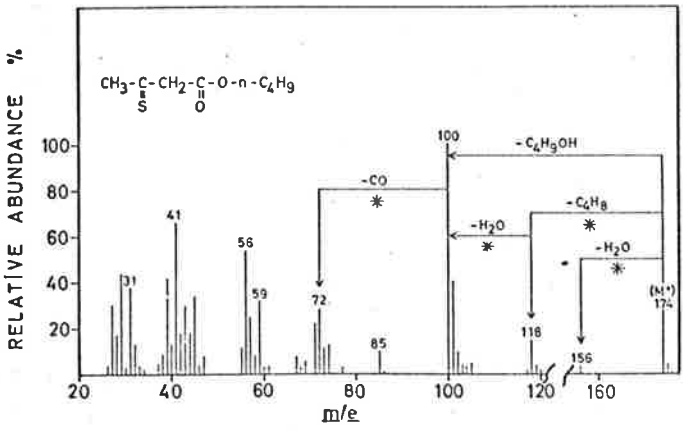

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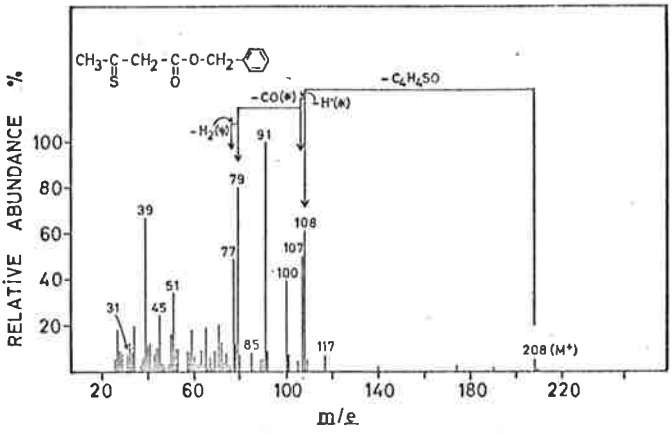

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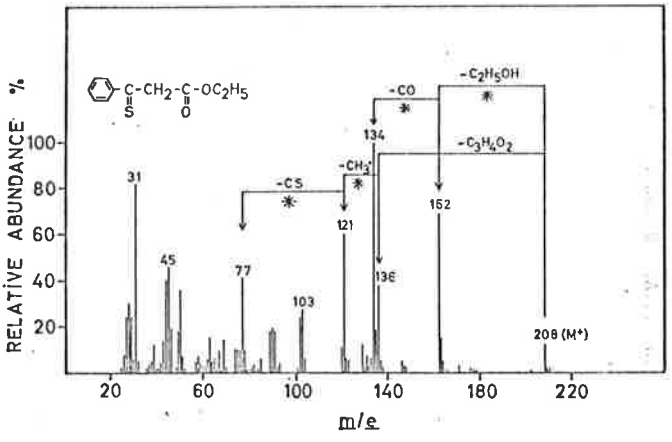

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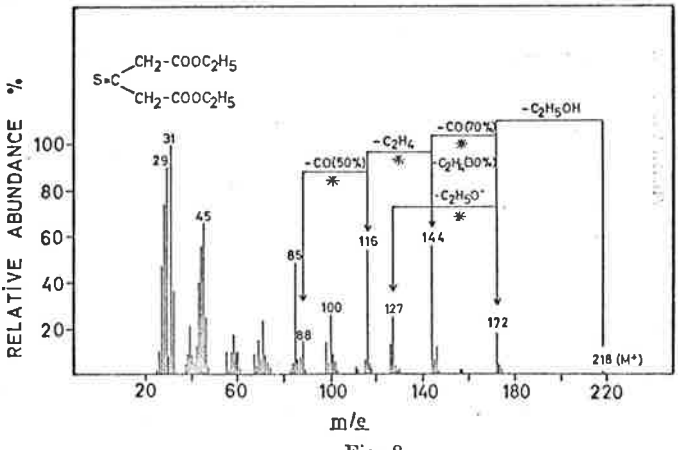


Fig. 8.

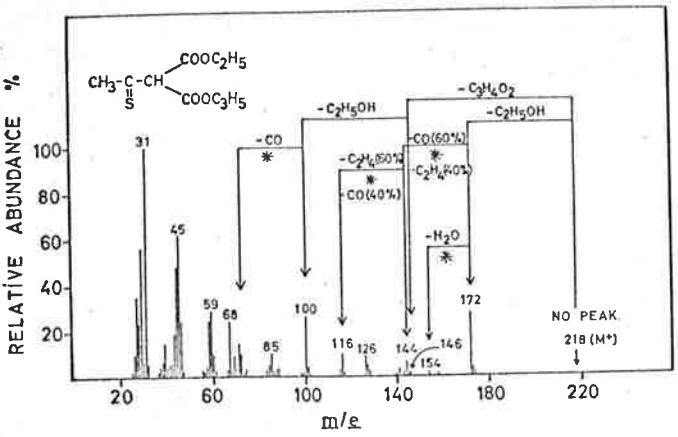


Fig. 9.

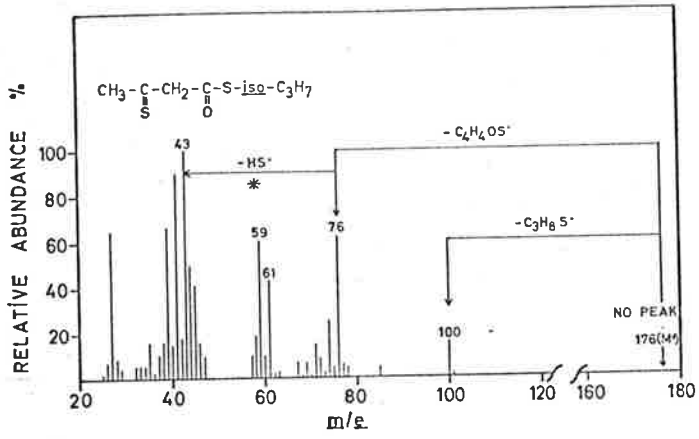


Fig. 10.

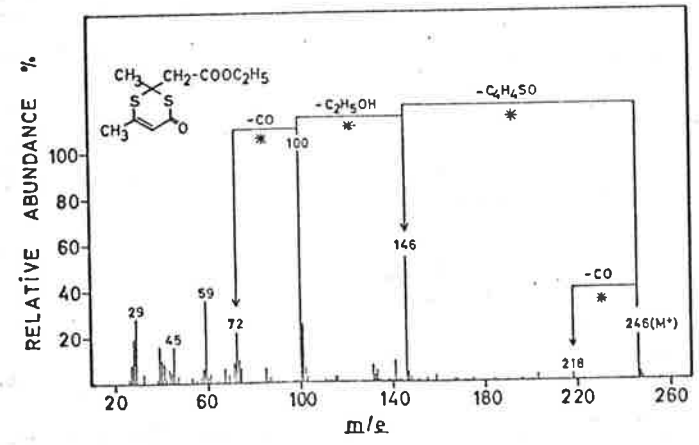


Fig. 11.

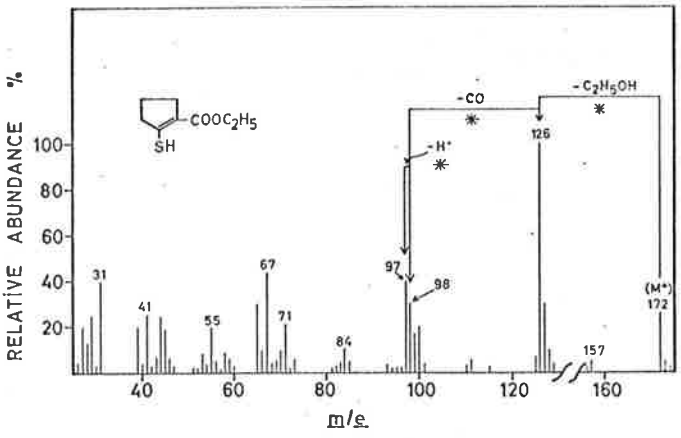
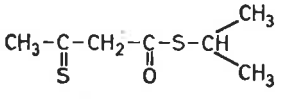
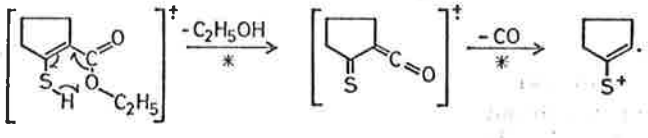


Fig. 12.



XVIII



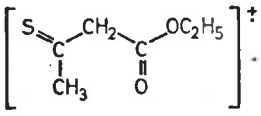
e, m/e 142 f, m/e 126 g, m/e 98

20 % of *m/e* 31 in the spectrum (Fig. 1) of ethyl thioacetoacetate is not formed by the processes *a* or *b*→*c*+*d*. In order to investigate the formation of *m/e* 31 further, the labelled esters II and III were synthesized, and their spectra are recorded in Figs. 2 and 3. Exact mass measurements (Table 1) allow the calculation of the relative shifts, which are summarised in Table 3. These results show that 15 % of *m/e* 31 in I originates by a methyl migration from carbon to oxygen. Either process *h*→*i* or *h*→*j* could explain this formation. There is no evidence for the formation of *i* (or its anticipated decomposition products), but 40 % of *m/e* 60 (Fig. 1) is C_3H_8O. It is possible that this could correspond to *j*, and the spectrum [16] of ethyl methyl

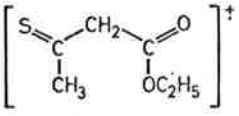
Table 3. Relative shifts of the *m/e* 31 peak in the spectra of I, II, and IX.

Compound	*m/e* 31 (CH_3O^+)	32 (CH_2DO^+)	33 (CHD_2O^+)
II	15 %	5 %	80 %
III	98 %	2 %	
IX	ca. 20 %	ca. 80 %	—

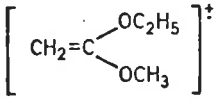
ether exhibits an *m/e* 31 ion [27 % of the base peak (molecular ion)]. Clearly, the rearrangement process is complex as the spectra of II and III both show small contributions from CH_2DO species (Table 3). It is conceivable that these ions may arise by randomisation of the label in *k* and *l*, respectively, but there is no evidence to support this supposition.



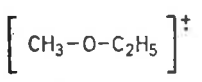
h, m/e 146



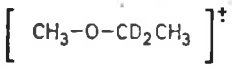
h



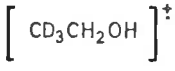
i, m/e 102



i, m/e 60



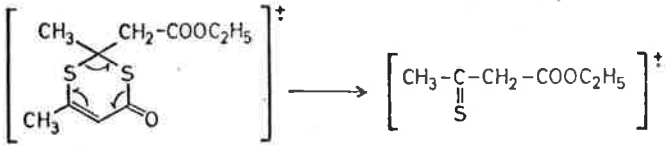
k, m/e 63



l, m/e 49

The other fragmentations of the simple esters I–VI, VIII, XI, and XIII are summarised in Figs. 1–6, 8, and 12, and do not merit special comment. The spectrum (Fig. 7) of the phenyl derivative VII shows a fragmentation not noted in the other spectra. Loss of the ester group with double hydrogen rearrangement (M-72) produces *m/e* 136, which is represented as the thioacetophenone radical ion. M-72 ions are also noted in the spectra of ethyl benzoylacetates [2]. This species fragments as indicated in Fig. 7.

The cyclic disulphide XII provides a further example of the retro-Diels-Alder process [17] in mass spectrometry. Fragmentation by the process $m \rightarrow n$ produces the keto form of the ethyl thioacetoacetate molecular ion (*m/e* 146). No peak at *m/e* 31 is observed in this spectrum, which possibly indicates either that sufficient energy is lost during the retro-Diels-Alder process to prelude both the formation of the ethanol radical ion (and the other rearrangement processes), or that the production of the ethanol radical ion (in I), proceeds completely via the enol form ($a \rightarrow c + d$).



m, m/e 246

n, m/e 146

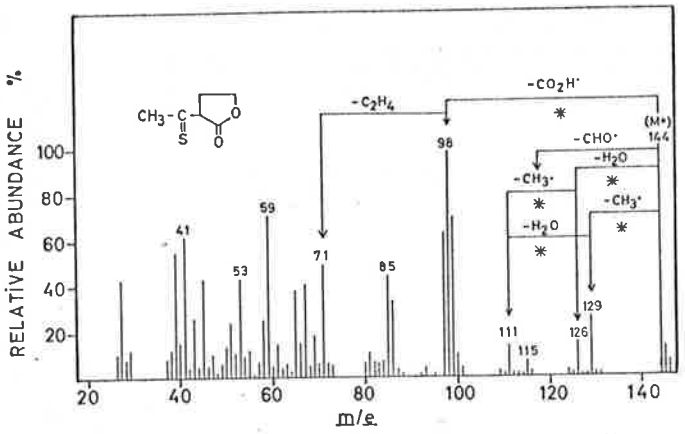


Fig. 13.

The spectrum (Fig. 13) of XV (which contains a γ-lactone moiety) bears little relation to those of the simpler esters. Fragmentation occurs mainly in the γ-lactone ring with the M–CO_2H process predominating. α-Cleavage to C=S is also observed, and other processes are summarised in Fig. 13.

Experimental

All mass spectra were measured with an Hitachi Perkin-Elmer R.M.U. 6D double focussing mass spectrometer with an inlet temperature of 100° and a source temperature of 150°. The spectra of IX, X, and XIV were obtained by introducing I, VII, and XIII into the source with D_2O [10]. Exact mass measurements were performed with an A.E.I. MS 9 mass spectrometer using a resolution of 14000 (10 % valley definition) with heptacosafluorotributylamine providing reference masses. All measurements were correct to within 15 ppm.

All compounds were tested for purity by vapour phase chromatography, NMR, and mass spectrometry. Previously published procedures were used for the preparation of I [18], IV [18], V [18], VII [18], VIII [18], XI [18], and XII [18]. II, III, and VI were prepared by treatment of the corresponding β-ketoesters (synthesized from diketene and alcohols [19]) with hydrogen sulphide and dry hydrogen chloride [18]. Below the detailed synthesis of VI is given as an example. The syntheses of XV [20] and XVIII [21] will be published in forthcoming publications.

Benzyl thioacetoacetate, VI

A solution of 19.2 g (0.1 mole) benzyl acetoacetate in 150 ml of acetonitrile was cooled to −60°. Keeping the temperature constant, a moderate stream of H_2S-gas was passed through the solution for 90 minutes followed by dry HCl for 40 minutes. During the night the reaction mixture was allowed to warm to −20°. Then it was poured into ice-water under stirring and extracted with benzene. The benzene layer was washed with a diluted natrium carbonate solution, then with water and dried over calcium sulphate.

The benzene was removed and the remaining oil distilled to give the title compound as a red oil, $bp_{0.05}$: 98° (uncorrected), $n_D^{21.5}$: 1.5665.

Yield: 16.2 g (78 %).

(Found: C, 63.35; H, 5.72; S, 15.52. $C_{11}H_{12}O_2S$ requires: C, 63.45; H, 5.81; S, 15.37.)

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Department of Organic Chemistry, Chemical Institute, University of Aarhus, 8000 Aarhus C, Denmark (F. D., S.-O. L.)

Department of Organic Chemistry, University of Adelaide, Adelaide, South Australia 5001 (J. H. B.)

University Chemical Laboratory, Lensfield Road, Cambridge, England (R. G. C.)

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MASS SPECTRA OF α-DIKETONES

I.† NON-ENOLIZED α-DIKETONES

By J. H. Bowie,‡ R. G. Cooks,§ G. E. Gream,‡ and M. H. Laffer‡

[*Manuscript received November* 3, 1967]

Summary

The mass spectra of a series of α-diketones are reported and discussed. Fragmentation patterns have been substantiated by exact mass measurements, metastable ions, and in two cases, by deuterium labelling studies. The McLafferty rearrangement is not observed in the spectra of aliphatic α-diketones; fragmentation proceeds by α-cleavage. The fragmentation modes of those cyclic α-diketones studied depend largely on the ring size. Molecular ions are observed in all spectra.

Although the mass spectra of β-diketones[1–6] and γ-diketones[7] have been discussed, the only spectra of α-diketones to be reported are those of biacetyl,[8] pentane-2,3-dione,[9] and octane-2,3-dione.[9] We have synthesized a series of non-enolized α-diketones (I–XII and XIV)‖ and their spectra are recorded in Figures 1–8 or Table 1. High-resolution data are summarized in Table 2. Although the structures of fragment ions are not known, nominal structures have been drawn in order that the fragmentation modes may be related to the structures of the molecules in the ground state. The presence of an appropriate metastable ion for any process is indicated (both in the text or a figure) by an asterisk.

The mass spectra (Fig. 1 and Table 1) of the symmetrical aliphatic α-diketones (I–VI) are very simple. These compounds exist predominantly in the keto form,¶ and

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‡ Department of Organic Chemistry, University of Adelaide, S.A. 5000.

§ University Chemical Laboratory, Lensfield Road, Cambridge, England.

‖ The mass spectra of enolizable cyclic α-diketones will be reported in a subsequent publication.

¶ Infrared and n.m.r. studies have not revealed the presence of any enolic components.

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RCOCOR′

	R	R′
(I)	Me	Me
(II)	Pr^n	Pr^n
(III)	Pr^i	Pr^i
(IV)	Bu^n	Bu^n
(V)	Bu^t	Bu^t
(VI)	n-C_5H_{11}	n-C_5H_{11}
(VII)	Bu^t	Pr^i
(VIII)	Ph	Ph
(IX)	[2,4,6-D]Ph	[2,4,6-D]Ph

cleavage of the C–C bond between the two carbonyl groups produces the base peak of the spectrum when each side-chain contains less than five carbon atoms, and is not branched. When the side-chain contains more than four carbon atoms, the base peak of the spectrum is the propyl cation ($C_3H_7^+$, *m/e* 43). When the side-chain is branched,

TABLE 1

MASS SPECTRA OF COMPOUNDS (I–III), (V), (VI), (XI), (XII), AND (XVI)

All peaks greater than 2% of the base peak (100%) are recorded

(I)	*m/e*	28	42	43	44	86(M)												
	I (%)	14	10	100	15	24												
(II)	*m/e*	27	28	29	39	41	42	43	44	69	71	72	73	113	142(M)			
	I (%)	17	4	8	8	29	6	100	6	11	100	7	8	3	12			
(III)	*m/e*	27	39	41	42	43	44	57	70	71	72	142(M)						
	I (%)	14	8	22	5	100	7	3	6	54	5	7						
(V)	*m/e*	27	29	39	41	42	56	57	58	85	170(M)							
	I (%)	4	14	6	22	5	5	100	6	16	5							
(VI)	*m/e*	27	29	39	41	42	43	44	55	57	71	72	99	100	141	155	169	
	I (%)	12	20	6	20	8	100	6	12	4	63	7	86	8	3	2	2	
	m/e	198(M)																
	I (%)	5																
(XI)	*m/e*	27	28	39	40	41	42	43	44	57	58	59	69	70	71	85	100	128
	I (%)	9	4	22	8	31	94	36	6	3	28	42	3	100	5	2	4	6
	m/e	156(M)																
	I (%)	6																
(XII)	*m/e*	27	28	38	39	40	50	51	52	62	63	65	74	75	76	77	78	79	89
	I (%)	10	6	7	36	5	29	57	11	9	20	15	13	13	16	44	43	4	7
	m/e	91	92	102	103	104	115	116	117	118	131	132	145	146	147				
	I (%)	30	3	14	59	7	29	11	88	42	100	11	35	94	12				
	m/e	174(M)																	
	I (%)	28																	
(XVI)	*m/e*	37	38	39	49	50	51	52	61	62	63	74	75	76	101	102	103	104	
	I (%)	4	6	10	6	37	40	11	6	8	13	20	21	36	9	86	9	7	
	m/e	129	130	131	158(M^+)														
	I (%)	6	100	14	9														

the base peak of the spectrum is produced by the appropriate alkyl cation (the tertiary cation being more stable and more abundant than a secondary cation). When the energy of the electron beam is reduced to 15 eV, the R–C≡O$^+$ (or R′–C≡O$^+$) species is always the base peak. In the spectrum (Fig. 1) of decane-5,6-dione (IV), α-cleavage produces *a* (*m/e* 85), which decomposes by loss of carbon monoxide to produce the n-butyl cation (*b*, *m/e* 57). No metastable ion is present to indicate that

TABLE 2
COMPOSITION OF SOME IONS IN THE SPECTRA OF COMPOUNDS (I–XV)

Compound	m/e	Composition
(II)	43	C_3H_7 (90%), C_2H_3O (10%)
	71	C_4H_7O
	73	C_4H_9O (60%), $C_3H_5O_2$ (40%)
	113	$C_6H_9O_2$
(III)	43	C_3H_7 (95%), C_2H_3O (5%)
	85	C_5H_9O
(IV)	99	$C_6H_{11}O$ (70%), $C_5H_7O_2$ (30%)
	113	$C_6H_9O_2$
	127	$C_7H_{11}O_2$
	141	$C_8H_{13}O_2$
(V)	43	C_3H_7 (95%), C_2H_3O (5%)
	141	$C_8H_{13}O_2$
	155	$C_9H_{15}O_2$
	169	$C_{10}H_{17}O_2$
(VIII)	152	$C_{12}H_8$
	181	$C_{13}H_9O$
	194	$C_{14}H_{10}O$
(X)	42	C_3H_6
	70	C_4H_6O
	83	C_6H_{11}
	98	C_7H_{14}
	126	$C_8H_{14}O$
(XI)	42	C_3H_6
	58	C_3H_6O
	59	C_3H_7O
	70	C_4H_6O
	85	C_5H_9O
	128	$C_7H_{12}O_2$
(XIII)	56	C_4H_8
	69	C_5H_9 (80%), C_4H_5O (20%)
	72	C_4H_8O
	112	C_8H_{16}
	140	$C_9H_{16}O$
(XIV)	43	C_3H_7 (70%), C_2H_3O (30%)
	55	C_4H_7 (70%), C_3H_3O (30%)
	67	C_5H_7
	69	C_4H_5O (70%), C_5H_9 (30%)
	77	C_6H_5
	79	C_6H_7
	81	C_6H_9
	82	C_6H_{10} (80%), C_5H_6O (20%)
	83	C_6H_{11} (96%), C_5H_7O (4%)
	95	C_7H_{11} (98%), C_6H_7O (2%)
	110	C_8H_{14} (70%), $C_7H_{10}O$ (30%)
	138	$C_9H_{14}O$
(XV)	69	C_4H_5O (80%), C_5H_9 (15%), C_5H_7D (5%)
	72	$C_5H_6D_3$

b [or its analogues in the spectra of (I–III) and (V–VII)] is formed directly from the molecular ion. The McLafferty rearrangement[10] is not observed in these spectra, even

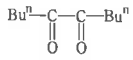
$$\text{(IV)} \xrightarrow[-C_5H_9O\cdot\ (*)]{-e,} \underset{a,\ m/e\ 85}{Me(CH_2)_3C{\equiv}O^+} \xrightarrow[*]{-CO} \underset{b,\ m/e\ 57}{Me(CH_2)_2CH_2^+}$$

when the energy of the electron beam is reduced to a nominal 10 eV. This is an important observation (cf.[9]) as the McLafferty rearrangement is generally a major process when the alkyl substituent attached to the carbonyl group contains three or more

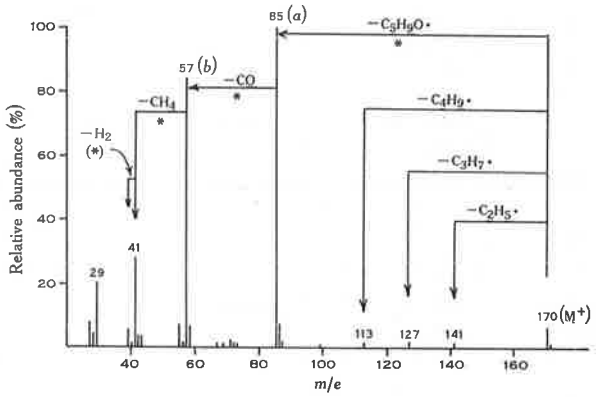
[10] McLafferty, F. W., *Analyt. Chem.*, 1959, **31**, 82.

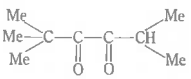
carbon atoms with at least one hydrogen attached to the γ-carbon atom (for compendia of these processes see[11,12]). The propensity of the α-cleavage process presumably precludes the operation of the β-cleavage process.

Fig. 1



(IV)





(VII)

Fig. 2

(*a*) 75 eV

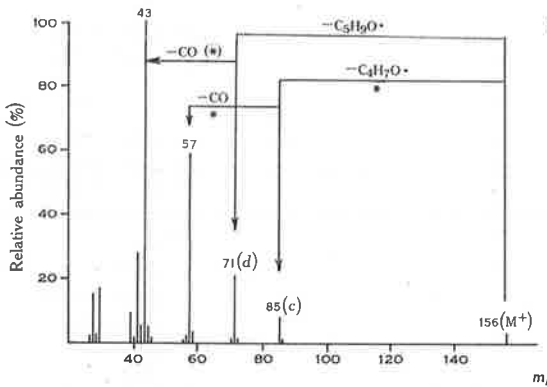
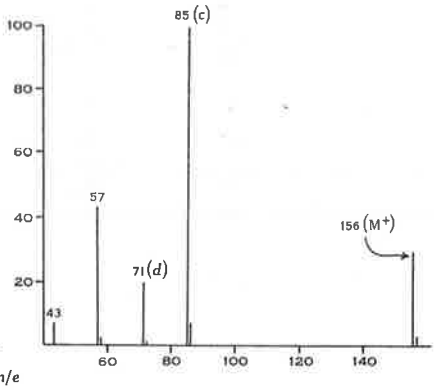


Fig. 2

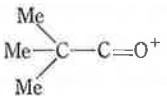
(*b*) 15 eV



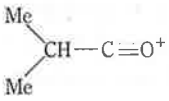
The spectrum (Fig. 2(*a*)) of 2,2,5-trimethylhexane-3,4-dione (VII) exhibits the species *c* and *d*, which are produced by the α-cleavage process. Surprisingly, the relative abundances of *c* and the t-butyl cation (*m/e* 57) are less than those of *d* and the isopropyl cation (*m/e* 43) respectively. This situation is reversed when the energy of the ion beam is reduced to 15 eV (see Fig. 2(*b*)).

[11] Budzikiewicz, H., Djerassi, C., and Williams, D. H., "Mass Spectrometry of Organic Compounds." (Holden-Day: San Francisco 1967.)

[12] Bowie, J. H., "Mass Spectrometry of Carbonyl Compounds" in "The Chemistry of the Carbonyl Group." (Ed. J. Zabicky.) Vol. II. (Interscience: London 1968.)

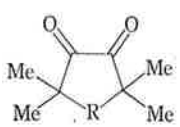


c, *m/e* 85

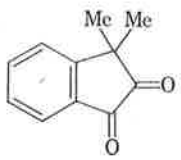


d, *m/e* 71

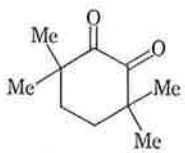
The spectrum (Fig. 3) of benzil (VIII) is noteworthy for the presence of a skeletal-rearrangement process of the type $[ABC]^{+\cdot} \rightarrow [AC]^{+\cdot} + B$ (cf.[13]). Examples of this type of process are relatively common in unsaturated systems (for reviews, see[12,14]). At present, only *a posteriori* statements can be given for these processes. The process observed in the spectrum of benzil is M—CHO· —CHO· to form *m/e* 152 (1% of the base peak), which is plausibly represented as the biphenylene radical ion. Although this process is a minor one, it is important, and benzil-d_6 (IX) was synthesized in order to see whether the hydrogen atoms that are lost come specifically from the *ortho* positions. The spectrum of (IX) is recorded in Figure 4, and it can be seen that the initial process (M—CHO·) in Figure 3, is now M—CDO· and M—CHO· in the ratio 3 : 2. The second loss of a formyl equivalent (although more complex) also follows this pattern. These results may be explained if the hydrogens on the aromatic rings are completely randomized upon electron impact. This hypothesis has been invoked previously, to explain results obtained from deuterium labelling studies, which were designed to clarify the formation of oxonium cations in the spectra of compounds of the general type Ph–CH–CH=CO–R.[15] Complete randomization of hydrogen atoms is also observed for toluene.[16] Randomization of the hydrogens in benzil occurs even at 15 eV.



(X) R = CH_2
(XI) R = O



(XII)



(XIII)

The fragmentations in the spectra (Figs. 5 and 6, or Table 1) of the monocyclic α-diketones (X–XIII) are largely dependent on the ring size. Extensive high-resolution studies (Table 2) were necessary to elucidate the fragmentation patterns.

The spectrum (Fig. 5) of the cyclopentanedione (X) exhibits fragmentation patterns which are very similar to that (Table 1) of (XI). Compound (X) exists in the keto form because of its substitution pattern, and two fragmentation processes are observed; viz. $e \rightarrow f \rightarrow g$, and $e \rightarrow h$ (base peak). Other fragmentations are

[13] Bowie, J. H., Williams, D. H., Madsen, P., Schroll, G., and Lawesson, S.-O., *Tetrahedron*, 1967, **23**, 305.

[14] Brown, P., and Djerassi, C., *Angew. Chem. int. Edn*, 1967, **6**, 477.

[15] Williams, D. H., Ronayne, J., and Bowie, J. H., *J. Am. chem. Soc.*, 1966, **88**, 4980.

[16] Grubb, H. M., and Meyerson, S., in "Mass Spectrometry of Organic Ions." (Ed. F. W. McLafferty.) Ch. 10. (Academic Press: New York 1963.)

indicated in Figure 5. A very different situation is observed when a benzene ring is fused to the cyclopentane-1,2-dione ring (as in XII). The base peak (*h*, *m/e* 70) in the spectrum of (X) is not observed in that of (XII). Instead, the base peak is

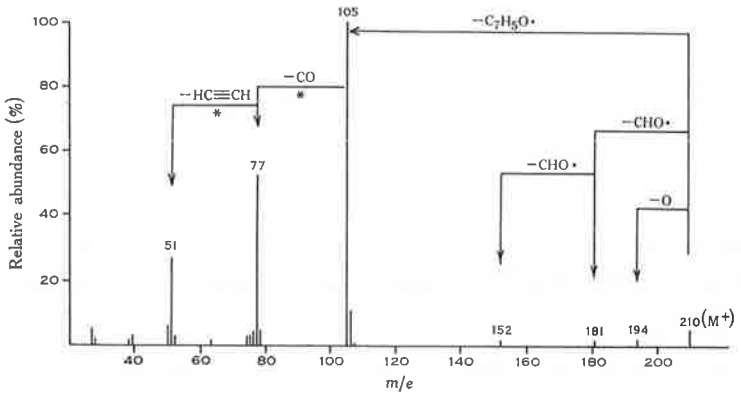
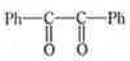


Fig. 3



(VIII)

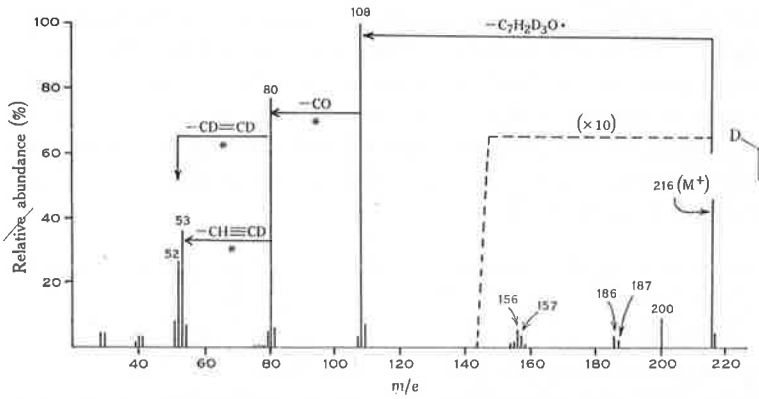
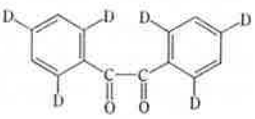


Fig. 4



(IX)

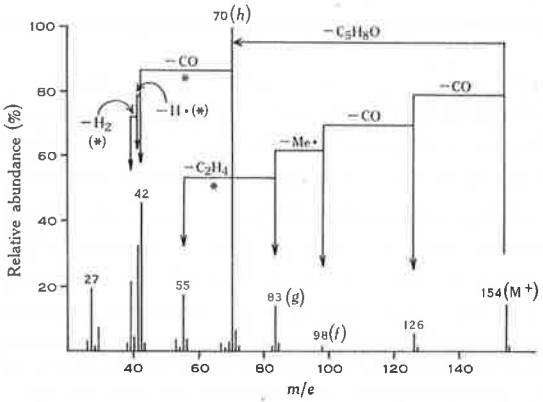
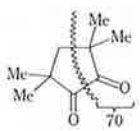
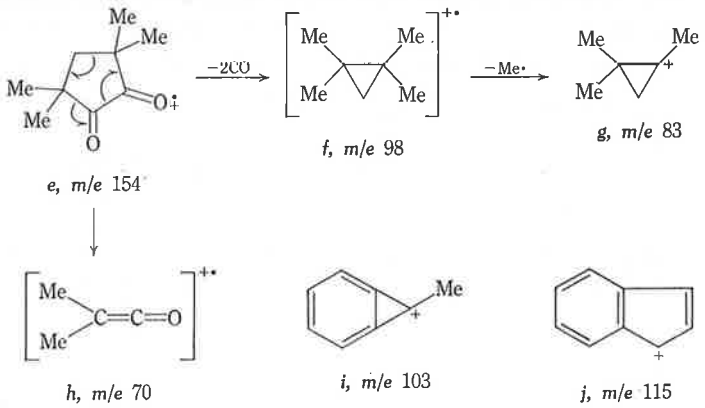


Fig. 5

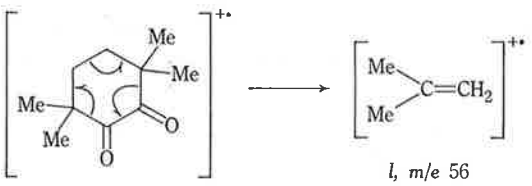


(X)

formed by the process M—CO—Me·, and the two major fragmentation schemes are M—CO—Me· —CO (possibly to *i*, *m/e* 103) and M—CO—CHO· —H_2 (to the indene cation, *j* *m/e* 115).



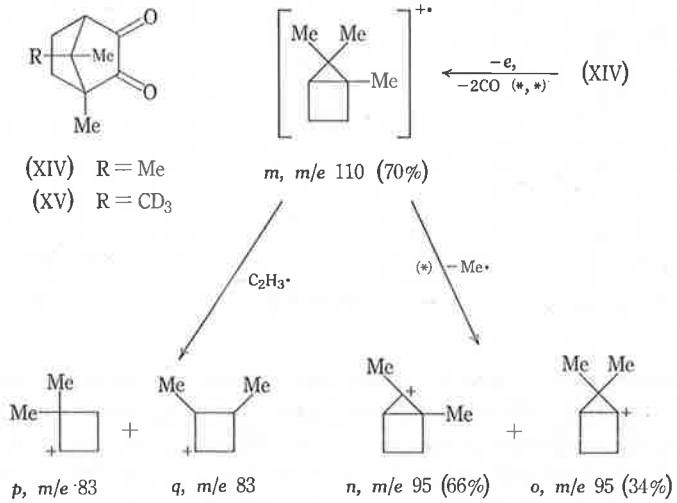
The spectra (Figs. 5 and 6) of the cyclic five- and six-membered diketones (X and XIII) are very different. The base peak in the spectrum (Fig. 6) of (XIII) is produced by the hydrocarbon species *m/e* 56, which may be formed by the process $k \rightarrow l$ (there is no evidence to suggest that this is a concerted process). No ion corresponding to *h* (*m/e* 70) is present in this spectrum, but the process M—CO—CO (analogous to $e \rightarrow f$ in X) is still observed.



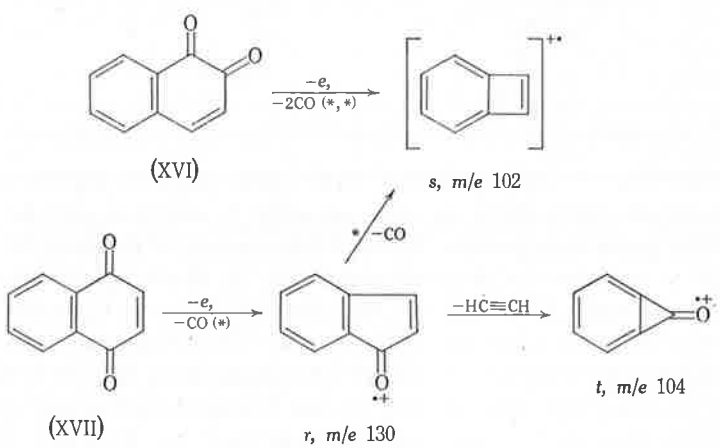
The behaviour of camphorquinone (XIV) upon electron impact is complex, and high resolution (Table 2) of the spectrum (Fig. 7) was necessary for the interpretation of the breakdown process. Through the courtesy of Professor W. L. Meyer we were able to measure the mass spectrum (Fig. 8) of the d_3-derivative (XV).[17] The bicyclic α-diketone (XIV) does not fragment either as a cyclopentane-1,2-dione or a cyclohexane-1,2-dione. Instead, the process M—CO—CO produces *m/e* 110 (70% C_8H_{14}), plausibly represented as *m*, which may fragment by loss of either methyl radical to *n* or *o* (*m/e* 95). Alternatively *m* may fragment by loss of $C_2H_3\cdot$ to *m/e* 83 (C_6H_{11}, 96%). This species loses ethylene to produce *m/e* 55 ($C_4H_7^+$, 70%). The analogous ion (*m/e* 86) in Figure 12 loses C_2H_4, C_2H_3D, and $C_2H_2D_2$; this indicates that *m/e* 83 probably exists in ring-expanded forms, e.g. *p* and *q*. Other fragmentations are complex; e.g. 70% of *m/e* 69 is $C_4H_5O^+$. The formation of this ion does not involve the labelled methyl group in (XV). The complement (30%) of *m/e* 69 corresponds to $C_5H_9^+$. In the spectrum of (XV), 50% of this peak remains at *m/e* 69 and 50% is

[17] Meyer, W. L., Lobo, A. P., and McCarty, R. N., *J. org. Chem.*, 1967, **32**, 1754.

shifted to *m/e* 72, indicating involvement of the bridging carbon atom and its two methyl substituents.



Finally, it is of interest to compare the spectra of 1,2- and 1,4-quinones. The spectra of 1,4-naphthaquinones[18,19] are characteristic, as they may decompose from the M—CO ion [e.g. (XVII) → *r*] by loss of acetylene (probably to *t*), or carbon monoxide (probably to *s*), that is, a "doublet" at M—54 and M—56 is observed.



1,2-Naphthaquinone (XVI), upon electron impact, does not fragment by the process M—CO—HC≡CH. Instead, loss of carbon monoxide from the molecular ion produces the base peak of the spectrum, and the process M—CO—CO is pronounced, indicative of the close proximity of the two carbonyl groups. Comparison of the spectra[18] of

[18] Beynon, J. H., and Williams, A. E., *Appl. Spectrosc.*, 1960, **14**, 156.
[19] Bowie, J. H., Cameron, D. W., and Williams, D. H., *J. Am. chem. Soc.*, 1965, **87**, 5094.

anthraquinone and phenanthraquinone also indicates that the M—CO process produces the base peak for phenanthraquinone but only 76% for anthraquinone.

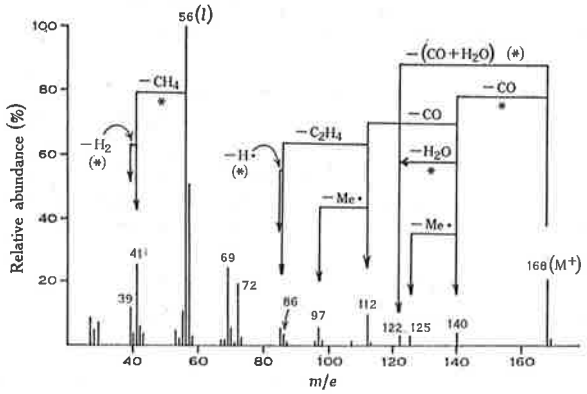
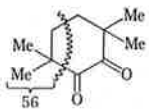


Fig. 6



(XIII)

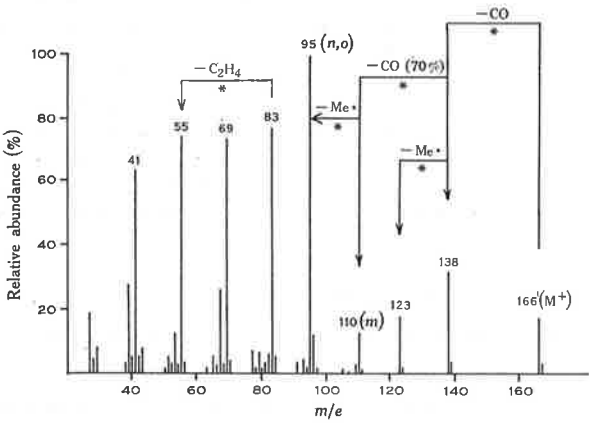
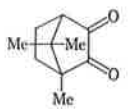


Fig. 7



(XIV)

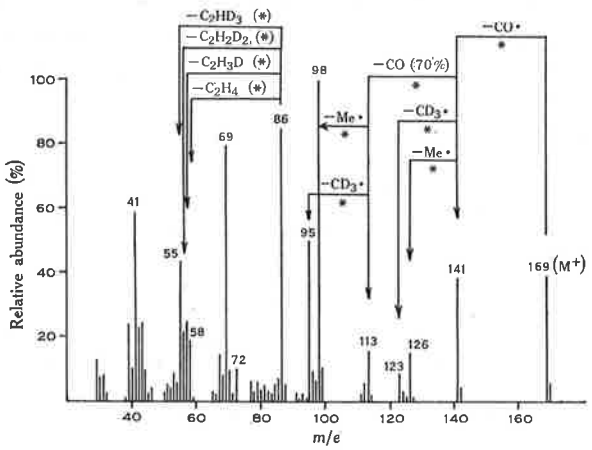
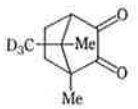


Fig. 8



(XV)

Experimental

All mass spectra were measured with an Hitachi Perkin–Elmer RMU 6D double-focusing mass spectrometer operating at 75 eV, with a source temperature of *c.* 150° and an inlet

temperature of 50–100°. Exact mass measurements were carried out with an A.E.I. MS9 mass spectrometer with a resolution of 15000 (10% valley definition) using heptacosafluorotributylamine to provide reference masses.

Liquid samples were purified by preparative gas chromatography, and solids by recrystallization. The purity of all samples was routinely checked by gas chromatography, n.m.r., and mass spectrometry.

Compounds (I), (VIII), and (XVI) were purified commercial samples. The following compounds were prepared by reported procedures: (II),[20,21] (III),[20,22] (IV),[20,21] (V),[20,22] (VI),[20,21] (X)[23] (by selenium dioxide oxidation of 2,2,4,4-tetramethylcyclopentanone[24]), (XI),[25] (XIII),[26] and (XIV).[27] Benzil-d_8 (IX) was synthesized from benzaldehyde-2,4,6-d_3[15] by the benzoin condensation followed by oxidation with nitric acid. The synthesis of compound (VII) caused unexpected difficulties and will be the subject of a communication in preparation.

3,3-Dimethylindane-1,2-dione

The experimental procedure is essentially that used for the preparation of camphorquinone (XIV).[27]

A mixture of 3,3-dimethylindan-1-one[28] (5·2 g), selenium dioxide (4·0 g), and acetic anhydride (4·0 ml) was heated under reflux in an atmosphere of nitrogen for 4 hr. A second portion of selenium dioxide (1·4 g) was then added and the mixture heated under reflux for a further 2 hr. After being cooled, the mixture was neutralized by the dropwise addition of aqueous sodium hydroxide (30%) followed by saturated sodium carbonate solution (25 ml). After removal of the precipitated selenium by filtration, the reaction mixture was extracted with ether (3 × 100 ml) and the combined ether extracts were washed with water, and dried ($MgSO_4$). After the dried extract had been allowed to stand over a few drops of mercury for 12 hr in order to remove residual selenium,[23] the ether was removed to yield 3,3-dimethylindane-1,2-dione (4·5 g, 79%), m.p. 104–106° (lit.[28] 106–107°) after recrystallization from light petroleum followed by sublimation at 75°/1·5 mm.

Acknowledgments

We are indebted to Professor W. L. Meyer for a sample of the labelled camphorquinone, and to Drs J. H. Beynon and R. F. C. Brown for preliminary mass-spectral data for compounds (X), (XI), and (XIV). One of us (R.G.C.) acknowledges the award of an Elsie Ballot Fellowship. The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee. We thank Mr B. K. Simons for preparing a sample of benzil-d_6.

[20] Snell, J. M., and McElvain, S. M., *J. Am. chem. Soc.*, 1931, **53**, 750.
[21] De Borgen, L., Anteunis, M., Lammens, H., and Venzele, M., *Bull. Soc. chim. Belg.*, 1964, **73**, 73.
[22] Newman, M. S., and Kahle, G. R., *J. org. Chem.*, 1958, **23**, 666.
[23] Sandris, C., and Ourisson, G., *Bull. Soc. chim. Fr.*, 1956, **23**, 958.
[24] Slomp, G., Inatome, M., Bowers, C. E., Derfer, J. M., Greenlee, K. W., and Boord, C. E., *J. org. Chem.*, 1960, **25**, 514.
[25] Korobitsyna, I. K., Yur'ev, Y. K., and Nefedova, O. I., *J. gen. Chem. USSR*, 1954, **24**, 191.
[26] Klenberg, D., *Ann. Acad. Sci. fenn.*, 1962, Ser. AII, No. 118.
[27] Eistert, B., Greiber, D., and Caspari, I., *Liebigs Ann.*, 1962, **659**, 64.
[28] Koelsch, C. F., and Le Claire, C. D., *J. org. Chem.*, 1941, **6**, 516.

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Skeletal-rearrangement ions in the mass spectra of nitrones[1]

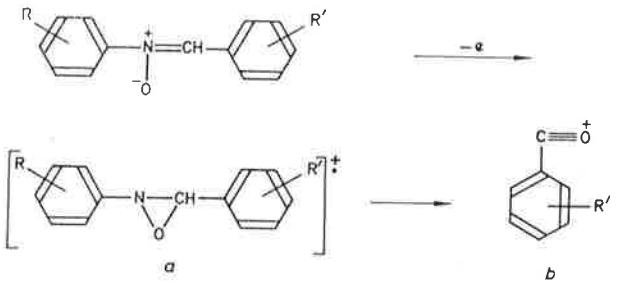
by B. Søgaard Larsen, G. Schroll and S. -O. Lawesson
Department of Organic Chemistry, Aarhus University, Aarhus C., Denmark
J. H. Bowie
Department of Organic Chemistry, University of Adelaide, South Australia, 5000
and R. G. Cooks
University Chemical Laboratory, Lensfield Road, Cambridge, UK

Because of our interest in the skeletal-rearrangement processes observed in the mass spectra of azoxybenzenes[2,3] and *N*-oxides,[4,6] we have determined the mass spectra of a series (1–12) of nitrones. Prominent rearrangement peaks due to substituted benzoyl cations are observed in all spectra. Their formation must result from migration of oxygen from nitrogen to the adjacent carbon atom. This should be compared with the rearrangement of azoxybenzenes, where the oxygen migrates to the aromatic ring furthest from the *N*-oxide link.[2,3] The results are summarised in the Table.

Table
Relative abundances of rearrangement peaks in the spectra of 1–12

Compound			*Rearrangement peak (m/e)*	*Relative abundance (%)*	*Metastable ion (m/e)*
	R	R′			
(1)	H	H	105	21	56·0
(2)	H	*p* Me	119	18	67·1
(3)	H	*p* Cl	139/141	12/5	—
(4)	H	*m* OH	121	47	68·8
(5)	H	*p* OMe	135	28	80·3
(6)	H	*m* NO_2	150	4	—
(7)	*p* Cl	H	105	24	47·6
(8)	*o* OH	H	105	7	—
(9)	*p* Cl	*p* Cl	139/141	26/10	73·0
(10)	*p* Cl	*o* OH	121	32	—
(11)	*p* Cl	*o* OMe	135	31	69·8
(12)	*p* Cl	*p* NO_2	150	8	—

The compositions of all rearrangement peaks have been established by exact mass measurements. Appropriate metastable ions are observed for many of the processes. This does not necessarily indicate that the formation of the rearrangement ion from the molecular ion involves a one-step process.[7] The formation of the rearrangement species possibly involves the formation of the cyclic intermediate *a*, which may decompose further to *b*. The formation of oxaziridine species of the type *a* has photochemical analogies.[8]



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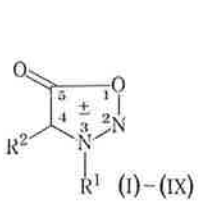
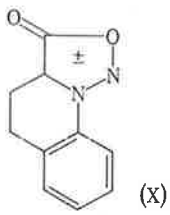
MASS SPECTRA OF SYDNONES*

By J. H. Bowie,† R. A. Eade,‡ and J. C. Earl†

Because of our interest[1,2] in the mass spectra of heterocyclic systems, we have measured the mass spectra of the sydnones (I)–(X). Their mass spectra are recorded in Figures 1–4 or in Table 1. The presence of a metastable ion for a particular process is indicated (both in the text and in Figures) by an asterisk. Structures drawn for fragment ions are nominal representations only but serve the important purpose of relating the fragmentation pattern to the structure of molecules in the ground state.



(I)–(IX)



(X)

	R^1	R^2		R^1	R^2		R^1	R^2
(I)	Ph	H	(IV)	*p*-$OMeC_6H_4$	H	(VII)	CH_2Ph	H
(II)	Ph	Me	(V)	*p*-$O_2NC_6H_4$	H	(VIII)	2-naphthyl	H
(III)	Ph	Cl	(VI)	$HO_2CCH_2C_6H_4$	H	(IX)	cyclohexyl	H

The mass spectra of the sydnones (I)–(X) all contain molecular ions, characteristic fragmentation patterns, and are devoid of skeletal-rearrangement fragments (cf.[3]). Consequently, mass spectrometry can be a useful aid to structure determination in this class of synthetically important compounds.[4,5]

The behaviour of sydnones upon electron impact, is typified by the spectrum (Fig. 1) of 3-phenylsydnone (I). Loss of the elements of NO· and CO from the molecular ion produces a species plausibly represented as the protonated benzoisonitrile cation *c* (*m*/*e* 104), which may decompose further by loss of HCN to yield *d*, $C_6H_5^+$ (it has been suggested that *d* is probably linear, and not the phenyl cation[6]).

* Manuscript received December 5, 1967. This paper also constitutes Part XXVIII in the series "Electron Impact Studies." Part XXVII, Lawesson, S.-O., Schroll, G., Bowie, J. H., and Cooks, R. G., *Chemy Ind.*, in press.

† Department of Organic Chemistry, University of Adelaide, S.A. 5000.

‡ School of Chemistry, University of New South Wales., P.O. Box 1, Kensington, N.S.W. 2033.

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The compositions of the major ions in the spectrum of (I) have been established by high-resolution measurements, and the fragmentation modes may be represented by the process (I) $\rightarrow d$. Many canonical forms may be written for the molecular ion of (I); *a* has been chosen only because it best illustrates the cleavage processes.

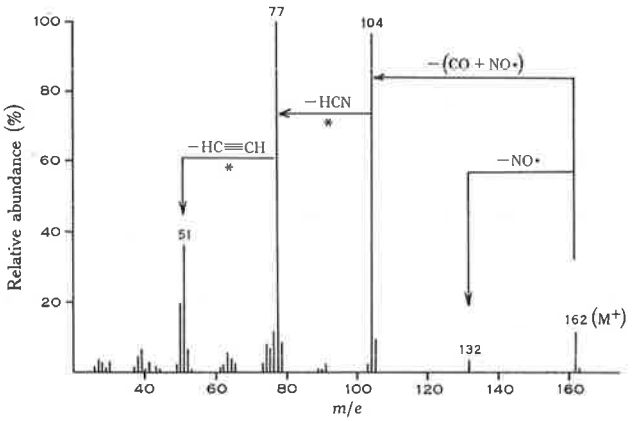
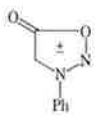
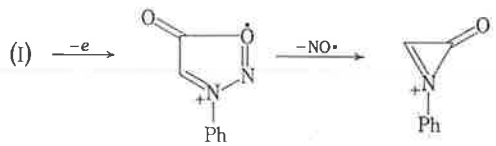


Fig. 1



(I)



a, *m/e* 162 *b*, *m/e* 132

d, *m/e* 77 *c*, *m/e* 104

The initial loss of NO· and CO (M—58) is the characteristic fragmentation process for all the sydnones studied, except for 3-benzylsydnone (VII) whose spectrum is so dominated by the tropylium cation (*m/e* 91) that the M—58 process is not observed. The M—58 process precedes the breakdown of the substituents on the sydnone ring system [it seems likely that the loss of NO· in the spectrum (Table 1) of (V), comes from the sydnone ring, but ^{15}N-labelling would be necessary to substantiate this supposition]. An appropriate example to illustrate this point is the spectrum (Fig. 3) of 3-(*p*-anisyl)sydnone (IV), where the M—30 peak is completely due to loss of NO· (high resolution).

In the spectrum (Fig. 1) of 3-phenylsydnone (I) there is no evidence to indicate whether the loss of NO· and CO is concerted or occurs in a stepwise manner. The process is certainly stepwise in the spectra of (IV), (VI), (VIII), and (X), where the

processes M—NO·—CO are substantiated by appropriate metastable ions. However, it is possible that the process is concerted in the spectra of (II), (III), and (IX), which contain no M—30 ions, but which also have no metastable ions for the process M—(NO·+CO) (M—58).

TABLE 1

MASS SPECTRA OF COMPOUNDS (II), (III), AND (V)–(IX)

All peaks having a relative abundance greater than 5% of the base peak, and molecular ions which are less than this value, are recorded.

(II)	*m/e*	28	39	50	51	52	59	63	74	76	77	78	104	117	118	119	176(M)
	I (%)	8	7	19	51	6	7	6	6	11	100	15	6	6	96	15	32
(III)	*m/e*	39	50	51	63	74	75	76	77	78	103	138	139	140	196(M)		198(M)
	I (%)	13	20	34	6	7	7	16	100	8	11	77	7	30	13		4
(V)	*m/e*	50	63	64	74	75	76	77	92	103	122	149	150	177	207(M)		
	I (%)	31	9	10	11	30	41	6	14	43	16	100	10	10	9		
(VI)	*m/e*	27	28	39	43	50	51	62	63	64	77	78	79	89	90	91	105	106
	I (%)	8	12	15	29	7	14	6	18	7	33	6	32	36	24	13	13	12
	m/e	107	117	135	162	163	190	220(M)										
	I (%)	9	13	33	100	15	18	4										
(VII)	*m/e*	28	38	39	41	45·5	50	51	62	63	64	65	77	89	91	92	176(M)	
	I (%)	8	6	33	7	13	9	11	6	16	6	41	30	6	100	9	3	
(VIII)	*m/e*	51	63	63·5	74	75	76	77	101	126	127	128	153	154	155			
	I (%)	7	9	7	6	8	5	22	9	19	100	13	6	74	11			
	m/e	182	212(M^+)															
	I (%)	29	3															
(IX)	*m/e*	27	28	29	39	41	43	53	54	55	56	67	83	84	87	110	168(M)	
	I (%)	18	10	12	20	55	8	7	9	100	8	9	86	8	6	6	20	

Although the M—58 ion is abundant in all spectra except that of (VII) (Table 2), there appears to be little correlation between the substitution patterns and the relative abundances of the M—30 ion (see Table 2). For example, in the spectra of the 3-phenyl- and 3-(2-naphthyl)-sydnone (I and VIII) it constitutes 3 and 29% respectively,

TABLE 2

RELATIVE ABUNDANCES OF M—30 AND M—58 IONS IN THE SPECTRA OF COMPOUNDS (I)–(VI) AND (VIII)–(X)

Compound	(I)	(II)	(III)	(IV)	(V)	(VI)	(VIII)	(IX)	(X)
M—30	3	0	0	28	10	19	29	0	24
M—58	96	96	77	100	100	100	74	86	100

while both electron-withdrawing and electron-introducing groups on the aromatic substituent (IV)–(VI) increase the relative abundance of the M—NO· ion when compared with that in (I). The M—NO· process is not thermal (see below) and is the major process observed in the spectra of (I) and (VIII) when the energy of the

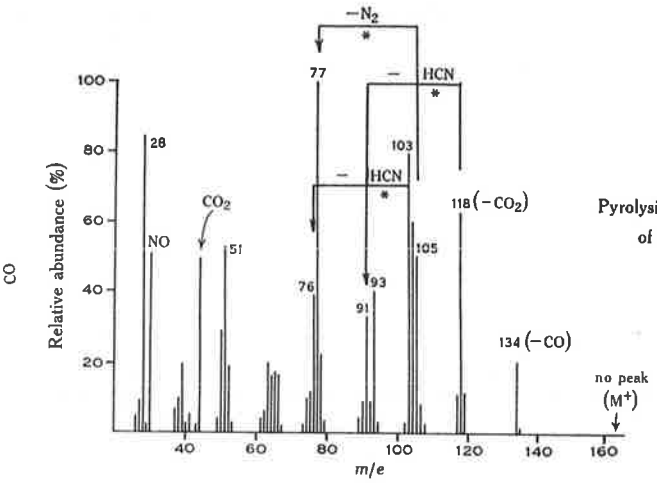


Fig. 2

Pyrolysis (200°/10^{-6} mmHg) of 3-phenylsydnone

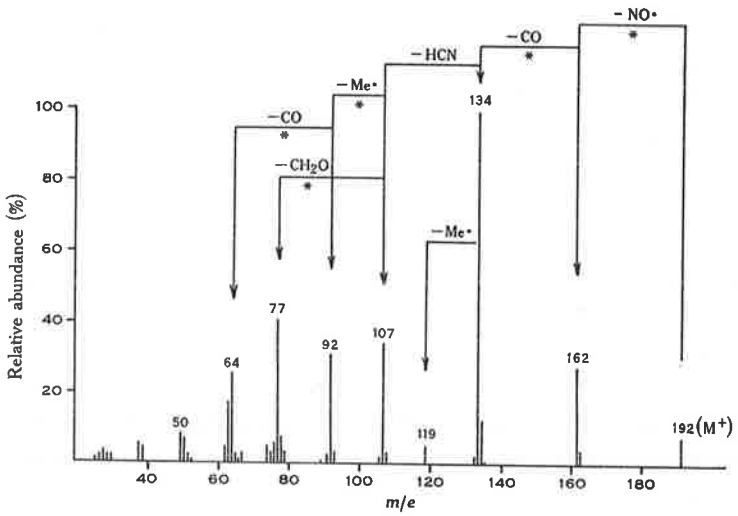
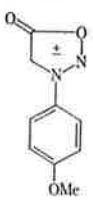


Fig. 3



(IV)

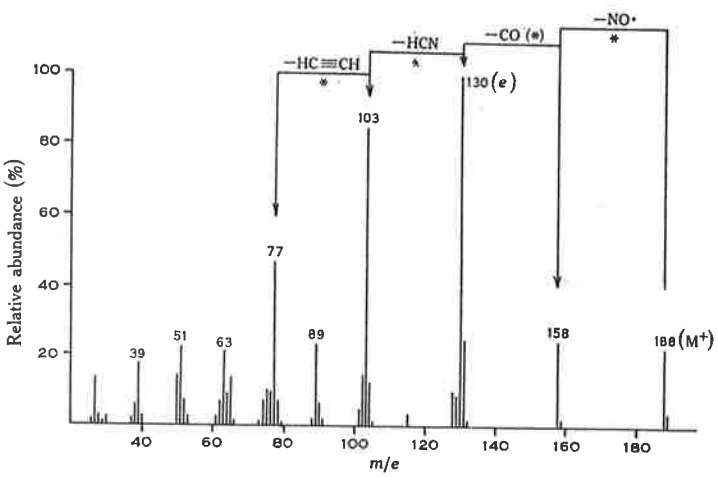
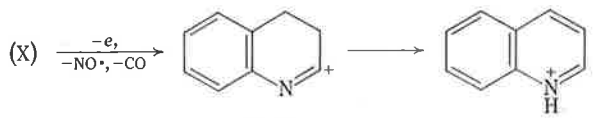


Fig. 4

(X)

electron beam is lowered to a nominal 10 eV, viz. for (VIII) (10 eV), M^+ (100%), M−30 (92%), M−58 (2%). It is of interest to note that this is not the case when the M−58 process may form an exceptionally stable cation, e.g., in the spectrum (Fig. 4) of the cyclic sydnone (X), it produces the species *e*, which probably rearranges to produce the stable protonated quinoline cation *f*. When the spectrum of (X) is measured at 10 eV, *m/e* 130 (*e*, M−58) is still the base peak.



e, *m/e* 130 *f*, *m/e* 130

All spectra were measured by the direct insertion technique, as it was found that sydnones [especially (I) and (III)] pyrolyse in the heated inlet system (*c.* 150–200° at 10^{-6} mmHg). 3-Phenylsydnone is the most unstable, and its mass spectrum (obtained at 200°) is illustrated in Figure 2. This should be compared with the true spectrum (Fig. 1) obtained by the direct insertion procedure. The compositions of the thermal decomposition products have been established by exact mass measurements. Species corresponding to the loss of CO (*m/e* 134) and CO_2 (*m/e* 118) are observed, but no product due to loss of NO is present. The most abundant decomposition product, *m/e* 103, corresponds to the benzoisonitrile molecular ion, and this representation is supported by its loss of HCN to *m/e* 76. Other ions noted in Figure 2 which are absent in Figure 1 are *m/e* 93 (C_6H_7N) which may correspond to aniline (both benzoisonitrile and aniline are produced when 4-chloro-3-phenylsydnone is treated with base[7]) and *m/e* 105 ($C_6H_5N_2^+$) which decomposes by loss of nitrogen and is possibly the diazonium cation.

Experimental

All mass spectra were measured with an Hitachi Perkin–Elmer RMU 6D double-focusing mass spectrometer (operating at 75 eV) by the "direct-insertion" procedure with source temperatures ranging from 50° (I and III) to 250° (VII and X).

Samples were synthesized by reported procedures: (I),[8] (II),[8] (III),[9] (IV),[10] (V),[11] (VII),[11] (VIII),[10] (IX),[11] and (X).[12]

p-*Ethoxycarbonylmethylphenylglycine Ethyl Ester*

A mixture of ethyl *p*-aminophenylacetate (18·0 g), anhydrous acetone (150 ml), anhydrous potassium carbonate (20 g), and ethyl bromoacetate (10 ml) was refluxed for 20 hr. Additional ethyl bromoacetate (2 ml) and potassium carbonate (10 g) were added after 10 hr. The hot acetone solution was filtered and the solvent was removed to give a crystalline product which was purified by the standard procedure.[10] The ester (15·4 g) separated from light petroleum (b.p. 60–80°) as needles, m.p. 49–50° (Found: C, 63·5; H, 7·4; N, 5·7. Calc. for $C_{14}H_{19}NO_4$: C, 63·4; H, 7·2; N, 5·3%).

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p-*Carboxymethylphenylglycine*

A mixture of the above diester (8·0 g), ethanol (5 ml), water (25 ml), and sodium hydroxide (2·6 g) were refluxed for 20 min. Careful acidification to pH 2 of the chilled reaction mixture gave the diacid (5·7 g) which separated as plates from water, m.p. 156–158° (dec.) (Found: C, 57·5; H, 5·3; N, 6·8. Calc. for $C_{10}H_{11}NO_4$: C, 57·4; H, 5·3; N, 6·7%).

N-*Nitroso*-N-p-*carboxymethylphenylglycine*

A suspension of the above diacid (2·08 g) in water (15 ml) was treated at 0° with a concentrated solution of sodium nitrite (0·8 g) in the absence of sunlight. After half an hour the clear reaction mixture was acidified. The crystalline nitroso derivative (2·23 g) which separated could be recrystallized from water to give prisms, m.p. 127–128° (dec.) (Found: C, 50·6; H, 4·4; N, 11·5. Calc. for $C_{10}H_{10}N_2O_5$: C, 50·4; H, 4·2; N, 11·8%).

3-(p-*Carboxymethylphenyl*)*sydnone*

The nitroso compound (1 g) gave at room temperature under the standard conditions,[10] 0·9 g of crude sydnone after four days' reaction. The sydnone separated as needles, m.p. 195–196° (dec.), from acetone (Found: C, 54·8; H, 3·9; N, 12·4. Calc. for $C_{10}H_8N_2O_4$: C, 54·6; H, 3·7; N, 12·7%).

Acknowledgment

The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

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ELECTRON IMPACT STUDIES—XXIX[1]

THE $C_{13}H_9$ SKELETAL-REARRANGEMENT FRAGMENT IN THE MASS SPECTRA OF HETEROCYCLIC SYSTEMS CONTAINING DIPHENYL SUBSTITUENTS. A DEUTERIUM LABELLING STUDY

J. H. BOWIE, P. F. DONAGHUE, H. J. RODDA and B. K. SIMONS

Department of Organic Chemistry, The University of Adelaide, South Australia 5001

(*Received in the UK* 13 *November* 1967; *accepted for publication* 12 *December* 1967)

Abstract—The *m/e* 165 ion ($C_{13}H_9$) has been noted in the mass spectra of a variety of heterocyclic systems containing two (or more) phenyl substituents. This skeletal-rearrangement fragment is most prominent in the spectra of particularly substituted oxazoles, imidazoles and thiazoles. Deuterium-labelling studies have allowed probable mechanistic formulations in the case of the 4,5-diphenylimidazoles, and the detection of two alternate rearrangement pathways in the spectrum of 2,4,5-triphenyloxazole. A comparison is made between the formation of *m/e* 165 in the spectrum of stilbene and 9,10-dihydrophenanthrene.

DURING a study of the mass-spectral fragmentations of substituted imidazoles,[2] it was observed that the spectra of 4,5-diphenylimidazoles exhibited pronounced skeletal-rearrangement fragments at *m/e* 165 ($C_{13}H_9^+$, high resolution). This ion is formed directly from the molecular ion, and its formation demands a Ph migration. Similar phenomena are observed[3] in the spectra of the isomeric diphenyloxazoles, and tentative mechanisms have been proposed for the genesis of the rearrangement ion. The $C_{13}H_9$ ion is also observed in the spectra of 2,5-diphenyl-1,2,4-oxadiazole

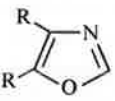
TABLE 1. RELATIVE ABUNDANCE OF *m/e* 165. FRAGMENTS IN THE MASS SPECTRA OF DIPHENYL HETEROCYCLES

Compound	Abund. of *m/e* 165 (%)	Compound	Abund. of *m/e* 165 (%)
4,5-Diphenylimidazole	42	2,4-Diphenylthiazole	1
2-Isopropyl-4,5-diphenylimidazole	26	3,5-Diphenylisoxazole	4
2,4,5-Triphenylimidazole	100	3,5-Diphenylpyrazole	7
4,5-Diphenyloxazole	75	3,4-Diphenylpyrazole	21
2-Methyl-4,5-diphenyloxazole	86	2,5-Diphenylfuran	3
2-Ethyl-4,5-diphenyloxazole	100	5-Methyl-2,3-diphenylpyrrole	2
2-*n*-Pentyl-4,5-diphenyloxazole	73	2,3-Diphenylthiophen	7
2,4,5-Triphenyloxazole	80	2,4-Diphenylthiophen	5
2,5-Diphenyloxazole	53	2,5-Diphenylthiophen	2
4,5-Diphenylthiazole	85	2-Chloro-5,6-diphenylpyrazine	2
2-Amino-4,5-diphenylthiazole	45	3,6-Diphenylpyridazine	0

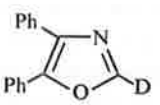
(53% of the base peak),[4] 4,5-diphenyl-2-pyrone (18%),[5] 3,4-diphenyl-4,5-epoxy-2-cyclopenten-1-one (21%)[5] diphenylmethane (29%),[6] stilbene (30%)[7] and 9,10-dihydrophenanthrene (30%).[8]

As a knowledge of skeletal-reorganization processes in mass spectrometry is extremely important,[9] it was decided to investigate (a) whether the presence of a prominent $C_{13}H_9$ peak is characteristic of all compounds containing the Ph—C=C—Ph unit, and (b) to study the genesis of the rearrangement ion in the spectra of the 4,5-diphenyloxazoles, the 4,5-diphenylimidazoles, stilbene and 9,10-dihydrophenanthrene, by deuterium-labelling studies. This paper deals primarily with these problems.

The relative abundances of the $C_{13}H_9$ fragments in the mass spectra of some heterocyclic compounds are summarized in Table 1. It can be clearly seen that the rearrangement fragment is pronounced in the spectra of 4,5-diphenyloxazoles (where in several cases it constitutes the base peak of the spectrum), 4,5-diphenylimidazoles, 4,5-diphenylthiazoles and 2,5-diphenyloxazoles. In the case of the 5-membered heterocycles containing one heteroatom, and with adjacent Ph substituents, the rearrangement peak is less than 10% of the base peak,* while the *m/e* 165 peak is either small or absent in the spectra of the two 6-membered compounds. Therefore, a pronounced $C_{13}H_9$ peak is not characteristic of the Ph—C=C—Ph moiety, but is generally confined to 5-membered heterocyclic systems containing two heteroatoms (normally in 1,3 positions), and to isolated instances, including diphenylmethane, stilbene and dihydrophenanthrene.

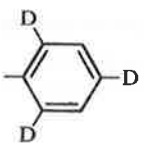


1: R = Ph



3

2: R =



The mass spectra of 4,5-diphenyloxazole **1** and the two labelled derivatives **2** and **3** are recorded in Figs 1–3. It has been shown previously that hydrogens on aromatic rings become equivalent upon electron impact[10,11] and that randomization does not occur for isolated hydrogen substituents attached to the oxazole nucleus.[12] This situation has also been apparent throughout this study, and consequently, even though the benzene rings are specifically labelled with deuterium, fragmentations involving loss of deuterium and/or hydrogen atoms from the benzene rings of **2** will occur in the ratio 3:2 (D:H) (ignoring possible isotope effects). In the spectrum (Fig. 1) of 4,5-diphenyloxazole **1**, *m/e* 165 may be formed by two pathways: viz.

* The skeletal-rearrangement fragments observed in the mass spectra of isoxazoles, pyrazoles, 2,5-diphenyl-furan, -pyrrole and -thiophen, will be the subject of a future publication.

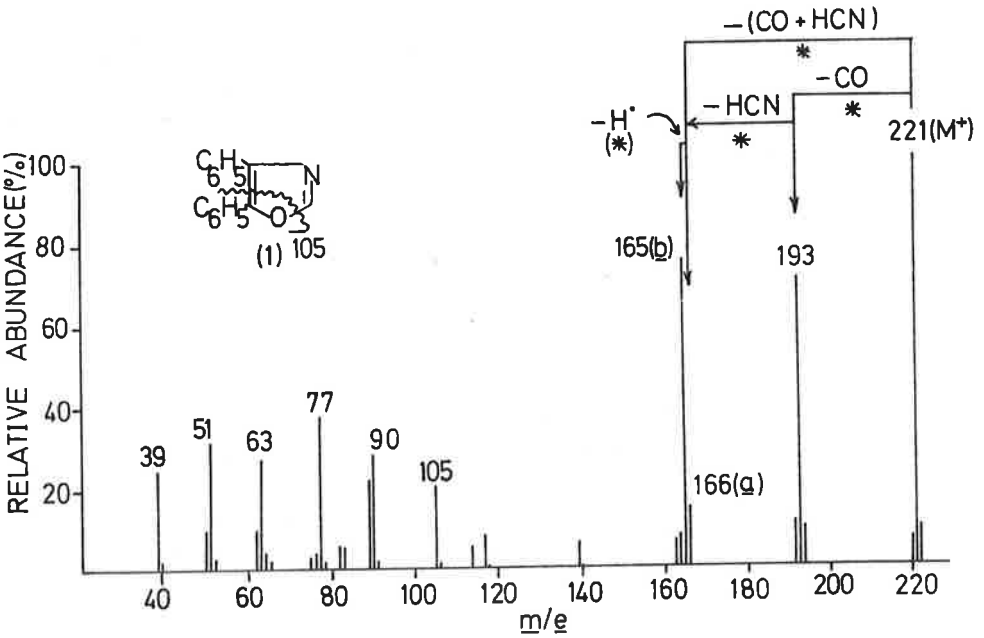

RELATIVE ABUNDANCE(%)
m/e
(1) 105
-(CO + HCN)
-CO
-HCN
-H·
(*)
221(M+)
165(b)
193
166(a)
39
51
63
77
90
105

FIG. 1.

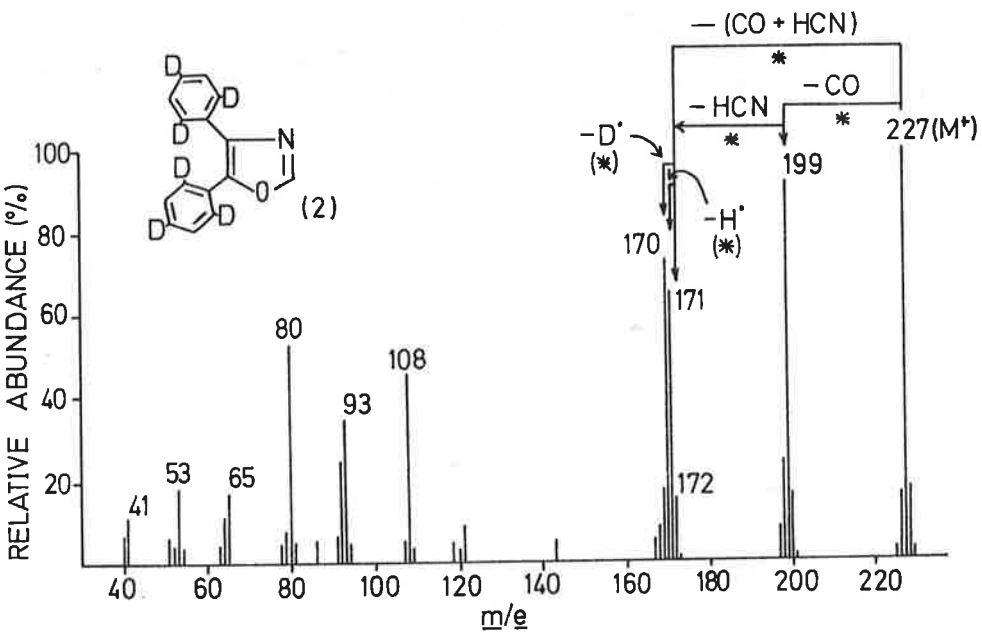

RELATIVE ABUNDANCE (%)
m/e
(2)
— (CO + HCN)
-CO
-HCN
-D·
(*)
227(M+)
199
-H·
(*)
170
171
172
41
53
65
80
93
108

FIG. 2

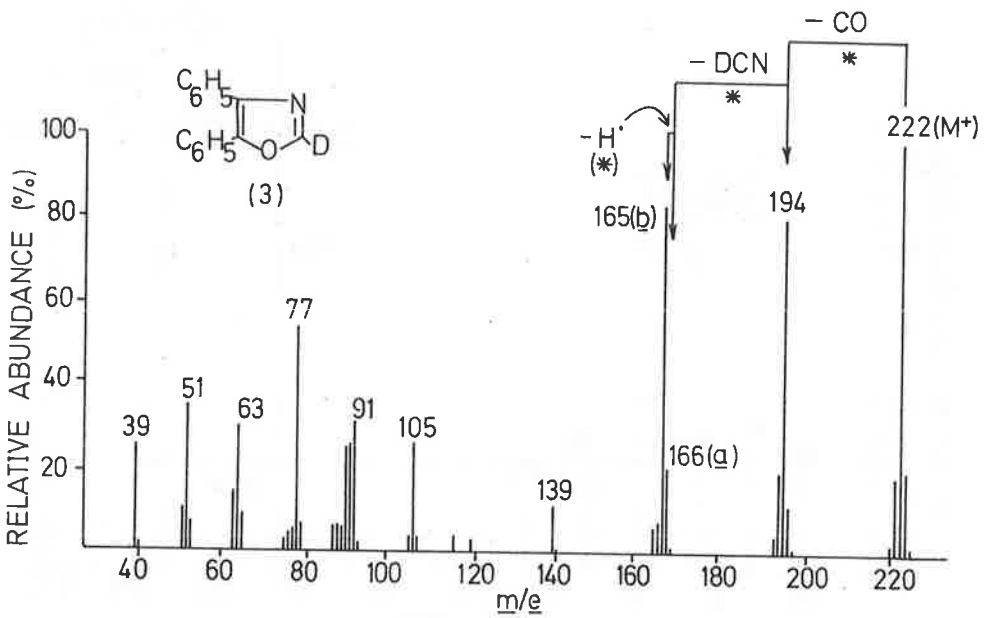
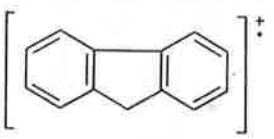
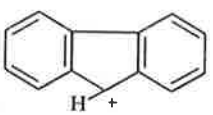


FIG. 3.

(a) M—(CO + HCN)—H· and (b) M—CO—HCN—H· [appropriate metastable ions (denoted by an asterisk in the Figs) substantiate all processes]. These processes are modified in the spectra of all the 2-substituted 4,5-diphenyloxazoles to M—(CO + RCN)—H· and M—CO—RCN—H·. When the energy of the electron beam is reduced to 10 eV, the process M → *m/e* 166 is always pronounced, with *m/e* 165 being the minor component. Even though structures drawn for fragment ions are nominal only, it is argued that the most plausible structures for *m/e* 166 and 165, correspond to the fluorene radical ion (*a*) and cation (*b*), respectively, although this does not preclude the possibility of more extensive rearrangement.



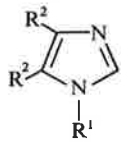
a: *m/e* 166



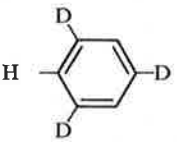
b: *m/e* 165

The spectra (Figs 2 and 3) of the labelled compounds **2** and **3** show that the two Ph rings are involved in the formation of the fluorene cation [i.e. the processes M—CO—HCN—H· or M—CO—HCN—D· produce *m/e* 171 or 170 respectively (Fig. 2)], and that the deuterium at C-2 in (**3**) is specifically lost in the initial process, and plays no part in the formation of the rearrangement ion. The latter observation negates the earlier mechanistic proposal[3] for the formation of *m/e* 165 from 4,5-diphenyloxazole, as this mechanism invokes the participation of the hydrogen at

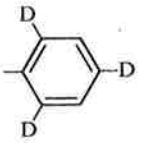
C-2 in the transformation. Nevertheless, the above observations still do not allow unequivocal proposals to be advanced for the mechanism.

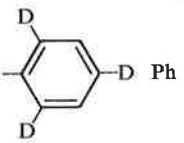


	R^1	R^2
4	H	Ph
5	D	Ph



	R^1	R^2	R^3
7	H	Ph	Ph
8	D	Ph	Ph





However, the spectra of the imidazoles **4**–**10** permits conclusions to be reached concerning the genesis of the ion *b*. The spectra (Figs 4 and 6) of 4,5-diphenylimidazole (**4**) and 2,4,5-triphenylimidazole (**7**) are different from that of 4,5-diphenyloxazole (**1**), as in these spectra, *b* (*m/e* 165) is formed directly from the molecular ions (concerted losses of $C_2H_3N_2\cdot$ and $C_8H_7N_2\cdot$ respectively). Metastable ions substantiate these processes, which, although concerted, do not necessarily occur by one-step processes.[13] The spectra (e.g. Fig. 6) of the N–d_1 derivatives **5** and **8** show incorporation of deuterium into the rearrangement peaks, and after a calculation (which is approximate because of M-1 and M-2 peaks) to allow for incomplete labelling, a value of $50 \pm 10\%$ is obtained for the incorporation of deuterium into the rearrangement ions (now *m/e* 165, 166 and 167). Such a value is much too high to be accounted for by randomization of the label, and a specific transfer process is indicated. It is of interest to note that the spectrum (Fig. 7) of **10** shows that the phenyl substituent at C-2 is not involved in the rearrangement process.

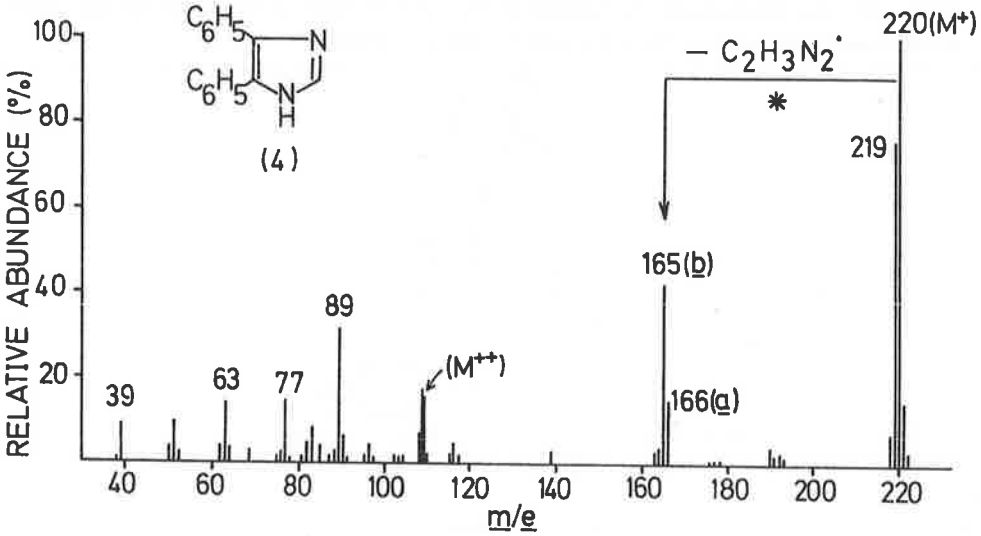

RELATIVE ABUNDANCE (%)
m/e
(4)
220(M+)
219
165(b)
166(a)
89
(M++)
39
63
77
– C2H3N2·
*

FIG. 4.

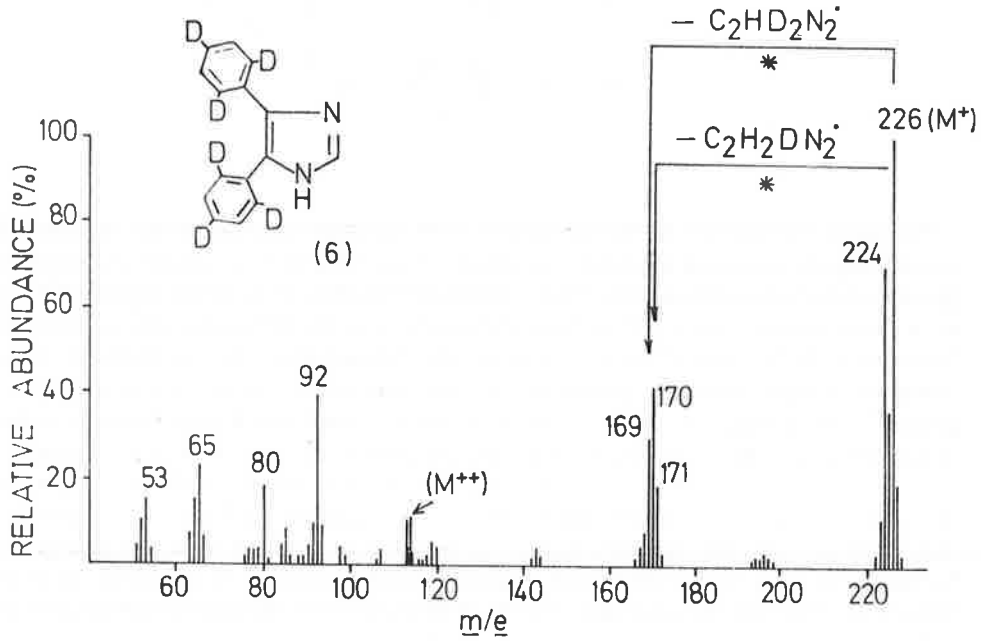

RELATIVE ABUNDANCE (%)
m/e
(6)
226 (M+)
224
92
65
80
53
(M++)
169
170
171
– C2HD2N2·
– C2H2DN2·
*

FIG. 5.

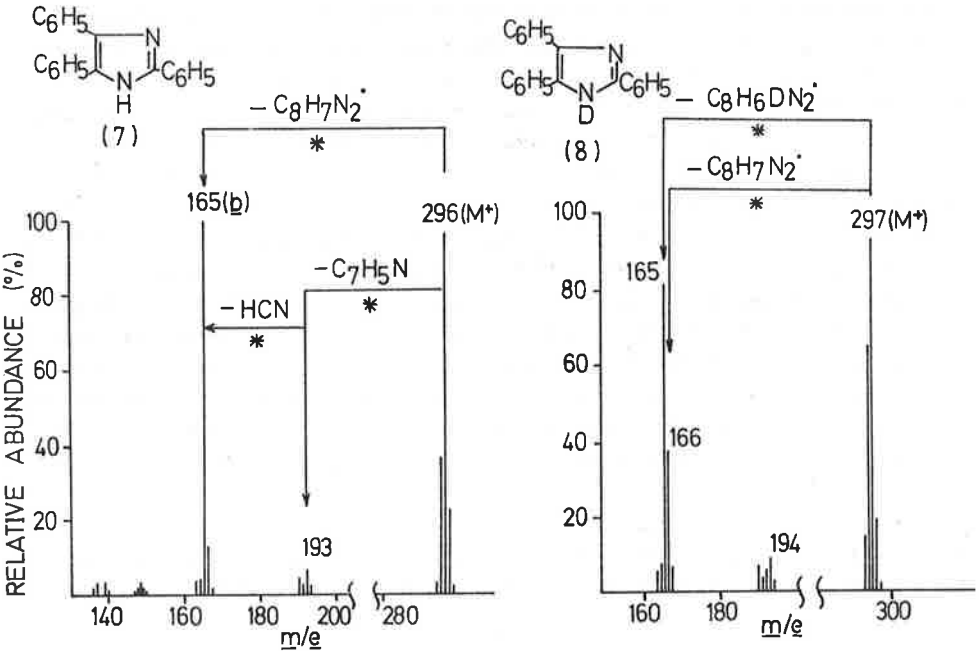

(7)
(8)
– C8H7N2·
– C8H6DN2·
– C7H5N
– HCN
165(b)
296(M+)
297(M+)
193
194
166
RELATIVE ABUNDANCE (%)
m/e

FIG. 6.

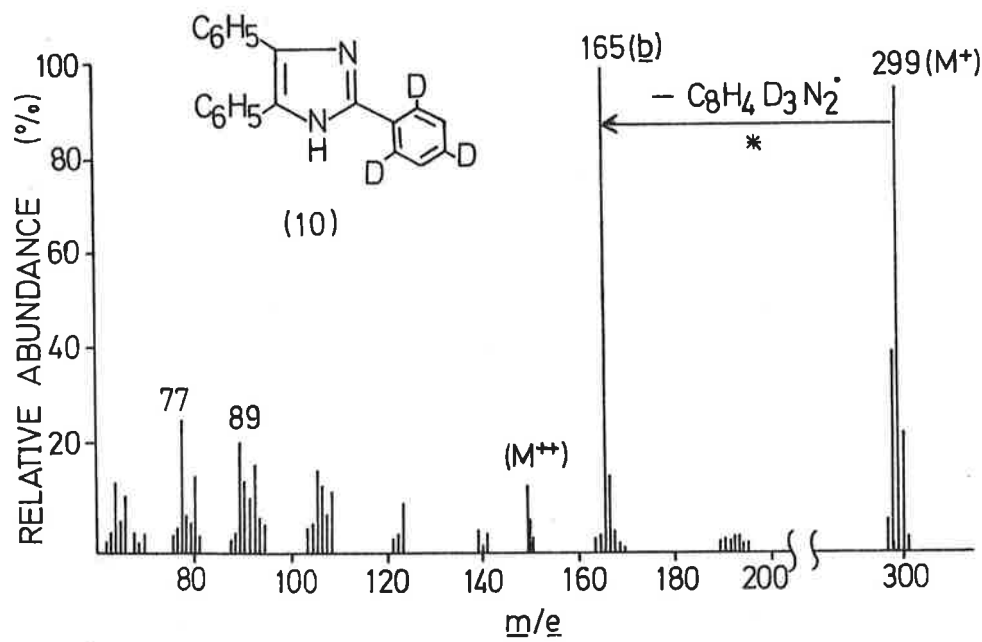
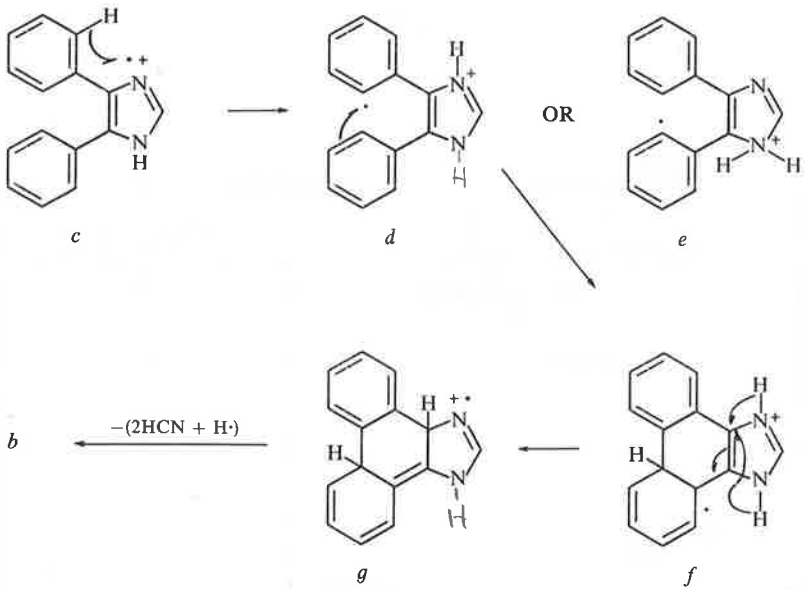

(10)
165(b)
299(M+)
– C8H4D3N2·
(M++)
77
89
RELATIVE ABUNDANCE (%)
m/e

FIG. 7.

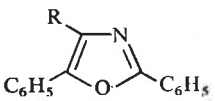
The spectra of the d_6-derivatives **6** and **9** demonstrate the participation of a second hydrogen-transfer process. The spectrum of **6** is illustrated in Fig. 5, and it should be noted that the ratios of *m/e* 169:170:171 are identical in the spectra of **6** and **9**, although the relative abundances of the peaks are not the same in the two spectra. Two concerted eliminations are noted, viz. in Fig. 5, M—$C_2H_2DN_2$· (to *m/e* 170) and M—$C_2HD_2N_2$· (to *m/e* 169). The presence of the second process can only mean that a deuterium has migrated from a Ph ring to the imidazole ring in order to allow the loss of the second D atom in the rearrangement. This migration must of course involve both D and H atoms in the ratio 3:2. To explain this double hydrogen rearrangement, Scheme 1 is proposed for the formation of *b*. Migration of a H atom to either nitrogen, produces *d* or *e*, which cannot be distinguished (we have a marginal preference for *d* because it forms symmetrical intermediates). The production of *d* (or *e*) provides an electron-deficient centre on one of the aromatic rings to which the other may migrate (e.g. $d \rightarrow f$). In order for the rearrangement to proceed, either hydrogen on nitrogen must migrate back to the "fluorene-centre". There is an equal probability of either hydrogen migrating, as *f* may be considered as a symmetrical intermediate, and although the acceptor-site of the rearrangement is not known, a possible formulation is *g* (it is possible that the imidazole ring may have opened by this stage), which may now readily fragment to the fluorene cation.

SCHEME 1

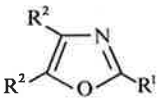


Although this rationale is speculative, it explains the hydrogen rearrangements, and may be correlated with the ratios of *m/e* 169:170:171 in the spectra of **6** and **9**. A simple calculation assuming deuterium/hydrogen rearrangement to nitrogen in the ratio 3:2, followed by 50% back exchange of each atom (H or D) on nitrogen together with the possible eliminations to produce the rearrangement ions, gives a calculated ratio for the *m/e* 169, 170 and 171 peaks as 1·0:2·1:1·2. When isotopic corrections,

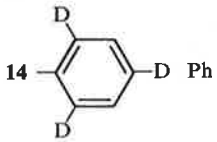
and approximate corrections due to incomplete labelling are made, the observed ratios are 1·0:1·5:0·9. These ratios are not inconsistent when the approximations inherent in the calculations are considered, and also as possible isotopic effects have been ignored. If one argues by analogy, a similar mechanism could apply to the formation of *b* in the spectra of the 4,5-diphenyloxazoles and -thiazoles, although it is recognized that this double-hydrogen rearrangement could not occur in such cases.



11: R = H
12: R = D



	R^1	R^2
13	Ph	Ph



The formation of the fluorene cation (*b*) in the spectrum of 2,5-diphenyloxazole (**11**) has been noted previously,[3] and a mechanism has been proposed for its formation. We wished to compare this rearrangement with that observed in the spectrum of 4,5-diphenyloxazole. The spectra of **11** and **12** are illustrated in Fig. 8, and it can be seen that the hydrogen at C-4 is not involved in the formation of *b*. Apart from the fact that Ph migration must occur, no concrete proposal can be presented for the mechanism, but it is noteworthy that the formation of *b* in the spectrum of 2,4-diphenyloxazole occurs only to the extent of 5%.[3] It has already been shown (*vide supra*) that the 2-phenyl group of 2,4,5-triphenylimidazole is not involved in the formation of *b*,

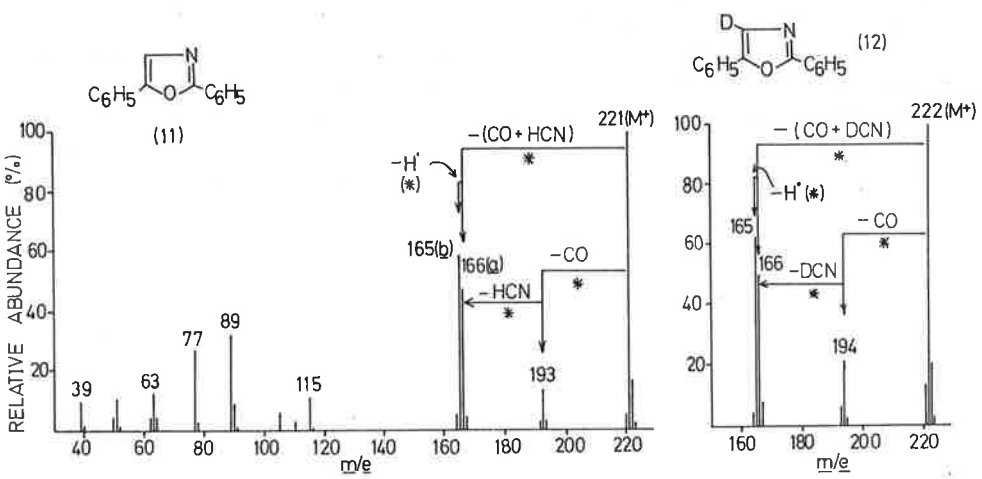


FIG. 8.

but because of the pronounced rearrangement occurring in the spectrum of 2,5-diphenyloxazole, the spectra (Fig. 9) of 2,4,5-triphenyloxazole (**13**) and **14** were examined. Fig. 9 shows the occurrence of two distinct processes, *viz.* (a) the formation of *b* from the 4,5-Ph groups via the normal pathway (60%), and (b) formation of the

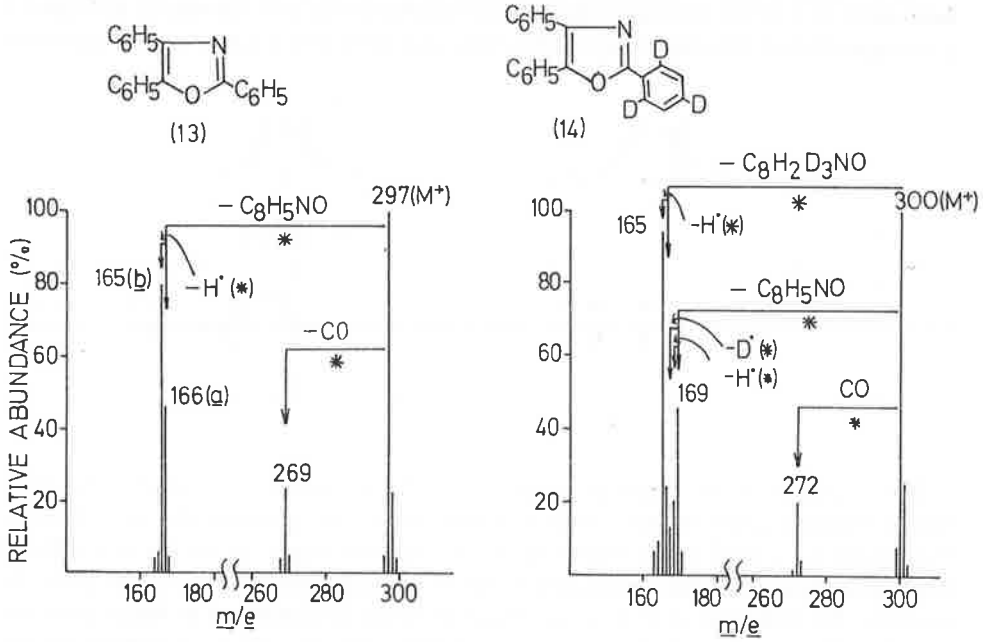
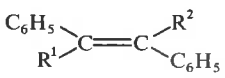


FIG. 9.

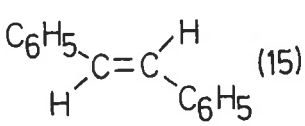
d_3-fluorene radical ion (*m/e* 169) from the 2,5-phenyl substituents (40%). This ion (*m/e* 169) may either lose a H atom (to *m/e* 168) or a D atom (to *m/e* 167). When the energy of the electron beam is reduced to 10 eV, only two ions are observed in the *m/e* 165–170 region; *m/e* 166 and 169 in the ratio 2:3. This implies that the formation of the fluorene radical ion (*a*) from the 2 and 5 Ph groups is more energetically favourable than its formation from the 4 and 5 Ph substituents. It is assumed that bond formation does not occur between the 2 and 4 Ph substituents, because of the small relative abundance of *b* in the mass spectrum of 2,4-diphenyloxazole. The loss of carbon monoxide from the molecular ions of 2,4,5-trisubstituted oxazoles has been reported previously.[12]



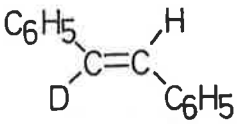
	R^1	R^2
15	H	H
16	H	D
17	D	D

18: R = H
19: R = D

Finally, it was of interest to examine the almost identical spectra of stilbene[7] and 9,10-dihydrophenanthrene,[8] which both lose a Me radical from their molecular ions to form *m/e* 165 (*b*, 30% of the base peak). In order to examine this feature, **17** was required. The synthesis of this compound was approached by equilibration of desoxybenzoin with MeOD/Na, then reduction with LAD followed by elimination of D_2O. Unfortunately, the initial step gives only 65% of the d_2 species, any further equilibration then results in deuteration of the aromatic system. As the final product contains only ca. 75% d_2, compound **16** was used for this study. The partial spectra of the stilbenes **15** and **16** are illustrated in Fig. 10. The ratios of the 165/166 peaks



(15)



(16)

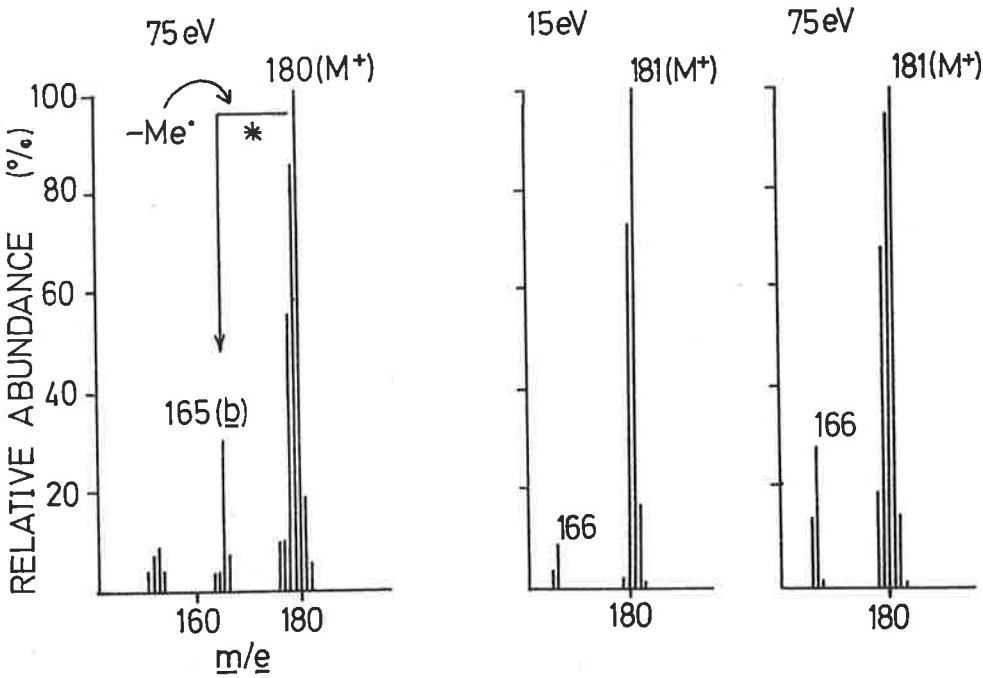
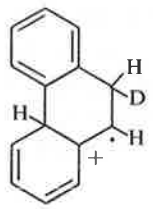


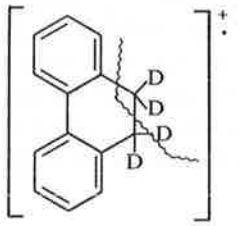
FIG. 10.

in the spectrum of **16** are unchanged at 75, 20, 15 and 10 eV and each spectrum shows 34% relative loss of $CH_2D\cdot$ and 66% of $CH_3\cdot$. This cannot be explained by randomization of the hydrogen (or deuterium) on the olefinic link with the aromatic hydrogens, nor can it be explained by an intermediate of the type *h*, which would be the species obtained from an adaptation of the mechanism outlined in Scheme 1 (the participation of such an intermediate is unlikely in any case, as it has been demonstrated above that the heteroatoms play a significant part in the mechanism

outlined in Scheme 1). Further rearrangement of *h* has been previously used to explain the loss of a methyl radical from the stilbene molecular ion.[14] Although the mechanism for the loss of Me· from the stilbene molecular ion is not clear, it seems that at least

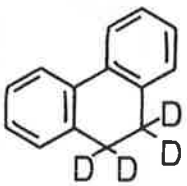


h: *m/e* 181



i: *m/e* 184

two processes may be involved. The loss of a methyl radical from 9,10-dihydrophenanthrene (**18**) is even more difficult to explain. The spectrum (Fig. 11) of the d_4-derivative (**19**) might be expected to exhibit loss of CD_3· (see *i*). However, the



(19)

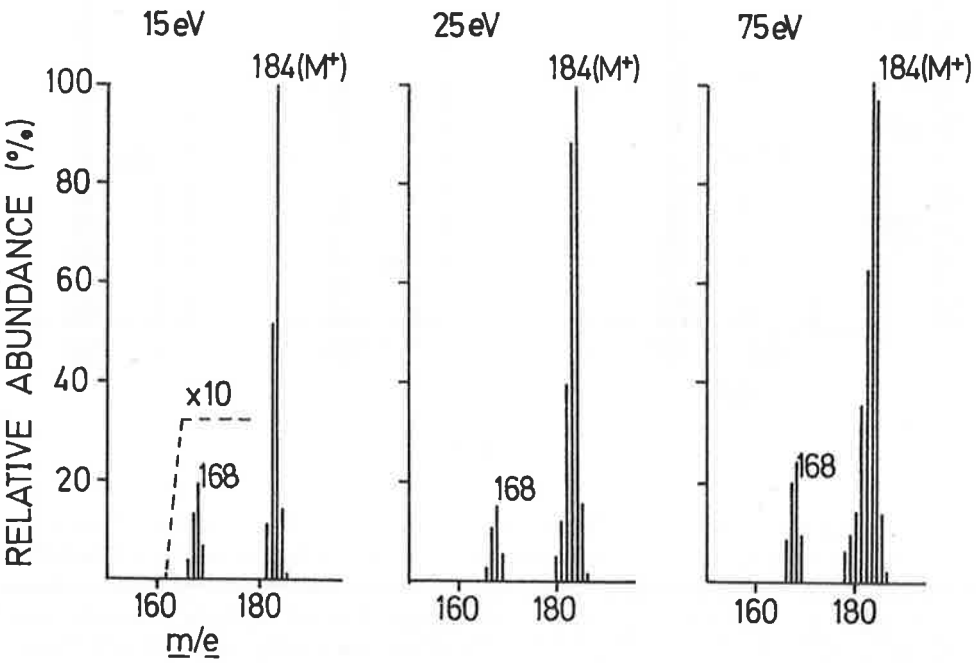


FIG. 11.

loss of CD_3· is minor, the major losses being CH_2D· and CD_2H·. Again, the *m/e* 166, 167, 168, 169 ratio is not markedly affected by decreasing the energy of the electron beam (see Fig. 11), and it appears that little randomization of deuterium occurs. In a previous paper[8] it was assumed that hydrogen lost in the M—H_2 process [to produce the phenanthrene molecular ion (*m/e* 178)] originated from the 9,10 positions of 9,10-dihydrophenanthrene. This is not the case, as the major loss in the spectrum of **19** is H_2 and not D_2, and probably indicates considerable rearrangement of the molecular ion. Although the losses of Me· from stilbene and 9,10-dihydrophenanthrene are complex, there is little doubt that the formation of *b* proceeds differently in these cases than it does for 4,5-diphenylimidazole.

These studies demonstrate yet again that extreme caution must be exercised when postulating mass-spectrometric mechanisms without the aid of the spectra of suitably labelled derivatives.

EXPERIMENTAL

All mass spectra were determined with an Hitachi Perkin–Elmer RMU 6D double focussing mass spectrometer operating at 75 eV (unless otherwise specified) with a source temp of approximately 150° and an inlet temp between 50° and 200°.

All samples used in this study were routinely checked for purity by nuclear magnetic resonance and mass spectrometry.

4,5-Diphenylimidazole, 2-isopropyl-4,5-diphenylimidazole and 2,5-diphenyloxazole were purified commercial samples. The following compounds were prepared by reported procedures: 2,4,5-triphenylimidazole,[15] 4,5-diphenyloxazole,[16] 2-methyl-4,5-diphenyloxazole,[17] 2-ethyl-4,5-diphenyloxazole,[18] 4,5-diphenyl-2-n-propyloxazole,[18] 2-n-pentyl-4,5-diphenyloxazole,[12] 2,4,5-triphenyloxazole,[17] 4,5-diphenylthiazole,[19] 2-amino-4,5-diphenylthiazole,[21] 2,4-diphenylthiazole,[22] 3,5-diphenylisoxazole,[23] 3,5-diphenylpyrazole,[23] 3,4-diphenylpyrazole,[24] 2,5-diphenylfuran,[25] 2,5-diphenylpyrrole,[26] 5-methyl-2,3-diphenylpyrrole,[27] 2,3-diphenylthiophen,[28] 2,4-diphenylthiophen,[29] 2,5-diphenylthiophen,[29] 2-chloro-5,6-diphenylpyrazine,[30] and 3,6-diphenylpyridazine.[31]

The spectra of 5 and 8 were obtained by introducing 4 and 7 into the source with deuterium oxide.[32]

Labelled compounds

2,4,6-d_3-*Benzaldehyde.* Prepared from 2,4,6-d_3-aniline by the method of Williams *et al.*[11]

2,4,6-d_3-*Benzoylchloride.* Prepared in quantitative yield by oxidation of 2,4,6-d_3-benzaldehyde with $KMnO_4$ aq, followed by treatment of 2,4,6-d_3-benzoic acid with $SOCl_2$.

2,4,6,2′,4′,6′-d_6-*Benzoin.* Prepared from 2,4,6-d_3-benzaldehyde by the benzoin condensation.

2,4,6,2′,4′,6′-d_6-*Benzil.* Prepared in quantitative yield by HNO_3 oxidation of 2,4,6,2′,4′,6′-d_6-benzoin. ($d_5 = 4\%$, $d_6 = 96\%$).

2-d-4,5-*Diphenyloxazole* (**3**). 4,5-Diphenyloxazole (0·58 g) in dry ether (10 cc) was added to a soln of n-BuLi [from Li (0·086 g) and n-BuBr (0·69 g)] in dry ether (20 cc) at −65°, under dry O_2-free nitrogen. After stirring for 30 min, D_2O (5 cc) was added, the ethereal soln was separated, dried (Na_2SO_4) and evaporated. The product was purified by preparative VPC (30% SE30, 12′). The NMR spectrum lacked the singlet at 2·19 τ indicative of the 2-H of 4,5-diphenyloxazole.[20]

4,5-*Di*(2,4,6-d_3-*phenyl*)*oxazole* (**2**). Prepared from d_6-benzoin by the method of Theilig.[18] Purified by preparative VPC (see above) b.p. 190–194°/14 mm Hg.

2-(2,4,6-d_3-*Phenyl*)4,5-*diphenyloxazole* (**14**). 2,4,6-d_3-Benzoylchloride (1·3 g) and benzoin (2·1 g) were warmed on a water bath for 1 hr. The benzoin-d_3-benzoate was cyclized to 14 by the method of Davidson *et al.*[17] The crude product was chromatographed over alumina in ether, and crystallized from EtOH as colourless prisms, m.p. 115–116°.

4-*Bromo*-2,5-*diphenyloxazole.* To a soln of 2,5-diphenyloxazole (4·4 g) in glacial AcOH (100 cc), boiling under reflux, was added a soln of Br_2 (3·2 g) in AcOH (15 cc) over a period of 1 hr. The mixture was cooled and a solid ppt removed. The filtrate was poured onto ice (800 g), extracted with ether (3 × 100 cc), and the combined extracts washed with Na_2CO_3 aq, water, and then dried (Na_2SO_4). Removal of the ether left a solid which was chromatographed over alumina in light petroleum:ether (92:8) to give

4-bromo-2,5-diphenyloxazole (1·1 g, 31%), which crystallized from light petroleum as colourless needles, m.p. 70–71°. (Found: C, 60·2; H, 3·5; N, 4·6; Br, 26·3. $C_{15}H_{10}Br$ requires: C, 60·5; H, 3·4; N, 4·7; Br, 26·6%). The NMR spectrum lacks the singlet at 2·68 τ attributed to the 4-H of the oxazole system.[20]

3-d_1-2,5-*Diphenyloxazole* (**12**). To 4-bromo-2,5-diphenyloxazole (0·3 g) in dry ether (10 cc) was added soln of n-BuLi [from Li (0·07 g) and n-BuBr (0·68 g)] in ether (20 cc), at −65°, for 1 hr, decomposed with D_2O (4 ml) and worked up as for 3. The product (0·2 g) was purified by sublimation, followed by preparative VPC (see above), m.p. 72–73°. The NMR spectrum completely lacked the characteristic singlet at 2·68 τ in the spectrum of 2,5-diphenyloxazole.[20]

4,5-*Di*(2,4,6-d_3)*phenylimidazole* (**6**). Prepared from d_6-benzil, formaldehyde and formamide (cf. Ref. 15). Crystallized from aqueous EtOH as colourless needles, m.p. 232–233°, yield 61%.

2-*Phenyl*-4,5-di(2,4,6-d_3)*phenylimidazole* (**9**). Prepared from d_6-benzil, benzaldehyde and formamide (cf. Ref. 15). Crystallized from aqueous EtOH as colourless needles, m.p. 270–272°, yield 60%.

2-(2,4,6-d_3)*Phenyl*-4,5-*diphenylimidazole* (**10**). Prepared from benzil, 2,4,6,-d_3-benzaldehyde and formamide as for 9, m.p. 273–274°.

d_1-*Stilbene* (**16**). Reduction of desoxybenzoin with LAD gave 1-d_1-1,2-diphenylethanol, which was dehydrated in DMSO to give d_1-stilbene, m.p. 124–125° (cf. Ref. 33). This was purified by preparative VPC. The NMR spectrum indicated quantitative incorporation of D (>99% d_1).

9,10-d_2-9,10-*Dideuterophenanthrene* (**19**). Reduction of the dimethyl ester of diphenic acid with LAD gave 2,2′-(d_2-hydroxymethyl)diphenyl, which was converted to 19 by the method of Hall *et al.*[34] Purification by preparative VPC gave 19, b.p. 174°/17 mmHg. The NMR spectrum indicated quantitative incorporation of D (>99% d_4).

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THE MASS SPECTRA OF NITRONES

C—O BOND FORMATION UPON ELECTRON IMPACT[1]

B. SØGAARD LARSEN, G. SCHROLL and S.-O. LAWESSON
Department of Organic Chemistry, Aarhus University, 8000 Aarhus C., Denmark

J. H. BOWIE
Department of Organic Chemistry, University of Adelaide, South Australia. 5000

and

R. G. COOKS
University Chemical Laboratory, Lensfield Road, Cambridge, England

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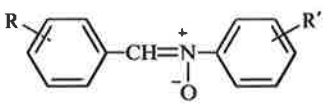
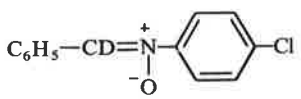
Abstract—The mass spectra of a series of nitrones are reported and discussed. All spectra contain molecular ions, and the majority of fragment ions owe their genesis to skeletal-reorganization of the molecular ion. Fragmentation modes have been substantiated by high-resolution data and appropriate metastable ions. Deuterium labelling has been used to elucidate the M—H$^{\cdot}$ process which is observed in many spectra.

THE mass spectra of pyridine N-oxides,[2] quinoline N-oxides,[3–5] Δ^1-pyrroline N-oxides,[2] phenazine and benzo[a]phenazine N-oxides[6] and aromatic azoxy compounds[7,8] have been reported. Skeletal-rearrangement fragments (produced by C—O bond formation) are observed in the mass spectra of N-oxides[4–6] and azoxy compounds.[7,8]

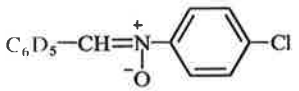
As a logical extension of the work on N-oxides[6] and azoxy compounds,[7,8] we have synthesized a series of nitrones (I–XV) and have measured their mass spectra.



	R	R′
I:	H	H
II:	*p*-Me	H
III:	*p*-Cl	H
IV:	H	*p*-Cl
V:	*m*-OH	H
VI:	*o*-OH	H
VII:	*o*-OD	H
VIII:	*p*-OMe	H
IX:	*m*-NO_2	H
X:	*p*-Cl	*p*-Cl
XI:	*o*-OH	*p*-Cl
XII:	*o*-OMe	*p*-Cl
XIII:	*p*-NO_2	*p*-Cl



XIV



XV

This study was also prompted from the knowledge[9] that nitrones undergo photochemical cyclization to oxaziridines. The spectra are recorded in Table 1 or Figs 1–8, exact mass measurements are listed in Table 2. The presence of an appropriate

TABLE 1. MASS SPECTRA OF V–VII, AND X–XIII*

V	*m/e*	26	27	28	29	38	39	40	41	43	44	45	46	50	51	52	53	55	57	63	64
	I(%)	6	20	13	16	13	40	8	18	23	13	16	8	16	51	8	8	7	7	16	16
		65	66	68	72	74	75	76	77	78	91	92	93	94	104	105	107				
		41	13	8	16	6	6	6	100	9	24	6	36	13	16	8	8				
		109	121	122	141	167	184	196	197	198	213(M)										
		7	47	36	6	8	7	65	70	11	18										
VI	*m/e*	28	39	50	51	52	65	64	65	66	76	77	78	91	92	93	94	104	105	120	
	I(%)	7	12	9	38	8	9	15	17	8	6	86	14	100	16	24	12	11	7	10	
		121	141	167	168	184	185	196	197	212	213(M)	214									
		15	6	15	12	13	19	76	41	6	61	14									
VII	*m/e*	27	28	38	39	40	50	51	52	63	64	65	66	76	77	78	91	92	93	94	
	I(%)	10	8	8	24	6	12	62	11	12	21	18	12	6	88	14	100	13	13	22	
		95	104	105	120	121	122	167	168	185	186	196	197	198	213	214(M^+)					
		11	8	7	6	11	11	9	6	8	7	35	24	14	15	23					
		$d_0 = 38$; $d_1 = 62\%$																			
X	*m/e*	38	39	50	51	62	63	64	73	74	75	76	77	87	89	90	99	111	112	113	
	I(%)	6	14	24	20	9	25	8	7	12	57	16	7	4	18	35	14	86	10	25	
		125	126	127	128	138	139	140	141	152	248	249	250	251	252	253	264				
		100	12	44	9	8	26	8	16	5	18	25	19	16	7	6	8				
		265(M)	266	267(M)																	
		13	7	8																	
XI	*m/e*	27	38	39	40	50	51	52	53	61	62	63	64	65	66	73	74	75	76	77	78
	I(%)	10	10	31	7	16	26	12	8	6	8	20	12	26	8	7	11	54	17	21	14
		85	90	91	92	93	94	111	112	113	120	121	122	125	126	127	128	129			
		6	17	10	7	10	7	58	10	21	15	32	18	100	11	43	10	10			
		138	139	140	141	166	167	168	219	230	231	232	233	247(M)	248						
		12	9	8	16	10	15	7	8	54	52	26	16	35	6						
		249(M)																			
		11																			
XII	*m/e*	27	37	38	39	50	51	52	62	63	64	65	66	75	76	77	78	89	90	91	92
	I(%)	10	10	16	35	43	46	9	12	30	13	30	12	71	11	58	7	12	32	62	23
		93	94	104	105	107	111	112	113	118	119	120	121	125	126	127	128				
		7	7	13	13	10	76	7	27	16	69	10	10	61	8	63	11				
		129	135	136	138	141	143	166	167	214	230	232	245	261(M)	263(M)						
		16	31	36	7	27	10	6	6	6	33	12	8	9	3						
XIII	*m/e*	39	50	51	63	75	90	111	113	125	126	127	128	150	151	152	166	260			
	I(%)	6	6	6	9	12	18	14	6	100	9	43	13	8	9	8	6	8			
		276(M)	278(M)																		
		18	6																		

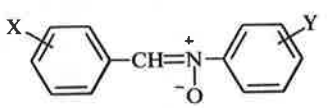
* All peaks greater than 5% of the base peak are recorded.

TABLE 2. COMPOSITIONS OF SOME IONS IN THE MASS SPECTRA OF I–XIII

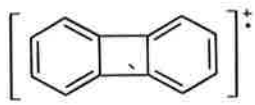
Compound	m/e	Composition
I	91	C_6H_5N (60%), C_7H_7 (40%)
	104	C_7H_6N
	105	C_7H_5O
	168	$C_{12}H_{10}N$
	169	$C_{12}H_{11}N$
	180	$C_{13}H_{10}N$
	181	$C_{13}H_{11}N$
II	91	C_7H_7
	119	C_8H_7O
	165	$C_{12}H_{10}N$
	183	$C_{13}H_{13}N$
III	105	C_7H_5O
	127	$C_6H_4NCl^{37}$ (90%), $C_6H_6NCl^{35}$ (10%)
	152	$C_{12}H_8$
IV	139	$C_7H_4OCl^{35}$ (95%), $C_{11}H_7$ (5%)
	141	$C_7H_4OCl^{37}$
	203/205	$C_{12}H_{10}NCl$
V	121	$C_7H_5O_2$
	122	$C_7H_6O_2$
	167	$C_{12}H_9N$
	185	$C_{12}H_{11}NO$
VIII	91	C_6H_5N
	150	$C_8H_8NO_2$
	167	$C_{12}H_9N$
	184	$C_{12}H_{10}NO$
	198	$C_{13}H_{10}O_2$
	199	$C_{13}H_{13}NO$ (50%), $C_{13}H_{11}O_2$ (50%)
IX	91	C_6H_5N
	150	$C_7H_4NO_3$ (80%), $C_{12}H_6$ (20%)
	167	$C_{12}H_9N$
	195	$C_{13}H_9NO$
X	125	$C_6H_4NCl^{35}$
	127	$C_6H_4NCl^{37}$ (95%), $C_6H_6NCl^{35}$ (5%)
	139/141	C_7H_4OCl
XI	121	$C_7H_5O_2$
	127	$C_6H_4NCl^{37}$ (90%), $C_6H_6NCl^{35}$ (10%)
	129	$C_6H_6NCl^{37}$
XII	127	$C_6H_4NCl^{37}$ (30%), $C_6H_6NCl^{35}$ (70%)
	129	$C_6H_6NCl^{37}$
	135	$C_8H_7O_2$
	136	$C_8H_8O_2$
	167	$C_{12}H_9N$
XIII	150	$C_7H_4NO_3$ (55%), $C_{12}H_6$ (45%)
	151	$C_7H_5NO_3$ (55%), $C_{12}H_7$ (45%)

metastable ion for any process is indicated, both in the text and in Figs, by an asterisk. Structures drawn for fragment ions are nominal only [work in many laboratories has shown that molecular ion rearrangements are no longer rare (cf. Ref. 10)] but relate the decomposition patterns to the structure of the intact molecule.

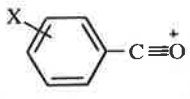
Many fragment ions observed in the mass spectra of the nitrones I–XV are produced by skeletal-rearrangement processes (Figs 1–8). These are all low energy processes and occur at 10 eV. The relative abundances of many ions produced by the major rearrangement processes are summarized in Table 3. Five specific classes of skeletal-rearrangements are observed. Consider the general cases XVI:



XVI



a: *m/e* 152



b

(1) M—CHNO—$X^{\bullet}$—$Y^{\bullet}$ or M—CHNO—H_2 (or other variations) to produce either the biphenylene radical ion (*a*) or substituted biphenylene radical ions. These processes are observed in most spectra, and are of the general type $[ABC]^{+\bullet} \rightarrow [AC]^{+\bullet} + B$.[11] A compendium of such processes is available.[10]

(2) M—CO, together with additional fragmentation through the substituents. This process is observed in the spectra (Figs 1–3 and 7) of I, II, III and VIII and demands C—O bond formation. M—CO ions are also present in the spectra (Table 1) of V, VI and XI, but as these compounds are phenolic, it is likely that at least some of the CO lost originates from the phenol moiety.[12]

(3) A process observed in all spectra is M—Y $C_6H_5N^{\bullet}$, which produces a species X $C_7H_4O^{+}$, best represented as the substituted benzoyl cation *b*. The formation of *b* necessitates C—O bond formation. This rearrangement has been reported previously.[13]

(4) The process M—X·C_7H_5O (to produce Y $C_6H_4N^{+\bullet}$) is noted in all spectra except that of II [where *m/e* 91 corresponds exclusively to the tropylium cation (Fig. 2, Table 2)].

(5) Skeletal-rearrangements involving the M—O ion. These are not observed in all spectra, but are of the general type $[ABC]^{+\bullet} \rightarrow [AC]^{+\bullet} + B$, e.g. M—O—$Cl^{\bullet}$—HCN to produce *a*, is observed in Fig. 4.

TABLE 3. RELATIVE ABUNDANCES (%) OF SOME FRAGMENT IONS IN THE SPECTRA OF I–VI AND VIII–XIII*

Compound	$M^{+\bullet}$	M—1	M—O	M—CO	$XC_6H_4CO^{+}$	$YC_6H_4N^{+}$	$YC_6H_4^{+}$	$XC_6H_4^{+}$
I	23	19	9	5	21	60	X = Y	Total = 41
II	21	20	7	6	18	0	28	100
III	16	9	17	2	12	100	39	32
IV	18	6	6	0	24	100	38	7
V	17	4	70	5	47	23	100	35
VI	61	6	41	19	16	100	86	24
VIII	30	18	9	4	27	30	46	6
IX	8	1	6	0	4	100	34	0
X	13	7	25	0	26	100	X = Y	Total = 87
XI	35	2	52	8	32	100	59	11
XII	9	2	7	0	31	61	76	11
XIII	18	1	8	0	8	100	15	0

* Where the fragment ion contains Cl, the relative abundance of the ^{35}Cl isotope is recorded.

Before considering the rearrangement types 2–5 in detail, it is convenient to discuss several of the normal decompositions of nitrones, as a knowledge of these is necessary for the understanding of two of the rearrangement modes. Two processes observed in all spectra are M—O and M—$H^{\bullet}$. M—O ions are of diagnostic value in the spectra of many compounds containing the —N^{+}—O^{-} group.[2–8] It is noteworthy that in no case does the intensity of the M—O ion (Table 3) vary more than 10% when the 'heated' and 'direct' spectra are compared, indicating that this process (which does not have an appropriate metastable ion) is mainly electron-impact induced. The general species produced will be *c*, and this representation is supported by the spectra

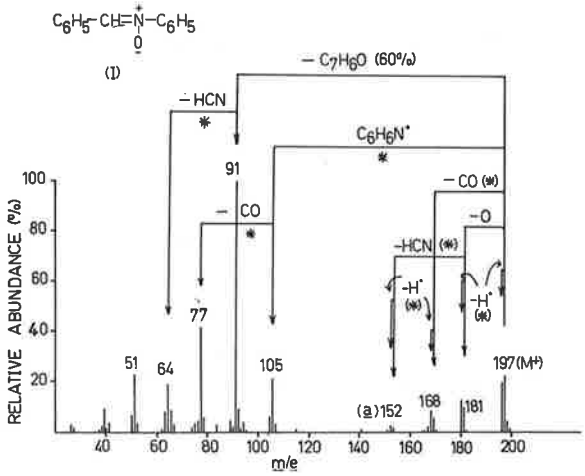


FIG. 1

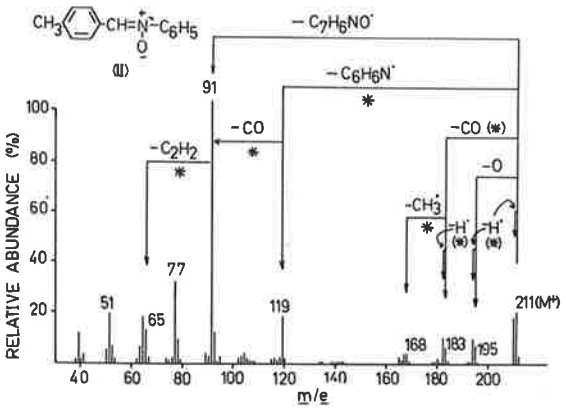


FIG. 2

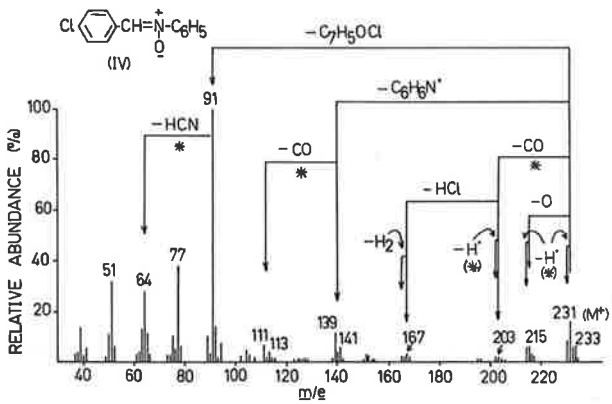


FIG. 3

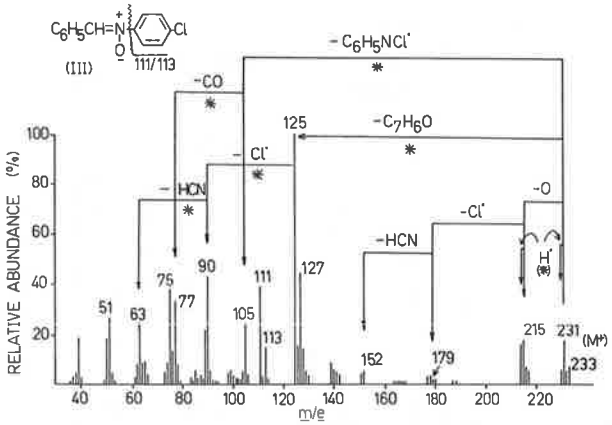


FIG. 4

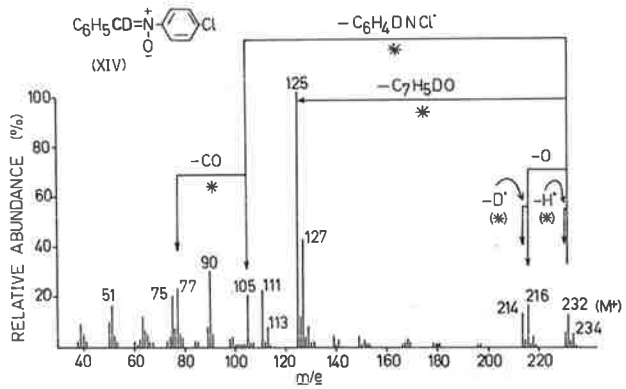


FIG. 5

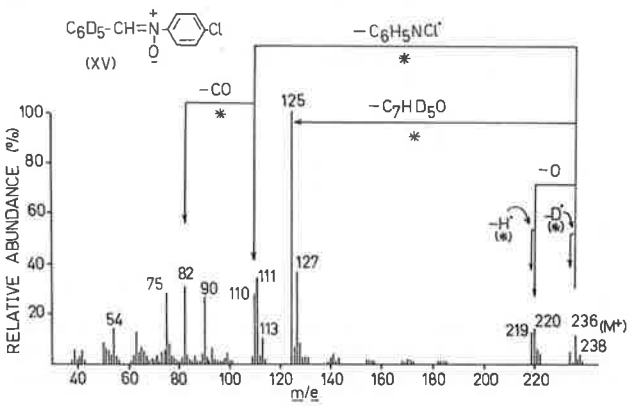


FIG. 6

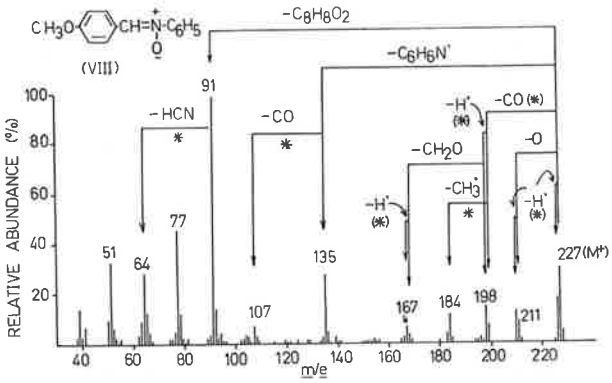


FIG. 7

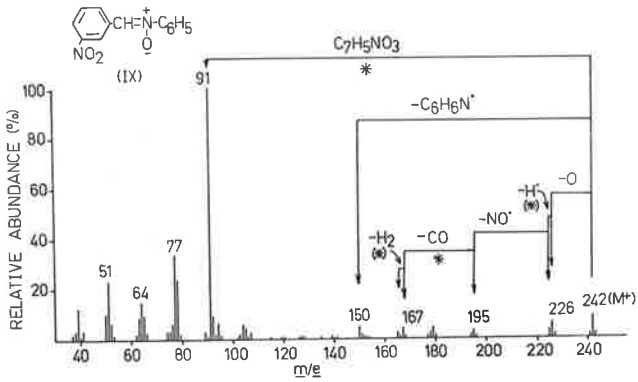
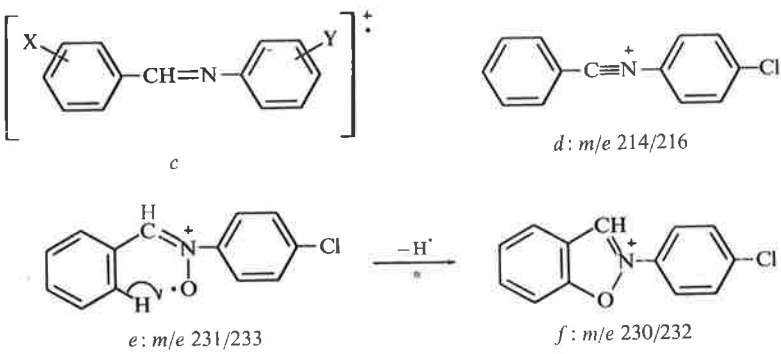
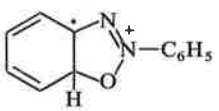


FIG. 8

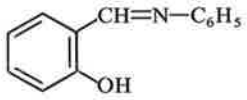
(Figs 4–6) of III and the labelled derivatives XIV and XV, where it can be seen that the process M—O—H$^{\bullet}$ of III becomes M—O—D$^{\bullet}$ in XIV. The ion produced is probably *d* (*m/e* 214/216). It has been shown[14] that the M—1 ion in the spectra of diaryl Schiffs' bases corresponds mainly (>85%) to ions analogous to *d*. Moreover, both the molecular ions and M—1 ions of Schiffs' bases undergo skeletal-reorganization reactions of the type ABC → AC + B,[14] thus clarifying the rearrangement process 5.



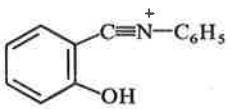
However, the hydrogen lost in the M—1 process of nitrones, does not originate from the methine position. Figures 4–6 show that the hydrogen comes from the aromatic ring furthest from the N—O group. The deuterium labelling studies are consistent with the formation of the stable cation *f* by an intermolecular aromatic substitution reaction, viz. $e \rightarrow f$. The presence of a strongly electron withdrawing nitro substituent on the ring from which the hydrogen atom is lost, reduces the proclivity of the M—1 process (Table 3 and Fig. 8). Intermolecular aromatic substitution reactions involving C—O bond formation have been reported previously,[15–17] and it has been shown[16] that the hydrogens attached to any one aromatic ring become equivalent during this reaction.



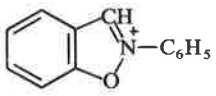
g



XVIII



h: *m/e* 196



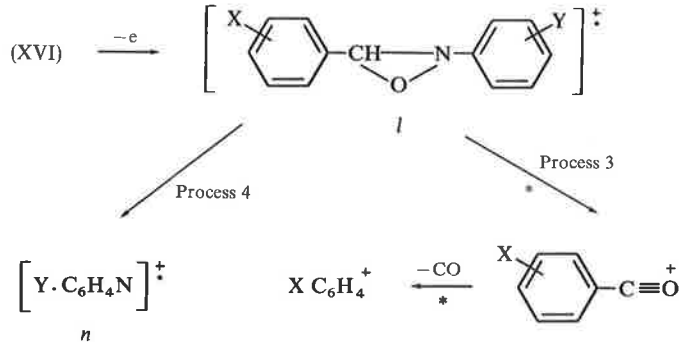
i: *m/e* 196

The skeletal-rearrangement fragments in the spectrum of azoxybenzene do not owe their genesis to the intermediacy of the *o*-hydroxyazobenzene radical ion, and breakdown of *g* has been invoked to rationalize the rearrangements.[8] Similarly, the M—CO process of the nitrone (I) cannot be explained by the formation of the molecular ion of the Schiffs base XVIII. The rearrangement modes in I are M—CO—H$^{\bullet}$ and M—H$^{\bullet}$—CO and in XVIII,[14] M—H$^{\bullet}$—CO and M—CHO$^{\bullet}$ (metastable ions substantiate all processes). Although two of these processes seem identical, they are not, as the M—1 ions are different in each spectrum, viz. *h* and *i* respectively. Moreover, several prominent ions in the spectrum[14] of XVIII are absent in that (Fig. 1) of I. The benzanilide radical ion is also not the reactive intermediate as this species does not exhibit an M—CO ion. An ion which best explains the M—CO process is *k* (analogous to *g* and *i*) which could originate by the process $j \rightarrow k$.

j: *m/e* 197 *k*: *m/e* 197

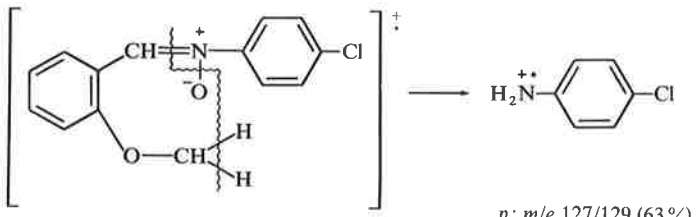
Processes 3 and 4 can be best explained by the formation of an oxaziridine intermediate. Although such a supposition is speculative, it has photochemical analogies.[9] An investigation of the mass-spectral breakdown of the oxaziridines postulated,

would probably not be meaningful because of the relative instability of such systems.[9] The formation of the substituted benzoyl cations [metastable ions usually substantiate the $M \rightarrow X{-}C_6H_4{-}C{\equiv}\overset{+}{O}$ process (Ref. 13 and Figs 1–8] could come from the intermediate *l*. Similarly, the ion *n* (Process 4) could arise from *l*.



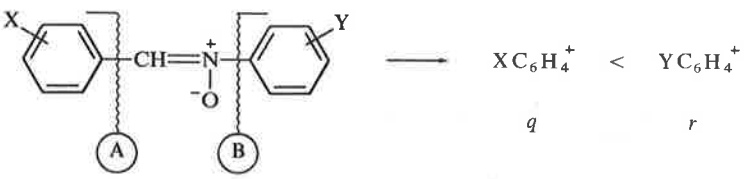
It is clear that these processes may be further complicated by the presence of substituents (X and Y), e.g. when X is hydroxy, o-methoxyl or nitro (e.g. V, VI, IX–XIII) ions due to both $X{\cdot}C_6H_4{\cdot}CHO^{+\cdot}$ and $X{\cdot}C_6H_4\ C{\equiv}O^+$ are observed. When Y is *p*-chloro (IV, X–XIII), high resolution (Table 2) indicates that as well as $Y{-}C_6H_4N^{\ddagger}$ species (*n*), small amounts of $Y{-}C_6H_4NH_2^{+\cdot}$ are also formed. A different hydrogen rearrangement is observed in the spectrum of I. 40% of *m/e* 91 (base peak) corresponds to the tropylium cation ($C_7H_7^+$), which can only be produced by a hydrogen rearrangement from the aromatic ring (adjacent to —N—O) to the methine group.

The fragmentations so far described have been due to reorganization of the molecular ion, which although of mechanistic interest, are of little use for structure elucidation. However, there are several processes which may be used for structure determination. The first of these is a specific hydrogen transfer process observed in the spectrum (Table 1) of XII (viz. $o \rightarrow p$). These processes have been noted previously in the



o: *m/e* 261/263

p: *m/e* 127/129 (63%)



q *r*

spectra of azoxybenzenes[8] and Schiffs bases[14, 18] and have been substantiated by deuterium labelling studies.[8] Processes of more general applicability are shown in XVII. In all cases [except for II (Fig. 2) where the formation of the exceptionally stable tropylium cation preponderates all other processes] cleavage B gives a more abundant ion than cleavage A, i.e. the relative abundance of X $C_6H_4^+$ (*q*) is less than that of Y $C_6H_4^+$ (*r*). The abundances of these ions are summarized in Table 3 and their relative intensities may be used to determine the position of the $-\overset{+}{N}-\overset{-}{O}$ group.

In summary, nitrones, in common with other compounds containing the N-oxide group, undergo complex reorganization on electron impact. As it is not possible to predict the presence of such processes with any certainty, only *a posteriori* statements may be made concerning them. Cleavage α to the —N—O moiety allows the determination of the position of this group, in compounds where alkyl groups are not attached to the aromatic rings.

EXPERIMENTAL

All spectra were determined by the direct-insertion procedure with an R.M.U. 6D double focusing mass spectrometer operating at 75 eV, and with a source temp between 100 and 150°. Exact mass measurements were performed with an A.E.I. MS 9 mass spectrometer, using a resolution of 10,000 (10% valley definition) with heptacosafluorotributylamine providing reference masses. All measurements were correct to within 10 ppm.

The spectra of VII was obtained by inserting VI into the source with D_2O.[19]

The following nitrones were synthesized by reported procedures;[20] I, II, IV–VI, VIII, and IX. Compounds III, VII, X and XI were prepared from arylaldehydes and N-arylhydroxylamines in ethanolic solution (cf. 20). The arylaldehydes were purified commercial samples, whereas the N-arylhydroxylamines were freshly prepared from the corresponding nitro compounds by reduction with zinc and ammonium chloride.[21, 22]

Compound	m.p. (°C)	Found C	Found H	Found N	Calculated C	Calculated H	Calculated N
III	95–96	79·8	6·1	6·6	79·6	6·2	6·6
VII	178	67·7	4·2	5·9	67·4	4·4	6·0
X	126–127	64·9	4·7	5·3	64·3	4·6	5·4
XI	192–193	56·3	3·5	9·8	56·4	3·3	10·1

Microanalyses by Mrs. B. Rasmussen, Aarhus University.

The deuterated nitrone (XIV) was prepared from commercial C_6H_5CDO, while (XV) was prepared from C_6D_5CHO (synthesized from commercial C_6D_5Br).[23]

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AUSTRALIAN JOURNAL OF CHEMISTRY

ELECTRON IMPACT STUDIES

XXXI.† SKELETAL-REARRANGEMENT FRAGMENTS IN THE MASS SPECTRA OF ANILS

By J. H. Bowie,‡ R. G. Cooks,§ J. W. Fisher,‡ and T. McL. Spotswood‡

[*Manuscript received March* 19, 1968]

Summary

Skeletal-rearrangement fragments are observed in the mass spectra of all anils derived from aromatic aldehydes. The rearrangement processes have been studied by high-resolution mass spectrometry and in certain cases by deuterium labelling. All processes are of the general type $[ABC]^{+\cdot} \rightarrow [AC]^{+\cdot} + B$.

The mass spectra of azomethines[1] and the normal fragmentations of anils[2] have been reported. Skeletal-rearrangement processes of the type $[ABC]^{+\cdot} \rightarrow [AC]^{+\cdot} + B$ are common features of the spectra of compounds having the general structure Ar–X=Y–Ar,[3] and these are especially important in the spectra of azobenzenes,[4] azoxybenzenes,[5] and nitrones.[6] As the previous publication on anils[2] does not specifically discuss skeletal-reorganization processes, we have undertaken a survey to study this problem, and this paper is concerned with both the rearrangement and normal cleavage processes in the spectra of (I)–(XXX).

Skeletal-rearrangement processes are recorded in Table 1, and examples of spectra are shown in Figures 1–10. The compositions of the rearrangement ions mentioned in Table 1, and of the fragment ions discussed in the text or indicated by schematic arrows in the figures, have been definitely established by exact mass measurements. The presence of an asterisk either in the text or a figure denotes the presence of an appropriate metastable ion for the process indicated.

† Part XXX, Larsen, B. S., Schroll, G., Lawesson, S.-O., Bowie, J. H., and Cooks, R. G., *Tetrahedron*, in press.

‡ Department of Organic Chemistry, University of Adelaide, P.O. Box 498D, Adelaide, S.A. 5001.

§ University Chemical Laboratory, Lensfield Road, Cambridge, England.

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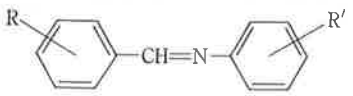
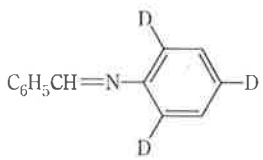
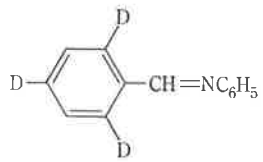


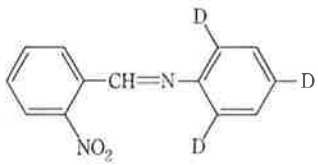
	R	R′		R	R′		R	R′
(I)	H	H	(X)	H	*p*-Cl	(XIX)	H	*p*-MeO
(II)	*o*-Me	H	(XI)	*p*-Br	H	(XX)	*o*-OH	H
(III)	*p*-Me	H	(XII)	H	*m*-Br	(XXI)	*p*-OH	H
(IV)	H	*o*-Me	(XIII)	H	*p*-Br	(XXII)	H	*p*-OH
(V)	H	*m*-Me	(XIV)	*p*-F	H	(XXIII)	*o*-NO_2	H
(VI)	H	*p*-Me	(XV)	*o*-MeO	H	(XXIV)	*m*-NO_2	H
(VII)	*o*-Cl	H	(XVI)	*m*-MeO	H	(XXV)	*p*-NO_2	H
(VIII)	*m*-Cl	H	(XVII)	*p*-MeO	H	(XXVI)	H	*m*-NO_2
(IX)	*p*-Cl	H	(XVIII)	H	*m*-MeO	(XXVII)	*p*-NMe_2	H



(XXVIII)



(XXIX)



(XXX)

TABLE 1

SKELETAL-REARRANGEMENT PROCESSES IN THE SPECTRA OF (I)–(XXVII)

All processes are substantiated by metastable ions except those indicated by placing the elimination product in parentheses. Rearrangement processes have been substantiated by high-resolution studies. Where several isomers (e.g. VII–IX) have identical rearrangement processes, exact mass measurements have been determined for only one isomer

Compound(s)	Rearrangement Process	Final Ion (*m/e*)	Rel. Abund. of Final Ion (%)
(I)	M−H·−HCN−H·	152	5
(II)–(VI)	M−H·−HCN−H_2	165	8, 6, 5, 4, 3
	M−H·−Me·−(HCN)	152	5, 4, 4, 4, 4
(VII)–(IX)	M−Cl·−H·−HCN	152	5, 3, 3
(X)	M−H·−Cl·−HCN	152	8
(XI)–(XIII)	M−Br·−H·−HCN	152	4, 18, 13
(XIV)	M−H·−HF−HCN	151	2
(XV)–(XIX)	M−H·−Me·−CO−HCN−(H_2)	139	2, 3, 3, 4, 4
	M−(MeO·)−(HCN)−H·	152	2, 3, 2, 3, 2
(XX)–(XXII)	M−CHO·−(HCN)−H_2	139	3, 2, 3
	M−H·−H_2O−HCN	151	2, 3, 2
(XXIII)	M−HO·−(NO·)−HCN	152	35
	M−HO·−CN_2O	152	35
(XXIV)–(XXVI)	M−NO_2·−H·−HCN	152	10, 12, 31
(XXVII)	M−H·−Me·−H·−HCN−H·−HCN	152	2

The interpretation of the rearrangement processes in the spectrum (Fig. 1) of (1) has been aided by the spectra (Fig. 2) of the labelled derivatives (XXVIII) and (XXIX). The overall process is M—H·—HCN—H· to produce *m/e* 152 ($C_{12}H_8$, h.r.), which is most plausibly represented as the biphenylene radical ion (*b*).

Fig. 1

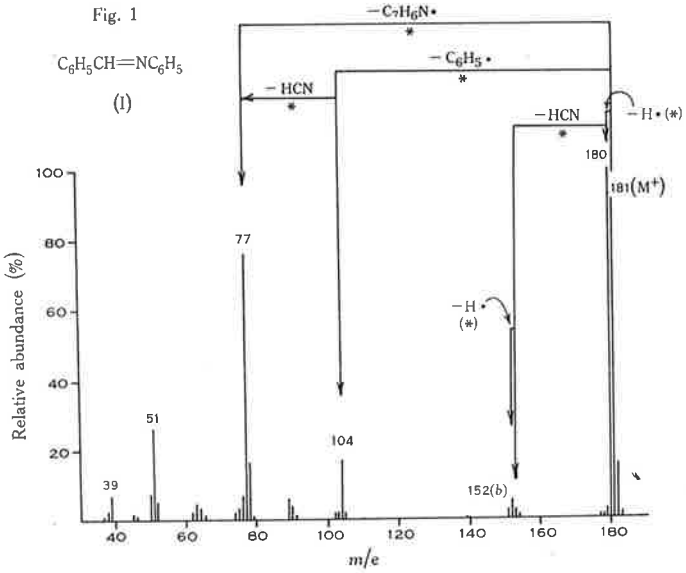
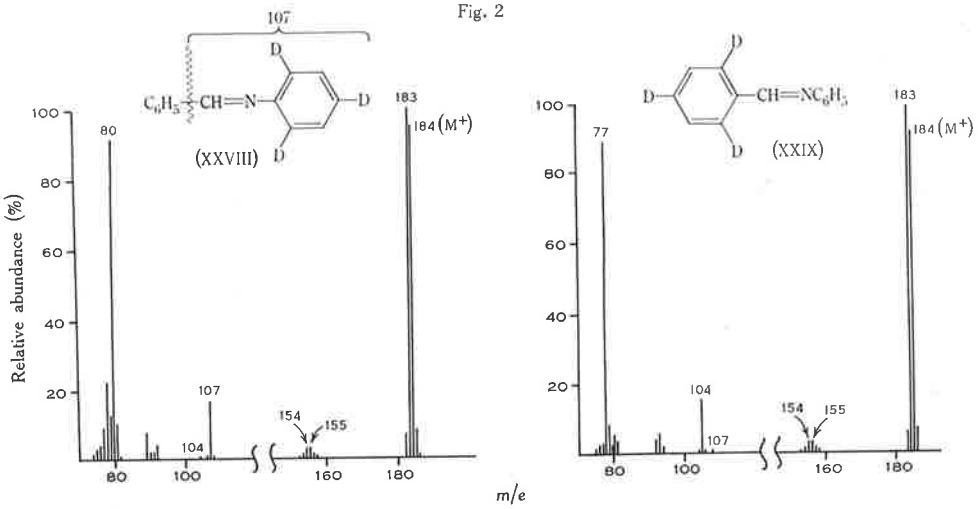
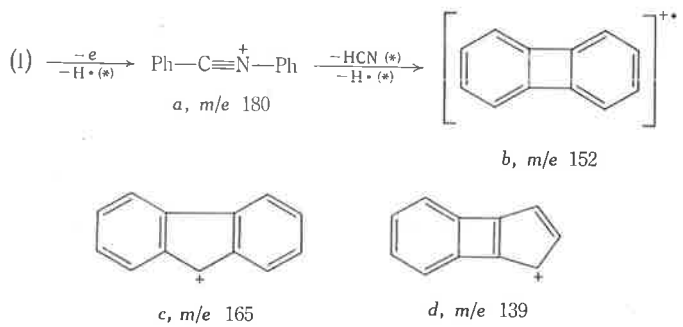


Fig. 2



The hydrogen lost in the M—H· decomposition comes almost exclusively (> 90%) from the azomethine moiety as evidenced by the spectra (Fig. 2) of (XXVIII) and (XXIX). The spectra of (XXVIII) and (XXIX) in the *m/e* 152–157 region are identical, indicating that the two hydrogen atoms involved in the last two decompositions come equally from each aromatic ring. It is not possible to determine

whether the hydrogens come specifically from *ortho* positions, as it is known[7–9] that, in general, the hydrogens on any one monosubstituted benzene ring become equivalent upon electron impact.† Consequently, D and H will be lost from the labelled aromatic ring in the ratio 3 : 2 (ignoring possible isotope effects). The rearrangement may therefore be represented by the scheme (I) → *b*.



The skeletal-rearrangement processes in the spectra of monosubstituted derivatives are modified by the substituent. When the substituents may fragment by *a*-cleavage to the aromatic ring (e.g. X = Me, Cl, Br, and NO_2),[10] then *b* is formed by either of the processes M−H·−X·−HCN or M−X·−H·−HCN (see Figs. 3, 4, and 7–9). The fluorine substituent should also fall into this classification, but the ion produced in this case is the biphenylene cation (*m/e* 151), not *b*. The relative abundances of *b* range from 2–35% of the base peaks, and are largest when X = NO_2. When X = Me (see Fig. 3), the cation *m/e* 165 ($C_{13}H_9^+$) is also formed. Even though structures drawn for fragment ions are nominal only, it is argued that the most plausible structure for this ion is the fluorene cation (*c*), although this does not preclude the possibility of more extensive rearrangement.

When the presence of an oxygenated substituent allows the additional loss of a ring carbon (e.g. X = OH or OMe),[10] then the ion produced by the overall rearrangement is *d*, *m/e* 139 ($C_{11}H_7$ h.r.) (see Figs. 5 and 6). For example, in the spectrum (Fig. 6) of (XXI) the major reorganization process is M−CHO·−HCN−H_2. Even in such cases *m/e* 152 ions are still present. The formation of *b* from the molecular ion of the dimethylamino derivative (XXVII) is complex, involving six successive eliminations, viz. M−H·−Me·−H·−HCN−H·−HCN (Fig. 10).

Although the simple cleavage processes of anils have been discussed previously,[2] there are certain features which need clarification. Cleavage of anils occurs *a* to the

† *Note added in proof*—For exceptions to this statement, see Williams, D. H., Ward, R. S., and Cooks, R. G., *J. Am. chem. Soc.*, 1968, **90**, 966.

[7] Grubb, H. M., and Meyerson, S., "Mass Spectrometry of Organic Ions." (Ed. F. W. McLafferty.) Ch. 10. (Academic Press: New York 1963.)

[8] Ronayne, J., Williams, D. H., and Bowie, J. H., *J. Am. chem. Soc.*, 1966, **88**, 4980.

[9] Bowie, J. H., Donaghue, P. F., Rodda, H. J., and Simons, B. K., *Tetrahedron*, 1968, **24**, 3965.

[10] Budzikiewicz, H., Djerassi, C., and Williams, D. H., "Interpretation of the Mass Spectra of Organic Compounds." (Holden–Day: San Francisco 1967.)

Fig. 3

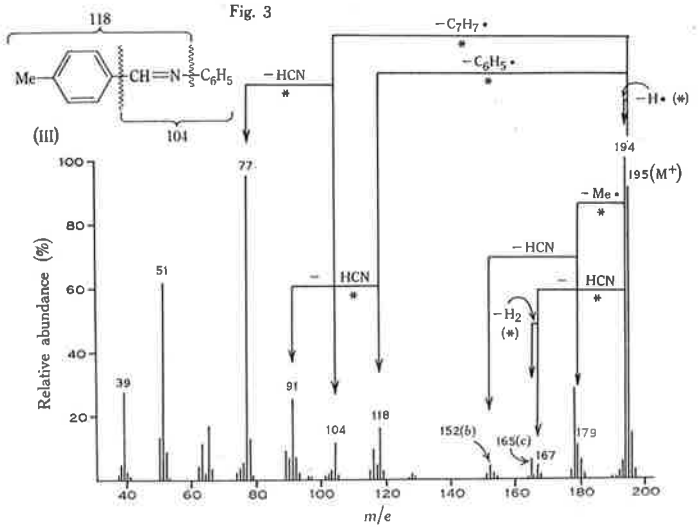


Fig. 4

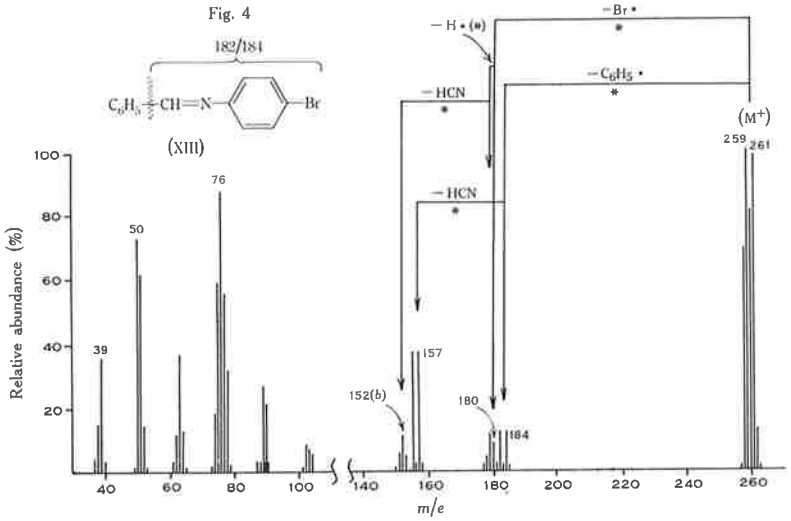


Fig. 5

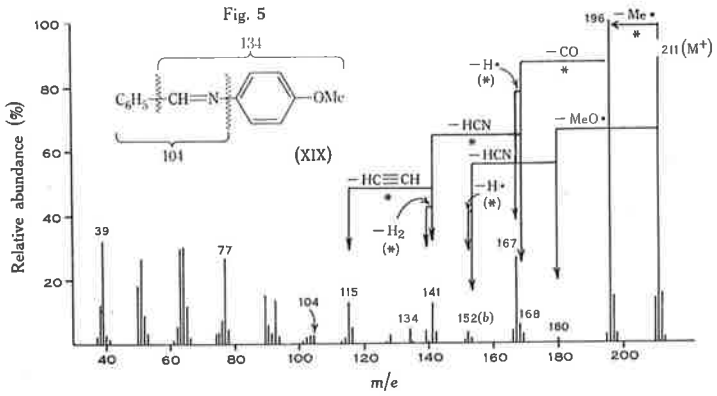


Fig. 6

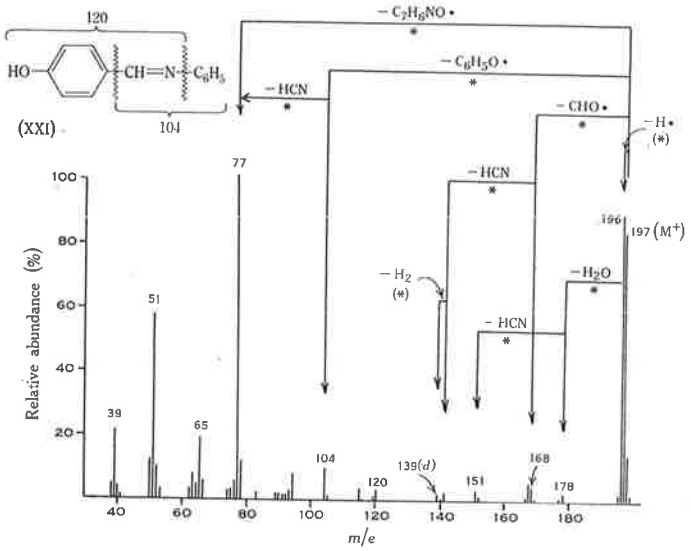
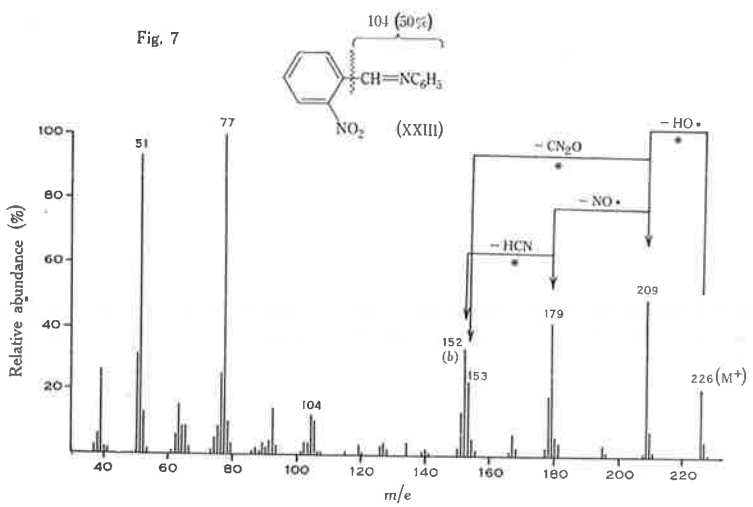
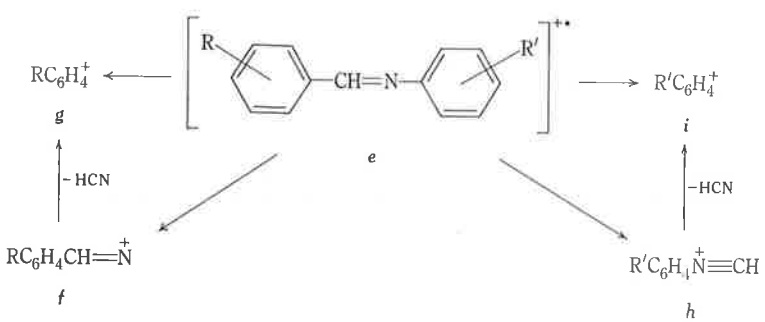


Fig. 7





Scheme 1

aromatic system either by C–C or C–N bond fission. These processes [which are normally substantiated by metastable ions (see Figs. 1–10)] are summarized in Scheme 1. Carbon–nitrogen bond cleavage is more facile than C–C bond cleavage. This is illustrated by the spectra (Fig. 2) of (XXVIII) and (XXIX) and in general the relative abundance of i is normally greater than that of g (for exceptions see

Fig. 8

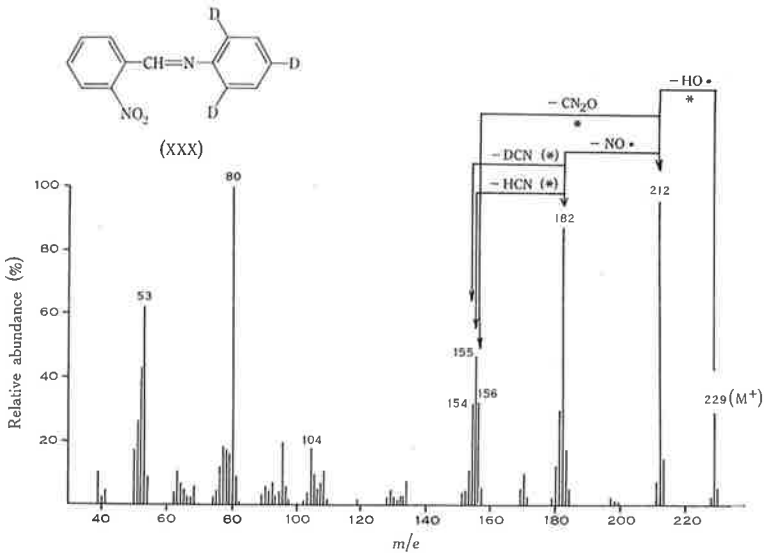
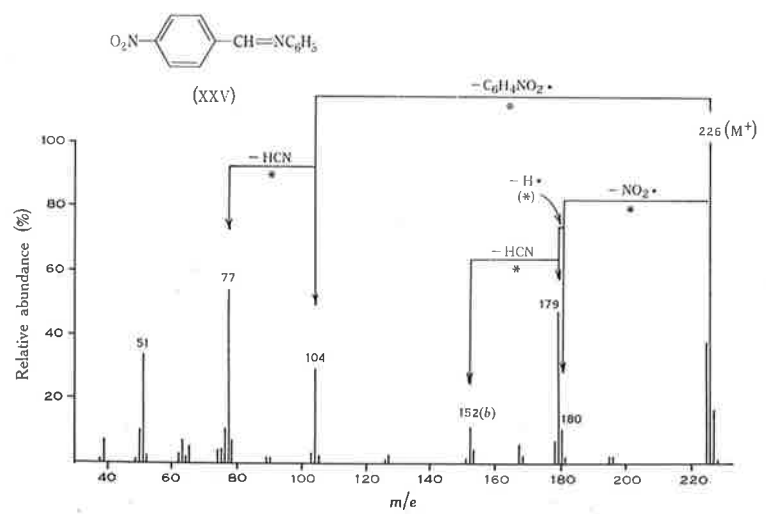


Fig. 9

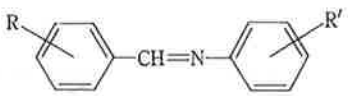


below). However, the relative abundance of h is generally greater than that of f, indicating that in this case, C–C bond fission produces a more stable cation than C–N bond fission. As the ions g and i are produced directly from the molecular ion and also by decomposition of f and h respectively, the additive effect should increase

the abundance of i at the expense of g, even though it is not possible to determine the relative extent of each process. The relative abundances of these ions in the spectra of (I)–(XXVII) are listed in Table 2. There are several exceptions to the two general rules (viz. $i > g$ and $h > f$) stated above. For example, $g > i$ (%) in the spectra of (XIX) and (XXVI) and $f > h$ in the spectra of (II), (III), (XVIII), and (XX). Caution should therefore be exercised when using the relative abundances of these ions to aid structure elucidation.

TABLE 2

RELATIVE ABUNDANCES (%) OF CLEAVAGE FRAGMENTS IN THE SPECTRA OF (I)–(XXVII)



Compound	$RC_6H_4CH{=}N^+$ (f)	$R'C_6H_4\dot{N}{\equiv}CH$ (h)	$RC_6H_4^+$ (g)	$R'C_6H_4^+$ (i)
(I)†	1	13	10	93
(II)	26	12	25	100
(III)	15	12	25	100
(IV)	4	100	14	55
(V)	2	16	14	79
(VI)	2	18	13	64
(VII)	2	22	2	100
(VIII)	2	28	3	100
(IX)	2	17	3	100
(X)	5	27	40	77
(XI)	0	18	2	100
(XII)	6	21	54	72
(XIII)	5	27	58	76
(XIV)	1	15	5	100
(XV)	0	6	2	51
(XVI)	0	19	4	100
(XVII)	2	7	2	100
(XVIII)	13	9	26	61
(XIX)	3	4	27	4
(XX)	17	10	2	60
(XXI)	2	10	5	100
(XXII)	2	19	12	16
(XXIII)	0	7	0	100
(XXIV)	0	39	0	100
(XXV)	0	29	0	29
(XXVI)	5	9	31	2
(XXVII)	0	8	5	39

† These values have been determined from the spectra of (XXVIII) and (XXIX).

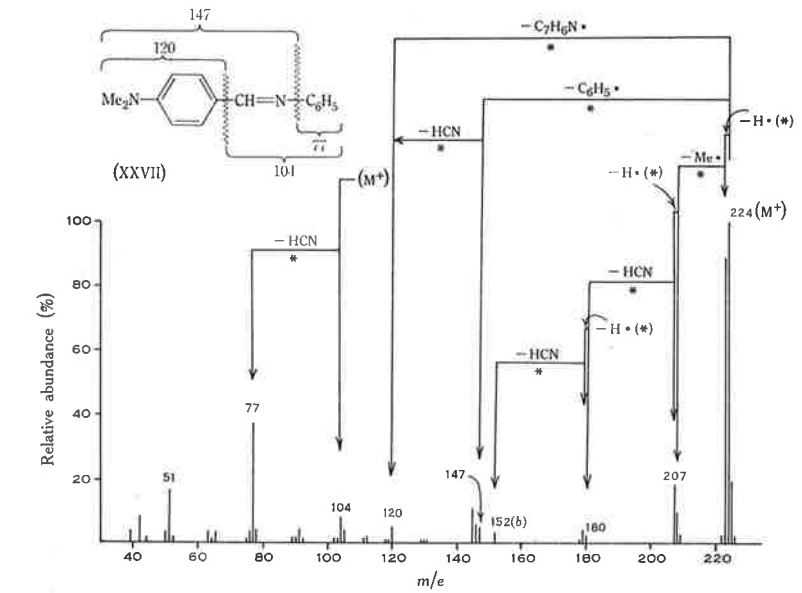
It has been shown that simple cleavage processes in the spectra of acetophenones,[11,12] benzophenones,[11,12] and azobenzenes[4] may be related semiquanti-

[11] McLafferty, F. W., *Analyt. Chem.*, 1959, **31**, 477.

[12] Bursey, M. M., and McLafferty, F. W., *J. Am. chem. Soc.*, 1966, **88**, 4484.

tatively to solution chemistry. This has been demonstrated for monosubstituted compounds by obtaining a straight line plot when a function of the relative abundance of a particular ion (which is common to a series of spectra) is plotted against the Hammett σ value for the *meta* or *para* substituent. The theoretical basis of this method has been discussed by McLafferty.[12] A similar plot for the C_6H_5—$\dot{N}$=CH

Fig. 10



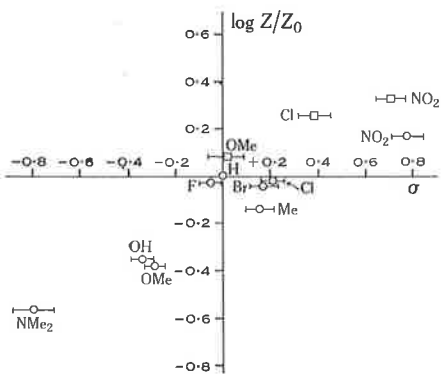


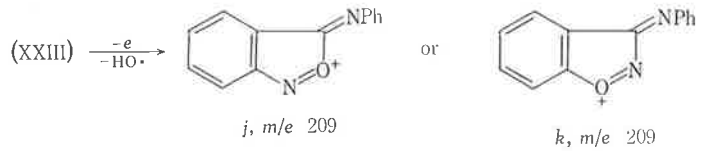
Fig. 11.—Plot of log Z/Z_0 *v.* σ:
○, *meta* substituent;
□, *para* substituent.

$$Z = \frac{\text{rel. ab. } [C_6H_5\dot{N}{=}CH]}{\text{rel. ab. } [XC_6H_4CH{=}NC_6H_5]}$$

$$Z_0 = \frac{\text{rel. ab. } [C_6H_5\dot{N}{=}CH]}{\text{rel. ab. } [C_6H_5CH{=}NC_6H_5]}$$

ion (*m/e* 104) in the spectra of compounds of the general type X—C_6H_4—CH=NC_6H_5 (X is *meta* or *para*) against the σ value for X, is illustrated in Figure 11. Although the scatter of points is pronounced, the trend is that electron-withdrawing substituents (e.g. NO_2) decrease the strength of the HC—C bond and increase the relative abundance of *m/e* 104, while electron-introducing substituents (e.g. NMe_2) decrease the abundance of the *m/e* 104 fragment.

Finally, when certain substituents occupy positions *ortho* to the azomethine moiety, proximity effects are observed in the mass spectra. Instances involving hydroxyl, methoxyl, and methyl groups have been cited.[2] Another can be seen from a comparison of the spectra (Figs. 7 and 9) of the nitro isomers (XXIII) and (XXV). A major fragmentation of the *ortho* derivative proceeds through an M—HO· ion (51%) which is absent in the spectrum of (XXV). The spectrum (Fig. 8) of



j, *m/e* 209 *k*, *m/e* 209

the deuterium-labelled derivative (XXX) shows that the hydrogen atom involved in the M—HO· process does not originate from the aromatic ring adjacent to nitrogen. As the spectra of nitrobenzene[13] and *o*-nitrobenzaldehyde are devoid of M—HO· peaks, the hydrogen atom is probably lost from the methine position. The M—17 ion may be represented either as *j* or *k*, depending on whether the ion is formed from the intact or rearranged[13] nitro group.

Experimental

All mass spectra were measured with an Hitachi Perkin–Elmer RMU 6D double-focusing mass spectrometer under identical recording conditions—source and inlet temperatures at 150°±5°, and identical ion currents. Exact mass measurements were performed on an A.E.I. MS9 mass spectrometer using a resolution of 10,000 (10% valley definition) with heptacosafluorotributylamine providing reference masses. All measurements were correct to within 15 p.p.m.

All the anils (I)–(XXVII) are known compounds and were prepared by standard procedures.

Compounds (XXVIII) and (XXX) were prepared from the appropriate aldehyde and [2,4,6-D_3]aniline.[14] Compound (XXIX) was prepared from aniline and [2,4,6-D_3]benzaldehyde.[8]

Acknowledgments

The award of an Elsie Ballot Fellowship (to R.G.C.) is gratefully acknowledged. The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Committee.

[13] Momigny, J., *Bull. Soc. r. Sci. Liége*, 1956, **25**, 93.
[14] Best, A. P., and Wilson, C. L., *J. chem. Soc.*, 1946, 241.

Reprinted from CHEMICAL COMMUNICATIONS, 1968, page 698.

Skeletal-rearrangement Fragments in the Mass Spectra of Substituted Thioglycollic Acids and Esters[1]

By J. Ø. MADSEN and S.-O. LAWESSON*

(*Department of Organic Chemistry, Aarhus University*, 8000 *Aarhus C, Denmark*)

J. H. BOWIE*

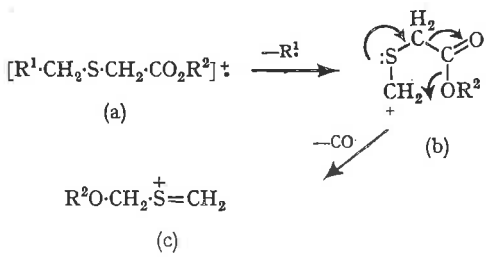
(*Department of Organic Chemistry, University of Adelaide, Adelaide, South Australia*, 5001)

and R. G. COOKS

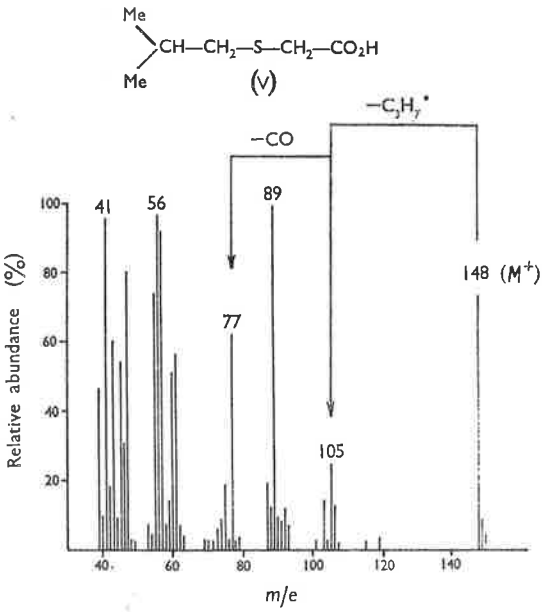
(*University Chemical Laboratory, Lensfield Road, Cambridge*)

THE presence of skeletal-rearrangement fragments in the mass spectra of organic compounds is currently exciting much interest.[2] Rearrangement ions are found in the spectra of a variety of sulphur compounds.[3] We report the occurrence of a novel rearrangement, which probably involves migration to a carbonium-ion centre.

The spectra of the thioglycollic acid derivatives (I—XII) contain ions of the general formula, $R^2C_2H_4SO^+$. The abundances of these species are recorded in the Table and they range from 3% (for VIII) to 63% (for V). The compositions of all ions have been established by high-resolution measurements. The rearrangement process is generally more pronounced in the spectra of the acids ($R^2 = H$) than the esters ($R^2 = Me$), and occurs when the thioglycollic acid (or ester) is of type $R^1CH_2{\cdot}SCH_2{\cdot}CO_2R^2$.



The majority of spectra contain $M - R^{1\cdot}$ ions as well as the rearrangement ions [$(M - R^{2\cdot})$ —CO]. Although the $M - R^{1\cdot}$ process is not substantiated



Relative abundances of rearrangement ions in the spectra of (I—XII)

Compound $R^1CH_2{\cdot}SCH_2{\cdot}CO_2R^2$			$M - R^{1\cdot}$ ($^+CH_2SCH_2CO_2R^2$)		$(M - R^{1\cdot}) - CO$ ($R^2OCH_2{}^+S{=}CH_2$)		
	R^1	R^2	*m/e*	(%)	*m/e*	(%)	Metastable ion
(I)	Me	H	105	2	77	13	
(II)	CD_3	H	,,	3	,,	9	
(III)	Et	H	,,	6	,,	34	
(IV)	Pr^n	H	,,	10	,,	38	
(V)	Pr^i	H	,,	25	,,	63	
(VI)	$CH_2{=}CH$	H	,,	0	,,	4	
(VII)	Ph	H	,,	0	,,	0	
(VIII)	Me	Me	119	0	91	3	
(IX)	Et	Me	,,	3	,,	6	69·4
(X)	Pr^n	Me	,,	5	,,	7	69·4
(XI)	Pr^i	Me	,,	13	,,	18	69·5
(XII)	Ph	Me	,,	0	,,	0	

by metastable ions, loss of carbon monoxide from $M - R^{1\bullet}$ is definitely established by appropriate metastable ions, in three cases (IX—XI). In these cases the probable mechanism is (a) → (c). Other examples of migration to carbonium ion centres have been reported.[2,4] Even though there are no $M - CO$ ions in many of the spectra [that of (I) contains a 1% $M - CO$ ion], a mechanism involving migration of R^2O to sulphur followed by β-cleavage (to sulphur) cannot be precluded for those spectra where metastable peaks do not substantiate the process (b) → (c).

(*Received, April 16th*, 1968; *Com.* 458.)

[1] Previous paper in this series: J. H. Bowie, G. E. Lewis, B. Søgaard Larsen, S.-O. Lawesson, and G. Schroll, *Austral. J. Chem.*, in the press.
[2] P. Brown and C. Djerassi, *Angew. Chem.*, 1967, **79**, 481.
[3] F. Duus, P. Madsen, S.-O. Lawesson, J. H. Bowie, and R. G. Cooks, *Arkiv Kemi*, 1968, **28**, 423 (and references therein).
[4] R. G. Cooks and D. H. Williams, *Chem. Comm.*, 1967, **51**.

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AUSTRALIAN JOURNAL OF CHEMISTRY

ELECTRON IMPACT STUDIES

XXXII.† NEGATIVE-ION MASS SPECTRA OF AROMATIC COMPOUNDS CONTAINING THE =Ṅ–O– SUBSTITUENT

By J. H. Bowie,‡ S.-O. Lawesson,§ B. S. Larsen,§ G. E. Lewis,‡ and G. Schroll§

[*Manuscript received March* 27, 1968]

Summary

The negative-ion mass spectra of aromatic azoxy compounds, nitrones, and *N*-oxides exhibit pronounced molecular ions and simple fragmentation processes. No skeletal-rearrangement fragments are produced upon electron impact, in marked contrast to those exhibited in the positive-ion spectra of these compounds.

The positive-ion spectra of aromatic azoxy compounds,[1] nitrones,[2,3] and certain *N*-oxides[4] contain pronounced skeletal-rearrangement ions, which owe their geneses to fragmentations of rearranged molecular ions. All rearrangement processes involve C–O bond formation. As the relative abundances of these rearrangement ions are so large (the base peak in the nitrone spectra is generally a rearrangement ion), the positive-ion spectra are of limited use for structure elucidation. The negative-ion spectra (for a review of negative-ion mass spectroscopy see[5]) of these compounds were determined in order to ascertain whether skeletal-rearrangement ions occur in negative spectra, and to see whether cleavage processes may be correlated with the structures of the intact molecules.

No skeletal-rearrangement ions are present in any of the negative-ion spectra. The molecular ion is the base peak in all spectra and this should be compared with the relative abundances of the molecular ions in the positive-ion spectra of nitrones

† Part XXXI, *Aust. J. Chem.*, 1968, **21**, 2021.

‡ Department of Organic Chemistry, University of Adelaide, P.O. Box 489D, Adelaide, S.A. 5001.

§ Department of Organic Chemistry, Aarhus University, 8000 Aarhus C., Denmark.

[1] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *Aust. J. Chem.*, 1967, **20**, 1601.

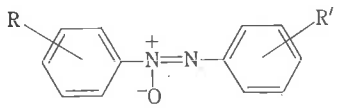
[2] Kinstle, T. H., and Stam, J. G., *Chem. Commun.*, 1968, 185.

[3] Larsen, B. S., Schroll, G., Lawesson, S.-O., Bowie, J. H., and Cooks, R. G., *Tetrahedron*, in press.

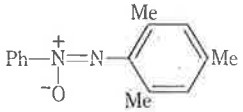
[4] Bowie, J. H., Cooks, R. G., Jamieson, N. C., and Lewis, G. E., *Aust. J. Chem.*, 1967, **20**, 2545.

[5] Melton, C. D., in "Mass Spectrometry of Organic Ions." (Ed. F. W. McLafferty.) (Academic Press: New York 1963.)

(5–30%) and azoxy compounds (15–70%). The cleavage processes of these two groups of compounds are very simple, but are quite different from the cleavage modes in the positive-ion spectra (the M—O fragmentation is an exception, and occurs in both types of spectra). Ions formed by fragmentation are generally of small relative abundance (< 15%), and may be directly correlated with structure.

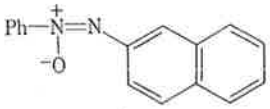


	R	R′
(I)	H	H
(II)	H	*p*-Me
(III)	*p*-Me	*p*-Me

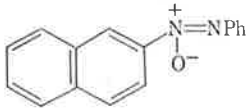


	R	R′
(IV)	H	*p*-NO_2
(V)	H	*p*-NMe_2

(VI)



(VII)



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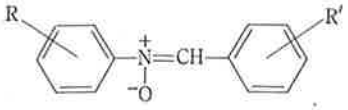
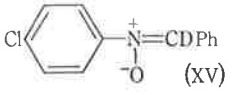
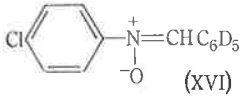


	R	R′
(IX)	H	H
(X)	H	*p*-Me
(XI)	*p*-Cl	H

	R	R′
(XII)	H	*p*-Cl
(XIII)	H	*m*-NO_2
(XIV)	*p*-Cl	*o*-OMe



(XV)



(XVI)

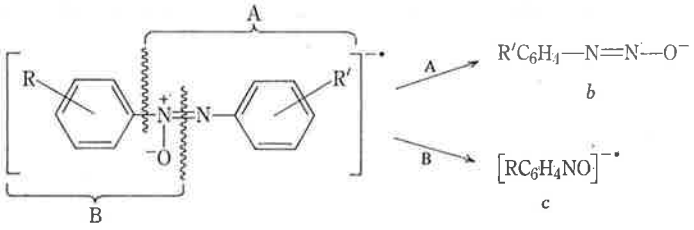
TABLE 1

RELATIVE ABUNDANCE OF FRAGMENT IONS IN THE NEGATIVE-ION SPECTRA OF (I)–(VIII)

Compound	M—O	M—RC_6H_4·†	M—$R'C_6H_4N$†	$RC_6H_4N^-$†	$R'C_6H_4N^-$†
(I)	1	6	3	3	0
(II)	4	6	2	2	0
(III)	2	4	6	0	0
(IV)	5	10	0	0	77
(V)	6	1	1	0	0
(VI)	7	2	4	2	0
(VII)	6	8	2	0	0
(VIII)	5	6	3	0	0

† Or the analogous ion in the spectra of (VI)–(VIII)

Fragment ions in the spectra of (I)–(VIII) are summarized in Table 1. Three processes are common to most spectra; viz., M—O, M—RC_6H_4·, and M—$R'C_6H_4N$. The M—O process is mainly electron-impact induced when the spectrum is obtained by the direct-insertion procedure, and the ion produced will be the corresponding azo radical anion. The other two processes are indicated in Scheme 1. Process A is common to all spectra and may be used to determine the position of the N–O moiety. Process B occurs in all spectra except that of the nitro compound (IV) (see below). Certain



d, *m/e* 136

Scheme 1

spectra (I, II, and VI) contain an ion $RC_6H_4N^-$ which may be produced by loss of oxygen from *c*. The very simple spectrum of (VII) is reproduced in Figure 1. The compositions of *m/e* 171 and 107 have been established by exact-mass measurements.

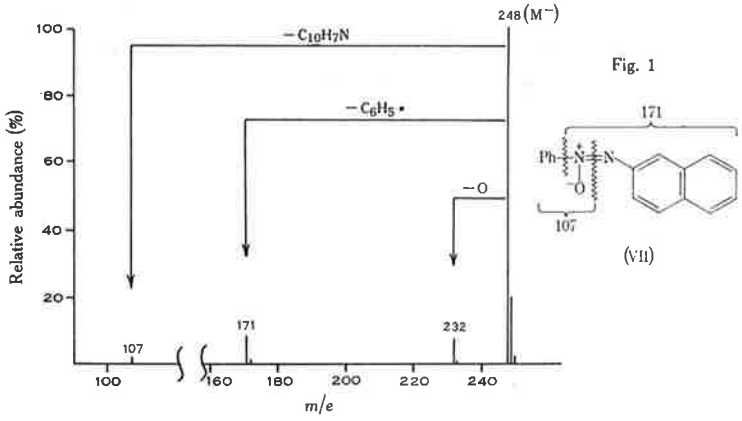


Fig. 1

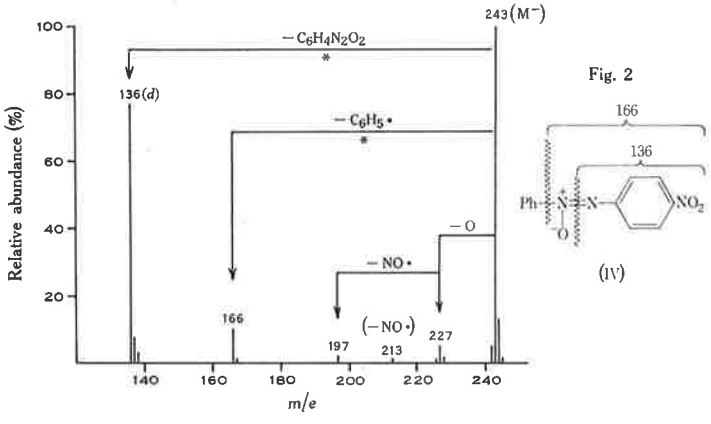


Fig. 2

When a nitro substituent is present (as in IV), cleavage B occurs, but the fragment *c* does not retain the charge. Instead *d*, *m/e* 136, is produced, and the large abundance of this ion must be due to its stabilization by delocalization, and to the weakening of the –N=N– bond by the electron-withdrawing substituent. The spectrum of (IV) is illustrated in Figure 2, and it is notable that this is one of the few cases where metastable ions (denoted by an asterisk) are present.

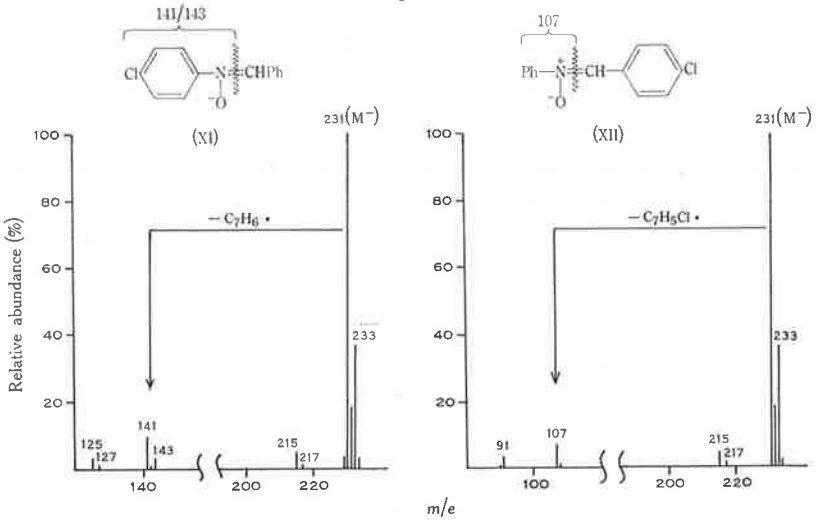
TABLE 2

RELATIVE ABUNDANCES OF FRAGMENT IONS IN THE NEGATIVE-ION SPECTRA OF (IX)–(XVI)

Compound	M—O	M—RC_6H_4·	M—$R'C_7H_5$	$RC_6H_4N^-$	$R'C_6H_4^-$
(IX)	1	2	7	7	0
(X)	2	0	8	0	0
(XI)	5	0	8	5	0
(XII)	5	0	7	2	0
(XIII)	17	0	2	3	8
(XIV)	2	4	13	0	0
(XV)	3	0	10	5	0
(XVI)	3	0	10	5	0

The spectra of the nitrones (IX)–(XVI) are even simpler than those considered above. The major fragment peaks are listed in Table 2. Only two fragmentations are common to all spectra, viz. M—O and M—$R'C_7H_5$·. The latter process (corresponding

Fig. 3



to B in *a*) allows the determination of the position of the N–O group. Only two spectra [of (IX) and (XIV)] contain M—RC_6H_4 ions, and this should be contrasted with the spectra of the azoxy compounds where M—RC_6H_4· is the diagnostic cleavage (process A in *a*). Ions due to RC_6H_4N anions are also present in many

spectra. The spectra of the two chloro isomers (XI and XII) are reproduced in Figure 3 [the compositions of *m/e* 141 (in XI) and 107 (in XII) have been established by high resolution]. The effect of a nitro substituent (as in XIII) is not as marked as it is in (IV), as no ion corresponding to *d* is produced. However, the electron-withdrawing substituent must weaken the =CH–C bond sufficiently to allow the additional formation of an $RC_6H_4^-$ species (*m/e* 120, 8% of the base peak).

The positive-ion spectra of phenazine *N*-oxides and benzo[*a*]phenazine *N*-oxides display pronounced M—CO fragments. The negative-ion spectra of phenazine *N*-oxide, phenazine di-*N*-oxide, the two isomeric benzo[*a*]phenazine *N*-oxides, benzo[*a*]phenazine di-*N*-oxide, phthalazine *N*-oxide, and benzo[*c*]cinnoline *N*-oxide contain no rearrangement ions. The only peaks are due to the molecular ion (base peak) and M—O and M—O—O (where applicable) fragments.

In summary, negative-ion spectra may be useful for diagnostic and structural purposes when positive-ion spectra are complicated by the presence of extensive skeletal-rearrangement processes. Moreover, for the compounds studied, the molecular ion is the base peak of the spectrum, and is therefore of use for molecular weight determination.

Experimental

All spectra were determined by the direct-insertion procedure (source 50–150°) with an Hitachi Perkin–Elmer RMU 6D mass spectrometer operating at 70 eV.

The compounds used have been reported previously.[1,3,4]

Acknowledgments

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