I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Date ......30 - 7 - 70..........   Signed

SOME ASPECTS OF COUPLING CONSTANTS

RELATED TO STEREOCHEMISTRY

A THESIS

PRESENTED FOR THE DEGREE OF

MASTER OF SCIENCE

in the

UNIVERSITY OF ADELAIDE

by

JOHN WAYNE FISHER, B.Sc.(Hons.)

Department of Organic Chemistry

January, 1970.

CONTENTS

* * * *

SUMMARY

$J_{(^{13}C - ^{1}H)}$ coupling constants in some hexachlorobicycloheptene, benzocyclobutene, cyclopropyl and vinyl compounds are reported here. The protons on the C atom β to the substituent, X, are found to be magnetically non-equivalent with respect to X.

Linear correlations are found when $J_{(^{13}C - H_B)}$ values (H_B being the proton *trans* or *gauche* to the substituent) are plotted against electronegativity or σ_I values of X. The slopes of these lines indicate the dependence of $J_{(^{13}C - H_B)}$ on the dihedral angle between $C - H_B$ and $C - X$.

Factors affecting $J_{(^{13}C - H_A)}$ (H_A being the proton *cis* to X) are also discussed.

Parameters obtained from the analysis of the proton magnetic resonance spectra of several 4-styryl-2-azetidinones are reported. From these values it may be deduced that (1) the spin-spin coupling constant, $J_{4'5}$, between protons on adjacent trigonal and tetrahedral C atoms (C_5 and C_4 respectively) depends on rotational conformation which is affected by the nature of the substituent in the 3-position on the 2-azetidinone ring; (2) the magnitude of the coupling constant $J_{4'5}$ varies with changing temperature indicating a dominance of the s-*trans* conformer at low temperatures with increasing concentration of *gauche* conformers at higher temperatures; (3) $J_{4'5}^{obs}$, and thus conformer population, depends on the polarity of solvent used.

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 $[ABC]^{+\bullet} \rightarrow [AC]^{+\bullet} + B$. Simple cleavage processes in *meta*- and *para*-substituted anils are found to be related to Hammett σ values of the substituents. Proximity effects observed in the mass spectra of *ortho*-substituted anils are reported.

STATEMENT

This thesis contains no material which has been accepted for the award of any other degree or diploma in any University, and to the best of my knowledge and belief contains no material previously published or written by another person, except where due reference is made in the text.

John W. Fisher

ACKNOWLEDGEMENTS

PUBLICATION

Part of the work described in this thesis has been published in the following paper:

"Skeletal-rearrangement Fragments in the Mass Spectra of Anils", J.W. Fisher, T.M. Spotswood, J.H. Bowie and R.G. Cooks, *Aust.J.Chem.*, *21*, 2021 (1968).

# CHAPTER 1. $J(^{13}C-^{1}H)$ COUPLING CONSTANTS AND STEREOCHEMISTRY

I. INTRODUCTION

1. Magnetic Non-equivalence of Protons

Protons of a methylene group removed by one or more bonds from a centre of molecular asymmetry may be magnetically non-equivalent and display AB-type nuclear magnetic resonance spectra.[1-4] The existence of preferred conformations of a methylene group with respect to an asymmetric centre is generally considered necessary for magnetic non-equivalence. However, the possibility of small contributions to magnetic non-equivalence arising from "intrinsic" asymmetry, which is independent of rotational conformer populations, has been indicated.[5] The problem of separating intrinsic non-equivalence from the effects of conformational populations still remains.[6-8] For example, non-equivalence of the methylene protons in acetals[9-11] results from the intrinsic internal asymmetry of the acetal grouping (1) and not ultimately from restricted rotation.
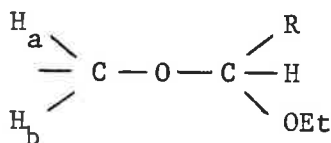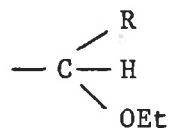
(1)   (2)

To the protons a and b of one (or other) methylenoxy group, the attached group (2) is asymmetric. The environment in each of the protons a and b is consequently distinct and the protons are diastereotopic. Each therefore expresses a different average environment from the other even though rapid rotation may equalise the populations of the separate conformers.

A complete analysis of the ^{13}C satellite spectrum of acetal[11] has shown that the methylene protons not only have different chemical shifts, but they have different $^{13}C-^1H$ couplings. It seems likely that the $^{13}C-^1H$ coupling parameter provides a new criterion for non-equivalence. This has the advantage of not being significantly affected by magnetic contributions which complicate the interpretation of chemical shifts.

2. Coupling Constants

The coupling constants considered here are those between

(a)   vicinal protons

(b)   geminal protons

(c) $^{13}C-^1H$.

(a)   Vicinal Coupling Constants (H — C — C' — H')

Karplus has indicated[12] that the size of vicinal proton-proton coupling constants, $J_{HH'}$, is expected on theoretical grounds to depend on many molecular properties. These include the C — C' bond length, hybridisation, dihedral angle ϕ, the bond angles θ and θ' in

Figure 1, the electronegativity of substituents, changes in π-bonding, ΔE variations and molecular vibrations.
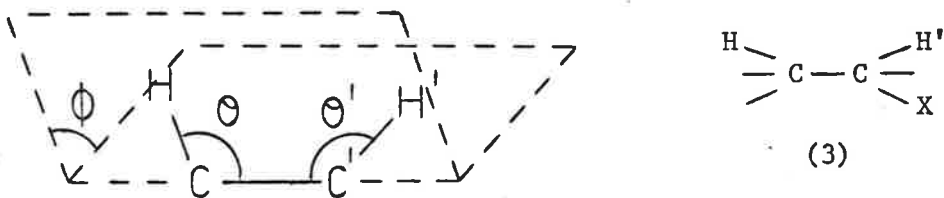
Figure 1

The dominant influence on the magnitude of $J_{HH'}$ is the dihedral angle φ between H and H' defined by the Karplus relation (1.1).[13]
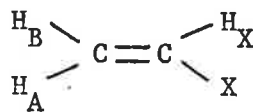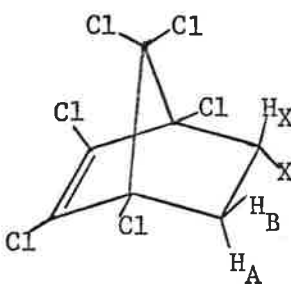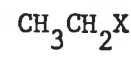
$$J_{HH'} = 8.5 \cos^2 \phi - 0.28 \text{ c.p.s. } (0° < \phi < 90°)$$

$$J_{HH'} = 9.5 \cos^2 \phi - 0.28 \text{ c.p.s. } (90° < \phi < 180°)$$

$$(1.1)$$

In the fragment (3) it is observed experimentally that the size of $J_{HH'}$ decreases as the electronegativity of the atom X increases. Over a limited range of Dailey electronegativity[14] the relationship appears to be approximately linear, i.e. of the form given in (1.2),

$$J_{HH'} = -aE_X + b \qquad (1.2)$$

with values of the constants a and b characteristic for each system. The decrease in vicinal coupling constants is most marked in ethylenic systems, less so in cyclopropanes, epoxides and norbornenes and least in simple acyclic molecules like the ethanes.[15]

Table 1. Effect of Substituents on Vicinal Coupling Constants[a]

(4) (Ref. 16)   (5) (Ref. 17)   (Ref. 18)

J_{AX}	J_{BX}	X	J_{AX}	J_{BX}	X	$J(CH_3, CH_2)$[b]	X
23.9	19.3	Li	3.81	9.73	H	8.90	Li
19.1	11.6	H	4.6	9.3	CN	8.0	H
17.2	10.4	CO_2H	3.2	8.0	Cl	7.23	Cl
14.3	7.0	OMe	2.5	7.7	OAc	6.97	OEt
13.9	6.3	OAc					
12.7	4.7	F					

[a] Only a few representative values from each system are given.

[b] Average coupling constant.

As well as their nature, the orientation of substituents with respect to the fragment H — C — C' — H' is important. This can be deduced from the fact that the lines of best fit corresponding to equation (1.2) constructed for various systems (e.g. those in Table 1) exhibit variations in slope not only between different systems

but also between J_{cis} and J_{trans} in the same system. Spectral data

for (6) *cis*- and (7) *trans*-2,6-dimethylpiperidine[19] in which

$J_{e_3 a_2}$ = 1.9 and $J_{a_3 e_2}$ = 4.6 c.p.s. support the earlier suggestion[20,21]
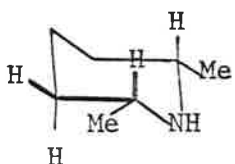
(6) (7)

that an electronegative substituent exerts a maximum effect

(leading to smallest J_{vic}) where a *trans* coplanarity relation exists

between a part of the 'coupling path' (indicated by heavy lines in

(6) and (7)) and the bond by which it is attached to the system

i.e. as in (6) but not (7), Further, it has been suggested[22] that

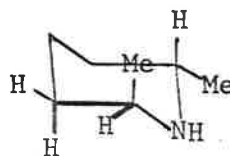in acyclic systems of known conformation, and presumably in the

chair forms of six-membered carbocyclic rings, J_{trans} in ethanic

fragments is significantly affected by the presence of electronegative

groups but the effect on J_{gauche} can be neglected unless stereo-

chemistry analogous to (6) is present.

Studies on a series of conformationally mobile ring systems

having similar geometry or similar vicinal polar substituents,[23] and

on open chain compounds,[24] have shown a linear relation exists

between the squares of the electric dipole moments and the sum of

the vicinal coupling constants $J_{AX} + J_{BX}$. It was shown that the

combination of dipole moment data with coupling constants yields

valuable quantitative information on Karplus parameters, ring
deformations and conformational equilibrium constants. The μ value
for the total compound and not that for the individual substituents
was used in these calculations. The dihedral angle is continually
changing, due to the mobility of the system, and the use of the
Karplus relation yielding $J_{AX} + J_{BX}$ is not really meaningful.

$J_{HH'}$ in ($H - C \equiv C' - H'$) exhibits very useful and regular
correlations with the nature of substituents, with ring size in
cyclic compounds and with the *cis-trans* relation between H and H'.
In substituted ethylenes (4), any variation in the electronegativity
of X will affect J_{BX}^{cis} slightly more than J_{AX}^{trans},[25] (see Table.1).

(b) <u>Geminal Coupling Constants</u> ($\diagdown C \diagup \diagdown$ H / H)

Pople and Bothner-By[26] have given a molecular orbital treatment
of geminal coupling constants which has provided a qualitative
rationalisation for the signs of observed coupling constants. The
value of the geminal coupling constant is considered to provide a
means of distinguishing between inductive and hyperconjugative electron
transfer. Barfield and Grant[27,28] obtained an excellent correlation
of data (experimental and theoretical) using a semi-empirical valence
bond description of hyperconjugative effects.

The main trends which have been established in geminal coupling
constants are:

(i) In the simplest hydrocarbons, the geminal proton-proton
coupling constant increases (i.e. becomes more positive) as the
hybridisation of the C-H bonds increases in s-character. The value

for methane (sp^3 hybridisation) is -12.4 c.p.s.[29] while that for

ethylene (sp^2 hybridisation) is +2.5 c.p.s.[30] The value for

cyclopropane (intermediate between sp^2 and sp^3 hybridisation) is

-4.34 c.p.s.[31]

   (ii)   Electronegative substituents on the carbon atom carrying
the geminal protons add positive increments to the coupling constants.
For freely rotating groups, or for groups with identical orientations
the effects are approximately additive.   The magnitude of the effects
can be estimated from some typical values (see Table 2).

   Table 2.   Geminal Coupling Constants in Substituted Methanes.

$$\begin{matrix} H_A \\ \\ H_B \end{matrix} \Big\rangle CH - X$$
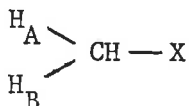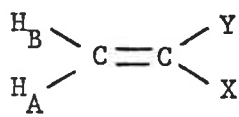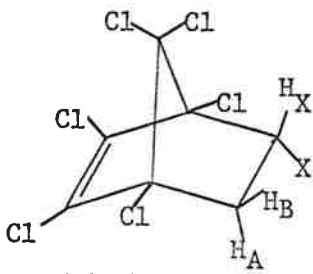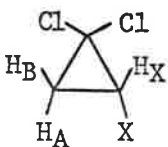
(Ref. 29,32)

J_{AB}	X
-12.4	H
-10.6	OMe
-10.2	Br
- 9.6	F
- 9.2	I

   (iii) In general, an increase in the electronegativity of
the β-substituent is associated with a negative increment in J_{gem}
but the relationship is not simple and appears to depend on

orientation. The values listed in Table 3 are in each case the extremes for large series covering most of the commonly encountered substituents.

Table 3. Selected Geminal Coupling Constants

(4) (Ref. 30)			(5) (Ref. 17)		(Ref. 33)	
J_{AB}	X	Y	J_{AB}	X	J_{AB}	X
+2.5	H	H	-12.6	CN	-4.9	$SiMe_3$
-1.3	Cl	H	-13.3	OAc	-9.1	OAc

In ethylene derivatives the magnitudes of J_{gem} are related to the nature of β-substituents [i.e. X and Y in (4)] and their effects are approximately additive. The relationship[34] of the form (1.3),

$$J_{gem} = -a(E_X + E_Y) + b \qquad (1.3)$$

where E_X and E_Y are the electronegativities of the substituents X and Y in (4), still appears to hold, contrary to Schaefer and Hutton's opinion (1.4)[16] even on an extended electronegativity range. The

mean deviations from a straight line of best fit using (1.3) are
no greater than those obtained using the reciprocal relationship (1.4).

$$J_{gem} = \frac{a}{E_X + E_Y} - b \qquad (1.4)$$

The present theory[12] can be rationalised to support (1.3) but there
is no theoretical or practical justification to warrant acceptance
of (1.4) even though this has been done.[35,36]

(c) $\underline{^{13}C-^{1}H \text{ Coupling Constants}}$

The nuclear spin-spin scalar coupling between ^{13}C and
directly bonded ^{1}H, $J(^{13}C-^{1}H)$, has been widely studied and
discussed.[10,37-42] The major contribution to the scalar coupling
arises from the Fermi contact term, which is proportional to the
contribution of s orbitals centred on carbon to the C-H bond. The
$2s_C$ orbital is the most important. On the basis of both theoretical
and empirical considerations it has been suggested[10] that $J(^{13}C-^{1}H)$ is
linearly related to the fractional s character α_H^2, of the C orbital
bonding to H; as indicated in the expression (1.5). The theoretical

$$J_{(^{13}C-^{1}H)} = 500 \ \alpha_H^2 . \qquad (1.5)$$

justification for the quantitative character of this relationship is
not perfect[42-44] but it is empirically very satisfactory in a series
such as CH_4, C_2H_4, C_2H_2. There is no doubt that it has value if

used carefully in suitable compounds. However other factors in the coupling constant expression may be important.[45] Whilst the values obtained appear reasonable for methane and the unsaturated hydro-carbons, they imply rather unusual interbond angles in some of the halogenated derivatives. This discrepancy can be accounted for by the concept of bent bonds,[37] i.e. the inter-orbital angles (which reflect the true state of hybridisation of an atom) may not be the same as the observed internuclear angles.

If the $^{13}C-^{1}H$ coupling constant does depend solely on the state of hybridisation of the carbon atom then it should be related to the C–H length.[38] For substituted methanes the empirical equation (1.6), where r_{C-H} is the bond length in Angstrom units, has been found.[37]

$$ r_{C-H} = 1.1597 - 0.000417 \times J_{(^{13}C-^{1}H)} \qquad (1.6) $$

In general, there is good agreement between observed and calculated[46] values of r_{C-H} unless the carbon atom has very electronegative substituents. A correction for this has been proposed.[47]

Grant and Litchman[44] have shown, by a consideration of charge transfer in some simple aliphatic halides, that changes in the effective nuclear charge of carbon (Z) can account for observed changes in $J_{(^{13}C-^{1}H)}$. Changes in hybridisation parameters are not necessary to obtain a correlation with the experimental coupling constants. Some experimental support for this view is provided by

an observed correlation between C-H stretching force constants and $J_{(^{13}C-^1H)}$.[48] It can be shown theoretically that the force constant should depend on C-H bond polarity (which will in turn depend on the electronegativity of the other groups attached to carbon) but not directly on the carbon atom hybridisation. Lunazzi and Taddei[49] have proposed the relationship (1.7),

$$J_{(^{13}C-^1H)} = 3.25 \, d \, E + 94.9 \qquad (1.7)$$

where d is the bond distance in $\overset{o}{A}$ and E is the substituent electronegativity, to account for the variation of $^{13}C-^1H$ coupling constants in monosubstituted methanes. Huheey[50] finds extremely good correlation between $J_{(^{13}C-^1H)}$ in halogenated methanes and the electronegativity of the substituents when orbital electronegativities[51] are used. That is, the effect of varying orbital occupancy upon different orbitals of the same atom is taken into account. Douglas[52] has pointed out that there is correlation between $J_{(^{13}C-^1H)}$ in CH_3X and the electronegativity of X within a particular period of the periodic table, but that the linear plots are of different slopes. He concludes that while factors other than C-H bond s-character can affect C-H coupling constants, consideration of changes of hybridisation cannot be neglected.

The present position is that variations of $J_{(^{13}C-^1H)}$ can be accounted for by changes in s-character if the electronegativity of the substituents varies little (e.g. amongst different saturated and

unsaturated hydrocarbons), and by changes in electronegativity
if the bulk of the substituents is roughly constant. The two factors
are actually related, and if both vary significantly then both must
be considered.

3. Rigid Stereochemical Systems Studied

The purpose of the work reported herein was to determine the
effect of various substituents on the coupling constants between
each of the methylene protons and the ^{13}C nucleus adjacent to the
substituted carbon atom. In order to determine the effect of
substituents of varying electronegativity on the magnitude of
$J_{(^{13}C-^{1}H)}$ it is necessary to have a system in which the stereochemistry
of the coupling protons remains fixed and known. Furthermore, the
system must have a minimum number of coupling protons to facilitate
complete, unambiguous analysis of the spectra. Finally, it must be
possible to introduce a variety of groups of differing electro-
negativity. For these reasons this study includes the n.m.r. spectra
of Diels-Alder adducts, formed from hexachlorocyclopentadiene and a
series of monosubstituted ethylenes (5), as well as substituted
benzocyclobutenes, cyclopropyl and vinyl derivatives.

Evidence for the conformational rigidity of the bicyclo-
[2.2.1]-heptene system has recently been given.[53,54] The compounds
used in this study are assumed, in accordance with the rule of Alder

and Stein,[55] to be *endo* isomers. The dihedral angles between the coupling protons are assumed to be 0° and 120°. The four-membered ring in benzocyclobutene is shown to be fixed and planar.[56] The rigid cyclopropane structure is well-known to provide an excellent system to study the influence of substituents on n.m.r. coupling constants.[36] The valence-bond calculations made by Karplus[13] and the molecular orbital treatment of Conroy[57] predict for sp^3 hybridisation a dependence of the vicinal coupling constant on the dihedral angle between the C — H bonds. For the geminal H — C — H angles of 114.5–118° for cyclopropanes[58] the corresponding dihedral angles are calculated to be 131–134° for *trans-* and 0° for *cis-* cyclopropyl hydrogens.

II. RESULTS

The coupling constants in the hexachlorobicyclo-[2.2.1]-heptene and benzocyclobutene systems were in each case calculated by an ABX[59] analysis of the spectrum (Table 4), although for the chloro and acetoxy derivatives, the calculated couplings are the same within experimental error as those obtained by direct measurement, because the chemical shifts between the coupling protons are so large. The lines for each proton in all spectra were very well resolved allowing assignments and line positions to be measured without ambiguity.

Table 4. Coupling Constants and Chemical Shifts
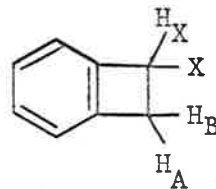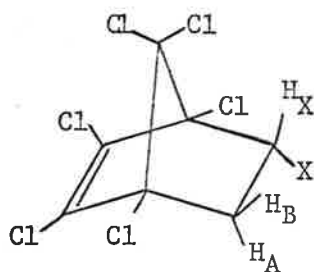
X =	CN	COMe	Br	Cl	OAc	Br
J_{AX}	4.2	3.8	3.4	3.03	2.45	2.02
J_{BX}	9.1	8.8	8.0	8.27	7.65	4.68
J_{AB}	−12.9	−12.4	−13.65	−13.4	−13.4	−14.6
ν_A	−411.9	−390.0	−385.5	−415.0	−384.4	−291.9
ν_B	−386.8	−409.5	−351.5	−372.4	−323.4	−275.2
ν_X	−335.7	−336.5	−246.3	−266.5	−154.7	−177.3
$J_{(^{13}C-H_A)}$	146.2	144.1	147.4	145.4	144.5	145.2
$J_{(^{13}C-H_B)}$	145.8	141.7	143.2	142.6	143.5	140.2
Electronegativity[14]	2.49	2.6	2.87	3.25	3.80	2.87

Each sample was run as *ca.* 150% solution in C_6D_6 with benzene as an external reference.
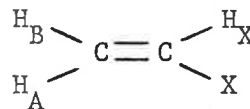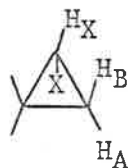
X =	OAc	CN	OAc
J_{AX}	3.03	18.09	14.0
J_{BX}	6.44	11.93	6.3
J_{AB}	−4.60	+0.88	−1.5

ν_A	105.8	269.35	288.5
ν_B	102.7	278.11	270.0
ν_X	238.4	331.40	436.0
$J_{(^{13}C-H_A)}$	163.6	164.2	158.5
$J_{(^{13}C-H_B)}$	164.2	166.6	162.0
Electronegativity[14]	3.80	2.49	3.80

Each sample was run neat. Cyclopropyl acetate and cyanoethylene had benzene and TMS as internal references, respectively. The spectrum of vinyl acetate was obtained by locking on the acetate peak.

First-order assignments were made in each case by inspection and introspection. This yielded quite accurate values for vinyl acetate. Use of the iterative program LAOCOON III[60] on the basis of these first-order assignments for cyclopropyl acetate and cyano-ethylene gave fairly rapid convergence. The plots of theoretical spectra agreed well with experimental spectra. The H — H coupling constants thus obtained agreed with those obtained from the normal spectrum to within 0.1 HZ. One-bond $^{13}C-^1H$ coupling constants as shown in Table 4 are taken as twice the difference between the effective chemical shift of the satellite spectra and the corresponding chemical shift obtained from the main spectra. After consideration of all possible sources of error the precision of the $^{13}C-^1H$ couplings cannot be claimed to be better than ±0.25 HZ. All other data are accurate to ±0.1 HZ.

Several other series of compounds which possess stereochemically rigid isolated 3-spin and related systems were synthesised. The $J_{(^{13}C-^1H)}$ values of these compounds were not precisely determined due to one or more of the following factors:

a. complex overlap of ^{13}C satellites

b. insufficient solubility of compound in benzene

c. lack of stability over extended periods of time necessary for determining the spectra.

d. unavailability of sufficient compound.

These compounds include 5-hydroxy-1,2,3,4,7,7-hexachlorobicyclo-[2.2.1]-hept-2-ene[a], -5-carboxylic acid[b] and -5-methylcarboxylate[a]; benzocyclobutene-1-carboxylic acid[b] and -1-methylcarboxylate[d]; acetyl-[a], bromo-[c] and chloro-[c] succinic anhydride; cyclopropyl derivatives[a]; 3-bromo-[c], 4-acetyl-[b] 3,4-dihydrocoumarin, -4-carboxylic acid[b] and -4-methylcarboxylate[d]; 3-bromo-4-chromanone[a]; *cis*-2,4-dibromobicyclo-[3.2.1]-octan-3-ol and bicyclo-[3.2.1]-octan-3-ol[d].

III. DISCUSSION

1. Non-equivalence of Protons

In the fragment (3r) protons H_A and H_B, which are symmetrically substituted about the C — C bond, should appear magnetically equivalent

$$H_X \searrow X \diagdown C - C \diagup H_B \diagdown H_A$$

(3r)
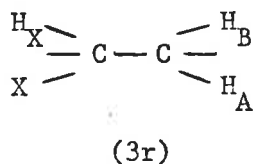
with respect to X if the electronic effects due to X are transmitted
through bonds. Unequal chemical shifts, proton coupling constants
and $J_{(^{13}C-^1H)}$ values in the compounds studied reveal magnetic
non-equivalence of the protons. Any effect on H_A and H_B produced
by electronic changes in X is most likely therefore to be transmitted
through space.

2. Factors affecting $J_{(^{13}C-H_B)}$

Schaefer et al.[34] have suggested that the coupling between
the proton *trans* to the substituent and the C atom bearing it,
$J_{(^{13}C-H_B)}$, for X=H, I, Br, Cl, F, CN in substituted ethylenes, varies
smoothly with the parameter μ/r, where μ is the substituent dipole
moment and r is the C—X bond length. This expression is not
grounded on a solid theoretical basis and the agreement obtained
for the compounds studied was purely fortuitous. The values for
vinyl acetate, vinyl cyanide and methyl vinyl ketone vary considerably
from the straight line plot. This expression does not yield any
regular correlation with $J_{(^{13}C-H_B)}$ in either of the cyclopropyl or
bicycloheptene systems studied here.

Several correlations have been described which attempt to relate magnitudes of couplings to substituent electronegativities. [16,33,61,62] All these treatments have used plots of coupling constants vs. electronegativity to derive a linear correlation. These linear relationships have all shown a significant scatter of points which suggests that a multiplicity of substituent effects influences these couplings although the most important one appears to be that of electronegativity. The $J_{(^{13}C-H_B)}$ values obtained in this work and from the literature[34,63] are plotted against the electronegativity of each substituent (see Figures 2a, b, c). A straight line correlation with minimum scatter is generally obtained for each of these systems. It is observed that the points corresponding to the cyano- and acetyl-groups lie above the line in the acetyl series as does the point corresponding to the cyanobicycloheptene.
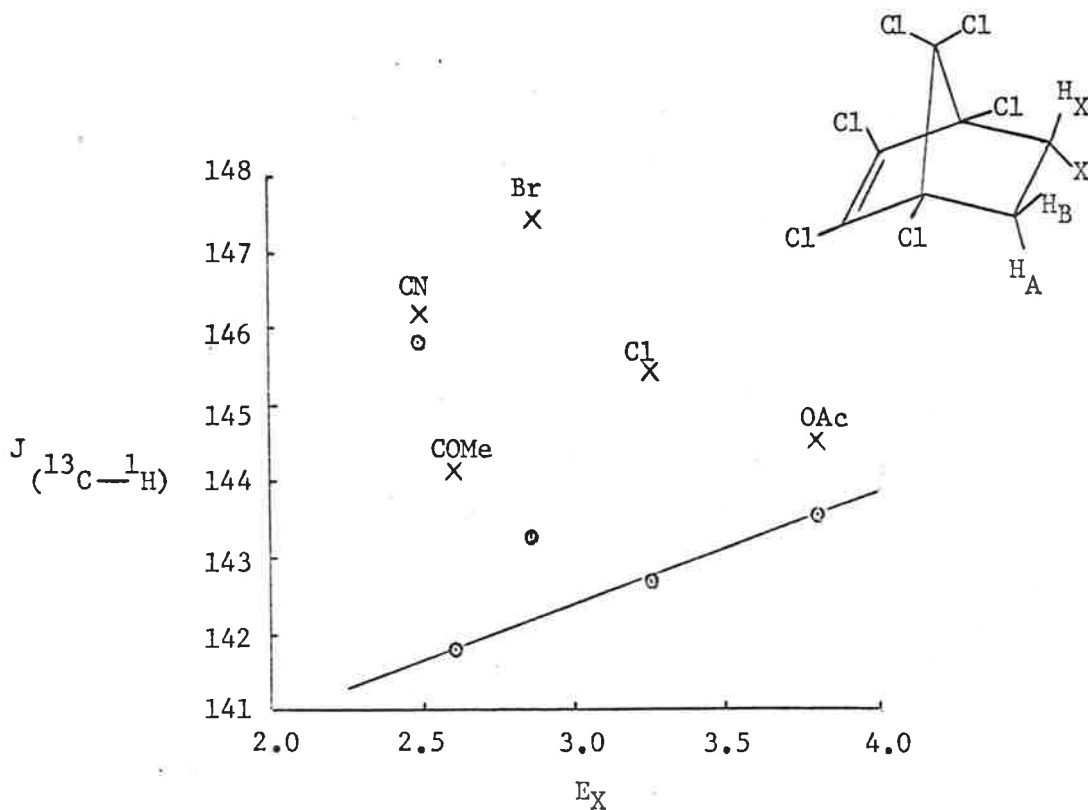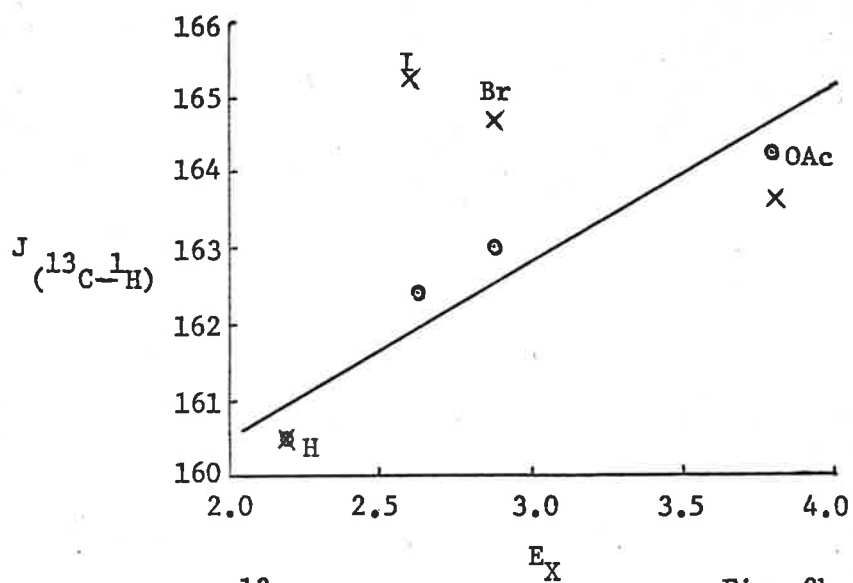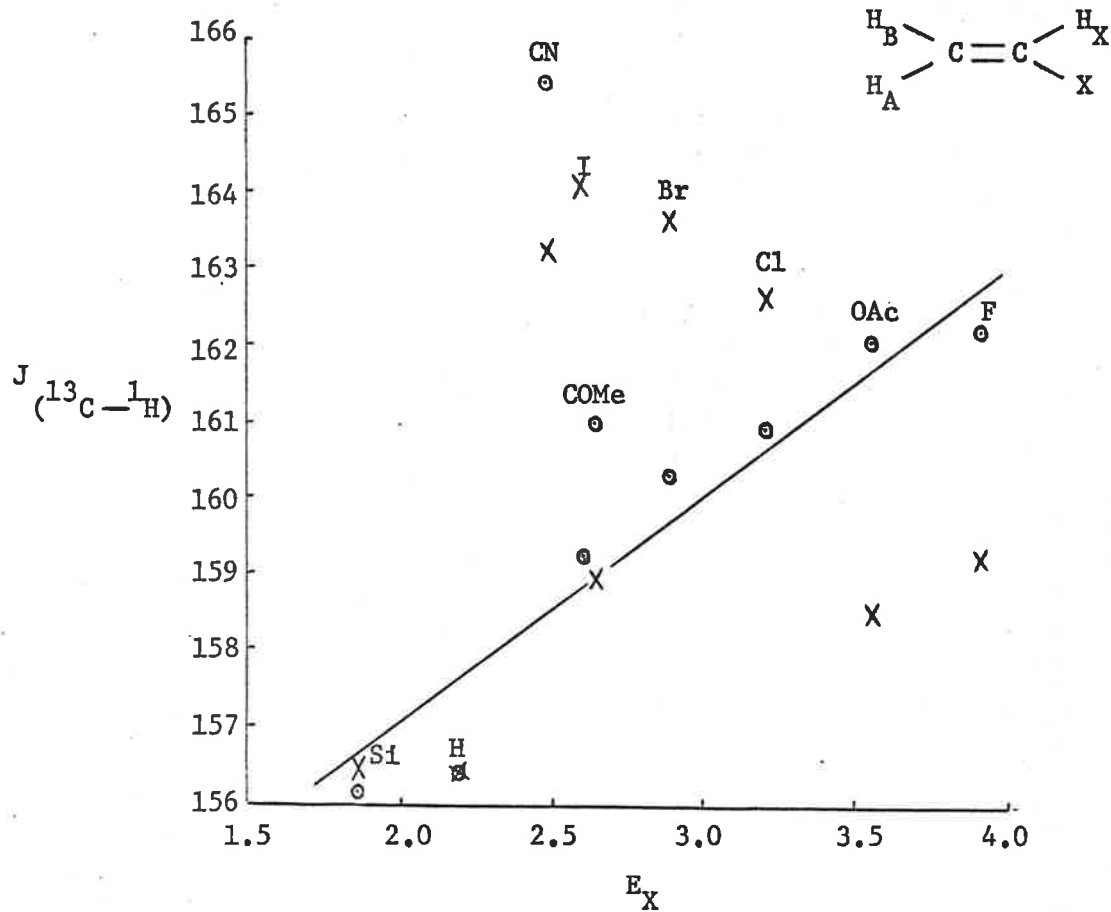

Fig. 2a

Fig. 2b

$\odot = J(^{13}C-H_B)$

$\times = J(^{13}C-H_A)$

Fig. 2c

An investigation of the slopes of these lines indicates that they can be represented by the expression (1.8) where ϕ is

$$\Delta J/\Delta E = 2.62 + 4.95 \cos^2 \phi \qquad (1.8)$$

the dihedral angle between the $C-X$ and $C-H_B$ bonds. The $^{13}C-^1H$ coupling constants thus depend on the dihedral angles as well as electronegativity. The larger the angle the greater is the value of $J_{(^{13}C-^1H)}$ obtained with the maximum effect coinciding with a *trans* anti parallel arrangement of the substituent and H_B i.e. in the ethylenes. The express-ion (1.5) yields sp^2 and approximate sp^2 hybridisation for the C atom β to X in the vinyl and cyclopropyl compounds respectively, with the bicycloheptenes and benzocyclobutenes approaching closer to sp^3 hybridisation.

The *trans-*, *cis-* and geminal proton coupling constants in the compounds studied correlate with the electronegativities of substituent groups[16,17,36] and are in the order expected from these electronegativities. Banwell and Sheppard noted,[25] in their study of coupling constants in vinyl compounds, that a substituent atom of high electronegativity would be expected to reduce the electron density around the nearby coupling protons which in turn should lead to less interaction between nuclear and electron spins and therefore algebraically lower values of coupling constants. The

dependence of $J_{(^{13}C-^1H)}$ is of the opposite sense to that of the other coupling constants, i.e. $J_{(^{13}C-H_B)}$ shows an algebraic increase as the electronegativity of the substituent increases. The $J_{(^{13}C-^1H)}$ values are absolutely positive in sign while J_{gem} are usually negative and J_{vic} positive. A comparison of the plots of the coupling constants vs. electronegativities indicates that $J_{(^{13}C-H_B)}$ is more strongly dependent on the electronegativity than the others. The slope of J vs electronegativity decreases in the order $J_{(^{13}C-H_B)} > J_{trans} > J_{cis} > J_{gem}$ for the cyclopropyl and bicycloheptene systems but J_{cis} is slightly greater than J_{trans} in the vinyl compounds.

It was mentioned earlier that the cyano- and acetyl-groups yield apparently anomolous values in the plots of J vs. electronegativity for certain compounds. There is a possibility that an additional mesomeric effect could be associated with the π-electron system in the vinyl compounds. A resonance contributing structure (8) in which π-electrons are removed from the carbon atom β to the substituent would leave that carbon atom with less p character i.e. apparent increase in s-character, with an associated larger $J_{(^{13}C-^1H)}$ value.

(8)
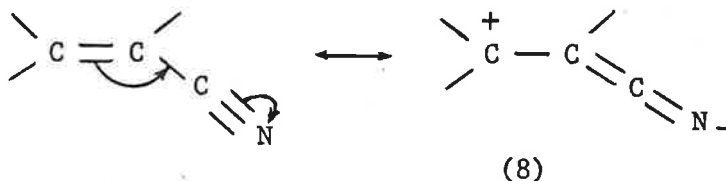
No such mesomeric effects are possible in the substituted bicycloheptenes but the cyano group with its large dipole moment could possibly induce a dipole in the $C-H_B$ bond to favour a contributing structure of the form C^-H^+. This would increase the s-character of the β carbon atom with a corresponding increase in the value of $J_{(^{13}C-H_B)}$.

If the major contributions to variations in $J_{(^{13}C-H_B)}$ values come from the electronegativity changes of the X substituents, then $J_{(^{13}C-H_B)}$ should also show a dependence on Taft σ values.[64] Qualitatively the σ values conform to the general picture of substituent effects with electron withdrawing groups having positive σ values. The $J_{(^{13}C-H_B)}$ values are plotted against σ_I, which measures the contributions to the σ value from non-conjugative (inductive)- and σ_R, which measures the contributions from conjugative (resonance)- interactions between the substituent and reaction centre. (see Figures 3a, b, c).

Fig. 3a

Fig. 3b

Fig. 3c

$\odot = \sigma_I$

$X = \sigma_I + \sigma_R$
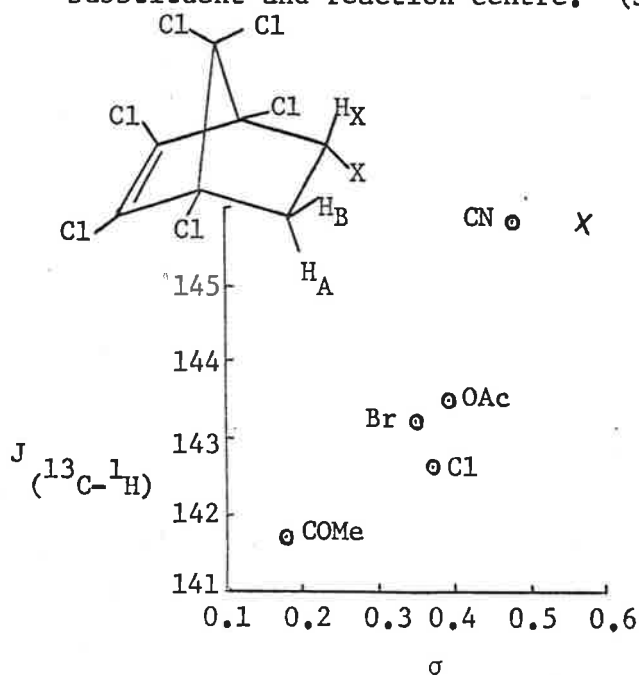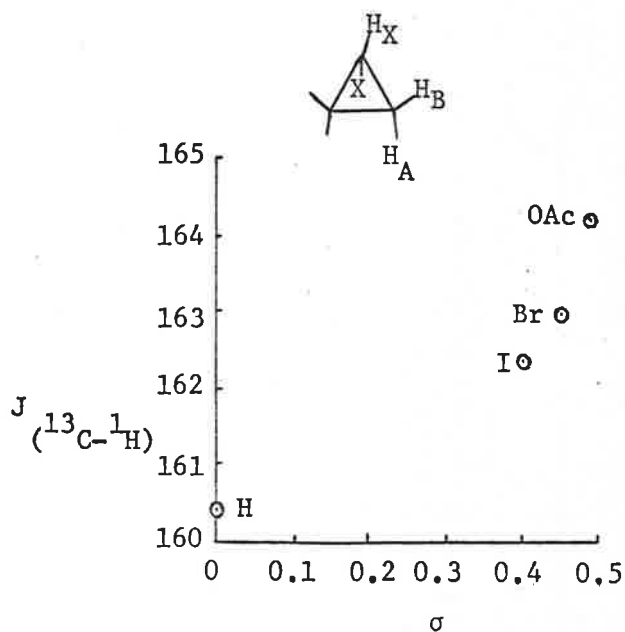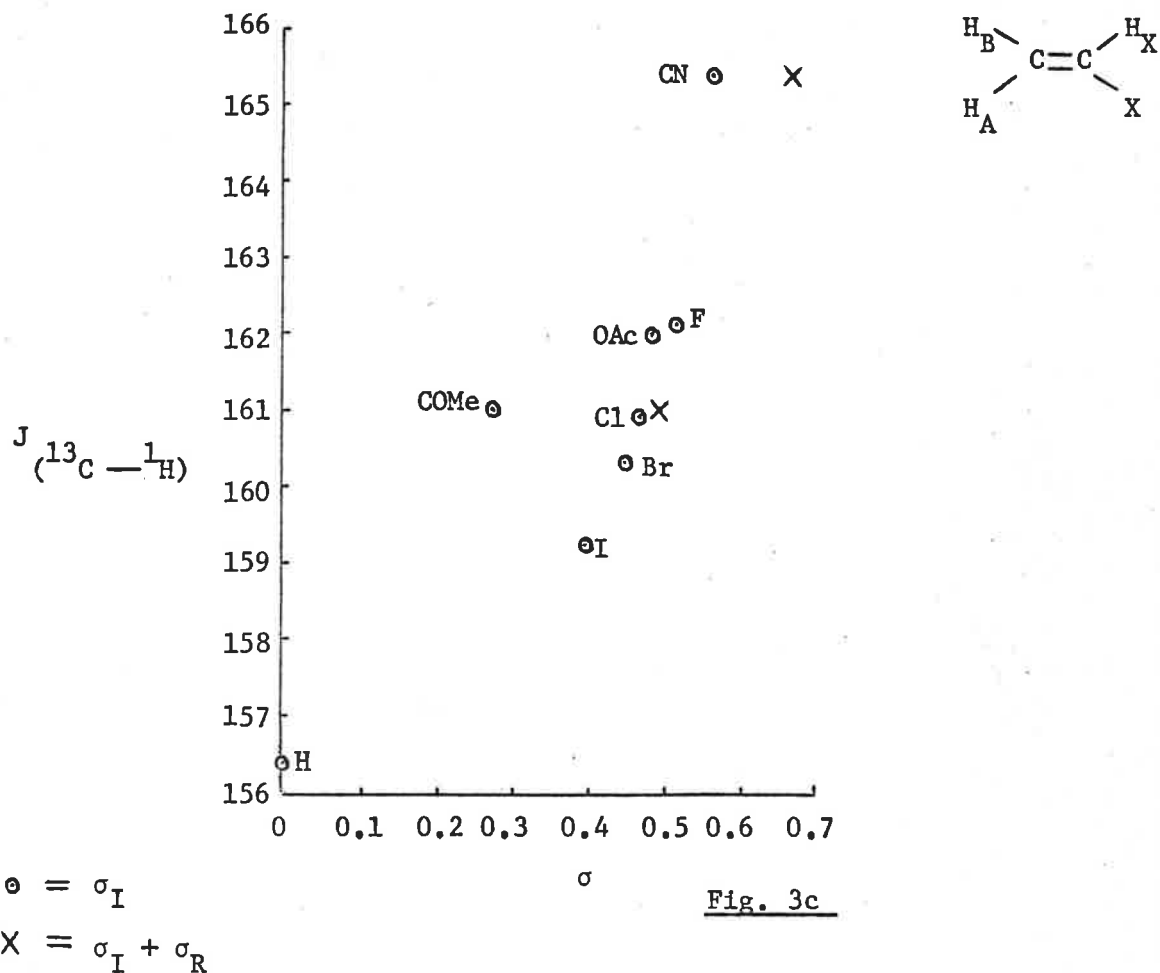
Linear correlations are generally observed for $J_{(^{13}C-H_B)}$ vs σ_I values in the vinyl-, cyclopropyl- and bicycloheptene-systems. The cyano- and acetyl- groupings again deviate from the linear plot in the vinyl system as does the cyano group in the bicycloheptene system.

A random distribution of points is obtained by plotting $J_{(^{13}C-H_B)}$ vs. σ_R.

If the values of $J_{(^{13}C-H_B)}$ for the -CN and -COMe groups in the vinyl system, and the -CN group in the bicycloheptene system are plotted against $\sigma_I + \sigma_R$ then these points fit well on the straight line plot of $J_{(^{13}C-H_B)}$ vs. σ_I for the other groups in these series. These results support the initial suggestion that the major factor affecting $J_{(^{13}C-H_B)}$ is the electronegativity of the substituent X with added resonance contributions from the cyano- and acetyl-groups.

These plots (Figs. 3a, b, c) are in the same sense as those obtained for $J_{(^{13}C-H_B)}$ vs. electronegativity values with the slopes of these straight lines again in the order vinyl > cyclopropyl > bicycloheptene. This supports the original view that $J_{(^{13}C-H_B)}$ is also dependent on the dihedral angle between C-X and C-H_B.

3. Factors affecting $J_{(^{13}C-H_A)}$

No regular correlations are found between the proton *cis* to the substituent and the C bearing it, $J_{(^{13}C-H_A)}$, and electronegativity, σ_I or σ_R values in the vinyl-, cyclopropyl- and bicycloheptene-systems studied here.

Juan and Gutowsky[65] suggest possible interactions between lone pairs of electrons on the substituent and the C-H bond, in substituted methanes, which affects $J_{(^{13}C-H)}$ without necessarily implying any alteration in the s-character of the C-H bond. The general trend of $J_{(^{13}C-H_A)}$ in the compounds studied here (see Figs. 2a, b, c) supports the possible operation of such an interaction. For example, the larger iodide group, in which there is more chance of neighbouring group

involvement between I and H_A, yields greater $J_{(^{13}C-H_A)}$ values than the smaller fluoride and acetate groups.

CHAPTER 2.   VARIABLE TEMPERATURE STUDIES OF COUPLING CONSTANTS

RELATED TO STEREOCHEMISTRY

I.   INTRODUCTION

1.   Vicinal coupling constants

N.m.r. has proved extremely valuable in conformational assignments for many systems.[66] In particular the variation in vicinal coupling constants, J_{HH}^{vic}, with dihedral angle[13] has been extensively used for substituted ethanes and for cyclohexane derivatives.

Over the past few decades there has accumulated considerable evidence for the existence of distinct rotational conformers in open-chain organic compounds containing a single bond between a tetrahedral and a trigonal carbon atom. Such conformers are sufficiently short lived that physical separation has not been feasible. Information about them has been obtained indirectly by physical measurements on mixtures.

In the compounds of type (9) with X=0 or $-CR_2$, the population of preferred rotational isomers varies with temperature, and so therefore does the vicinal coupling constant, J_{AB}.[76]

$$X = C \underset{\displaystyle H_A}{\overset{\displaystyle H_B}{\diagdown}} \underset{\displaystyle Y}{\overset{\displaystyle Y}{\diagup}}$$
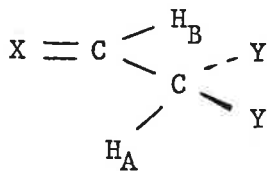
(9)

From a consideration of the vibrational frequencies, Mizushima *et al.*[67-70] have suggested that for carbonyl-containing compounds, one of the stable conformations is that in which the carbonyl oxygen is eclipsed with a substituent on the tetrahedral carbon.

Microwave spectroscopy has been applied in order to ascertain the structures in the cases of acetaldehyde[71] and propene.[72] While the symmetry of the methyl group precludes the existence of distinguishable rotational conformers in this case, the most stable conformation is confirmed as that in which one of the substituents on tetrahedral carbon is eclipsed with the carbonyl oxygen or the vinyl methylene.

Abraham and Pople[73] have studied the n.m.r. spectra of acetaldehyde and propionaldehyde and have found for propionaldehyde a dependence of J_{HH} (aldehyde proton to methylene proton) on temperature. This is interpreted in terms of a temperature dependence of rotamer population, and leads to the conclusion that the preferred conformation in liquid propionaldehyde is that in which the methyl group is eclipsed with the carbonyl.

Karabatsos and Hsi[74] extended this investigation by measuring the vicinal H—H coupling constant at various temperatures in the series $R.CH_2.CHO$. In the neat liquids, where R is methyl, ethyl, n-propyl, isopropyl or phenyl the energy difference favours the *trans* rotamer (10a). Where R is *t*-butyl, the *gauche* isomer (10b)
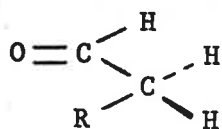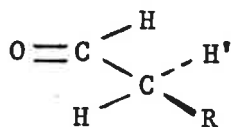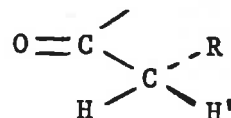
(10a)   (10b)   (10c)

or (10c) is more stable. In di-*t*-butylacetaldehyde the steric
interference between the *t*-butyl group and the carbonyl, when they
are eclipsed, is large. The conformer with the carbonyl and proton
eclipsed [(10b) or (10c) with H'=R=*t*-butyl] is favoured.[75]

In propene, the three most stable rotational conformations
are energetically indistinguishable. In the case of the monosubstituted
propenes (11) [analogous to (10) above], the introduction of bulkier
alkyl groups increases the populations of the forms (11b) and (11c)
at the expense of (11a). Calculation of coupling constants from
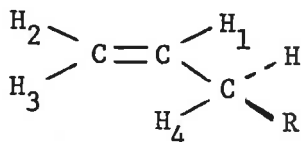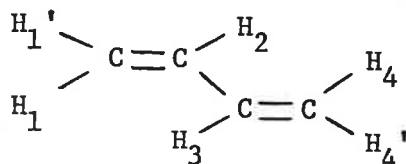
(11b)   (12)

rotamer populations and observed vicinal couplings in substituted
propenes yields a lower limit for J_{14}^{trans} of 11.1 c.p.s. and an
upper limit for J_{14}^{gauche} of 3.9 c.p.s.[75]

Hobgood and Goldstein[77] have published accurate n.m.r. data
for 1,3-butadiene and several derivatives to which they appended
some comments on the significance of their results for conformational
purposes. It seems generally agreed that 1,3-butadiene itself (12)
and most of its simple derivatives exist principally in the planar

s-*trans* conformation; butadiene itself has been said[78] to be at least 97% s-*trans*. In a number of 1,4-disubstituted-1,3-butadienes the average vicinal coupling constant $J_{23}^{s\text{-}trans}$ was found to be *ca.* 11 c.p.s.[79,80]

It has been assumed that only the s-*trans*- and the s-*cis*-conformations (ϕ = 180° and 0°, respectively) of vinyl cyclopropane are stable, because only in these is the nonbonded interaction between hydrogen atoms minimal.[81] However, a dihedral angle of 0° would not yield a value of 5 c.p.s. for J_{HH}^{vic}, as used in these calculations, according to the Karplus relation as it holds for medium sized cyclo-olefins.[83] Gunther and Wendisch[82] support an opposing view that for vinyl cyclopropane derivatives (13) a *trans*
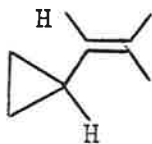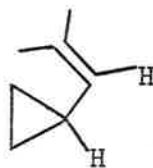
(13) *trans* conformer   one *gauche* conformer

(ϕ = 180°) and two *gauche* forms (ϕ = *ca.* 40°) are the stable conformers.

The study of styryl-azetidinones reported here extends the scope of variable temperature work already completed on substituted ethylenes.

2. Stereochemistry of 1-Phenyl-2-azetidinones

A study of the u.v. spectra[84] and n.m.r.[84-88] spectra of
2-azetidinones indicates that the heterocyclic ring is planar and
that in N-aryl-2-azetidinones the three valences of nitrogen are
nearly planar with the N-aryl ring and almost in the plane of the
2-azetidinone ring. These features have been confirmed by X-ray
diffraction studies of the chloro and bromo 2-azetidinones (14).

(14)   X = Cl, Br
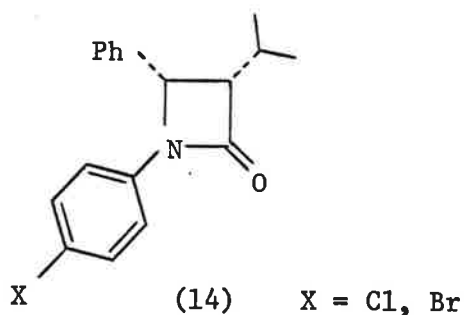
Some of the parameters obtained for these compounds are
listed in Table 5.

TABLE 5

X-RAY DIFFRACTION DATA FOR COMPOUNDS (14)

			X Cl	X Br
Angle between the four-membered ring	C_4	Ph	79±2°	80±2°
and the aryl groups	N	Ar	8±1°	5±1°
Angle between the N-Ar bond and the mean plane of the 2-azetidinone ring			9.3°	8.5°
Angle between the plane of the Ar group and mean plane of the 2-azetidinone ring			8.0°	5.6°

II. RESULTS

A number of 1-phenyl-4-styryl-2-azetidinones (Fig. 4), which were synthesised either via the reaction of cinnamylidene aniline with α-bromoesters or by reacting diphenylketene with cinnamylidene aniline, were characterised on the basis of i.r. and n.m.r. spectra.

R_3	$R_{3'}$
H	H
Me	H
Et	H
iso-Pr	H
Me	Me
Ph	Ph
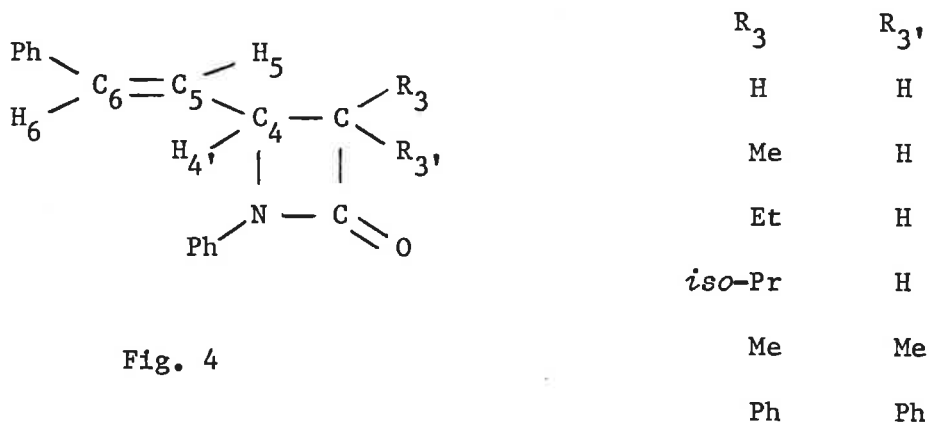
Fig. 4

The i.r. spectra of the products showed bands at 1740–1750 cm^{-1} (C$=$O of 2-azetidinone ring). The n.m.r. spectra displayed coupling constants characteristic of the 2-azetidinone ring ($J_{33'}$ = 14 c.p.s., $J_{3'4'}^{cis}$ = 5.9 c.p.s.) and normal *trans* olefinic coupling (J between 15 and 16 c.p.s.).

The coupling between the olefinic proton H$_5$ and ring proton H$_{4'}$ on the β-lactam ring, $J_{4'5}$, was found to vary with changing temperature as well as with the nature of substituents attached to C$_3$ (i.e. R$_3$ and R$_{3'}$) of the 2-azetidinone ring (see Table 6).

TABLE 6

VARIATIONS OF $J_{4'5}$ WITH TEMPERATURE

	$R_3=R_3{'}=H$		$R_3=Me, R_3{'}=H$		$R_3=R_3{'}=Me$		$R_3=R_3{'}=Ph$
Temp (°C)	$J_{4'5}^{obs}$ (c.p.s.)	Temp.	$J_{4'5}^{obs}$	Temp.	$J_{4'5}^{obs}$	Temp.	$J_{4'5}^{obs}$
+100*	7.42	+120*	7.36	+100*	7.38		
+ 80*	7.58	+100*	7.43	+ 80*	7.49		
+ 60*	7.73	+80*	7.51	+ 60*	7.59		
+ 40*	7.89	+ 60*	7.58	+ 40*	7.67		
+ 40†	7.62	+ 40*	7.65	+ 40†	7.54	+40†	9.13
+ 20†	7.76	+ 40†	7.50	+ 30†	7.61	+30†	9.15
0†	8.01	+ 10†	7.63	- 10†	7.81	0†	9.28
- 20†	8.14	- 10†	7.71	- 30†	7.93	-20†	9.39
- 40†	8.36	- 30†	7.83	- 40†	7.96	-40†	9.54
- 45†	8.47	- 50†	7.92	- 50†	8.13	-50†	9.64
- 55†	8.53						

* Measured on 10% D.M.S.O. solutions

† Measured on 10% $CDCl_3$ solutions

The 3,3'-disubstituted compounds yielded 3-spin systems which were analysed as typical ABX-type spectra.[18] The 3-monosubstituted- and 3-unsubstituted-2-azetidinones yielded slightly more complex 4- and 5-spin systems which were analysed by inspection to yield the $J_{4'5}$ values recorded above.

A study of the chemical shift values (Table 7) indicates that a slight shift to higher field (positive sign) occurred as the temperature increased.

TABLE 7

CHANGES IN CHEMICAL SHIFT VALUES WITH TEMPERATURE

Substituents	Proton	Temp. range	$\Delta\nu$ (c.p.s.)
$R_3=R_{3'}=H$	H_5	$-55°$ to $+40°C^{\neq}$	$+0.8$
		$+40°$ to $+100°C*$	$+3.0$
$R_3=Me$, $R_{3'}=H$	H_5	$-50°$ to $+40°C^{\neq}$	$+2.0$
	$H_{4'}$		$+0.7$
	H_5	$+40°$ to $+120°C*$	$+6.0$
	$H_{4'}$		$+2.3$
$R_3=R_{3'}=Me$	H_5	$-50°$ to $+40°C^{\neq}$	$+3.4$
	$H_{4'}$		$+4.8$
	H_5	$+40°$ to $+100°C*$	$+4.2$
	$H_{4'}$		$+2.0$
$R_3=R_{3'}=Ph$	H_5	$-50°$ to $+40°C$	$+0.4$
	$H_{4'}$		$+2.8$

The olefinic coupling constants, J_{56}, observed in the styryl-β-lactams were found to increase slightly with increase in temperature (see Table 8).

TABLE 8

OLEFINIC COUPLING CONSTANTS

$R_3 = R_{3'} = H$

Temp. (°C)	$- 55^{\dagger}$	$+40^{\dagger}$	$+40^{*}$	$+100^{*}$
J_{56} (c.p.s.)	15.7	16.05	15.7	15.9

$R_3 = Me,\ R_{3'} = H$

Temp.	$- 50^{\dagger}$	$+40^{\dagger}$	$+40^{*}$	$+120^{*}$
J_{56}	15.9	15.95	15.85	16.0

$R_3 = R_{3'} = Me$

Temp.	$- 50^{\dagger}$	$+40^{\dagger}$	$+40^{*}$	$+100^{*}$
J_{56}	15.95	16.0	16.0	16.0

$R_3 = R_{3'} = Ph$

Temp.	$- 50^{\dagger}$	$+40^{\dagger}$
J_{56}	15.2	15.4

The values of $J_{3'4'}^{cis}$ in the compound 3-methyl-1-phenyl-4-styryl-2-azetidinone (Table 9) remained fairly constant in the temperature range studied indicating a fixed angular stereochemical relationship between these two ring protons.

TABLE 9

VARIATION OF $J_{3'4'}^{cis}$ WITH TEMPERATURE

Temp. (°C)	− 50[†]	+40[†]	+40*	+120*
$J_{3'4'}^{cis}$ (c.p.s.)	5.95	5.85	5.95	6.0

The 3-substituted-1-phenyl-4-styryl-2-azetidinones, with ethyl and iso-propyl groups *cis* and *trans* to the styryl linkage, were not isolated in sufficient degree of purity to allow accurate $J_{4'5}$ values to be obtained from variable temperature studies on them.

III. DISCUSSION

1. Variable Temperature Dependence on Rotamer Populations

In 4-styryl-β-lactams a number of distinct rotational conformers are possible due to rotation about the bond joining the styryl group to the 2-azetidinone ring (i.e. the C_4-C_5 bond in Fig. 4). There are three preferred rotamers in which the olefinic double bond could be eclipsed with adjacent single bonds (c.f. vinyl cyclopropanes[82]). These are the s-*trans* (t) (Plate 1, Fig. 5),

in which the $C_5 = C_6$ bond is eclipsed with the $C_4 - H_{4'}$ bond giving an angle of 180° between $H_{4'}$ and H_5; *gauche* (g) (Plate 2, Fig. 6), in which the $C_5 = C_6$ bond eclipses the $C_4 - N$ bond; and *gauche'* (g') (Plate 3, Fig. 7), in which the $C_5 = C_6$ bond is eclipsed with the $C_4 - C_3$ bond. A study of ball-and-stick models yields dihedral angles between H_5 and $H_{4'}$ of *ca.* 310° and 40° in the g and g' conformers, respectively.

With respect to orientation of the styryl group relative to the β-lactam ring, the results obtained indicate that there is an equilibrium between the s-*trans* form (t) and the two *gauche* forms (g and g'). Because interconversion between the rotamers t, g and g' is rapid in the temperature ranges studied, only a mean value is observed for the coupling constant $J_{4'5}$. $J_{4'5}^{trans}$ is certainly larger than $J_{4'5}^{gauche}$. It therefore follows from the fact that $J_{4'5}^{obs}$ increases with decreasing temperature that the concentration of the s-*trans* conformer increases. The 3,3'-diphenyl-4-styryl-β-lactam possesses the largest value of $J_{4'5}$ ($J_{4'5}^{obs} > 9$ c.p.s.) indicating that this compound has the greatest contribution from the s-*trans* conformer (value of $J_{4'5}^{s-trans} = 11$ c.p.s.) in the series studied.

Variation in $J_{4'5}^{obs}$ with changing temperature, ΔJ (see Table 10), gives an indication of the rotamer population. The greatest change in ΔJ is experienced by the 3,3'-unsubstituted-β-lactam indicating the relative freedom of rotation of the styryl group about the
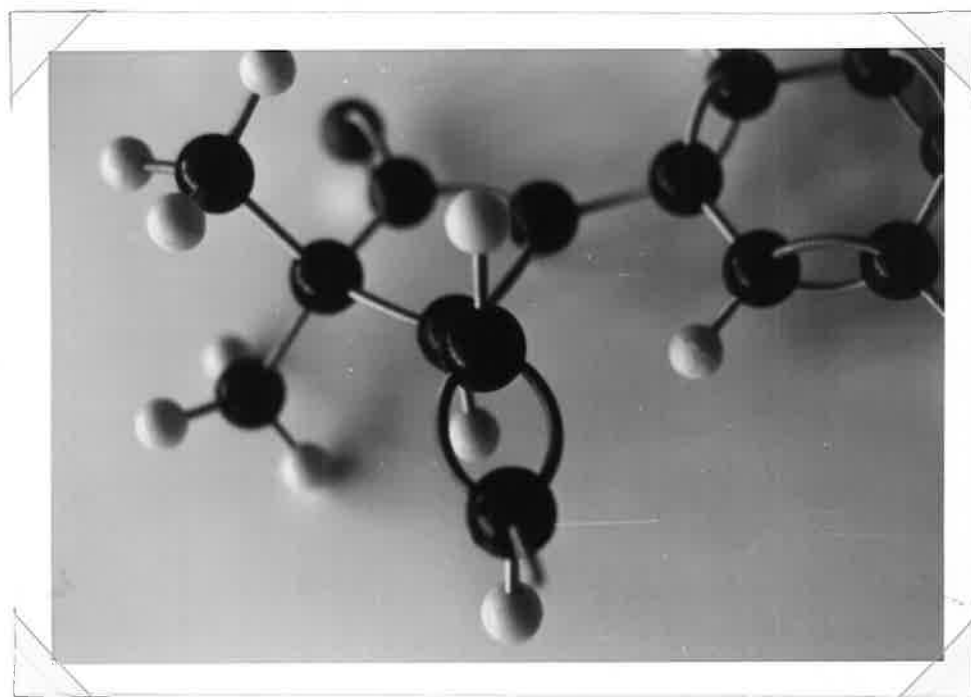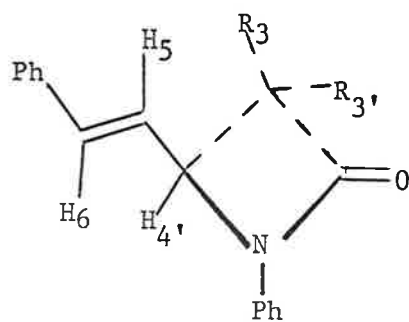
s-*trans* conformer (t)

Plate 1

Fig. 5

gauche conformer (g)
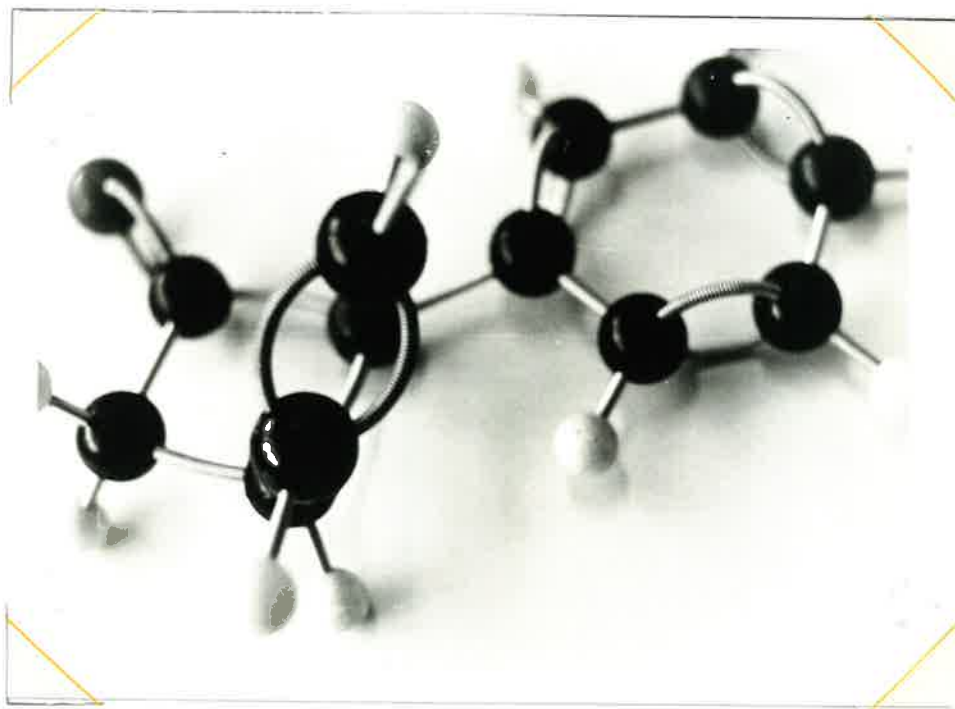
Plate 2
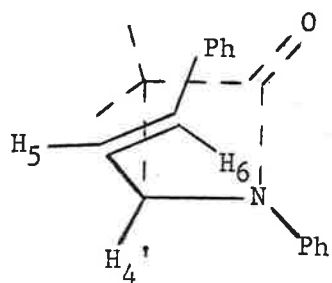
Fig. 6

gauche' conformer (g')
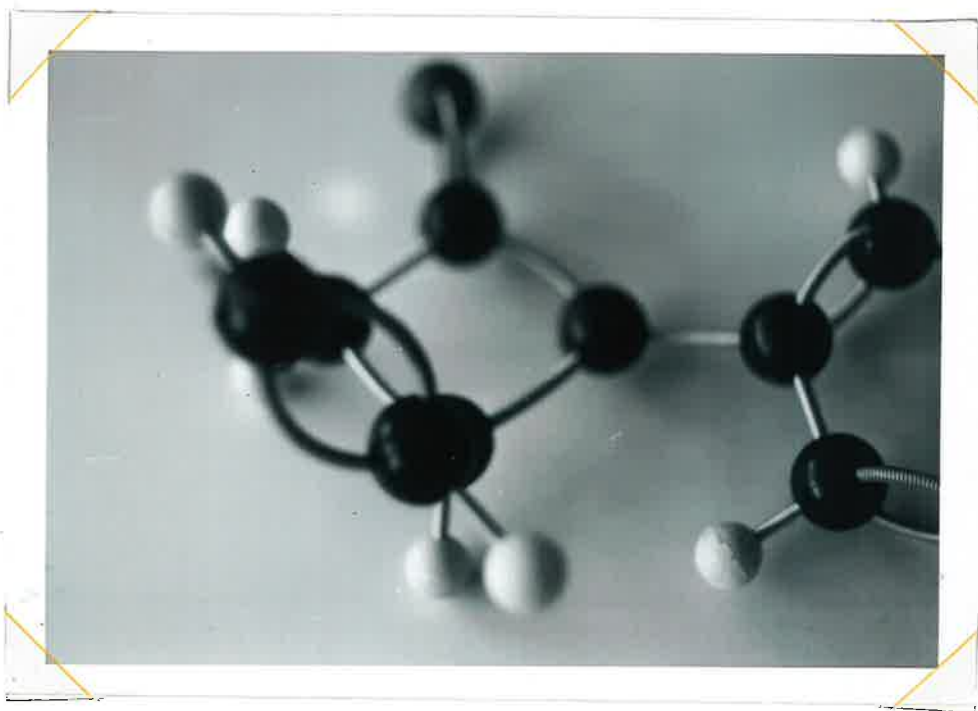
Plate 3
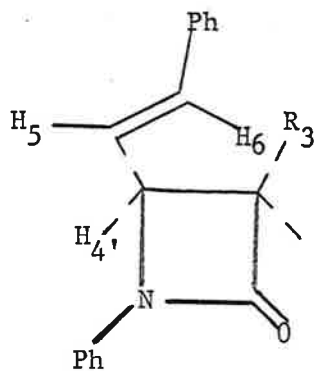
Fig. 7

TABLE 10

ΔJ VALUES FOR 4-STYRYL-β-LACTAMS

Temperature Range (°C)	-50 to +40$^{\neq}$	+40 to +100*
$R_3 = R_{3'} = H$	-0.88	-0.47
$R_3 = Me$, $R_{3'} = H$	-0.42	-0.22
$R_3 = R_{3'} = Me$	-0.59	-0.29
$R_3 = R_{3'} = Ph$	-0.51	

Note: A negative sign indicates an algebraic decrease in the value of J.

C_4-C_5 bond leading to a rapid increase in the concentration of the *gauche* conformers (g, g') in this compound. The rotamer population does not change very markedly in the 3-methyl-β-lactam whereas the 3,3'-dimethyl- and 3,3'-diphenyl-compounds exhibit noticable increases in the concentrations of *gauche* conformers at higher temperatures but these are not as great as in the case of the 3,3'-unsubstituted compound.

A study of models indicates that the steric interference between R_3 and H_6 would preclude a contribution from the g' conformer in the 3-substituted-4-styryl-2-azetidinones. The only contribution to $J_{4'5}^{obs}$ for these compounds would thus be from the s-*trans* and *gauche* (g but not g') conformers.

These trends are supported by the estimated values of x_t (mole fraction of the s-*trans* conformer) obtained from the approximate calculations in which it is assumed that $J_{4'5}^t$ lies between 11 and 12 c.p.s.[75] and $J_{4'5}^g$ between 4 and 6 c.p.s.[89] The values in Table 11 were obtained from the expression

$$J_{4'5}^{obs} = x_t \, J_{4'5}^t + x_g \, J_{4'5}^g + x_{g'} \, J_{4'5}^{g'}$$

using the values $J_{4'5}^t = 11$ c.p.s., $J_{4'5}^g = 4$ c.p.s., $J_{4'5}^{g'} = 6$ c.p.s. J^g and $J^{g'}$ were estimated using the Karplus expression

$$J^{vic} = 10.6 \cos^2 \phi \qquad (0° < \phi < 90°)$$

for vicinal couplings in medium rings with dihedral angles corresponding to those pertaining to the compounds studied here.

TABLE 11

MOLE FRACTION OF S-*TRANS* CONFORMER PRESENT WITH

VARYING T

$R_3=R_{3'}=H$		$R_3=Me, R_{3'}=H$		$R_3=R_{3'}=Me$		$R_3=R_{3'}=Ph$	
Temp. (°C)	x_t	Temp. (°C)	x_t	Temp. (°C)	x_t	Temp. (°C)	x_t
+100*	0.40	+120*	0.48	+100*	0.48		
+ 80*	0.43	+100*	0.49	+ 80*	0.50		
+ 60*	0.46	+ 80*	0.50	+ 60*	0.51		
+ 40*	0.48	+ 60*	0.51	+ 40*	0.52		

+ 40[†]	0.44	+ 40*	0.52	+ 40[†]	0.51	+ 40[†]	0.72
+ 20[†]	0.46	+ 40[†]	0.50	+ 30[†]	0.52	+ 30[†]	0.73
0[†]	0.50	+ 10[†]	0.52	- 10[†]	0.54	0[†]	0.75
- 20[†]	0.52	- 10[†]	0.53	- 30[†]	0.56	- 20[†]	0.77
- 40[†]	0.56	- 30[†]	0.55	- 40[†]	0.57	- 40[†]	0.79
- 45[†]	0.58	- 50[†]	0.56	- 50[†]	0.59	- 50[†]	0.81
- 55[†]	0.59						

*   10% D.M.S.O. solution

[†]   10% $CDCl_3$ solution

2.   Solvent Dependence on Rotamer Populations

A dependence on polarity of the solvent is indicated at 40°C by the 4-styryl-β-lactams (e.g. see 3,3'-unsubstituted compound, Fig 8).

Fig. 8.   Variation of $J_{4'5}$ with Temperature and Solvent in 1-Phenyl-4-styryl-2-azetidinone.
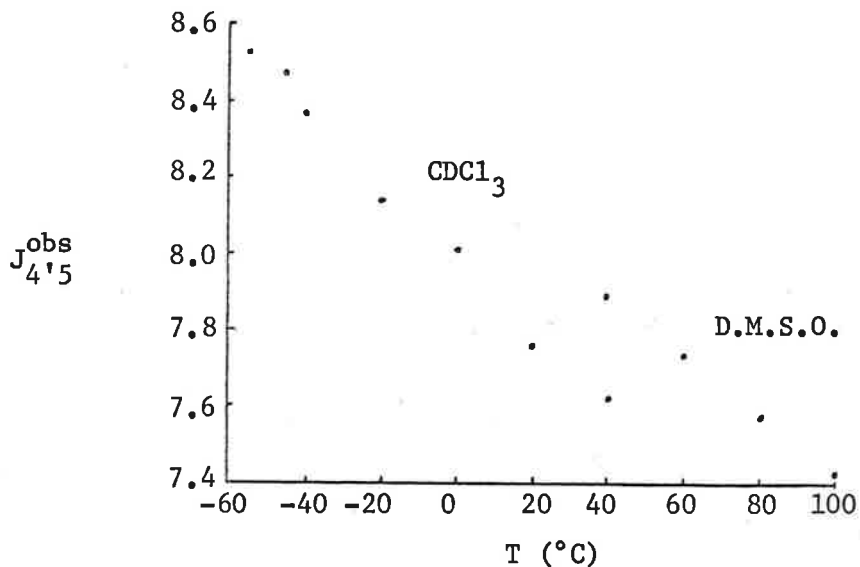
The coupling constant $J_{4'5}^{obs}$ and thus the population of the s-*trans* conformer increases with increasing polarity of the solvent e.g. from $CDCl_3$ to D.M.S.O. (c.f. propionaldehyde[74]).

CHAPTER 3. SKELETAL-REARRANGEMENT FRAGMENTS IN THE MASS SPECTRA OF

ANILS

I. INTRODUCTION

Mass spectrometry has become a useful physical technique which can aid in the elucidation of structures of organic molecules. The application of high resolution data and labelling studies has assisted in the interpretation of fragmentation processes in the mass spectra of many types of organic molecules. Details of the theory, mode and application of fragmentation processes in organic molecules have been extensively discussed in texts[100,107-12] and require no further discussion here.

The mass spectra of azomethines[90] and the normal fragmentation of anils[91] 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 $Ar-X=Y-Ar$,[92] and these are especially important in the spectra of azobenzenes,[93] azoxybenzenes[94] and nitrones.[95] Since the previous publication on anils[91] did not specifically discuss skeletal-rearrangement processes, a study of this problem was undertaken, and this work is concerned with both the rearrangement and normal cleavage processes in the spectra of compounds (I)-(XXX). Some of these compounds were used previously in the synthesis of substituted 1-aryl-4-aryl-2-azetidinones.[85]

II. RESULTS

Skeletal-rearrangement processes are recorded in Table 1M, and examples of spectra are shown in Figures 1M-10M. The compositions of the rearrangement ions mentioned in Table 1M, and of the fragment ions discussed in the text or indicated by schematic arrows in the figures, have been established by exact mass measurement. The presence of an asterisk either in the text or a figure denotes the presence of an appropriate metastable ion for the process indicated. All

	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)

TABLE 1M

SKELETAL-REARRANGEMENT PROCESSES IN THE SPECTRA OF (I)-(XXVII)

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
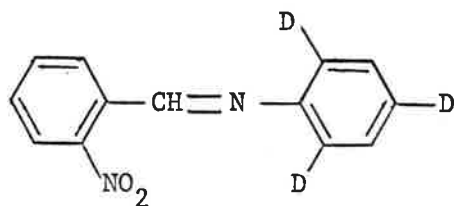
(XXX)

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.

Fig. 1m

$C_6H_5CH=NC_6H_5$

(I)

Fig. 2m

(XXVIII)

(XXIX)

Fig. 3m

Fig. 4m

Fig. 5m

Fig. 6m

Fig. 7m

Scheme 1

Fig. 8 m

(XXX)

Fig. 9 m

(XXV)
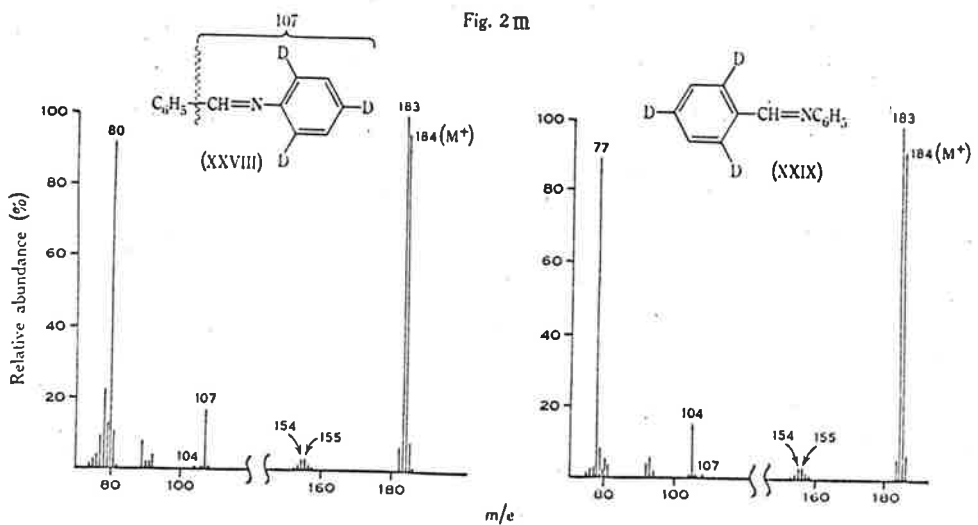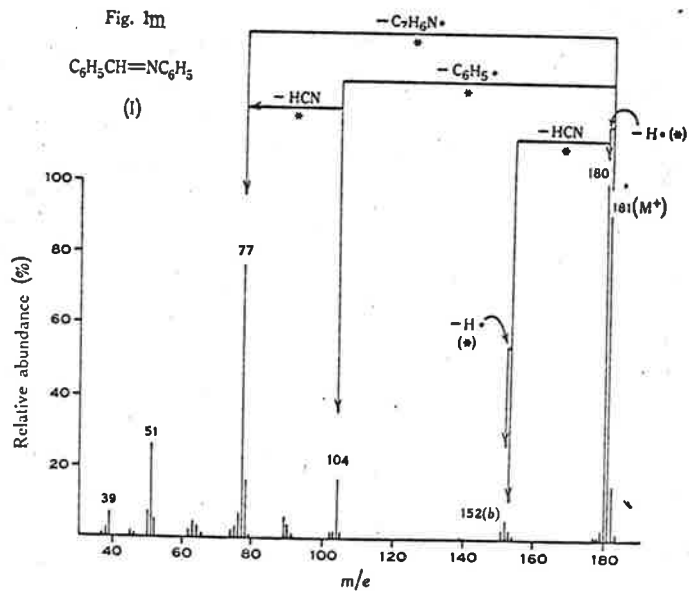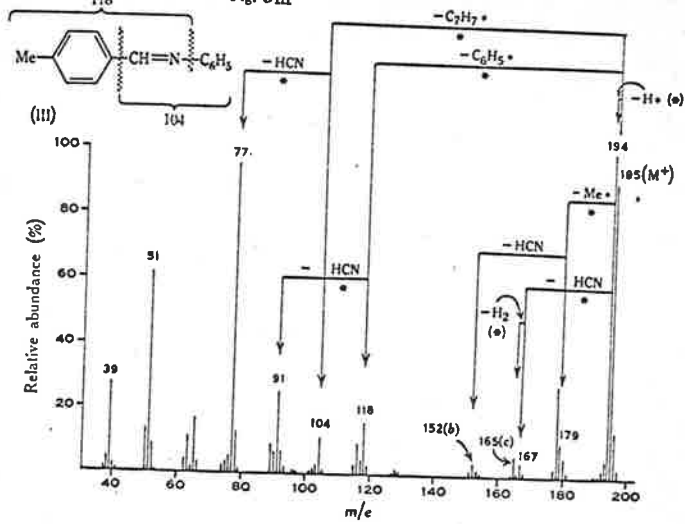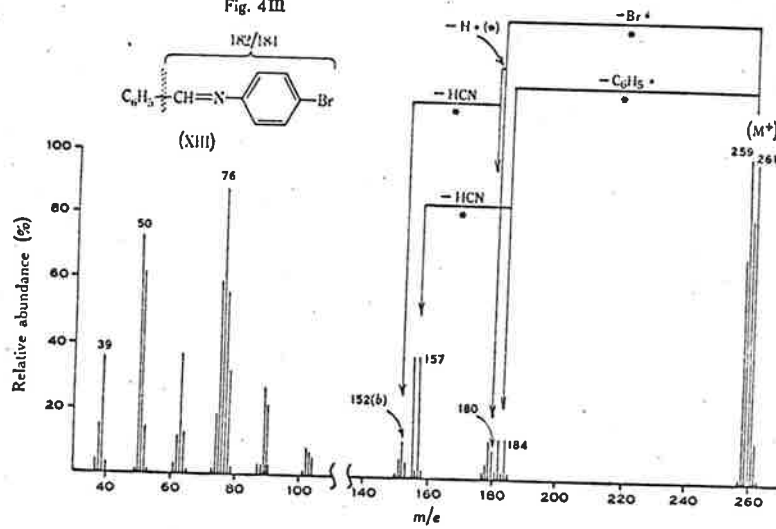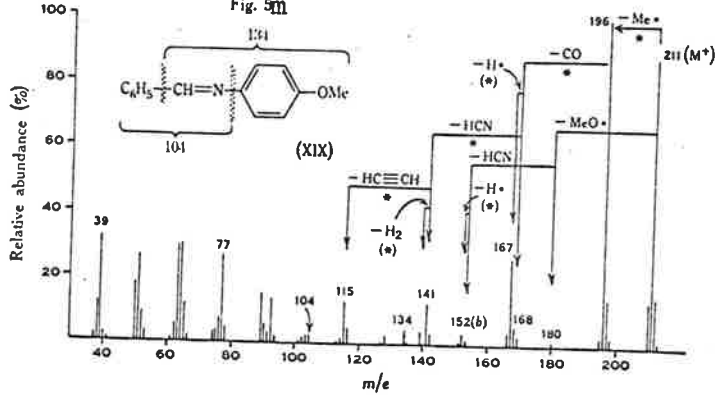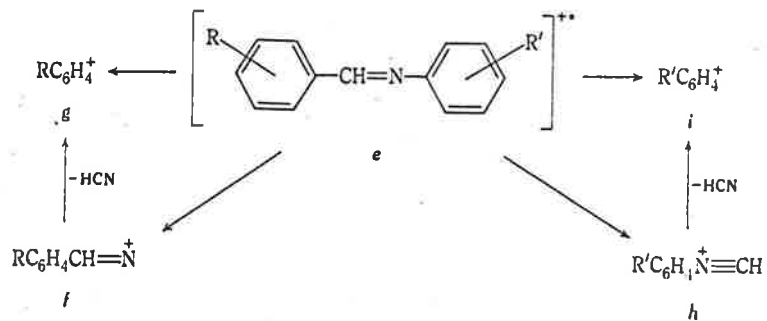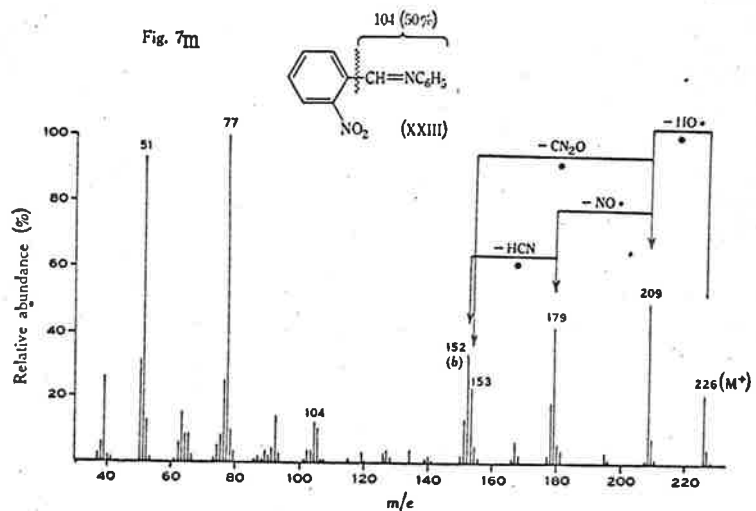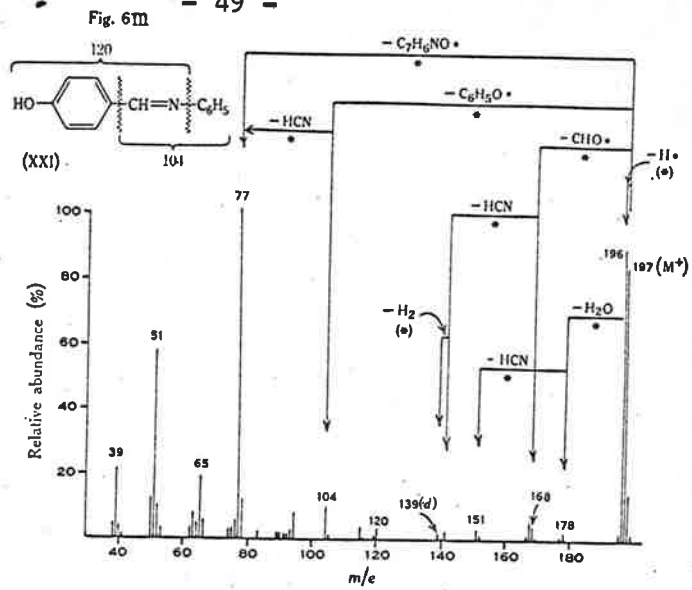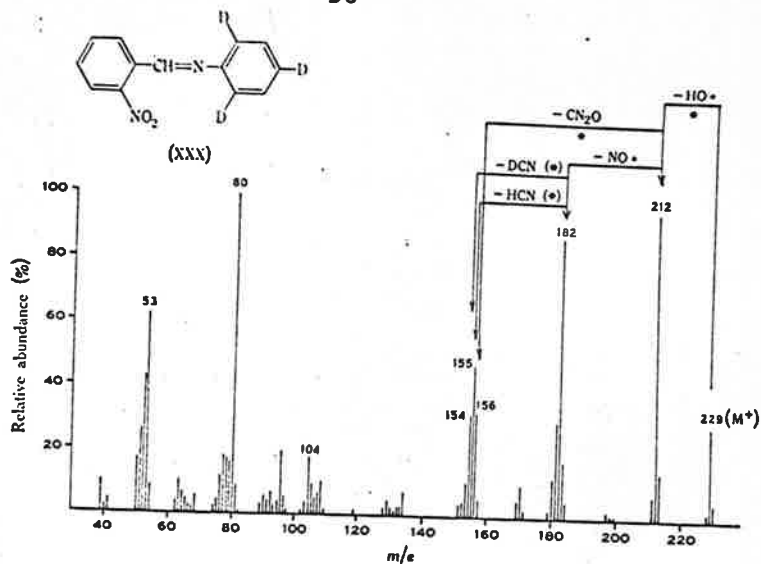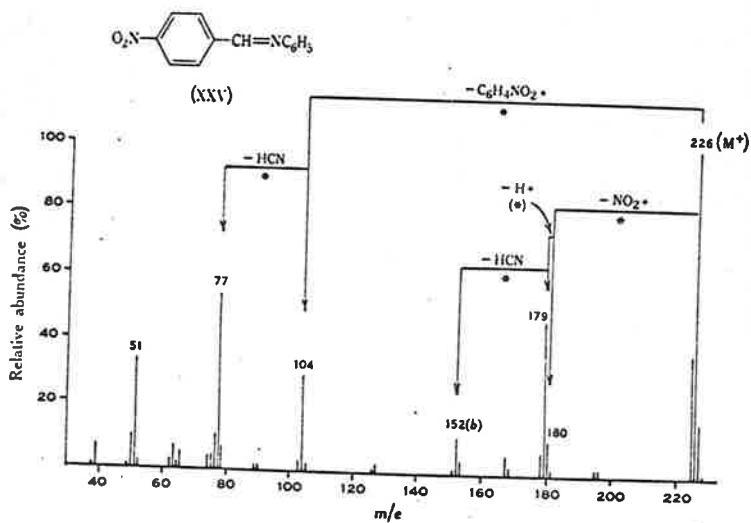
Fig. 10 m
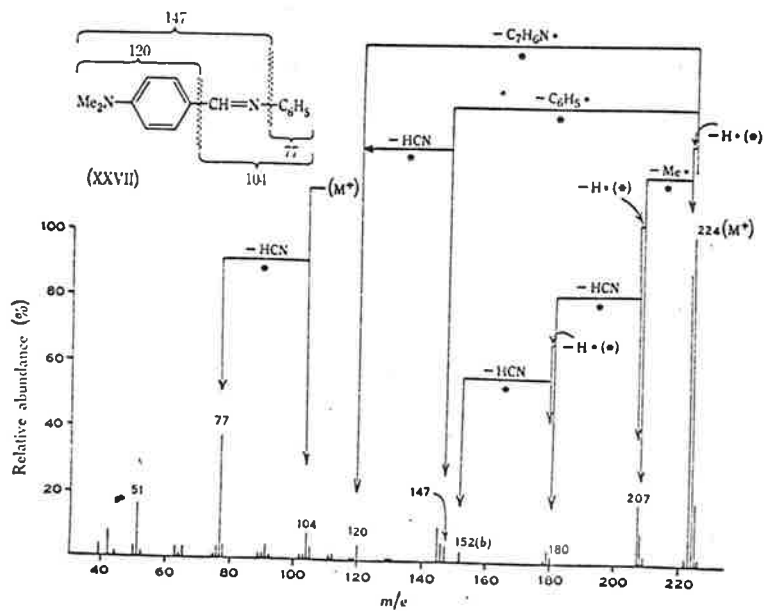
(XXVII)

III. DISCUSSION

1. General Rearrangement Processes in Anils

The interpretation of the rearrangement processes in the spectrum of (I) (Fig. 1M) has been aided by the spectra of the labelled derivatives (XXVIII) and (XXIX) (Fig. 2M). The overall process is $M - H\cdot - HCN - H\cdot$, the end product having m/e 152 ($C_{15}H_8$, h.r.), which is most plausibly represented as the biphenylene radical ion (b). It was initially thought that the hydrogen lost in the $M - H\cdot$ decomposition came almost exclusively (> 90%) from the azomethine moiety as indicated by the spectra of (XXVIII) and (XXIX) (Fig. 2). Further work[105] has shown a more accurate value to be about 75%. The spectra of (XXVIII) and (XXIX) are identical in the m/e 152-157 region. This indicates 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 since it is accepted[96-98] that the hydrogens on any one monosubstituted benzene ring generally become equivalent upon electron impact. There are, however, exceptions to this statement.[99] D and H will therefore be lost from the labelled aromatic ring in the ration 3:2, if possible isotope effects are ignored. A possible rearrangement may be represented by the scheme (I) → b.

$$(I) \quad \xrightarrow[{-H \cdot \ (*)}]{-e} \quad Ph-C \overset{+}{\equiv} N-Ph \quad \xrightarrow[{-H \cdot \ (*)}]{-HCN \ (*)} \quad \left[\right]^{+\cdot}$$

$$a, \ m/e \ 180 \qquad\qquad\qquad\qquad\qquad\qquad b, \ m/e \ 152$$
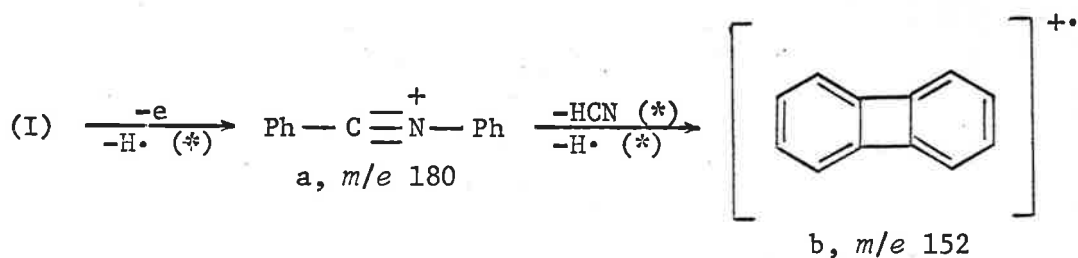
2. Skeletal-rearrangement Processes in Monosubstituted Anils.

In the spectra of monosubstituted derivatives the skeletal-rearrangement processes are modified by the substituent. If it is possible for the substituents to fragment by α-cleavage to the aromatic ring (e.g. X=Me, Br, Cl and NO_2),[100] then b is formed by either of the processes M — H• — X• — HCN or M — X• — H• — HCN displayed in Figs. 3M, 4M and 7M-9M. This classification should also hold for the fluorine substituent, 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. The cation m/e 165 ($C_{13}H_9^+$) is also formed when X=Me (see Fig. 3). Although structures drawn for fragment ions are only nominal, the most plausible structure for the ion m/e 165 is considered to be the fluorene cation (c). This does not, however, preclude the possibility of more extensive rearrangement.

If an oxygenated substituent, which allows the additional loss of a ring carbon, is present (e.g. X=OH or OMe),[100] then the ion produced by the overall rearrangement is d, m/e 139 ($C_{11}H_7$, h.r.)

(see Figs. 5M and 6M). For example, in the spectrum of (XXI)
(Fig. 6M) the major reorganisation process is $M - CHO\cdot - HCN - H_2\cdot$
The m/e 152 ions still occur in these cases. The formation of b
from the molecular ion of the dimethylamino derivative (XXVII) is
complete, involving six successive eliminations, viz. $M - H\cdot - Me\cdot -$
$H\cdot - HCN - H\cdot - HCN$ (see Fig. 10M).
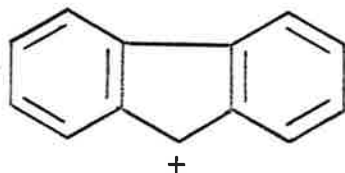
c, m/e 165
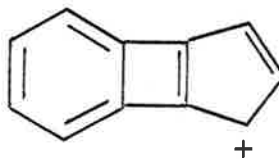
d, m/e 139

3. Cleavage Processes in Anils

The simple cleavage processes of anils have previously been
discussed,[91] but there are certain features which need to be clarified.
Cleavage of anils occurs α to the aromatic system either by $C - C$
or $C - N$ bond fission. These processes, which are normally
substantiated by metastable ions (see Figs. 1M-10M), are summarised
in Scheme 1.

The spectra of (XXVIII) and (XXIX) (Fig. 2M) illustrate that
$C - N$ bond cleavage is easier than $C - C$ bond cleavage. The
relative abundance of i is generally greater than that of g.
However, the relative abundance of h is normally greater than that
of f, indicating that in this case, $C - C$ bond fission produces a

more stable cation than C—N bond fission. Since 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 2M. 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). It is, therefore, necessary to exercise caution when using the relative abundances of these ions to aid structure elucidation.

TABLE 2M

RELATIVE ABUNDANCES (%) OF CLEAVAGE FRAGMENTS IN THE SPECTRA OF
(I)- (XXVII)

Compound	$RC_6H_4CH\overset{+}{=}N$ (f)	$R'C_6H_4\overset{+}{N}=CH$ (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).

4. Relation of *m*- and *p*-substituted anils to Hammett σ values.

Simple cleavage processes in the spectra of acetophenones,[101,102] benzophenones,[101,102] and azobenzenes[93] may be related semiquantitatively 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. McLafferty[102] has discussed the theoretical basis of this method. A similar plot for the $C_6H_5 - \overset{+}{N} = CH$ ion (*m/e* 104) in the spectra of compounds of the general type $X - C_6H_4 - CH = NC_6H_5$, with X *meta* or *para*, against the σ value for X, is illustrated in Fig. 11M. A definite scatter of points exists with the obvious trends being 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.

Fig. 11M. Plot of log Z/Z_0 vs. σ

$$Z = \frac{rel.ab.[C_6H_5\overset{+}{N} = CH]}{rel.ab.[XC_6H_5CH = NC_6H_5]}$$

○   *meta* substituent

□   *para* substituent

$$Z_0 = \frac{rel.ab.[C_6H_5\overset{+}{N} = CH]}{rel.ab.[C_6H_5CH = NC_6H_5]}$$
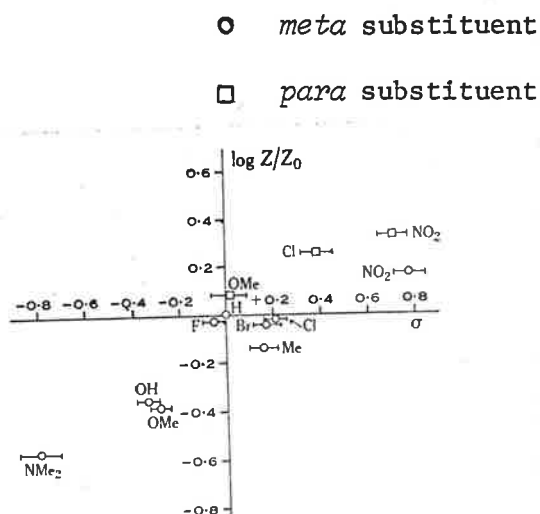
5. Proximity Effects in *o*-Substituted Anils

Proximity effects are observed in mass spectra when certain substituents occupy positions *ortho* to the azomethine moiety. Cases involving hydroxyl, methoxyl, and methyl groups have been recorded.[91,105,106] A comparison of the spectra of the nitro isomers (XXIII) and (XXV) (Figs. 7M and 9M) yields another example of this proximity effect. A major fragmentation of the derivative proceeds via an M — HO• ion (51%) which is absent in the spectrum of (XXV). The spectrum of the deuterium labelled derivative (XXX) (Fig. 8M) indicates that the H atom involved in the M — HO• process does not originate from the aromatic ring adjacent to nitrogen. Since the spectra of nitrobenzene[103] and *o*-nitrobenzaldehyde do not possess M — HO• peaks, it is probable that the hydrogen atom is lost from the methine position. Depending on whether the M-17 ion is formed from the intact or rearranged[103] nitro group, it may be represented by either j or k, respectively.

(XXXIII) $\xrightarrow[-HO\bullet]{-e}$

j, *m/e* 209   or   k, *m/e* 209
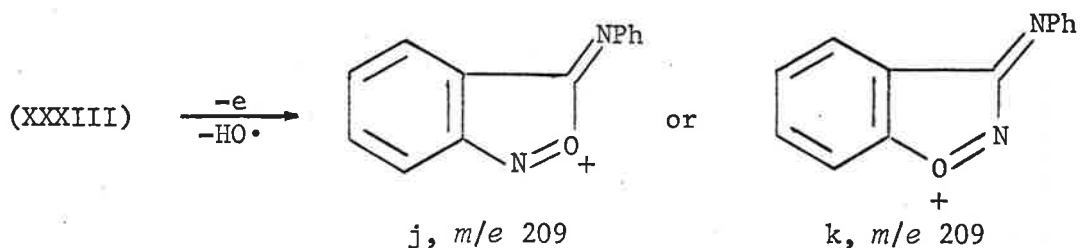
CHAPTER 4. EXPERIMENTAL

1. Instrumentation

Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected.

Infrared (i.r.) spectra were recorded on a Perkin-Elmer 237 I.R. spectrophotometer.

Nuclear magnetic resonance (n.m.r.) spectra were recorded on a Varian DA-60-IL spectrometer operating at 60 Mc/s. The spectra were run in the frequency sweep mode. Variable temperature spectra were run using the variable temperature accessory V6040.

Mass spectra (m.s.) were measured with an Hitachi Perkin-Elmer RMU 6D double-docussing 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 are correct to within 15 p.p.m.

Microanalyses were performed by the Australian Microanalytical Service, Melbourne.

2. Diels-Alder Adducts of Hexachlorocyclopentadiene and Monosubstituted Ethylenes.

endo-5-Acetoxy-1,2,3,4,7,7-hexachlorobicyclo-[2.2.1]-hept-2-ene

This compound was prepared by refluxing equimolar quantities of vinyl acetate and hexachlorocyclopentadiene for 8 hours at 150-180°C. Distillation yielded the colourless viscous adduct (80%) b.p. 110°/.6 mm (lit.[113] b.p. 113°/.6 mm).

endo-5-Hydroxy-1,2,3,4,7,7-hexachlorobicyclo-[2.2.1]-hept-2-ene

A solution of the acetoxy compound in ethanol was stirred and refluxed with conc. hydrochloric acid for 2 hours. The clear solution was poured into water. The orange oil was ether extracted, dried over sodium sulphate and ether distilled off leaving the hydroxy compound (95%) as white crystals m.p. 154-155° (lit.[113] 155°) ex n-heptane.

endo-5-Bromo-1,2,3,4,7,7-hexachlorobicyclo-[2.2.1]-hept-2-ene

Vinyl bromide (5.4 g) and hexachlorocyclopentadiene (13.7 g) were heated at 120° in a sealed tube for 20 hours. Distillation of the reaction mixture yielded 2 fractions:

    a.   hexachlorocyclopentadiene (5.1 g) b.p. 64°/.7 mm

    b.   required bromo compound (11.9 g, 96%) b.p. 140°/.7 mm.

(Found: C, 22.47; H, 0.94; Br, 21.1; Cl, 56.1; $C_7H_3BrCl_6$ requires C, 22.1; H, 0.79; Br, 21.05; Cl, 56.05%). ν_{max} (mull) 1603 (C $=$ C str.) cm^{-1}.

endo-1,2,3,4,5,7,7-Heptachlorobicyclo-[2.2.1]-hept-2-ene

Vinyl chloride was passed into hexachlorocyclopentadiene for 48 hours at 2 atmospheres pressure and 120 ± 2°C. Distillation at 20 mm yielded unchanged hexachlorocyclopentadiene b.p. 122-130° and crude chloro compound (90%) b.p. 130-140°. Repeated sublimation at 70°/.05 mm yielded the pure chloro compound m.p. 128-132° (lit.[114] ca. 125-136°).

endo-5-Cyano-1,2,3,4,7,7-hexachlorobicyclo-[2.2.1]-hept-2-ene

Acrylonitrile, hexachlorocyclopentadiene, 4-t-butylcatechol and glacial acetic acid were heated for 24 hours at 100°C. Steam distillation of the mixture yielded unreacted diene and the waxy cyano adduct (67%) b.p. 170-174°/.9 mm (lit.[115] m.p. 143°).

endo-5-Acetyl-1,2,3,4,7,7-hexachlorobicyclo-[2.2.1]-hept-2-ene

The reaction between methylvinylketone, hexachlorocyclopentadiene, 4-t-butylcatechol and glacial acetic acid yielded the acetyl adduct (98%) which on repeated sublimation had m.p. 71-72° (lit.[115] m.p. 70°)

endo-1,2,3,4,7,7-Hexachlorobicyclo-[2.2.1]-hept-2-ene-5-carboxylic acid

Equimolar quantities of acrylic acid and hexachlorocyclopenta-diene were heated for 24 hours at 130°. After repeated sublimation the carboxylic acid adduct (85%) had m.p. 175-178° (lit.[116] m.p. *ca.* 180°). ν_{max} (mull) 1705 (C$=$O) cm^{-1}.

endo-1,2,3,4,7,7-Hexachlorobicyclo-[2.2.1]-hept-2-ene-5-methyl carboxylate

Method A. The carboxylic acid (1.8 g) was treated with diazo-methane in ether to yield the methyl ester (1.7 g, 90%) m.p. 36-38°. (Found: C, 30.37; H, 1.68; Cl, 59.1; O, 8.85. $C_9H_6Cl_6O_2$ requires C, 30.08; H, 1.67; Cl, 59.33; O, 8.91%). ν_{max} (mull) 1740 (C$=$O) cm^{-1}.

Method B. The carboxylic acid in methanol, with a trace of conc. sulphuric acid, was refluxed for 24 hours to yield the methyl ester (75%) m.p. 36-38°.

Attempted synthesis of endo-5-methoxy-1,2,3,4,7,7-hexachlorobicyclo-[2.2.1]-hept-2-ene

When the corresponding hydroxy compound was treated with diazomethane in ether a quantitative recovery of starting material was obtained.

3. Benzocyclobutene and Derivatives

w,w,w',w'-Tetrabromo-o-xylene

This compound was prepared by the method of Thiele and Gunther[117] and was obtained as a light brown powder m.p. 116° (lit.[117] m.p. 116°).

1,2-Dibromobenzocyclobutene

w,w,w',w'-Tetrabromo-*o*-xylene was treated with sodium iodide by the method of Cava and Napier[118] to yield 1,2-dibromobenzocyclobutene as colourless crystals m.p. 52-53° (lit.[118] m.p. 52.4-52.8°).

Benzocyclobutene

1,2-Dibromobenzocyclobutene (5 g) was hydrogenated at room temperature in ethanol (500 ml) in the presence of 50% Pd/C (2 g) and sodium ethoxide. The reaction mixture on fractionation yielded pure benzocyclobutene (1.7 g, 85%) b.p. 150°/760 mm (lit.[119] b.p. 150°/748 mm).

w,w'-Dibromo-o-xylene

This compound, prepared by Perkin's method,[120] was obtained as colourless crystals m.p. 93° (lit.[120] m.p. 93°).

Attempted alternative synthesis of benzocyclobutene

The method used was that of Hall *et al.*[121] for the preparation of dihydrophenanthrene from dibromoditolyl.

Freshly made lithium wire (1 g) was cut into a nitrogen-filled flask containing dry ether (75 cc) and bromobenzene (12 g) was gradually added. When the interaction was completed, a solution of w,w'-dibromo-*o*-xylene (16 g) in ether (200 cc) was added as fast as refluxing allowed. Ice and water were then introduced and the two layers separated. Distillation of the dried ethereal layer gave a quantitative recovery of w,w'-dibromo-*o*-xylene.

1-Bromobenzocyclobutene

Benzocyclobutene (12 g) in carbon tetrachloride (120 cc), N-bromosuccinimide (21.6 g) and benzoyl peroxide (1.2 g in 5 cc $CHCl_3$) were heated to reflux and the reaction continued without further heating being completed in 10 minutes. The succinimide was filtered off at the pump and the filtrate distilled yielding 1-bromobenzocyclo-butene (12 g, 57%) b.p. 60°/1 mm (lit.[122] b.p. 55–59°/1 mm).

Benzocyclobutene-1-carboxylic acid

The Grignard reagent, formed from 1-bromobenzocyclobutene (4.02 g) and Mg (0.7 g) in the usual manner, was exchanged with carbon dioxide (by bubbling dried CO_2 through the ethereal solution). This reaction yielded the acid (1.7 g, 53%) which on sublimation had m.p. 74–75° (lit.[122] m.p. 75°).

Benzocyclobutene-1-methylcarboxylate

This compound was prepared by treating the acid (300 mg) with diazomethane in ether and yielded a colourless liquid (221 mg, 66%) b.p. 64°/0.5 mm (lit.[122] b.p. 64°/0.5 mm).

4. Monosubstituted Succinic Anhydrides

Acetyl succinic anhydride

This compound was prepared by refluxing l-malic acid (13 g) with acetyl chloride (25 g) until the solid dissolved (2 hours). Distillation yielded acetyl succinic anhydride (10 g, 65%) b.p. 166°/ 14 mm (lit.[123] b.p. 160-162°/14 mm).

Attempted isolation of chloro succinic anhydride

The method of Anschutz and Bennert[124] was used by heating fumaric acid (3.3 g) in acetic acid (12 g) with acetyl chloride (7 g) in a sealed tube for 10 hours at 120°. The mixture was then concentrated under reduced pressure (0.5 mm) to remove the acetic acid and excess acetyl chloride.

First attempt. The n.m.r. spectrum run on the reaction mixture showed the presence of chloro succinic anhydride but other impurities present did not allow a satisfactory complete interpretation of the spectrum.

Subsequent attempts. The reaction mixture was ether extracted. The ethereal solution was washed with a saturated sodium bicarbonate solution. A white solid (1 g) which precipitated and was filtered off was identified as fumaric acid (sublimed at 200°C). The ether extract was dried over sodium sulphate and ether distilled leaving an off-white solid (1.8 g) which was identified as maleic acid m.p. 139° alone and admixed with an authentic sample.

Attempted isolations of bromo succinic anhydride

Method A. Several attempts using the above method[124] with fumaric acid, acetyl bromide and acetic acid yielded fumaric and maleic acids as the major products.

Method B. Bromo succinic acid (5 g) was refluxed with acetyl chloride (12 cc) until the solid dissolved (4 hours). Distillation yielded maleic anhydride (2.3 g, 92%) b.p. 150°/26 mm.

5. Cyclopropane Derivatives

Cyclopropanol

Cyclopropanol, prepared from epichlorohydrin by reacting it with magnesium bromide and ethyl magnesium bromide by the method of Stahl and Cottle,[125] was obtained as a colourless oil b.p. 48-52°/97 mm (lit.[125] b.p. 53-55°/100 mm).

Cyclopropyl-p-toluene sulphonate

This compound prepared by the method of Sekera and Marvel[127] was obtained as a colourless oil b.p. 118-119°/0.06 mm (lit.[127] b.p. 110-120°/0.1-0.5 mm).

Cyclopropyl acetate

Acetyl chloride reacted with cyclopropanol in pyridine and the reaction mixture treated in the usual manner to yield cyclopropyl acetate b.p. 110-112° (lit.[126] b.p. 108-111°).

Methyl-cyclopropane carboxylate

Cyclopropane carboxylic acid (2.2 g) in ether was treated with diazomethane to yield the methyl ester (2.2.g, 85%) as a colourless liquid b.p. 118-119° (lit.[139] b.p. 119°/764 mm).

Phenyl-cyclopropane carboxylate

Cyclopropane carboxylic acid was treated with phenol in the usual manner to yield the phenyl ester as a colourless liquid b.p. 112°/12 mm (lit.[128] b.p. 117-118°/13 mm).

6.   3,4-Dihydrocoumarin Derivatives

o-Hydroxyphenylsuccinic acid

Coumarin (50 g) was heated for 6 hours in ethanol (1500 cc) with a solution of potassium cyanide (30 g) in water (150 cc). The alcohol was removed, residue was dissolved in a small amount of water and was then extracted with ether. The residue was warmed with potassium hydroxide (5 g) for another hour on the water bath, acidified with hydrochloric acid, filtered and the filtrate extracted with ether. Removal of the ether yielded crystals (45 g, 73%), m.p. 148-150° (lit.[129] m.p. *ca.* 150°).

3,4-Dihydrocoumarin-4-carboxylic acid

o-Hydroxyphenylsuccinic acid was heated in boiling xylene containing phosphoric oxide for 30 mins. The product (83% yield) was crystallised from ethyl acetate-petroleum ether (b.p. 40-60°) m.p. 135° (lit.[130] m.p. 135°).

4-Acetyl-3,4-dihydrocoumarin

Method A. *o*-Hydroxyphenylsuccinic acid (1 g) was boiled under reflux with acetic anhydride (10 ml) for 1 hour where-upon carbon dioxide evolution ceased. The product (1 g), after removal of acetic anhydride *in vacuo*, was crystallised from aqueous ethanol as needles m.p. 121-122° (lit.[130] m.p. 122°).

Method B. 3,4-Dihydrocoumarin-4-carboxylic acid (0.5 g) was warmed on a steam bath with acetic anhydride (3 ml) and 3-picoline (3 ml) for 30 mins at which time carbon dioxide evolution ceased. After evaporation at 100° *in vacuo*, the residue was recrystallised ex ethanol (using norite).

3,4-Dihydrocoumarin-4-methyl carboxylate

The carboxylic acid (128 mg) in methanol was treated with diazomethane to yield crystals (98 mg, 73%) m.p. 88° (lit.[130] m.p. 89°).

4-Bromo-3,4-dihydrocoumarin

This compound, prepared by Ebert's method[131] of adding hydrogen bromide to coumarin, was obtained as white crystals m.p. *ca.* 45° (lit.[131] m.p. 42-45°). This compound is very unstable and on standing for even a short time evolution of HBr occurs yielding a white solid identified as coumarin m.p. 67° alone and admixed with an authentic sample.

3,4-Dihydrocoumarin

Coumarin (29.2 g) was hydrogenated by treating an ethereal solution with Raney nickel (5 g) at 100°C, 1800 p.s.i. of hydrogen, for $^1/_2$ hour to yield a colourless liquid (26.6 g, 90%) b.p. 130°/ 8 mm (lit.[132] b.p. 140-141°/14 mm).

Attempted isolation of 3-bromo-3,4-dihydrocoumarin

Method A. An equimolar quantity of bromine (in CCl$_4$) was added dropwise to 3,4-dihydrocoumarin (in CCl$_4$) at 0°. When addition was complete the solution stood over calcium carbonate. An n.m.r. spectrum run on the reaction mixture verified the presence of 3-bromo-3,4-dihydrocoumarin. If the temperature of the reaction mixture rose above 0°, evolution of HBr occurred yielding coumarin m.p. 67°.

Method B. 3,4-Dihydrocoumarin (in CCl$_4$), N-bromosuccinimide and a trace of benzoyl peroxide were heated under reflux for 5 mins, cooled, and succinimide was filtered off. The white solid left, after CCl$_4$ was removed under reduced pressure, was identified as coumarin.

Method C. All attempts to catalytically reduce α-bromocoumarin,[134] made from coumarin dibromide,[133] led to the unfavourable removal of the bromine atom before reducing the double bond.

7. Substituted Chromanones

3-Bromo-4-chromanone

This compound was made by the method of Arndt and Kallner[135] from chromanone and 1 mole of bromine in chloroform. Repeated sublimation yielded off-white crystals m.p. 69-70° (lit.[135] m.p. 69-70°).

Phloroglucinol dimethyl ether

This compound, prepared by the method of Pratt and Robinson,[136] was obtained as a colourless liquid b.p. 198-199°/35 mm (lit.[136] b.p. 198-200°/35 mm).

Condensation of phloroglucinol dimethyl ether and acetonitrile

This condensation yielded 4-hydroxy-2,6-dimethoxyacetophenone as pale yellow crystals m.p. 184-185° (lit.[136] m.p. 185.5°) and the isomeric compound 2-hydroxy-4,6-dimethoxyacetophenone m.p. 80-81° (lit.[136] m.p. 80-81°).

Attempted synthesis of 5,7-dimethoxy-3-hydroxy-4-chromanone

A mixture of 2-hydroxy-4,6-dimethoxyacetophenone (2 g), sodium dust (1 g) and methyl formate (20 g) was kept for 40 hours then shaken with ice and water. The ethereal solution was washed with water and dried ($MgSO_4$). The ether and methyl formate were removed on a water bath. The residual oil after solidifying was crystallised ex ethanol as a pale yellow solid m.p. 320°. The required compound has m.p. 104°.[137]

8. Bicyclo-[3.2.1]-octan-3-one derivatives

2,3-Dibromobicyclo-[3.2.1]-oct-2-ene

This compound, prepared by treating norbornylene with potassium

tert-butoxide and bromoform, was obtained as a colourless oil
b.p. 104°/1 mm (lit.[138] b.p. 104°/1 mm).

3-Bromobicyclo-[3.2.1]-oct-2-ene

This compound, prepared by reacting 2,3-dibromobicyclo-
[3.2.1]-oct-2-ene with lithium aluminium hydride, was obtained as
a colourless oil b.p. 42-44°/1 mm (lit.[138] b.p. 40-44°/1 mm).

Bicyclo-[3.2.1]-octan-3-one

This compound, made by reacting 3-bromobicyclo-[3.2.1]-
oct-2-ene with conc. sulphuric acid, was obtained, after sublimation,
as a colourless solid m.p. 132-133° (lit.[138] m.p. 132-133°).

2-Bromobicyclo-[3.2.1]-octan-3-one

Bicyclo-[3.2.1]-octan—3-one was brominated using bromine
in acetic acid to yield this compound as a colourless solid m.p. 49-50°
(lit.[138] m.p. 49-50°).

cis-2,4-Dibromobicyclo-[3.2.1]-octan-3-one

This compound, prepared by brominating bicyclo-[3.2.1]-octan-
3-one with pyridinium perbromide, was obtained as a colourless
crystalline solid m.p. 89° (lit.[138] m.p. 87-88°).

trans-*2,4-Dibromobicyclo*-[*3.2.1*]-*octan-3-one*

The *cis*-dibromoketone in acetic acid was treated with 40% aqueous hydrobromic acid. The reaction mixture was left at 40 ± 3° for 3 days. After the usual treatment there was obtained a mixture of two products one of which was *cis*-2,4-dibromobicyclo-[3.2.1]-octan-3-one. N.m.r. indicated that 80 ± 10% epimerisation had occurred.

cis-*2,4-Dibromobicyclo*-[*3.2.1*]-*octan-3-ol*

By treating *cis*-2,4-dibromobicyclo-[3.2.1]-octan-3-one in ethanol with boric acid and sodium borohydride the required compound was obtained as a colourless crystalline solid m.p. 110-112°, (lit.[138] 115-116°).

Compound obtained from cis-*2,4-dibromobicyclo*-[*3.2.1*]-*octan-3-ol*

An attempt to purify this compound by sublimation at 140°/0.05 mm yielded a colourless crystalline solid m.p. 160-161° which exhibited a typical ABX-type n.m.r. spectrum and showed *m/e* 202, 204. This compound is believed to be 2-bromo-3,4-epoxybicyclo-[3.2.1]-octane.

Bicyclo-[*3.2.1*]-*octan-3-ol*

Bicyclo-[3.2.1]-octan-3-one in methanol was treated with sodium borohydride and let stand at room temperature for 2 hours. After the usual treatment a crystalline product, which was shown to

be a mixture by t.l.c., was obtained. This mixture when
-chromatographed on silica yielded with petroleum ether-ether
(15%) mixture a colourless crystalline compound m.p. 224–225° (lit.[138]
m.p. 225°) exhibiting an axial-OH in n.m.r. and ν_{max} (mull) 3620
(OH) cm^{-1}.

Elution with pure ether yielded another colourless compound
m.p. 116–118° (lit.[138] 116–117°) which exhibited an equatorial-OH
in n.m.r. and ν_{max} (mull) 3620 (O–H) cm^{-1}.

9. Cyclobutanone Derivatives

2-Isopropylidene cyclobutanone and 2,4-diisopropylidene cyclobutanone

A mixture of acetone (35 g), cyclobutanone (10 g) and 1N
caustic soda (100 ml) was stirred in a closed flask for 48 hours. A
yellow layer appeared on the surface. The reaction mixture was
neutralised with acetic acid, the upper layer decanted and the aqueous
phase extracted several times with benzene and ether. The organic
phases were combined, dried over sodium sulphate and the solvents
distilled. A pinch of phosphorus pentoxide was added to the residue
which was slowly distilled yielding 2-isopropylidene cyclobutanone
(3.5 g) b.p. 70–72°/21 mm (lit.[140] b.p. 71–72°/21 mm), and 2,4-
diisopropylidene cyclobutanone b.p. 135°/21 mm (lit.[140] b.p. 135°/
21 mm) which crystallises on freezing m.p. 75–77° (lit.[140] m.p. 75–79°).

Attempted synthesis of 2-t-butyl-4-isopropylidene cyclobutanone

2,4-Diisopropylidene cyclobutanone (in anhydrous THF) was added dropwise to methyl magnesium iodide (in anhydrous THF) and a pinch of cuprous chloride was added at 0°. The reaction would not take place. The solvent was removed and distillation of the residue yielded the starting material.

10. Photoreaction Between Phenanthraquinone and Styrene

Phenanthraquinone (1 g) and freshly distilled styrene (2 g) in benzene (50 cc) were exposed for 4 days. After the benzene was removed and the residue treated with light petroleum (b.p. 30-50°), concentration of the extract yielded almost colourless crystals m.p. 125-135°d (lit.[141] *ca.* 130°d) after washing with ether.

11. 1-Phenyl-4-styryl-2-azetidinones

1-Phenyl-4-styryl-2-azetidinone

The reaction of cinnamylidene-aniline (10.35 g) and ethyl-α-bromoacetate (10.0 g) gave 10 g of a brown oil. This oil was absorbed on alumina (250 g) packed in benzene and eluted with benzene/ether. The fractions collected containing 15-20% ether yielded the required compound as colourless needles (2 g, 20%) m.p. 87° (lit.[142] m.p. 87°).

3-Methyl-1-phenyl-4-styryl-2-azetidinone

The reaction of cinnamylidene-aniline (10.35 g) and ethyl-α-bromopropionate (10.1 g) gave the required compound as pale brown plates (6.8 g, 59%) m.p. 142-144° (lit.[85] m.p. 142-144°) ex ethanol, shown by n.m.r. to be a mixture of *cis* and *trans* isomers. Repeated recrystallisation ex ethanol yielded a small amount of the pure *cis* isomer m.p. 146-148°.

3-Ethyl-1-phenyl-4-styryl-2-azetidinone

Cinnamylidene-aniline (10.35 g) on reaction with ethyl-*t*-bromo-*n*-butyrate (10.5 g) gave a deep red viscous oil (10 g, 83%) b.p. 170°/0.1 mm which was shown by n.m.r. to be a mixture of *cis*- and *trans*-3-ethyl-1-phenyl-4-styryl-2-azetidinone

3-Isopropyl-1-phenyl-4-styryl-2-azetidinone

The reaction of cinnamylidene-aniline (10.35 g) and ethyl-α-bromo-isovalerate (10.5 g) gave an orange solid (5 g) b.p. 135°/0.2 mm, which had no $C = O$ absorption *ca.* 1740 cm^{-1} in i.r., so no further investigation was done on this compound, and a red liquid (6 g, 50%) b.p. 170°/0.2 mm which was shown to be a mixture of *cis*- and *trans*-3-isopropyl-1-phenyl-4-styryl-2-azetidinone by n.m.r.

Attempted synthesis of 1,3-diphenyl-4-styryl-2-azetidinone

The reaction of cinnamylidene-aniline (5 g) with ethyl-α-bromo-phenyl acetate (5 g) gave a brown solid (0.84 g, 15%) containing an NH band at 3300 cm^{-1} in i.r. This compound was identified as ethyl-3-anilino-1,4-diphenylpent-1-enate by n.m.r.

3,3-Dimethyl-1-phenyl-4-styryl-2-azetidinone

The reaction of cinnamylidene-aniline with ethyl-α-bromo-iso-butyrate gave this compound as yellow needles m.p. 131-132° (lit.[85] m.p. 131-132°).

1,3,3-Triphenyl-4-styryl-2-azetidinone

This compound, prepared by Staudinger's method from cinnamylidene-aniline and diphenylketene was obtained as a white solid m.p. 173-174° (lit.[143] m.p. 171-172°).

12. Schiff's bases

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.[104] Compound (XXIX) was prepared from aniline and [2,4,6-D$_3$]benzaldehyde.[97]

REFERENCES

1. E.I. Snyder, *J.Amer.Chem.Soc.*, *85*, 2624 (1963).

2. K. Deutsch and I. Deutsch, *Ann.Physik*, *16*, 30 (1965).

3. R.K. Hill and T. Chan, *Tetrahedron*, *21*, 2015 (1965).

4. N.S. Bowman, D.E. Rice and B.R. Switzer, *J.Amer.Chem.Soc.*, *87*, 4477 (1965).

5. J.S. Waugh and F.A. Cotton, *J.Phys.Chem.*, *65*, 562 (1961).
    J.A. Pople, *Mol.Phys.*, *1*, 3 (1958).

6. C. van Der Vlies, *Rec.Trav.Chim.*, *84*, 1289 (1965).

7. E.I. Snyder, *J.Amer.Chem.Soc.*, *88*, 1150 (1966).

8. M. Raban, *Tetrahedron Letters*, 3105 (1966).

9. J.A. Elvidge and R.G. Foster, *J.Chem.Soc.*, 988 (1964).

10. H.S. Gutowsky and C. Juan, *J.Chem.Phys.*, *37*, 2198 (1962).

11. L.S. Rattet, L. Mandell and J.H. Goldstein, *J.Amer.Chem.Soc.*, *89*, 2253 (1967).

12. M. Karplus, *ibid.*, *85*, 2870 (1963).

13. M. Karplus, *J.Chem.Phys.*, *30*, 11 (1959).

14. J.R. Cavanaugh and B.P. Dailey, *ibid.*, *34*, 1099 (1961).

15. P. Laszlo and P. von R. Schleyer, *J.Amer.Chem.Soc.*, *85*, 2709 (1963).

16. T. Schaefer and H.M. Hutton, *Can.J.Chem.*, *45*, 3153 (1967).

17. K.L. Williamson, *J.Amer.Chem.Soc.*, *85*, 516 (1963).

18. A.A. Bothner-By, in 'Advances in Magnetic Resonance', ed. J.S. Waugh, Acad. Press, New York, Vol. 1 (1965).

19. H. Booth and G.C. Gidley, *Tetrahedron*, *21*, 3429 (1965).

20. N.S. Bhacca and D.H. Williams, *J.Amer.Chem.Soc.*, *86*, 2742 (1964).

21. H. Booth, *Tetrahedron Letters*, 411 (1965).

22. R.J. Abraham, L. Cavalli and K.G.R. Pachler, *Mol.Phys.*, *11*, 471 (1966).

23. (a) C. Altona, H.R. Buys, H.J. Hageman and E. Havinga,
         Tetrahedron, *23*, 2265 (1967).

     (b) C. Altona and A.P.M. van der Veek, *ibid.*, *24*, 4377 (1968).

24. C. Altona, H.R. Buys and E. Havinga, *Tetrahedron Letters*,
         3067 (1967).

25. C.N. Banwell and N. Sheppard, *Disc.Farad.Soc.*, *34*, 115 (1962).

26. J.A. Pople and A.A. Bothner-By, *J.Chem.Phys.*, *42*, 1339 (1965).

27. Reference 18, p. 149.

28. M. Barfield and D.M. Grant, *J.Amer.Chem.Soc.*, *85*, 1899 (1963).

29. H.J. Bernstein and N. Sheppard, *J.Chem.Phys.*, *37*, 3012 (1962).

30. R.C. Cookson, T.A. Crabb, J.J. Frankel and J. Hudec, *Tetrahedron*
         Suppl. 7, 355 (1966).

31. V.S. Watts and J.H. Goldstein, *J.Chem.Phys.*, *46*, 4165 (1967).

32. C.G. MacDonald, J.S. Shannon and S. Sternhell, *Aust.J.Chem.*,
         19, 1527 (1966).

33. K.L. Williamson, C.A. Lanford and C.R. Nicholson, *J.Amer.Chem.Soc.*,
         86, 762 (1964).

34. F. Hruska, G. Kotowych and T. Schaefer, *Can.J.Chem.*, *43*, 2827
         (1965).

35. S. Sternhell, *Quart.Rev.*, *23*, 236 (1969).

36. P.A. Scherr and J.P. Oliver, *J.Mol.Spectry*, *31*, 109 (1969).

37. N. Muller and D.E. Pritchard, *J.Chem.Phys.*, *31*, 768, 1471 (1959).

38. N. Muller, *ibid.*, *36*, 359 (1962).

39. J.H. Goldstein and R.T. Hobgood, *ibid.*, *40*, 3592 (1964).

40. M. Karplus and D.M. Grant, *Proc.Natl.Acad.Sci.(U.S.)*, *45*, 1269 (1959).

41. H. Dreeskamp and E. Sackmann, *Z.Physik.Chem.*, *34*, 273 (1962).

42. J.A. Pople and D.P. Santry, *Mol.Phys.*, *8*, 1 (1964); *9*, 301, 311 (1965).

43. W.J. Considine, *J.Chem.Phys.*, *42*, 1130 (1965).

44. D.M. Grant and W.M. Litchman, *J.Amer.Chem.Soc*, *87*, 3994 (1965).

45. G.W. Smith, *J.Chem.Phys.*, *42*, 435 (1965).

46. W. McFarlane, *Quart.Rev.*, *23*, 187 (1969).

47. J. Ranft, *Anal.Phys.*, *10*, 399 (1963).

48. T.L. Brown and J.C. Puckett, *J.Chem.Phys.*, *44*, 2238 (1966).

49. L. Lunazzi and F. Taddei, *Spectrochim.Acta*, *23A*, 841 (1967).

50. J.E. Huheey, *J.Chem.Phys.*, *45*, 405 (1966).

51. J. Hinze and H.H. Jaffe, *J.Amer.Chem.Soc.*, *84*, 540 (1962).

52. A.W. Douglas, *J.Chem.Phys.*, *45*, 3465 (1966).

53. J.F. Chiang, C.F. Wilcox and S.H. Bauer, *J.Amer.Chem.Soc.*, *90*, 3149 (1968).

54. K.L. Williamson, Y.L. Hsu, F.H. Hall, S. Swager, and M.S. Coulter, *ibid.*, *90*, 6717 (1968).

55. K. Alder and G. Stein, *Angew.Chem.*, *50*, 510 (1937).

56. G. Fraenkel, Y. Asaki, M.J. Mitchell and M.P. Cava, *Tetrahedron*, *20*, 1179 (1964). This paper is correct in its Table but has reversed assignments in the text.

57. H. Conroy, *Advan.Org.Chem.*, 2, 265 (1960).

58. E. Goldish, *J.Chem.Educ.*, 36, 408 (1959).

59. J.W. Emsley, J. Feeney and L.H. Sutcliffe, "High Resolution
     N.M.R. Spectroscopy", Pergamon Press, 1965, p. 362.

60. S. Castallano and A.A. Bothner-By, *J.Chem.Phys.*, 41, 3863 (1964).

61. R.E. Glick and A.A. Bothner-By, *ibid.*, 25, 362 (1956).

62. V. Sheppard and J.J. Farmer, *Proc.Roy.Soc.(London)*, A252,
     506 (1959).

63. G. Schrumpf and W. Luttke, *Tetrahedron Letters*, 2635 (1969).

64. P.R. Wells, "Linear Free Energy Relationships", Academic Press,
     London, N.Y. 1968, p. 19.

65. C. Juan and H.S. Gutowsky, *Disc.Farad.Soc.*, 34, 52 (1962).

66. H.S. Gutowsky, *Pure Appl.Chem.*, 7, 93 (1963).

67. S. Mizushima, T. Shimanouchi, T. Miyazawa, I. Ichishima, K.
     Kuratani, I. Nakagawa and N. Shido, *J.Chem.Phys.*, 21,
     815 (1953).

68. I. Nakagawa, I. Ichishima, K. Kuratani, T. Miyazawa, T. Shimanouchi
     and S. Mizushima, *ibid.*, 20, 1720 (1952).

69. S. Mizushima, T. Shimanouchi, I. Ichishima, T. Miyazawa,
     I. Nakagawa and T. Araki, *J.Amer.Chem.Soc.*, 78, 2038 (1956).

70. A. Miyake, I. Nakagawa, T. Miyazawa, I. Ichishima, T. Shimanouchi
     and S. Mizushima, *Spectrochim.Acta*, 13, 161 (1958).

71. R.W. Kilb, C.C. Lin and E.B. Wilson, *J.Chem.Phys.*, 26, 1695 (1967).

72. D.R. Herschbach and L.C. Krisher, *ibid.*, 28, 728 (1958).

73. R.J. Abraham and J.A. Pople, *Mol.Phys.*, *3*, 609 (1960).

74. G.J. Karabatsos and N. Hsi, *J.Amer.Chem.Soc.*, *87*, 2864 (1965).

75. (a) A.A. Bothner-By, C. Naar-Colin and H. Gunther, *ibid.*, *84*, 2748 (1962).

    (b) A.A. Bothner-By, S. Castellano, S.J. Ebersole and H. Gunther, *ibid.*, *88*, 2466 (1966).

76. W.A. Thomas, *Ann.Rev.N.M.R.Spectry.*, *1*, 43 (1968).

77. R.T. Hobgood and J.H. Goldstein, *J.Mol.Spectry.*, *12*, 76 (1964).

78. L.M. Sverdlov and E.N. Bolotina, *Russ.J.Phys.Chem.English Transl.*, *86*, 1502 (1962).

79. A.A. Bothner-By and R.K. Harris, *J.Amer.Chem.Soc.*, *87*, 3445 (1965).

80. A.A. Bothner-By and R.K. Harris, *ibid.*, *87*, 3451 (1965).

81. W. Luttke and A. DeMeijere, *Angew.Chem.internat.Edit.*, *5*, 512 (1966).

82. H. Gunther and D. Wendisch, *ibid.*, *5*, 251 (1966).

83. G.V. Smith and H. Krilov, *J.Amer.Chem.Soc.*, *85*, 2016 (1963).

84. M.S. Manhas, S. Jeng and A.K. Bose, *Tetrahedron*, *24*, 1237 (1968).

85. K.D. Barrow, Ph.D. Thesis, University of Adelaide, 1966.

86. J.L. Luche, H.B. Kagan, R. Parthasarathy, G. Tsoucaris, C. de Rango and C. Zelmar, *Tetrahedron*, *24*, 1275 (1968).

87. K.D. Barrow and T.M. Spotswood, *Tetrahedron Letters*, 3325 (1965).

88. C.L. Moret and L.M. Trefonas, *J.Heterocyclic Chem.*, *5*, 549 (1968).

89. J.B. Lambert, L.J. Durham, P. Lepoutere and J.D. Roberts, *J.Amer.Chem.Soc.*, *87*, 3896 (1965).

90. M. Fischer and C. Djerassi, *Chem.Ber.*, *99*, 1541 (1966).

91. D.J. Elias and R.G. Gillis, *Aust.J.Chem.*, *19*, 251 (1966).

92. P. Brown and C. Djerassi, *Angew.Chem.internat.Edit.*, *6*, 477
     (1967).

93. J.H. Bowie, R.G. Cooks and G.E. Lewis, *J.Chem.Soc.(B)*,
     621 (1967).

94. J.H. Bowie, R.G. Cooks and G.E. Lewis, *Aust.J.Chem.*, *20*,
     1601 (1967).

95. B.S. Larsen, G. Schroll, S.O. Lawesson, J.H. Bowie and R.G.
     Cooks, *Tetrahedron*, *24*, 5193 (1968).

96. H.M. Grubb and S. Meyerson, "Mass Spectrometry of Organic Ions",
     Ed. F.W. McLafferty, Acad. Press, N.Y. 1963.

97. J. Ronayne, D.H. Williams and J.H. Bowie, *J.Amer.Chem.Soc.*, *88*,
     4980 (1966).

98. J.H. Bowie, P.F. Donaghue, H.J. Rodda and B.K. Simons,
     Tetrahedron, *24*, 3965, (1968).

99. D.H. Williams, R.S. Ward and R.G. Cooks, *J.Amer.Chem.Soc.*, *90*,
     966 (1968).

100. H. Budzikiewicz, C. Djerassi and D.H. Williams, "Interpretation of
     the Mass Spectra of Organic Compounds" Holden-Day, San
     Francisco (1967).

101. F.W. McLafferty, *Analyt.Chem.*, *31*, 477 (1959).

102. M.M. Bursey and F.W. McLafferty, *J.Amer.Chem.Soc.*, *88*, 4484 (1966).

103. J. Momigny, *Bull.Soc.r.Sci.Liege*, *25*, 93 (1956).

104. A.P. Best and C.L. Wilson, *J.Chem.Soc.*, 241 (1946).

105. D.J. Elias and R.G. Gillis, *Aust.J.Chem.*, *22*, 2249 (1969).

106. J.H. Bowie and P.J. Hoffmann, *ibid.*, *22*, 1219 (1969).

107. K. Biemann, "Mass Spectrometry: Organic Chemical Applications", McGraw-Hill Book Co. Inc., N.Y., 1962.

108. J.H. Beynon, "Mass Spectrometry and Its Applications to Organic Chemistry", Elsevier Publishing Co., Amsterdam, 1960.

109. J.D. Waldron (Ed.), "Advances in Mass Spectrometry", Pergamon Press, London, 1959.

110. H. Budsikiewicz, C. Djerassi and D.H. Williams, "Structural Elucidation of Natural Products by Mass Spectrometry", Holden-Day, San Francisco, 1964.

111. F.W. McLafferty, "Interpretation of Mass Spectra", W.A. Benjamin, N.Y., 1966.

112. H.C. Hill, "Introduction to Mass Spectrometry", Heyden and Son, London, 1966.

113. E.K. Fields, *J.Amer.Chem.Soc.*, *78*, 5821 (1956).

114. H. Bluestone, *C.A.*, *48*, 8474b (1954).

115. E.A. Prill, *J.Amer.Chem.Soc.*, *69*, 62 (1947).

116. S.B. Soloway, J.G. Morales and J. van Overbeek, *C.A.*, *50*, 17307b (1956).

117. J. Thiele and O. Gunther, *Ann.*, *347*, 107.

118. M.P. Cava and D.R. Napier, *J.Amer.Chem.Soc.*, *79*, 1704 (1957).

119. M.P. Cava and D.R. Napier, *ibid.*, *78*, 500 (1956).

120. W.H. Perkin, *J.Chem.Soc.*, *53*, 5 (1888).

121. D.M. Hall, M.S. Lesslie and E.E. Turner, *ibid.*, 711 (1950).

122. L. Horner, W. Kirmse and K. Muth, *Chem.Ber.*, *91*, 432 (1958).

123. R. Anschutz, *ibid.*, *14*, 2791 (1881).

124. (a) R. Anschutz and C. Bennert, *Ann.*, *254*, 155 (1889).

     (b) L.E. Erickson, *J.Amer.Chem.Soc.*, *87*, 1867 (1965).

125. G.W. Stahl and D.L. Cottle, *ibid.*, *65*, 1782 (1943).

126. J.D. Roberts and V.C. Chambers, *ibid.*, *73*, 3177 (1951).

127. V.C. Sekera and C.S. Marvel, *ibid.*, *55*, 345 (1933).

128. S. Skraup and O. Binder, *Chem.Ber.*, *62*, 1133 (1929).

129. J. Bredt and J. Kallen, *Ann.*, *293*, 366 (1896).

130. A. Lawson, *J.Chem.Soc.*, 144 (1957).

131. G. Ebert, *Ann.*, *226*, 347 (1884).

132. P.J. deBenneville and R. Connor, *J.Amer.Chem.Soc.*, *62*, 283 (1940).

133. W.H. Perkin, *J.Chem.Soc.*, *23*, 368 (1870).

134. W.H. Perkin, *ibid.*, *24*, 38 (1871).

135. F. Arndt and G. Kallner, *Chem.Ber.*, *57*, 206 (1923).

136. D.D. Pratt and R. Robinson, *J.Chem.Soc.*, *125*, 193 (1924).

137. (a) P.C. Joshi and K. Venkataraman, *J.Sci.Ind.Research,*
         11B, 347 (1952).

     (b) P.C. Joshi and K. Venkataraman, *J.Chem.Soc.*, 513 (1934).

138. B. Waegell and C.W. Jefford, *Bull.Soc.Chim.France*, 844 (1964).

139. G.J. Ostling, *J.Chem.Soc.*, *101*, 472 (1912).

140. J.M. Conia, *Bull.Soc.Chim.France*, 2747 (1965).

141. A. Schonberg and A. Mustafa, *J.Chem.Soc.*, 387 (1944).

142. R. Pfleger and A. Jager, *Chem.Ber.*, *90*, 2460 (1957).

143. H. Staudinger, *Ann.*, *356*, 51 (1907).

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.

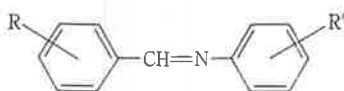[1] Fischer, M., and Djerassi, C., *Chem. Ber.*, 1966, **99**, 1541.

[2] Elias, D. J., and Gillis, R. G., *Aust. J. Chem.*, 1966, **19**, 251.

[3] Brown, P., and Djerassi, C., *Angew. Chem. int. Edn*, 1967, **6**, 477.
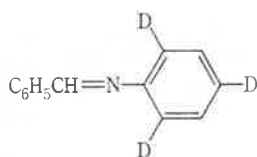
[4] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *J. chem. Soc. (B)*, 1967, 621.

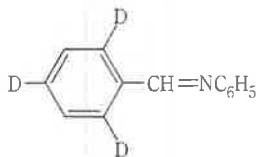[5] Bowie, J. H., Cooks, R. G., and Lewis, G. E., *Aust. J. Chem.*, 1967, **20**, 1601.

[6] Larsen, B. S., Schroll, G., Lawesson, S.-O., Bowie, J. H., and Cooks, R. G., *Tetrahedron*, in press.
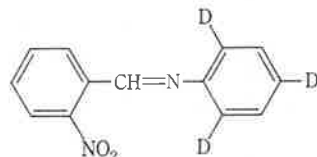
	R	R′		R	R′		R	R′
(I)	H	H	(X)	H	*p*-Cl	(XIX)	H	*p*-MeO
(II)	*o*-Me	H	(XI)	*p*-Br	H	(XX)	*o*-OH	H
(III)	*p*-Me	H	(XII)	H	*m*-Br	(XXI)	*p*-OH	H
(IV)	H	*o*-Me	(XIII)	H	*p*-Br	(XXII)	H	*p*-OH
(V)	H	*m*-Me	(XIV)	*p*-F	H	(XXIII)	*o*-NO$_2$	H
(VI)	H	*p*-Me	(XV)	*o*-MeO	H	(XXIV)	*m*-NO$_2$	H
(VII)	*o*-Cl	H	(XVI)	*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
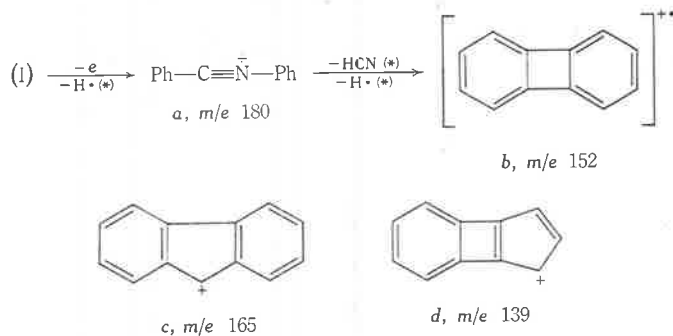
Compound(s)	Rearrangement Process	Final Ion (*m/e*)	Rel. Abund. of Final Ion (%)
(I)	$M - H \cdot - HCN - H \cdot$	152	5
(II)–(VI)	$\begin{cases} M - H \cdot - HCN - H_2 \\ M - H \cdot - Me \cdot - (HCN) \end{cases}$	165 152	8, 6, 5, 4, 3 5, 4, 4, 4, 4
(VII)–(IX)	$M - Cl \cdot - H \cdot - HCN$	152	5, 3, 3
(X)	$M - H \cdot - Cl \cdot - HCN$	152	8
(XI)–(XIII)	$M - Br \cdot - H \cdot - HCN$	152	4, 18, 13
(XIV)	$M - H \cdot - HF - HCN$	151	2
(XV)–(XIX)	$\begin{cases} M - H \cdot - Me \cdot - CO - HCN - (H_2) \\ M - (MeO \cdot) - (HCN) - H \cdot \end{cases}$	139 152	2, 3, 3, 4, 4 2, 3, 2, 3, 2
(XX)–(XXII)	$\begin{cases} M - CHO \cdot - (HCN) - H_2 \\ M - H \cdot - H_2O - HCN \end{cases}$	139 151	3, 2, 3 2, 3, 2
(XXIII)	$\begin{cases} M - HO \cdot - (NO \cdot) - HCN \\ M - HO \cdot - CN_2O \end{cases}$	152 152	35 35
(XXIV)–(XXVI)	$M - NO_2 \cdot - H \cdot - HCN$	152	10, 12, 31
(XXVII)	$M - H \cdot - Me \cdot - H \cdot - HCN - H \cdot - HCN$	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 $M-H\cdot-HCN-H\cdot$ to produce m/e 152 ($C_{12}H_8$, h.r.), which is most plausibly represented as the biphenylene radical ion (b).

Fig. 1
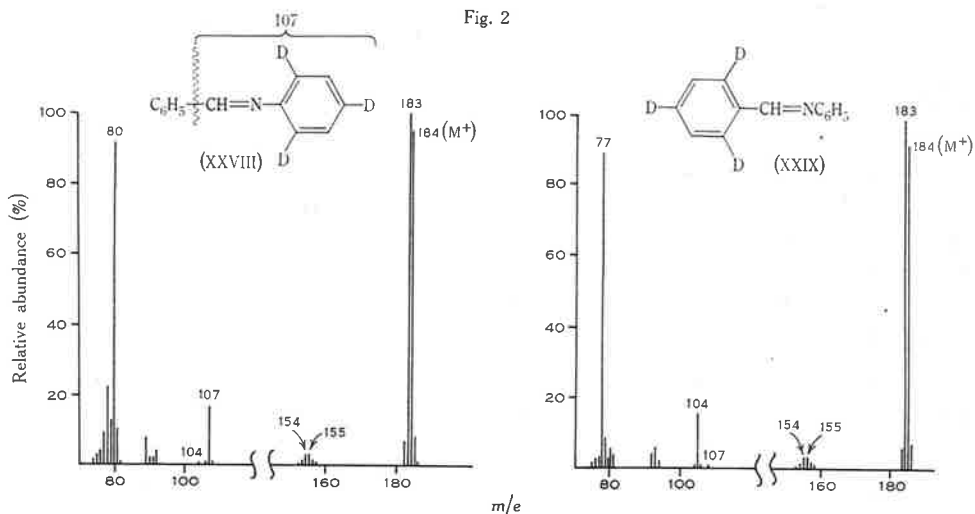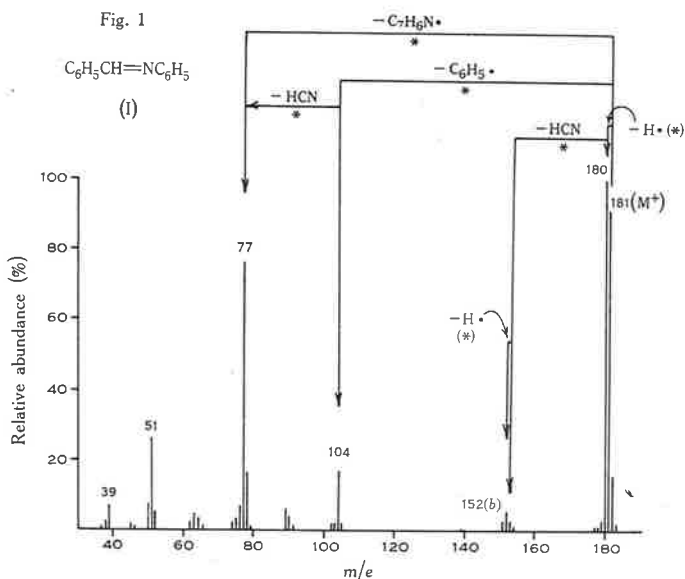
Fig. 2

The hydrogen lost in the $M-H\cdot$ 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*.

$$(I) \xrightarrow[-H\cdot(*)]{-e} \quad Ph-C\equiv\bar{N}-Ph \xrightarrow[-H\cdot(*)]{-HCN\ (*)}$$

a, m/e 180

b, m/e 152

c, m/e 165

d, m/e 139

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.)
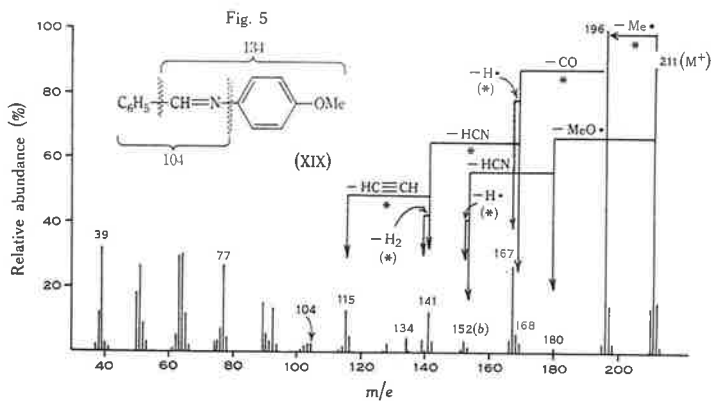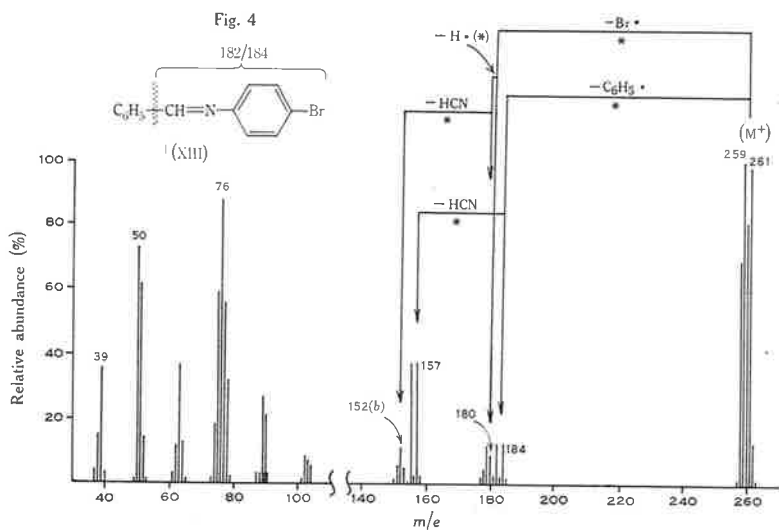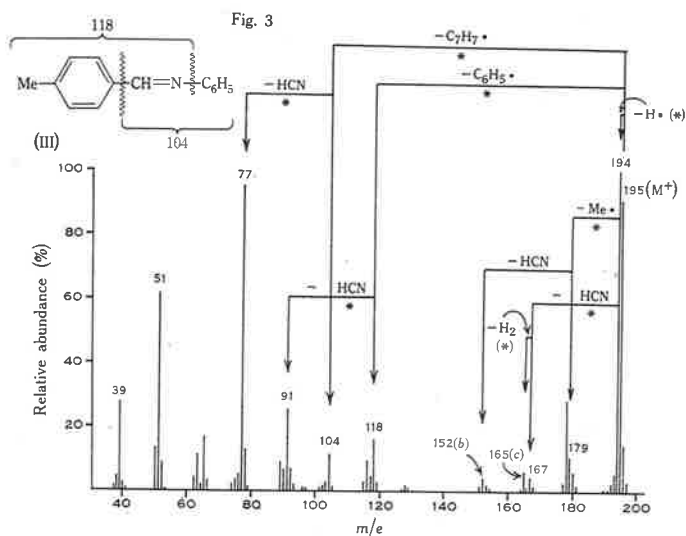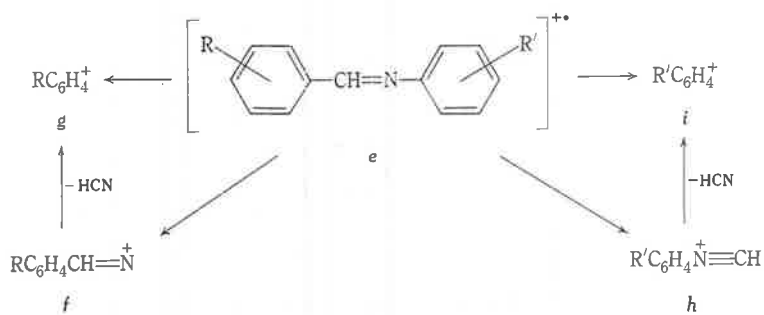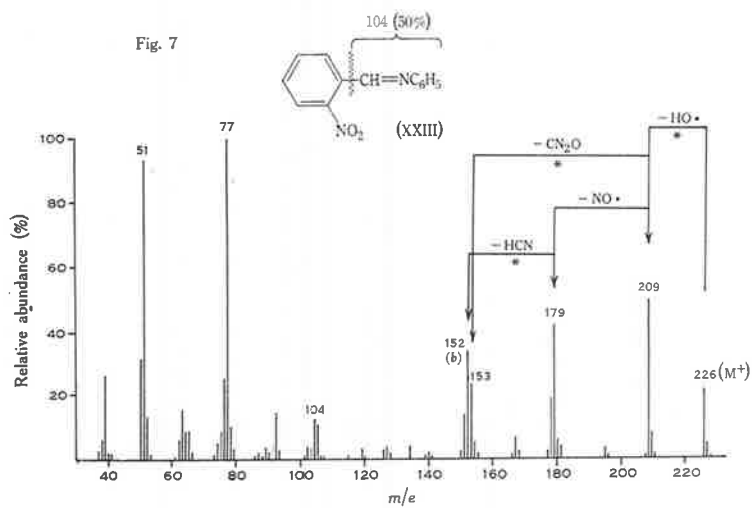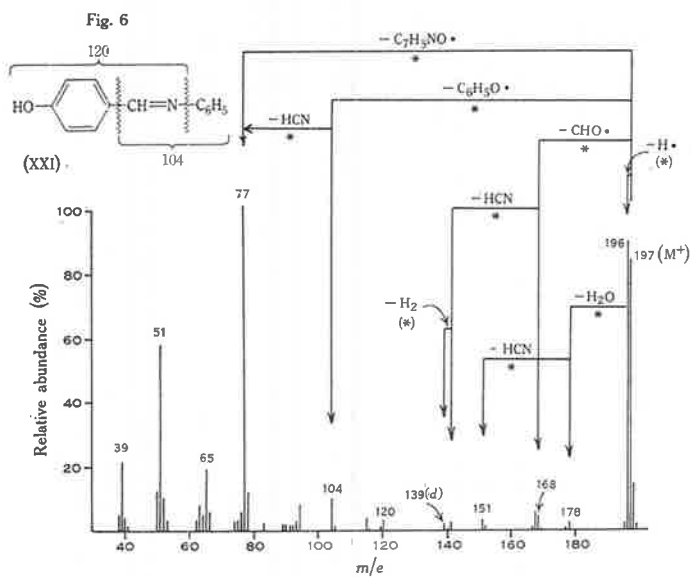
Fig. 3

Fig. 4

Fig. 5

Fig. 6

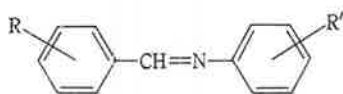
(XXI)

Fig. 7

(XXIII)

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
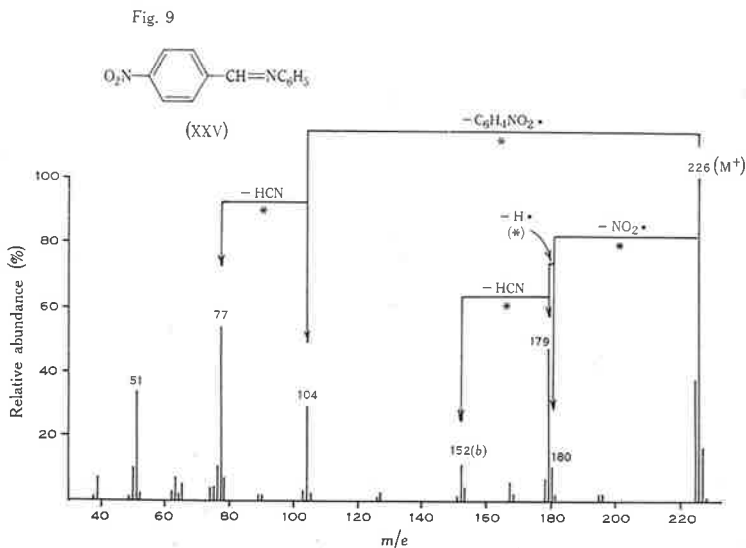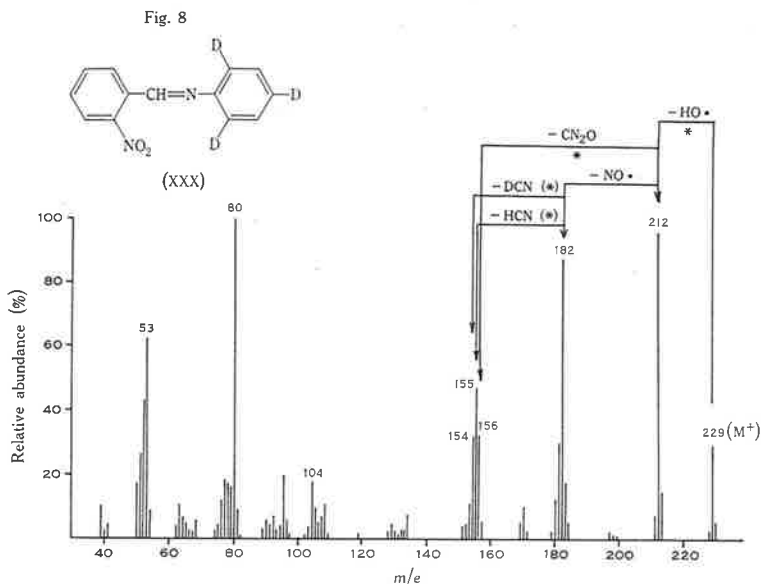
below). However, the relative abundance of h is generally greater than that of f, indicating that in this case, C–C bond fission produces a more stable cation than C–N bond fission. As the ions g and i are produced directly from the molecular ion and also by decomposition of f and h respectively, the additive effect should increase

J. H. BOWIE *ET AL.*

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 aceto-phenones,[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 $C_6H_5\overset{+}{-}\overset{\cdot}{N}\equiv CH$
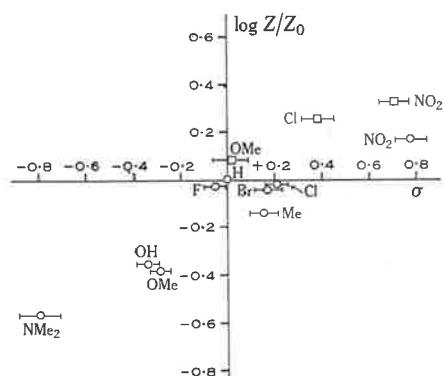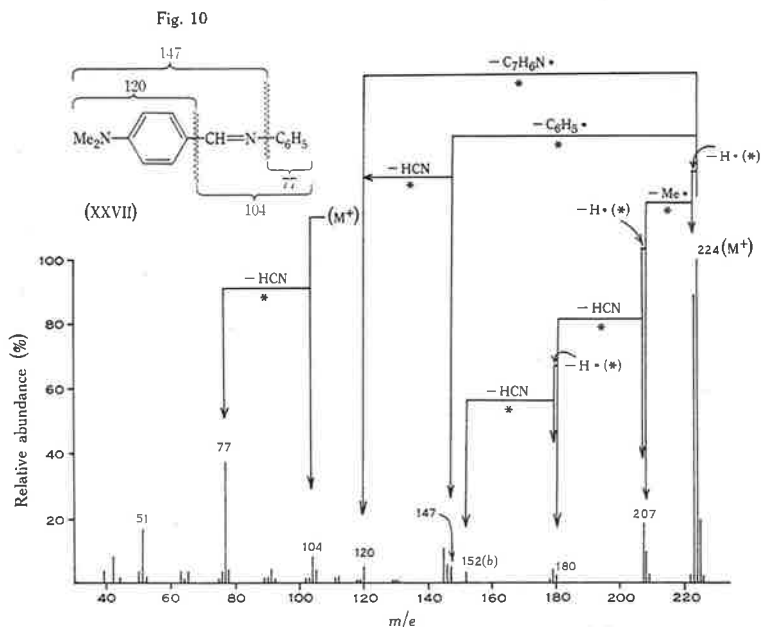

Fig. 10


Fig. 11.—Plot of $\log Z/Z_0$ v. σ:
○, *meta* substituent;
□, *para* substituent.

$$Z = \frac{\text{rel. ab. } [C_6H_5\overset{\cdot}{N}\equiv CH]}{\text{rel. ab. } [XC_6H_4CH=NC_6H_5]}$$

$$Z_0 = \frac{\text{rel. ab. } [C_6H_5\overset{\cdot}{N}\equiv CH]}{\text{rel. ab. } [C_6H_5CH=NC_6H_5]}$$

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 $M-HO\cdot$ ion (51%) which is absent in the spectrum of (XXV). The spectrum (Fig. 8) of

$$(\text{XXIII}) \xrightarrow[-\text{HO}\cdot]{-e} \qquad j, m/e \ 209 \qquad \text{or} \qquad k, m/e \ 209$$
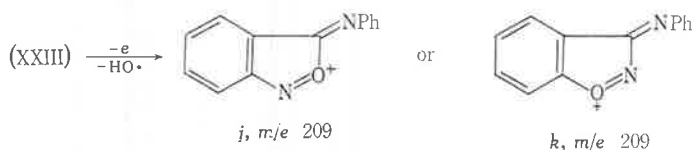
the deuterium-labelled derivative (XXX) shows that the hydrogen atom involved in the $M-HO\cdot$ process does not originate from the aromatic ring adjacent to nitrogen. As the spectra of nitrobenzene[13] and *o*-nitrobenzaldehyde are devoid of $M-HO\cdot$ peaks, the hydrogen atom is probably lost from 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 $150° \pm 5°$, 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 heptacosafluoro-tributylamine 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 $[2,4,6\text{-}D_3]$aniline.[14] Compound (XXIX) was prepared from aniline and $[2,4,6\text{-}D_3]$benzaldehyde.[8]

Acknowledgments

[13] Momigny, J., *Bull. Soc. r. Sci. Liége*, 1956, **25**, 93.
[14] Best, A. P., and Wilson, C. L., *J. chem. Soc.*, 1946, 241.