MECHANISTIC STUDIES IN THE BICYCLO[2,2,1]HEPTYL SERIES.

A Thesis

Presented for the Degree of

Doctor of Philosophy

in

The University of Adelaide

by

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Department of Organic Chemistry,

1973.

CONTENTS.

SUMMARY.

In order that a comprehensive study of the oxidative decarboxylation of carboxylic acids with lead tetraacetate could be carried out, the exo and endo isomers of 2-carboxy-2,3,3-trimethylnorbornane were required. Successful, as well as several unsuccessful routes to the synthesis of exo- and endo-2-carboxy-2,3,3-trimethylnorbornane are described. During the course of the synthetic work a potentially useful method of converting a bicyclo[2,2,1]heptyl derivative bearing an exocyclic methylene group into the corresponding bicyclo[3,2,1]octanone derivative was encountered and investigated.

A study of the oxidative decarboxylation of exo- and endo-2-carboxybornane, exo- and endo-2-carboxy-2,3,3-trimethylnorbornane and β-(2,2,3-trimethylcyclopent-3-enyl)propionic acid using lead tetraacetate was carried out in benzene and dimethylsulphoxide in the absence of, and presence of copper II acetate. It is suggested that the oxidative decarboxylation of the above acids with lead tetraacetate initially involves the formation of alkyl radicals which may be oxidised by lead carboxylates by two distinct mechanisms:

(i) oxidation by a lead IV carboxylate involving an electron transfer to give a cation and a lead III carboxylate.

(ii) oxidation by lead III to form a lead IV alkyl which may decompose either by a cyclic cis-elimination to give olefins or by a cyclic S_Ni mechanism to give acetates.

In the copper catalysed decarboxylation reactions, copper alkyls are proposed as intermediates. The formation of olefins by the decomposition of copper alkyls is suggested to occur via a cyclic cis-elimination reaction.

In order to complement the study of the oxidative decarboxylation reactions, the behaviour of the α-campholenyl radical was investigated under non-oxidative conditions.

The anodic oxidation of exo- and endo-2-carboxybornane and exo- and endo -2-carboxy-2,3,3-trimethylnorbornane in methanol at platinum and carbon electrodes was found to give an equilibrium mixture of the 1,7,7-trimethylnorborn-2-yl and 2,3,3-trimethylnorborn-2-yl cations, having properties very similar to that formed by methanolysis of the respective chlorides. Under the same conditions of electrolysis, β-(2,2,3-trimethylcyclopent-3-enyl)propionic acid gave very low yields of products (including those of cyclisation), the nature of which depended markedly on the type of anode used.

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STATEMENT.

The work described in this thesis incorporates no material previously submitted for a 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.

C.F. Pincombe.

ACKNOWLEDGEMENTS.

I wish to express my sincere thanks to Dr. G.E. Gream for his guidance, encouragement, and enthusiasm during the supervision of this work. I also wish to thank Dr. W.H. Atwell of the Dow Corning Corporation for a generous gift of the dimethoxymethyltrimethoxysilane used in this work.

Part of this work was carried out during the tenure of a Postgraduate University Research Grant, which I gratefully acknowledge.

Finally, I wish to thank my wife Julie for her patience and understanding during the completion of this work and the preparation of this thesis.

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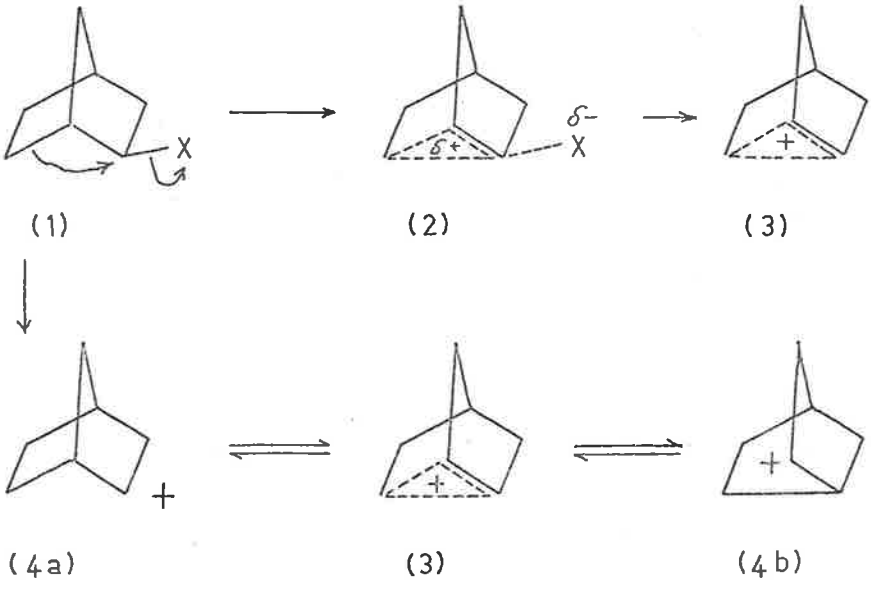
INTRODUCTION.

1. The structure of the norbornyl and substituted norbornyl cations.

Since the pioneering work[1] of Winstein, Ingold, Cram, and Roberts a vast number of reports of non-classical carbonium ion intermediates have appeared in the literature, and the subject has been extensively reviewed.[1-14] In 1962, Brown[15] questioned the concept of non-classical cations generally and the non-classical norbornyl cation in particular. Since Brown's paper, many workers have attempted to clarify the problem. In particular, most activity has been centred around the norbornyl and substituted norbornyl cations. A brief summary of the non-classical vs. classical cation question in the case of the norbornyl and substituted norbornyl systems is given below.

Several definitions of a non-classical cation have been proposed. Bartlett[2] suggested that an ion was non-classical if its ground state had delocalised, bonding σ-electrons. Brown[16] defined an ion as being non-classical if the position of one or more atoms was markedly different from that predicted on the basis of classical structural principles. A more comprehensive definition has also been put forward by Sargent.[7] Recently Olah[17] has suggested that trivalent (classical) ions be known as "carbenium ions" to differentiate the classical ion from three-centre bond, penta- or tetra-coordinated (non-classical) "carbonium" ions. "Carbocation" was suggested as a general term for all cations of carbon atoms. However, for the purposes of this thesis Olah's system of nomenclature will not be rigorously applied.

Until Brown's controversial paper,[15] the evidence of Winstein[18] and Roberts[19] for the existence of non-classical ions in the norbornyl series was generally accepted. Winstein's work[18] led to the postulate of the non-classical ion (3) as an intermediate in solvolytic reactions of exo-2-norbornyl derivatives (1). According to Winstein's mechanism for the solvolysis of (1), ionisation proceeds simultaneously with rearrangement [by way of the transition state (2)], to the non-classical ion (3), which is more stable than the classical ion (4). The ionisation is depicted in Scheme 1 and the energy profile in Fig. 1a. Three criteria, i.e. A, B, and C were used by Winstein to support the hypothesis of



(1) (2) (3)

Scheme 1 (Winstein)

(4a) (3) (4b)

Scheme 2 (Brown)

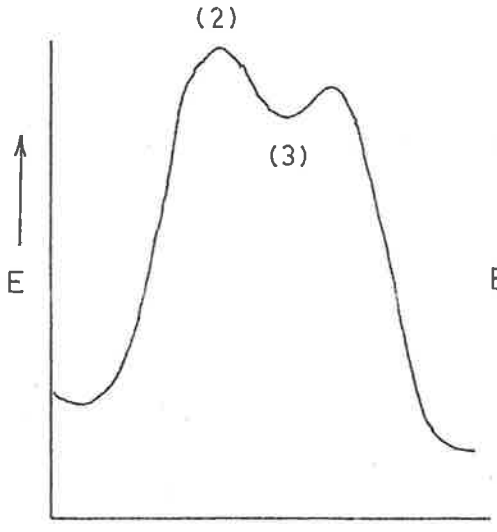
direct formation of the non-classical ion (3).

A. High solvolysis rates of exo-norbornyl derivatives.

B. High exo to endo rate ratios.

C. Exclusive exo substitution.

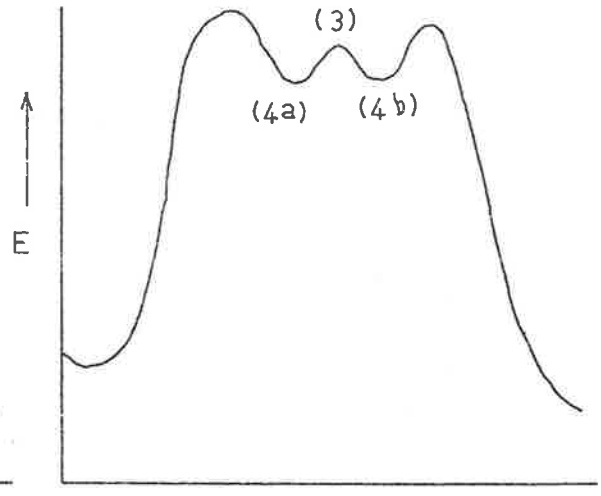
The validity of these three criteria has been disputed by Brown[8,9,16] who has suggested that the intermediate ion may be a set of rapidly equilibrating cations (4a) and (4b), which are more stable than the non-classical cation (3). Hence, in Brown's mechanism, the non-classical cation (3) serves only as a transition state for the equilibration of (4a) and (4b). This implies that rearrangement occurs after ionisation to the initially formed classical ion (4). Brown's mechanism is depicted in Scheme 2, and the corresponding energy profile in Fig. 1b.



Reaction Coordinate

WINSTEIN

Fig. 1a.

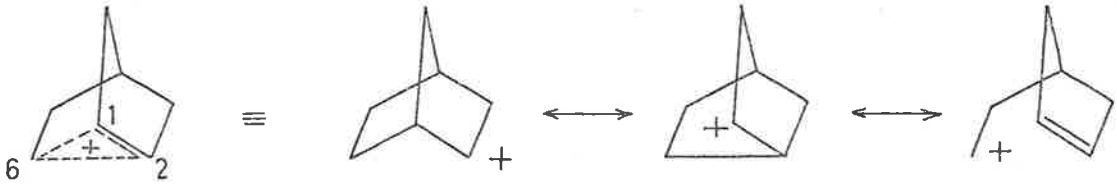


Reaction Coordinate

BROWN

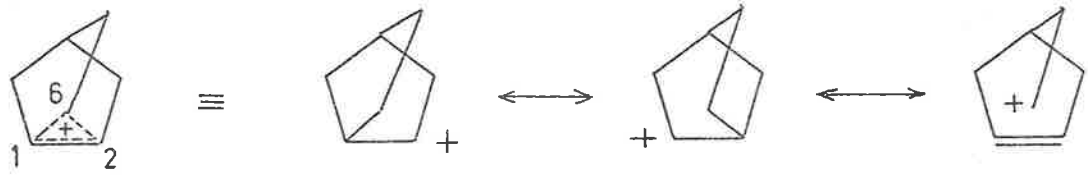
Fig. 1b.

Winstein's non-classical structure (3) can be represented as a resonance hybrid of the classical ions (4a), (4b), and (5a).



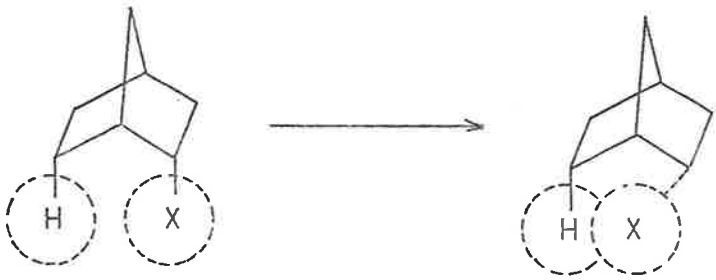
(3) (4a) (4b) (5a)

Hückel,[10] a strong opponent of the non-classical ion concept in the case of the norbornyl cation has objected to this representation because of the contravention of one of the conditions of resonance (i.e. that the positions of the atoms must be the same, or nearly the same, in each of the contributing structures). He has suggested that the non-classical norbornyl cation should be represented by a structure such as (3a), which has a similar geometry to nortricyclene (37). The contributors (4c), (4d), and (5b) to the resonance hybrid (3a) would then conform to the above condition of resonance.



(3a) (4c) (4d) (5b)

As a result of systematic studies,[8,9] Brown has cast doubt on the validity of the results of kinetic studies as being compelling evidence for C_1-C_6 electron pair participation in the solvolysis of norbornyl derivatives. The high solvolysis rates of exo norbornyl derivatives and the high exo to endo rate ratios (i.e. criteria A and B used by Winstein in support of non-classical ion formation) have been interpreted by Brown to mean that the exo derivative solvolyses at a "normal" rate, while the endo derivative solvolyses at an abnormally slow rate.[15,23] It was suggested that such a slow endo rate might result from a steric hindrance to ionisation since the leaving group X in the endo compound (6) has to pass unusually close to the endo hydrogen atoms at C_5 and C_6 in approaching the transition state (7) for ionisation.

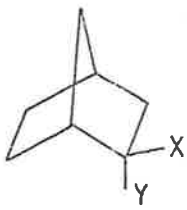


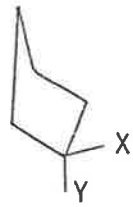
(6) (7)

The concept of steric hindrance to ionisation was proposed in order to account for the low solvolysis rates of endo norbornyl derivatives and hence high exo:endo rate ratios. Brown has also demonstrated that the rate of solvolysis of strained exo-2-norbornyl derivatives is not abnormally high when compared with the corresponding cyclopentyl derivatives (Table 1). It should be noted that criterion A, which led

TABLE 1.

Rate ratios for solvolysis of norbornyl and cyclopentyl derivatives.





Y	X	Solvent	Rate ratio norbornyl/cyclopentyl
H	OB_s *	MeOH	3.9
H	OB_s	EtOH	3.6
H	OB_s	HAc	12.4
CH_3	Cl	EtOH	5.3
CH_3	OPNB /	60% aq. dioxane	4.0
C_6H_5	Cl	EtOH	7.5
C_6H_5	OPNB	60% aq. dioxane	2.6

* OB_s = p-bromobenzenesulphonate

/ OPNB = p-nitrobenzoate

Winstein to postulate that exo norbornyl derivatives solvolyse with C_1-C_6 electron pair participation, was based on the assumption that these compounds solvolysed much faster than the corresponding cyclohexyl derivatives. Brown[20] however, considered that a comparison of the solvolytic behaviour of the exo-2-norbornyl derivatives with the similarly strained cyclopentyl derivatives, would be more valid than comparison with the strain-free cyclohexyl series. This would appear to be borne out by the fact that norbornan-2-one (22) exhibits a carbonyl absorption characteristic of a cyclopentanone rather than a cyclohexanone derivative.

Further evidence in support of the concept of steric hindrance to ionisation has been presented by Brown.[14] It was found that the rates of acetolysis of a series of p-toluenesulphonates decreased, as the steric interaction between adjacent alkyl groups and the leaving group increased (Fig. 2)

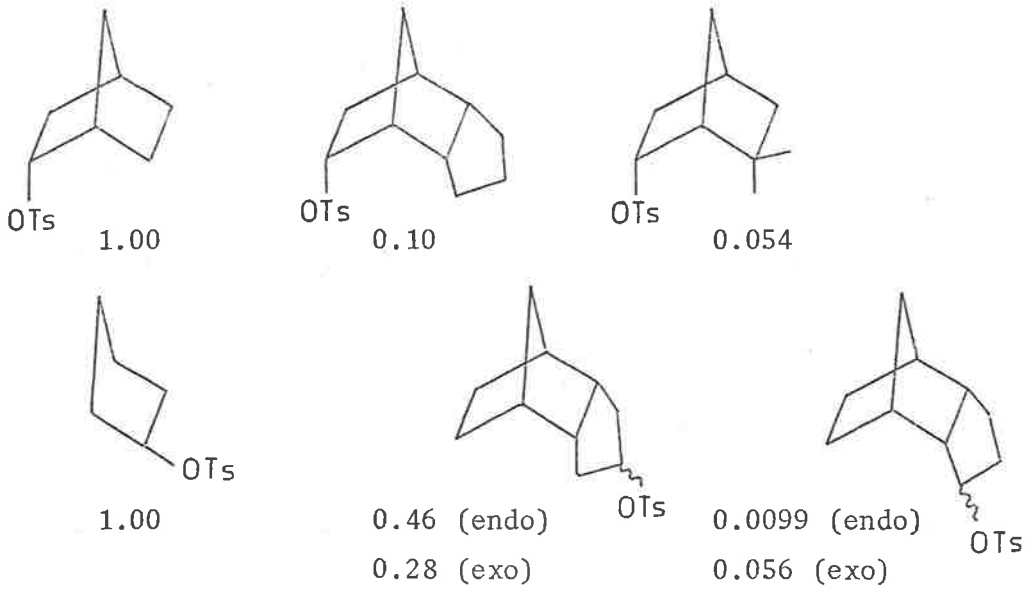
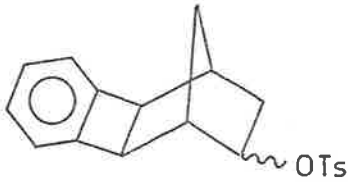
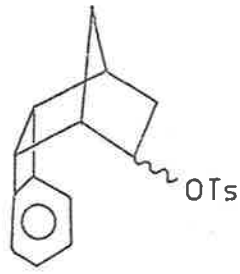


Fig. 2

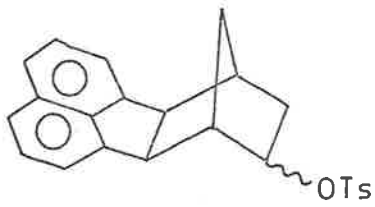
A similar result was observed when exo- and endo-5,6-(o-phenylene)- and -(1,8-naphthylene)-2-norbornyl p-toluenesulphonates (8-11) were solvolysed.[21]



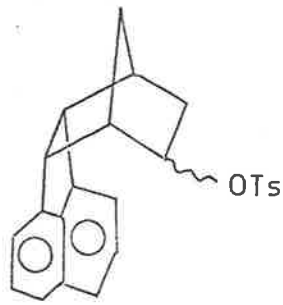
(8 a,b)



(9 a,b)



(10 a,b)



(11 a,b)

a = exo

b = endo

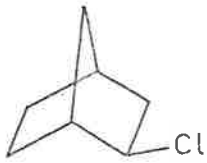
The rates of acetolysis of (8-11) at 75^{o} and 100^{o} are summarised in Table 2. In the cases where steric hindrance to ionisation may have been an important factor i.e. (9b) and (11b), a significant decrease in the rate of acetolysis was observed.

TABLE 2.

Rates of solvolysis in acetic acid.

Substrate	k_{75}^{o} (sec^{-1})	k_{100}^{o}
(8a)	79.5	1429
(8b)	45.8	683
(9a)	2675	
(9b)	1.2	25.0
(10a)	66.5	1250
(10b)	34.3	517
(11a)	385	
(11b)		9.41

It has been pointed out by Brown[20] that since the non-classical norbornyl cation has its positive charge equally distributed over C_1 and C_2, a substituent at either the 1- or 2-position should have an identical effect on the stability of the non-classical ion and a similar effect on the rate of solvolysis. The observed rates of ethanolysis of 1-phenyl-exo-norbornyl chloride (13) and 2-phenyl-exo-norbornyl chloride (14) relative to 2-exo-norbornyl chloride (12) were clearly contrary to this expectation and suggested that the solvolysis of (13) and (14) did not proceed through transition states which closely resembled the non-classical ion (15). Thus solvolysis of 2-phenyl-exo-norbornyl chloride (14) would appear to involve the classical ion (16), especially



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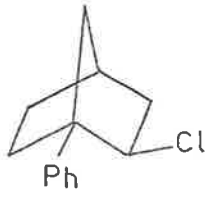

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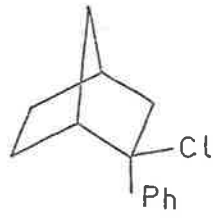
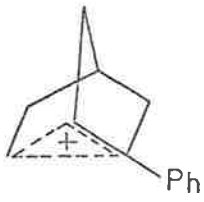


(14)

k_{rel} (25^{o})	1.00	3.9	3.9×10^{7}



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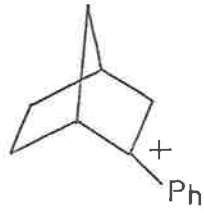
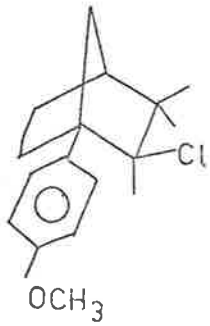


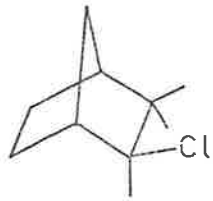
(16)

since it undergoes ethanolysis only 7.5 times faster than 1-phenyl-1-chlorocyclopentane (Table 1).

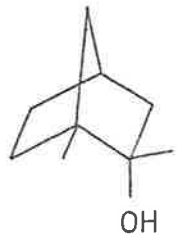
Similar studies by Brown and coworkers[22] on the solvolysis of 1-(p-anisyl)-camphene hydrochloride (17) and the p-nitrobenzoate esters of the epimeric alcohols (19) and (20) indicated that, in the view of the above workers, these tertiary derivatives solvolysed via essentially classical, rather than non-classical ions.



(17)



(18)



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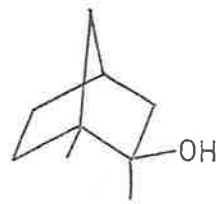


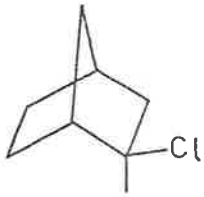
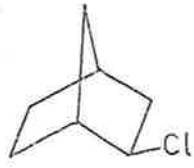
(20)

The presence of the p-anisyl group at C_1 in (17) would have been expected to lead to a rate enhancement if C_1-C_6 electron pair participation occurred during ionisation. However, the rate of ethanolysis of 1-(p-anisyl)-camphene hydrochloride was found to be 0.6 times slower than camphene hydrochloride (18).

A comparison of the effects of methyl and phenyl substituents at C_2 in exo-2-norbornyl derivatives by Brown[23,24] with the corresponding effects in aliphatic and alicyclic systems, has shown that the effects are remarkably constant in all cases and that the effect of substituents in the exo-2-norbornyl series was very similar to the observed substituent effects in the aliphatic and acyclic derivatives (Table 3).

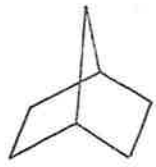
TABLE 3.

Rates of ethanolysis at 25° of R-Cl.

R	rate ratio
t Butyl : iso Propyl	55,000
1-methylcyclopentyl : cyclopentyl	175,000
1-methylcyclohexyl : cyclohexyl	33,000
1-methylcycloheptyl : cycloheptyl	90,000
 : 	63,000

These results would seem to suggest that the solvolytic behaviour of exo-2-norbornyl derivatives is not exceptional and does not require C_1-C_6 electron pair participation during ionisation.

The third criterion C, i.e. exclusive exo substitution, which has been used to rationalise the postulation of non-classical ions has also been questioned by Brown.[8,9,15,16] He has argued that exo substitution in simple norbornyl derivatives, rather than being exceptional, is in fact to be expected. That "substitution should be directed along the less hindered approach to the carbonium ion centre", would appear to be borne out in a number of reactions of norbornyl derivatives. For example, free radical substitutions[25,26] of norbornane (21), reductions with complex metal hydrides, the addition of Grignard reagents and alkylations of norbornan-2-one (22) occur from the exo side.[27,28,29] Oxidative hydroboration (a reaction that is sensitive to steric factors) of norbornene (23) affords 99.5% of the exo-norborneol (24) with only 0.5%



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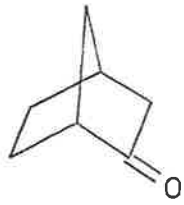

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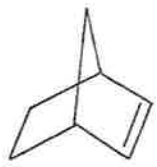

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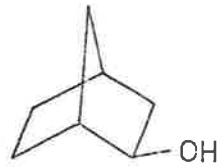


(24)

of the endo isomer.[15] It has also been reported[30] that elimination reactions of exo- and endo-2-norbornyl derivatives involve exclusive

participation of the 3-exo hydrogen atom. Thus exo norbornyl derivatives undergo cis E2 elimination, whereas endo norbornyl derivatives undergo trans E2 elimination.

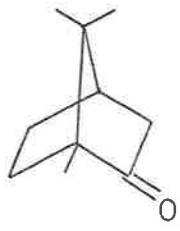
As an alternative to his argument that "substitution should be directed along the less hindered approach to the carbonium ion centre", Brown[15,16] has also suggested that the "windshield wiper effect" may explain the predominance of exo substitution in the norbornyl series. Postulation of the pair of rapidly equilibrating cations (4a) and (4b) as an alternative to the non-classical norbornyl cation (3) led Brown to suggest that the rapid movement of the ethylene bridge between C_1 and C_2 might prevent accumulation of solvent on the endo side and thereby favour exo substitution. Winstein[31] in turn, has questioned this proposal and has pointed out that exclusion of solvent from the endo

(4a) (4b)

side of the molecule would be thermodynamically unsound since desolvation of the classical ion should be associated with a corresponding destabilisation. Winstein also claimed that the rate of

equilibration* would have to be greater than kT/h in absolute rate theory to explain the almost 100% racemic nature of the exo-norbornyl acetate obtained from the solvolysis of exo-norbornyl p-bromobenzene-sulphonate in aqueous acetone.[33]

Brown's argument that the exo side in norbornyl derivatives was the more sterically accessible side of the molecule appeared to break down when applied to norbornyl derivatives possessing bulky 7-syn substituents, e.g. camphor (25) and apocamphor (26). In these cases the endo side of the molecule is less hindered as judged by the results of reductions with complex metal hydrides and the addition of Grignard reagents.[28,34] However, solvolysis of apoisobornyl (27) and isobornyl derivatives (28) results in exclusive exo substitution.[12]



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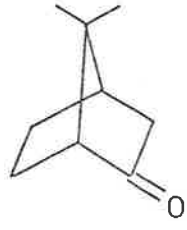

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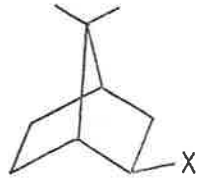

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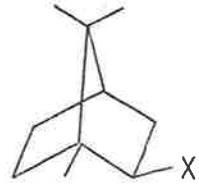

(28)

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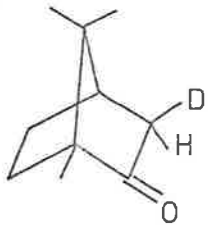
* The estimate of the rate of equilibration was based on the assumption that the rate of 6-2 hydride shift observed for the norbornyl cation in aqueous acetone was the same as for the cation in the n.m.r. solvent, SbF_5-SO_2-SO_2F_2.[32] Brown[8] has since questioned this assumption.

However, the validity of stereochemical results in the postulation of non-classical norbornyl cations has been brought into question by the following observations. Base catalysed deuterium exchange[35] of camphor (25) has been shown to result in exclusive incorporation of deuterium into the 3-exo position (29).



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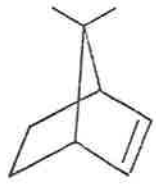

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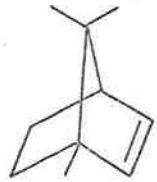
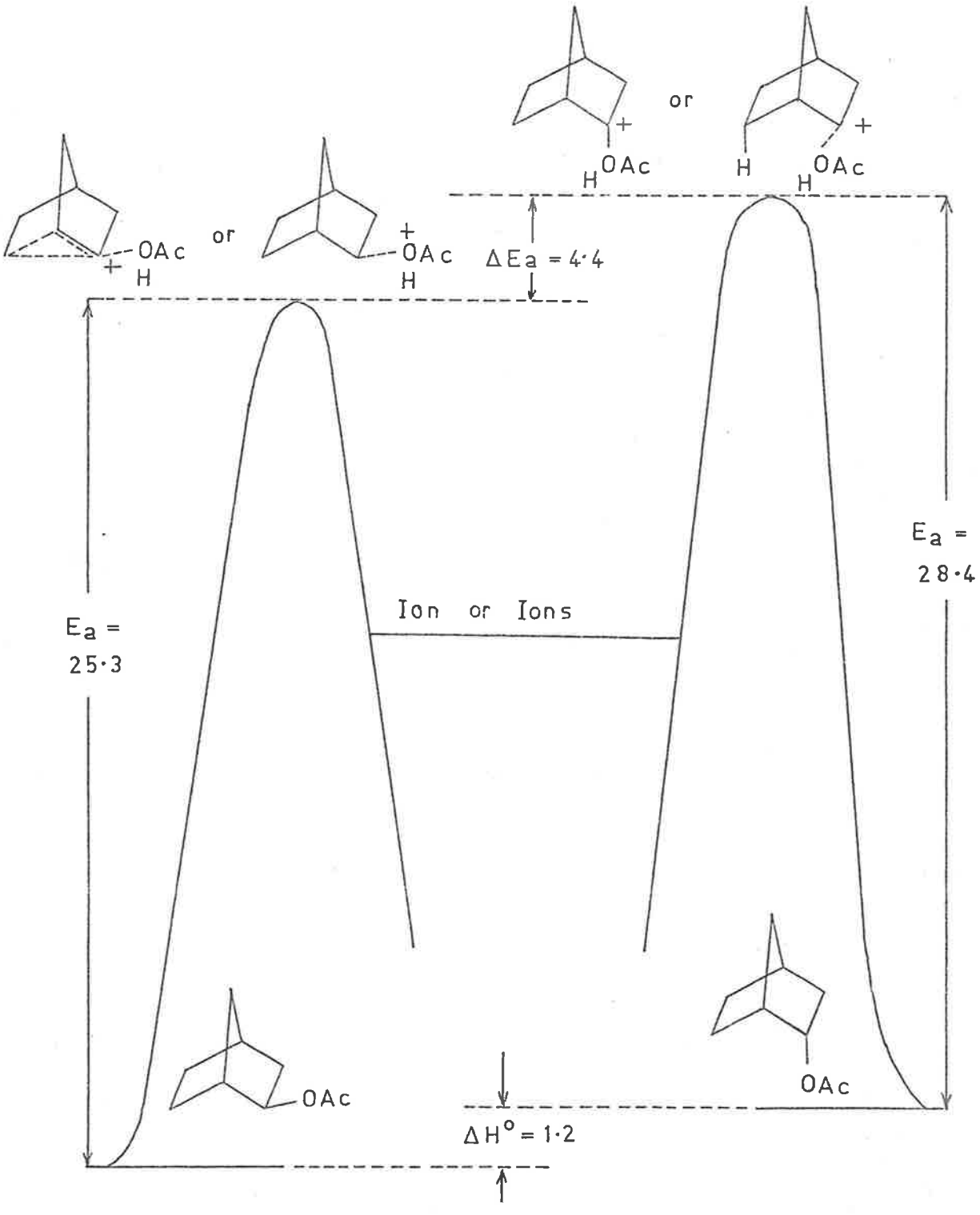


(31)

Oxymercuration[36] of apobornylene (30) and bornylene (31) has been observed to produce exclusively exo products. The observation of almost exclusive exo substitution in norbornyl derivatives bearing bulky 7-syn substituents under conditions where a cationic intermediate is not involved would appear to cast doubts on the validity of stereochemical arguments being used to postulate the intermediacy of non-classical ions.

A further important contribution[8,9,37] has been Brown's interpretation of the Goering-Schewene diagram.[38] Goering and Schewene studied the acid-catalysed acetolysis of exo- and endo-norbornyl acetates. From a study of the rates of racmisation, rates of exchange and the equilibration of the products these workers compiled the now well-known Goering-Schewene diagram (Fig. 3).

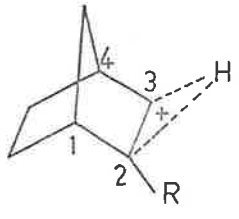


Modified Goering-Schewene Diagram: Acetolysis of exo- and endo-norbornyl acetate.

Fig. 3.

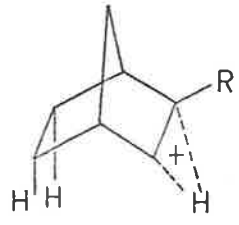
It should be noted that the energy of activation for the ionisation of the exo acetate is 3.2 kcal mole^{-1} lower than that of the endo acetate. The endo acetate also has a higher ground state energy (1.2 kcal mole^{-1}) than the exo derivative. Thus the difference in energy betwee the two transition states becomes 4.4 kcal mole^{-1}. Brown[8,9,37] reasoned that the factor responsible for the difference in energy between the exo and endo transition states must also be responsible for the stereoselectivity leading to the almost exclusive formation of the exo product. Hence the amount of bridging that may or may not be present in the free ion, would not be directly involved in the stereoselectivity of substitution, and the amount of bridging in the exo transition state, or whatever factor is responsible for the difference in transition state energies, would control the exo : endo product distribution.

Another explanation for the stereospecificity of reactions of norbornyl derivatives (e.g. exclusive exo 3,2-shifts, exo substitution and the high exo to endo rate ratios) has been put forward by von Schleyer.[39] He proposed that torsional effects may explain the observed stereospecificity in these reactions. It was suggested that an examination of models of the transition states for both exo (32) and endo (33), 3,2-shifts indicated that the arrangements about the C_1-C_2 and C_3-C_4 bonds in the exo transition state (32) were ideally "skewed". By contrast, in the endo conformation (33), arrangements about the same bonds were almost exactly eclipsed. von Schleyer proposed that the endo transition state was



exo shift

(32)

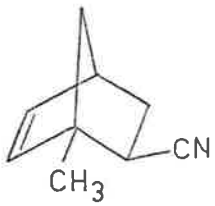


endo

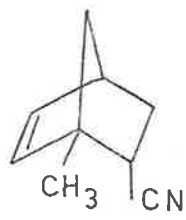
(33)

destabilised by the eclipsing interactions with the bridgehead substituents by up to 6 kcal $mole^{-1}$. The amount of destabilisation of the endo transition state (33) was considered to be more than sufficient to account for the experimentally observed degree of specificity of 3,2-shifts without recourse to either bridging or to non-bonded steric effect arguments. However, independent experimental tests[40,41] have failed to provide confirmatory evidence for its importance. Jindal and Tidwell,[42] in an attempt to evaluate the effect of torsional strain in bicyclic ring systems, studied the base catalysed deuterium exchange reaction of substituted norbornanones and the stereochemistry of the hydroboration of substituted norbornenes. These workers concluded that the effects of torsional strain in the norbornyl series appeared to be either minor, or were obscured by other factors.

In an attempt to evaluate the effect of torsional strain in the bicyclo[2,2,1]heptyl series, Mellor[43] studied the equilibration of various alkyl substituted exo- and endo-2-cyanonorborn-5-enes, e.g. (34) and (35).



(34)

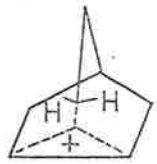


(35)

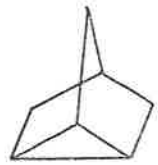
The equilibration of either (34) or (35) in t-butanol containing potassium t-butoxide at 83° afforded a 36 : 64 mixture of the exo and endo isomers (34) and (35) respectively. However, when the methyl substituent was placed at either the 4-, 5-, or 6-positions, equilibration gave an approximately 50 : 50 mixture of exo and endo

isomers. These results were interpreted to mean that torsional effects were important in determining relative ground state energies of epimeric norbornenes and it was suggested that the effect should be greater in transition states where an eclipsing of substituents at C_1 and C_2 was possible.

As well as arguments based on kinetic data and product studies of sovolytic reactions of norbornyl derivatives, attempts have been made to observe the norbornyl cation directly. The direct observation of the norbornyl cation was first reported by Olah and von Schleyer[32,44,45] in 1964. The cation was observed by n.m.r. spectroscopy as its hexafluoroantimonate salt in SbF_5, SbF_5-SO_2, SbF_5-SO_2-SO_2F_2, or SbF_5-FSO_3H-SO_2 solutions. However, this early work failed to positively identify the norbornyl cation as either a set of equilibrating classical cations or a non-classical σ-delocalised cation. Olah[46] recently has reported the study of a number of norbornyl (i.e. 2-norbornyl, 2-methylnorbornyl, 2-ethylnorbornyl, and 2-phenylnorbornyl) cations using ^1H and ^{13}C nuclear magnetic resonance spectroscopy and laser Raman spectroscopy. Examination of the 2-norbornyl cation at -154° in SbF_5-SO_2ClF-SO_2F_2 solution by ^1H and ^{13}C n.m.r. spectroscopy produced spectra which Olah believed were consistent only with a non-classical structure for the cations thus formed. The spectral data was considered to be consistent with a corner protonated nortricyclene [i.e. it contained a penta-coordinated bridging carbon atom in a 3-centre bond formation (36)]. The Raman spectrum of the norbornyl cation was also found to indicate nortricyclene, rather than norbornane-type skeletal symmetry.



(36)

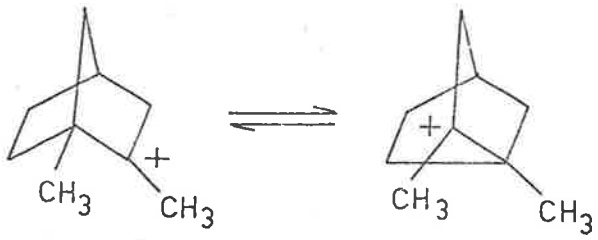


(37)

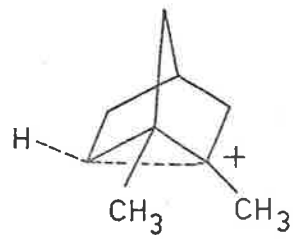
Quenching of the norbornyl cation at -78° with tertiary base (pyridine) gave almost exclusively nortricyclene (37).

Similar studies of the 2-methyl- and 2-ethylnorbornyl cations indicated that these cations showed some 6,2-σ-delocalisation without, however, a nortricyclene-type skeleton. The 2-phenylnorbornyl cation was found to be basically classical in nature, with negligible σ-delocalisation.

Using the same techniques as described above, Olah[47] has also examined the stable, long-lived 1,2-dimethylnorbornyl cation (38). He concluded that the cation was a partially delocalised ion (39),

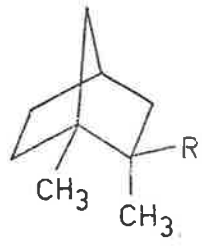


(38a) (38b)



(39)

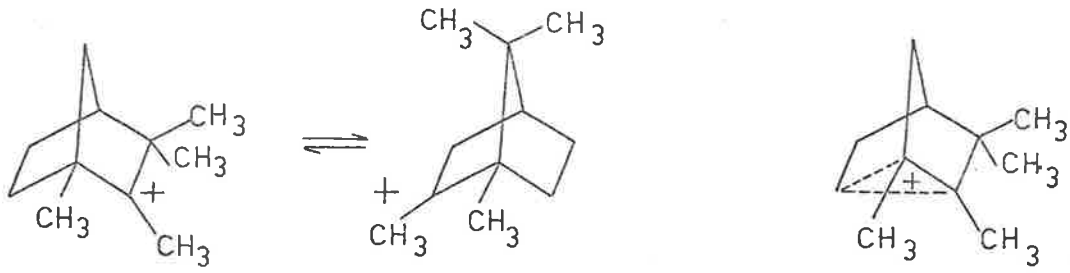
undergoing a rapid 1,2 Wagner-Meerwein shift. It was estimated that the degree of σ-delocalisation in the 1,2-dimethylnorbornyl cation was the same as that found in the 2-methylnorbornyl cation. The conclusions reached by Olah may be subject to some doubt however, because of the comparison of observed chemical shifts to those expected of various "models".



(40)

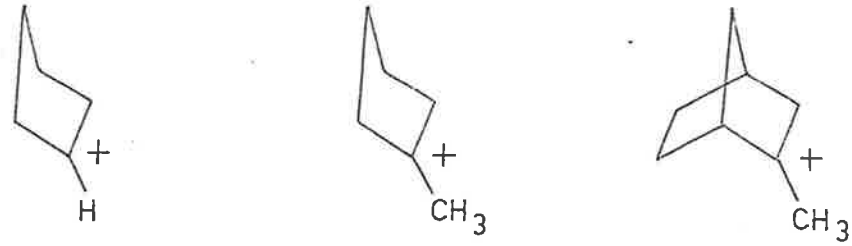
Goering[48,49] has studied the solvolysis of optically active exo derivatives of 1,2-dimethylnorbornane (40), e.g. R = -OPNB, -Cl. In both cases optically active products were detected. The results were interpreted as being direct evidence of the intermediate 1,2-dimethylnorbornyl cation existing as a set of asymmetric, equilibrating classical ions (38a) and (38b). Sorensen[50] also, has presented strong evidence in favour of the 1,2,3,3-tetramethyl-2-norbornyl cation existing as a set of classical, equilibrating cations (41a) and (41b), rather than a symmetrical, bridged intermediate (42).

Olah[51] has also applied the relatively new technique of X-ray photo-electron spectroscopy to an examination of the norbornyl cation. Because of the very short time scale (c. 10^{-16} sec) in the electron



(41a) (41b) (42)

spectroscopic process, definite ionic species may be characterised, regardless of their possible intra- and intermolecular interactions (e.g. Wagner-Meerwein rearrangements, hydride shifts, proton exchange). By comparison of the electronic spectrum of the norbornyl cation, with a series of related model ions [e.g. cyclopentyl (43), methylcyclopentyl (44), and 2-methylnorbornyl (45)] with varying degrees of charge localisation, Olah was able to make an estimation of the charge delocalisation in the norbornyl cation. The electron spectrum of the norbornyl cation, in Olah's view was consistent only with the σ-delocalised non-classical norbornyl cation (36). Hence the electron



(43) (44) (45)

spectroscopic data is in excellent agreement with the results of the proton and carbon-13 magnetic resonance spectra, as well as the Raman spectroscopic data presented earlier by Olah.[46]

That the long-lived norbornyl cation exists as a methylene-bridged, penta-coordinated carbonium ion (36), i.e. a "non-classical" ion in the super-acid medium used in the generation of the stable cation, would appear to be supported by a large amount of spectroscopic evidence. However, even in the unusual super-acid medium, tertiary norbornyl cations have been observed to exist as essentially classical ions. Thus the majority of evidence tends to support the view that the substituted norbornyl cation is classical in nature. In the case of the norbornyl cation itself, whether symmetrical bridging is reached under solvolytic conditions, where solvent capture may compete with σ-delocalisation of the C_1-C_6 bond is still open to question.

2. Oxidative decarboxylation of carboxylic acids with lead tetraacetate.

After Fieser and coworkers[52,53] and Waters[54,55] had shown that aromatic compounds could be C-methylated using lead tetraacetate, Waters[54,55] postulated that free methyl radicals were intermediates in these reactions (Scheme 3).

$$Pb^{IV}(OAc)_4 \rightarrow Pb^{II}(OAc)_2 + 2CH_3\dot{C}O_2$$

$$2CH_3\dot{C}O_2 \rightarrow 2CH_3^{\cdot} + 2CO_2$$

Scheme 3.

Waters[54] also found that a mixture of red lead and anhydrous organic acids decomposed smoothly to form acyloxy radicals and lead II carboxylate. As a follow-up to this work, Kharasch[56] demonstrated that the decomposition of lead tetraacetate gave products similar to those obtained by the decomposition of acetyl peroxide. However, it should be noted that the product ratios varied in the two reactions.

Mosher and Kehr[57] studied the decomposition of a series of carboxylic acids in the presence of lead tetraacetate in acetic acid as solvent. As a result of this study the above workers asserted that lead IV carboxylates decomposed by an ionic mechanism (Scheme 4), in which the intermediate carbonium ions could form both alkenes and acetates. Although unusually high yields of alkenes were formed from the supposed cations, the above workers did not comment on this fact. If acyloxonium ions were important intermediates in the oxidative

decarboxylation of organic acids, the large variations in the rates of decarboxylation which are observed for primary, secondary, and tertiary acids, would appear to be anomalous.

$$Pb^{IV}(OAc)_4 + 4RCO_2H \rightleftarrows Pb^{IV}(RCO_2)_4 + 4\ HOAc$$

$$Pb^{IV}(RCO_2)_4 \rightarrow R\text{-}\underset{\underset{O^-}{|}}{C}{=}O + R\text{-}\underset{\underset{O^+}{|}}{C}{=}O + Pb^{II}(RCO_2)_2$$

$$\downarrow H^+ \qquad \downarrow$$

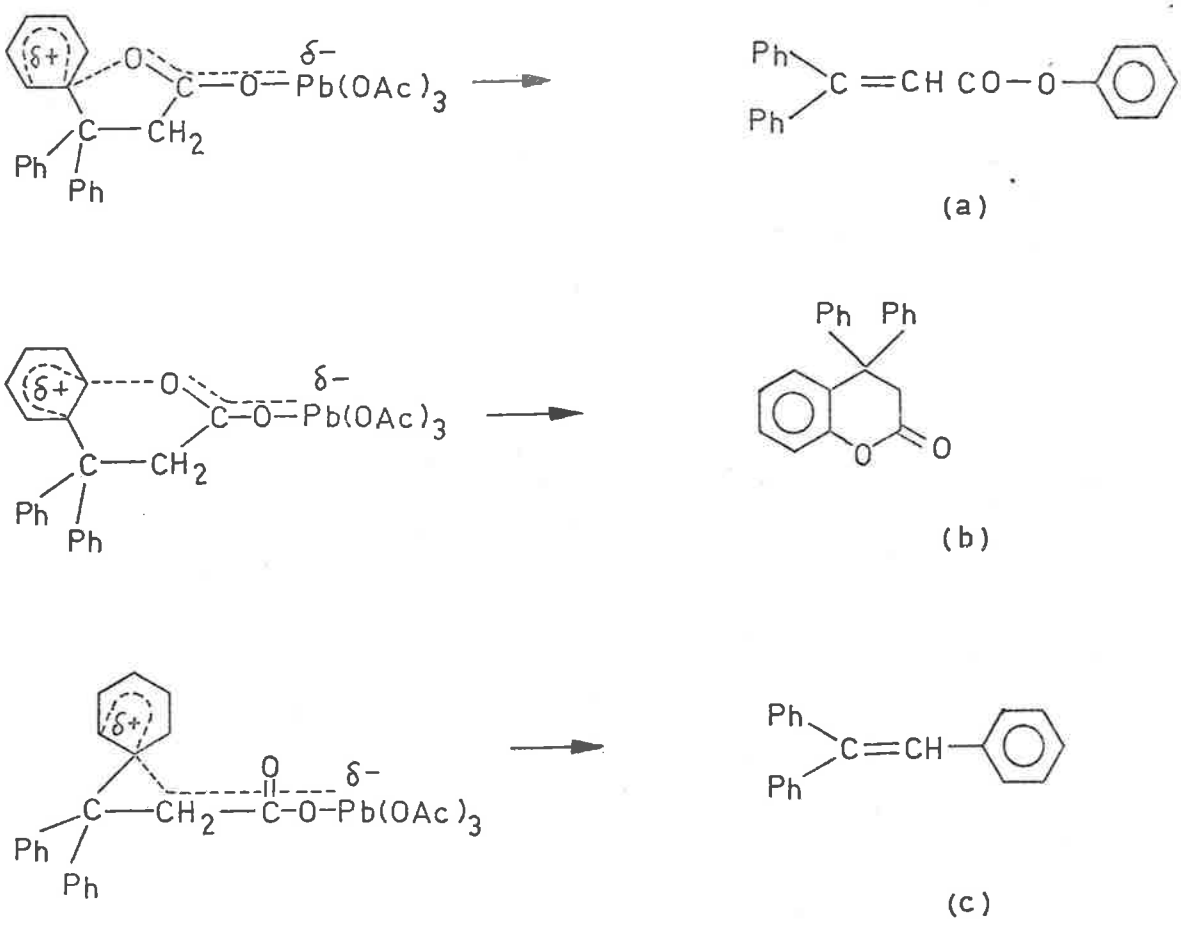
$$R\text{-}CO_2H \qquad R^+ + CO_2$$

Scheme 4.

In 1964, Starnes[58] observed products arising from rearrangement (a), cyclisation (b), and decarboxylation (c) in the reaction of 3,3,3-triphenylpropionic acid with lead tetraacetate (Scheme 5). Starnes suggested that free acyloxy radicals were not intermediates in the reaction and he postulated a concerted homolytic or heterolytic process with neighbouring group participation.

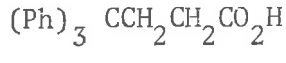
More recently, Starnes[59] has studied the oxidative decarboxylation of 4,4,4-triphenylbutyric acid (46). When the above acid was treated with lead tetraacetate in the absence of oxygen, the only product formed was the substituted indane (47). A similar treatment of (46) in the presence of oxygen gave the cyclic ether (48) as the only identifiable product. It was suggested that the 3,3,3-triphenylpropyl radical (49) was the primary intermediate in the reaction and that anchimeric assistance due to phenyl group participation was not

involved.



Scheme 5.

Davies and Waring have studied the reactions of 2'-substituted biphenyl-2-carboxylic acids[60] (50, X=H, CO_2H, NO_2, Cl, OCH_3, or CO_2CH_3) and p-substituted 5-aryl pentanoic acids[61] (51, X=H, NO_2) with lead tetraacetate in benzene. In the case of (50), the major product was



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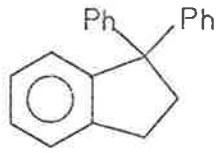

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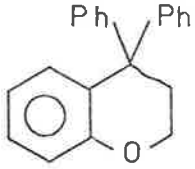

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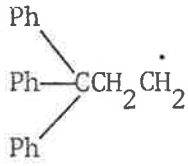


(49)

found to be 3,4-benzocoumarin (52), while substituted 1,2,3,4-tetrahydronaphthalene derivatives (53) were formed when p-substituted 5-aryl pentanoic acid derivatives (51) were treated under the same conditions. In each case, intramolecular cyclisation of free-radical intermediaces was proposed to account for the observed products. Decomposition of (50) were thought to involve an acyloxy radical (54) and in the decarboxylation of (51), the arylalkyl radical (55) was proposed as an intermediate.

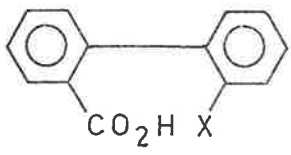
In recent years, Kochi and coworkers[62-66] have presented considerable evidence in support of a free-radical chain process (Scheme 6), in the oxidative decarboxylation of carboxylic acids by lead tetra-acetate. The reactions of primary,[62] secondary,[62] tertiary,[64] and α-arylakyl[64] carboxylic acids with lead tetraacetate were all found to exhibit the following diagnostic tests for the presence of free-radical intermediates:

(1) inhibition of the reaction by oxygen;

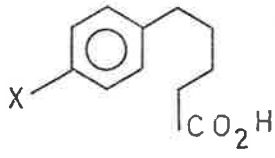
(2) scavenging of the free radicals by butadiene;

(3) similarity of the thermally and photochemically induced reactions, and high quantum yield of the photochemical reaction;

(4) detection by electron spin resonance spectroscopy.



(50)



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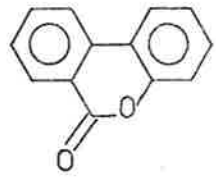

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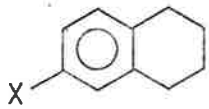

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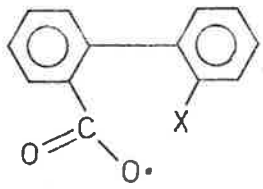
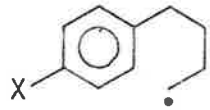


(54)



(55)

A summary of Kochi's suggested mechanism is shown in Scheme 6 and it is discussed in more detail following.

$$Pb^{IV}(OAc)_4 + nRCO_2H \rightleftarrows Pb^{IV}(OAc)_{4-n}(RCO_2)_n + nHOAc \quad (1)$$

$$Pb^{IV}(OAc)_{4-n}(RCO_2)_n \rightarrow Pb^{III}(OAc)_{4-n}(RCO_2)_{n-1} + \dot{R} + CO_2 \quad (2)$$

$$Pb^{III}(OAc)_{4-n}(RCO_2)_{n-1} \rightarrow Pb^{II}(OAc)_{4-n}(RCO_2)_{n-2} + \dot{R} + CO_2 \quad (3)$$

$$Pb^{IV} + R^{\cdot} \rightarrow Pb^{III} + R^{+} \quad (4)$$

$$Pb^{III} + R^{\cdot} \rightarrow Pb^{II} + R^{+} \quad (5)$$

$$Cu^{II} + R^{\cdot} \rightarrow Cu^{I} + R^{+} \quad (6)$$

$$Cu^{I} + Pb^{IV}/Pb^{III} \rightarrow Cu^{II} + Pb^{III}/Pb^{II} \quad (7)$$

$$R^{\cdot} + HS \rightarrow R\text{-}H + S^{\cdot} \quad (8)$$

Scheme 6.

Initiation of the reaction (equation 2) is dependent upon homolysis of the lead IV carboxylate to give a lead III carboxylate and either an acyloxy radical or an alkyl radical and carbon dioxide. Pyridine and nucleophiles (e.g. acetate, halide, cyanide, and thiocyanate anions) have been shown to labilise the lead IV carboxylate and markedly increase the rate of decarboxylation. It should be noted that the rate of decarboxylation is dependent on the stability of the radical generated.

i.e. CH_3 < primary < secondary < tertiary

Hence competition by decarboxylation of acetic acid is generally unimportant in these reactions.

The propagation of the free-radical chain reaction (equation 3)

is achieved by decomposition of the hypothetical lead III carboxylate, which, as yet has not been detected by electron spin resonance spectroscopy.[62,64,65] An analagous process has been reported by Wang and coworkers,[67] in which the triethyl lead IV cation was reduced with one electron reductants to a proposed lead III species, which rapidly fragmented to lead II and ethyl radicals. A similar tin III intermediate has also been postulated for radical chain reductions with trialkyl tin hydrides.[68]

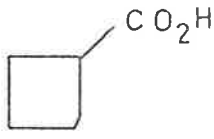
The ease of oxidation of the generated free radicals (tertiary > secondary > primary) by lead IV and lead III (equations 4 and 5) follows the ionisation potential of these radicals. In the case of primary and secondary radicals, reactions such as hydrogen abstraction may compete effectively with the oxidation reaction. On the addition of cupric acetate to the reactions, oxidation by lead IV and lead III (equations 4 and 5) is superseded by copper (equation 6), and the products obtained are similar to those derived from the copper catalysed decomposition of peroxides. In the case of tertiary acids, the addition of cupric acetate has little effect on the product ratios, indicating that lead salts are competing effectively with cupric salts for the oxidation of tertiary radicals.

Termination of the radical chain process occurs either by oxidation of the alkyl radical by a lead III species (equation 5) or by removal of the radical by a reaction such as hydrogen abstraction from the solvent (equation 8).

The intermediacy of free radicals in the decarboxylation of

primary and secondary acids has also been demonstrated by Forshult[69] and Heusler[70] using electron spin resonance spectroscopy.

Kochi[66] has studied the effect of solvent on the oxidation of alkyl radicals generated by the treatment of the corresponding carboxylic acid with lead tetraacetate, both in the presence and absence of copper II salts. In particular, treatment of cyclobutanecarboxylic acid (56), under the conditions described above, afforded products of elimination (e.g. olefins) and substitution (e.g. alkyl esters).



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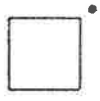
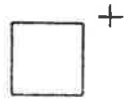


(57)

(58)



(59)

In the case of cyclobutanecarboxylic acid, some of the results obtained by Kochi are summarised in Table 4. It was found that when lead IV was the only oxidant present, the product distribution was not markedly altered by changes in solvent, and products of substitution (e.g. acetates) predominated. However, the oxidation of cyclobutyl radicals in the presence of copper II acetate was found to be highly dependent on the solvent employed. In most solvents, in the presence of copper II, oxidation of cyclobutyl radicals (57) to cyclobutene (58) appeared to be the preferred mode of reaction, despite the thermodynamic instability of the olefin (58). It was only in acetonitrile (and its homologues) that

copper II salts promoted products arising from substitution reactions. In this case the products were similar to those obtained when lead IV was the only oxidant present.

TABLE 4.

Oxidative decarboxylation of cyclobutanecarboxylic acid.

Solvent*	Oxidant	Products (mole %)		
				Acetates
benzene	Pb^{IV}	2	5	41
/DMSO	Pb^{IV}	0.2	2	19
CH_3CN	Pb^{IV}	1	16	49
benzene	Pb^{IV} ; Cu^{II}	78	0	7
DMSO	Pb^{IV} ; Cu^{II}	34	2	7
CH_3CN	Pb^{IV} ; Cu^{II}	3	8	58

* all containing 10% (V/V) acetic acid.

/ i.e. dimethylsulphoxide.

The unique effect of acetonitrile on the course of the reaction was attributed by Kochi,[66] to a specific coordination of the solvent with the copper II oxidant (equation 9). Because the formation of

$$Cu^{II}(OAc)_2 + nCH_3CN \rightarrow Cu(NC\text{-}CH_3)_n(OAc)_2 \quad (n=1\text{-}6) \qquad (9)$$

cyclobutene (58) from reactions of cyclobutyl radicals or cyclobutyl cation (e.g. from solvolysis of cyclobutyl derivatives[71]) is rarely observed, Kochi asserted that the cyclobutyl cation (59) was not an intermediate in cyclobutene (58) formation. Instead he postulated that the oxidative elimination of alkyl radicals by copper II involved a specific intramolecular removal of the β-hydrogen, with a synchronous electron transfer process. It was further suggested that part of the driving force for such a process may have been provided by synergic bonding between the incipient olefinic bond and copper I.[72] Kochi proposed that the oxidative elimination of alkyl radicals by copper II complexes involved copper alkyl species; the transition state, as depicted by Kochi, is shown below (Fig. 4). Furthermore, Kochi proposed that the formation of substitution

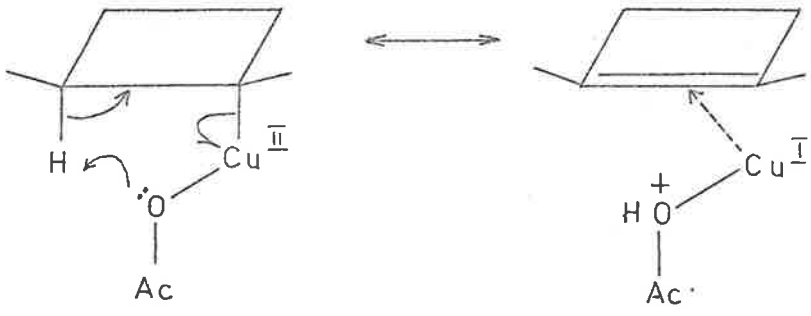
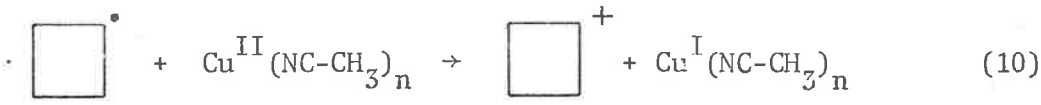


Fig. 4

products, in the presence of lead IV or $Cu^{II}(NC\text{-}CH_3)_n$ involved the intermediacy of the cyclobutyl cation (59), since the products observed were extensively rearranged.

The difference between copper II acetate and copper II acetonitrile complexes was proposed[66] to be due (at least in part) to the higher oxidation potential of the latter. Thus a greater driving force for electron transfer (equation 10) may be derived from the formation of the more stable copper I acetonitrile complex.[73] It was also postulated that the competing elimination reaction was minimised by (i) displacement of the acetato ligands in the copper II complex by acetonitrile, and (ii) reduction of the synergic bonding to the alkene by the presence of acetonitrile ligands in the complex.[72b]



(10)

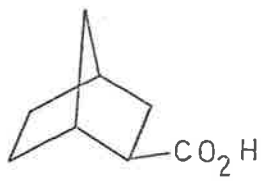
The dichotomy of mechanism observed in the oxidation of the cyclobutyl radical (57) by copper II is not unique and has also been observed for the allylcarbinyl,[66] α-phenylalkyl,[74] and 2-p-methoxyphenyl ethyl[75] radicals.

In a very recent report[76] Kochi has demonstrated that the course of reaction on oxidation of alkyl radicals (generated by the decomposition of the corresponding peresters) by copper II complexes may be dramatically altered by the addition of certain salts. For example, oxidation of the cyclobutyl radical by copper II acetate in most solvents (excluding acetonitrile) proceeds via an oxidative elimination process to give cyclobutene (58).[66] However, on the addition of lithium perchlorate, products of oxidative substitution were mainly formed. A similar result was observed when the acetato ligand was replaced by

trifluoromethanesulphonate.

Also of particular interest is the observation that in certain systems (e.g. norbornyl and substituted norbornyl), the oxidative decarboxylation of carboxylic acids produces no products that can be directly attributed to free radical intermediates.

Corey and Casanova[77] found that optically active exo- or endo-2-carboxynorbornane (60) or (61), underwent conversion to predominantly exo-norbornyl acetate (62) upon treatment with lead tetraacetate and pyridine in a suitable solvent. The acetate from the exo acid was essentially the pure exo acetate, while the acetate from the endo acid contained c. 3% of the endo acetate. The exo acetate was formed with 43% net retention of optical activity in benzene, and with 33% retention in the more polar acetonitrile as solvent. Although no decision could be made as to whether the initial decarboxylation was homolytic or heterolytic in nature, it was concluded that, the acetates were derived from a cationic intermediate which was largely unsymmetrical, i.e. the classical norbornyl cation (4a).



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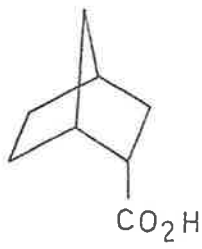

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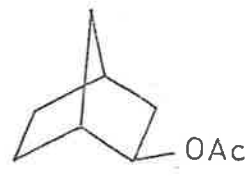
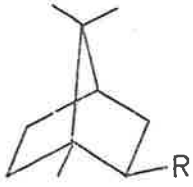
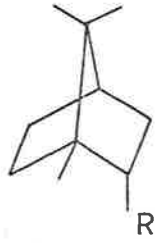


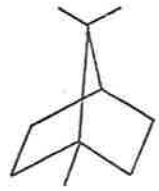
(62)

As a result of the above work, Gream and Wege,[78] in a preliminary

study, examined the oxidative decarboxylation of exo- and endo-2-carboxybornane (85) and (86), using similar conditions to those employed by Corey.[77] It was found that treatment of either acid with 1.25 equivalents of lead tetraacetate in benzene containing pyridine gave the same products in the same proportions (Table 5). These workers could detect no products [e.g. bornane (65)] which were derived from free radical precursors. They concluded that if the initial step was homolytic in nature, then the intermediate bornyl radical (66) was oxidised extremely rapidly.

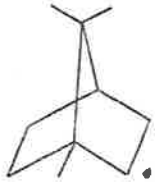


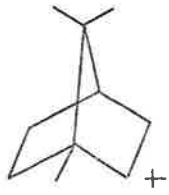


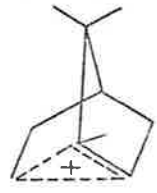


(63, R = $OCOCH_3$) (64, R = $OCOCH_3$) (65)

(85, R = CO_2H) (86, R = CO_2H)







(66) (67) (68)

Also of interest was that the ratio of bornyl (64) to isobornyl (63) acetates was 32 : 68, for both the exo and endo acids. This was assumed to be due to the formation of a common, product determining intermediate during the oxidative decarboxylation. Bornyl acetate (64) was considered to be derived from the classical bornyl cation (67), by

the addition of a nucleophile or transfer of a ligand, to the less hindered endo side of the cation. However, if the bornyl cation was the only intermediate present, a much higher ratio (c. 9 : 1) of bornyl : isobornyl acetate may have been expected, since the 7-syn methyl group causes the exo side of the molecule to be the more hindered. Hence the above workers concluded that the initially formed classical cation (67) was largely converted into the non-classical camphenehydro-isobornyl cation (68).

TABLE 5.

Composition of products of the oxidative decarboxylation of exo or endo-2-carboxybornane.

Product	Yield (%)
Tricyclene	2
Camphene	53-57
8-Methylcamphene*	3-4
Isobornyl acetate	11-13
Bornyl acetate	5-6
Camphene hydrate acetate	9
Acetates A, B, and C*	12-14

* These were shown to be secondary products formed from camphene by the action of lead tetraacetate.

Soon after the present investigation was initiated a study of

the cupric ion oxidation of a series of alkyl radicals (generated by oxidative decarboxylation of the corresponding carboxylic acids) was undertaken by Dr. Cross[79] in this department. For convenience, the results of his work, where relevant to those of the present work, will be incorporated into the Results and Discussion section of this thesis.

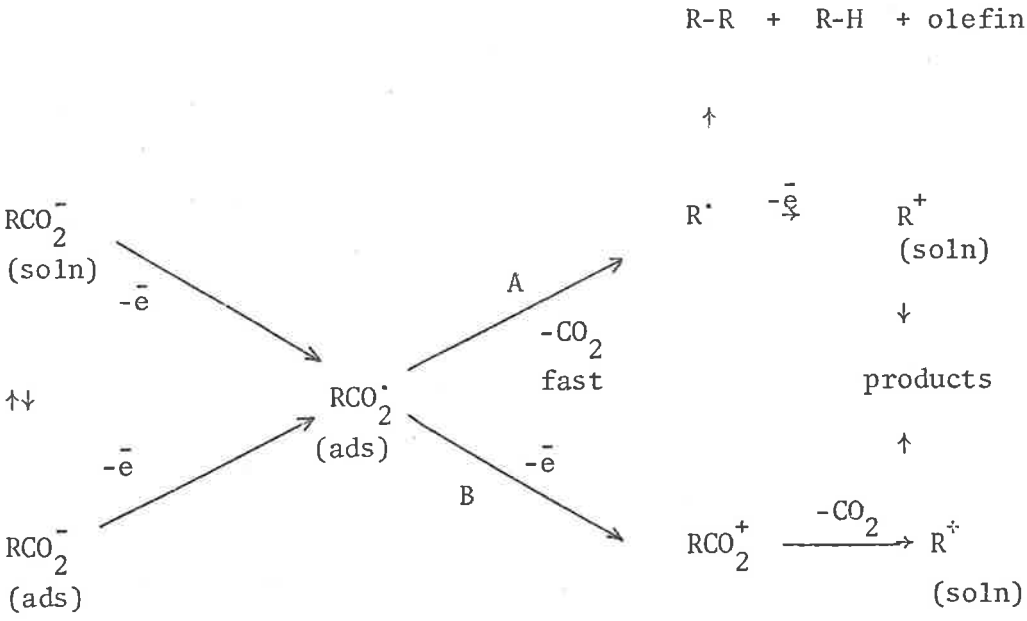
3. Anodic oxidation of carboxylic acids.

The Kolbe electrolysis of carboxylic acids has been known for many years. In his original study, Kolbe[80] suggested that the formation of a symmetrical hydrocarbon on electrolysis of the carboxylate anion occurred via the following process:

$$2RCO_2^- \rightarrow R\text{-}R + 2CO_2 + 2\bar{e}$$

The development of the reaction and its applications have been extensively reviewed.[81-90] It has also been observed that as R is changed from a primary, to a secondary, to a tertiary alkyl group, a number of side reactions become increasingly evident. The formation of olefins (more than can be attributed to disproportionation of the alkyl radical, R$^{\cdot}$) has been observed. Esters, alcohols (in aqueous solutions), and ethers (in alcoholic solutions), often rearranged, may be formed during the electrolytic process. Treatment of α-amino, α-hydroxy, and α-halo carboxylic acids may produce aldehydes and ketones.[90] The addition of some salts (e.g. sodium bicarbonate or sodium persulphate) has been found to promote the formation of olefins and alcohols (or ethers) at the expense of the dimerisation product. This is known as the Hofer-Moest reaction.[91]

The mechanism of the Kolbe reaction has been the subject of much research.[85,92-94] Several mechanisms, most of them radical in nature, have been proposed for the reaction. A summary of the possible reaction pathways for the Kolbe reaction is depicted in Scheme 7.



Scheme 7.

The mechanistic starting point is the acyloxy radical formed either by a one electron oxidation at the anode or in aqueous solution, involving oxidation by peroxide, which may be formed by the anodic oxidation of water.

$$2H_2O \rightarrow H_2O_2 + 2H^+ + 2\bar{e}$$

The acyloxy radical may dimerise to give the acyl peroxide or couple with a hydroxyl radical to give a peracid. These products may, in turn, decompose to produce radicals, esters, and so forth. If coupling does not occur, the acyloxy radical may lose carbon dioxide to produce the alkyl radical (i.e. route A, Scheme 7) which may dimerise to give the Kolbe product, i.e. R-R, or couple with an acyloxy or hydroxyl radical

to give an ester or an alcohol. The other possible reaction course open to the alkyl radical is a disproportionation reaction to give equal amounts of alkane and olefin.

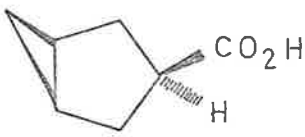
Criticism of the above mechanistic approach has been put forward on the basis that alkyl acyloxy radicals (but not aryl acyloxy radicals) have very short lifetimes (c. 10^{-9} sec)[95,96] and that they might not exist long enough to undergo coupling to any appreciable extent. However, this argument is based on the assumption that radicals generated (and possibly adsorbed) at the electrode surface, may be compared with radicals produced in homogeneous solution. This assumption has been questioned[97,98] and in fact it may be that an adsorbed acyloxy radical has a much longer lifetime than a free acyloxy radical.

The fact that although the normal Kolbe dimer is never rearranged, while the abnormal Kolbe products (e.g. alcohols and esters) often are, would appear to cast doubts on a strictly radical interpretation of the Kolbe reaction. Normally radicals do not undergo 1,2-hydrogen or 1,2-alkyl shifts.[99,100] Although it may be argued that the electrode surface may facilitate such shifts, the absence of rearrangement in the Kolbe dimer would render this an unlikely proposition.

The most likely explanation for the formation of rearranged products is that further oxidation of the alkyl radical may occur at the electrode surface to form the corresponding carbonium ion. The presence of cationic intermediates would then readily explain the formation of esters, alcohols, and rearranged products. Walling[101] was apparently the first to suggest that carbonium ion intermediates, as

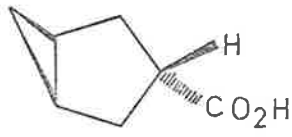
well as radicals were involved in the mechanism of the anodic oxidation reaction. Since then many workers have presented evidence in support of the carbonium ion postulate.[102]

An alternative to the mechanistic pathway depicted in Scheme 7, route A involves the transfer of a second electron from the adsorbed acyloxy radical to form an acyloxonium ion (Scheme 7, route B). Gassman[103] has postulated acyloxonium ions as possible intermediates in the anodic oxidation of cis and trans-3-carboxybicyclo[3,1,0]hexane, i.e. (69) and (70) respectively, although the available experimental data did not allow a definite decision as to whether or not acyloxonium ions were involved. In contrast, Skell[104] has suggested that acyloxonium ions are not intermediates in the anodic oxidation of alkyl carboxylates.



cis

(69)

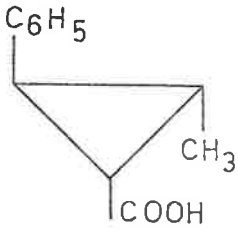


trans

(70)

Shono and coworkers[105] have investigated the stereochemistry of ring opening in the anodic oxidation of cyclopropyl carboxylic acids. The anodic oxidation of the acids (71), (72), (73), and (74) was studied using carbon electrodes in methanolic sodium methoxide at -30^{o} to -40^{o}. The experimental results indicated that concerted, stereospecific ring opening of the cyclopropane ring had occurred. Since cyclopropyl

radicals have been shown not to retain their stereoconfiguration and not to yield ring opened products at low temperatures,[106] and that cyclopropyl cations may give non-stereospecific allylic products,[107] these two species were considered as unlikely intermediates in the anodic oxidation of the acids (71), (72), (73), and (74). However, it was considered that the loss of carbon dioxide from an intermediate acyloxonium ion, would result in concerted opening of the cyclopropane ring yielding allylic products in a stereospecific manner. The possibility that stereospecific adsorption of the cyclopropyl radical to the electrode surface had occurred was considered, but this process had not been previously observed.[108] Hence, at least in the case of cyclopropyl carboxylic acids, the intermediacy of acyloxonium ions appeared to be a possibility.



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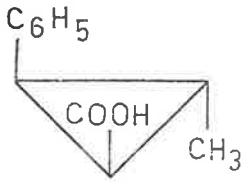

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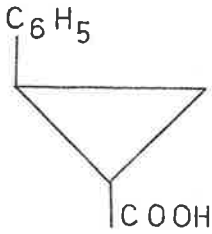
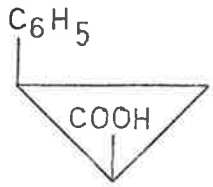


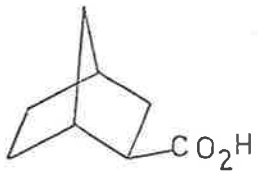
(73)



(74)

The postulation of a radical precursor to the cation in anodic oxidation does not necessarily require that epimeric carboxylic acids give the same products in the same proportions. The stereochemistry of the radical may be determined by such effects as adsorption on the electrode surface or characteristics of the electrolyte-electrode interface.

The experimental evidence available does not readily allow an assessment as to whether or not stereochemical control is maintained. The anodic oxidation of exo- and endo-2-carboxynorbornane (60) and (61) respectively gave identical product mixtures.[109] Similarly exo- and endo-2-carboxybicyclo[3,2,1]octane (75a) and (75b) showed little or no difference in product distributions after anodic oxidation.[110] However, electrolysis of cis- or trans-3-carboxybicyclo[3,1,0]hexane, (69) or (70), did not give identical product mixtures, although the differences were small.[103] Hence it would appear that in some, but not all cases, some degree of stereochemical control is maintained in the anodic oxidation of epimeric carboxylic acids.



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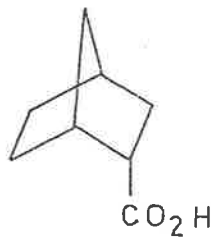

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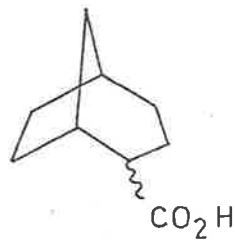


(75a,b)

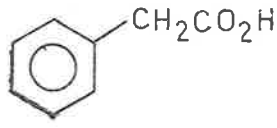
a = exo

b = endo

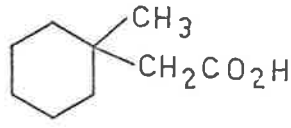
In some cases, the nature of the electrode has been found to have a dramatic effect on the course of the anodic oxidation of carboxylic acids. The change in product composition in the Kolbe reaction that could result from substituting a carbon anode for the usual platinum electrode was first reported by Koehl.[111] The electrolysis of acetic acid at platinum electrodes produced ethane and carbon dioxide, while

electrolysis at carbon electrodes yielded methyl acetate almost exclusively. The results were rationalised by assuming that the predominant reaction mode on platinum was a one-electron transfer to give a free radical intermediate, and on carbon, the preferred reaction path was an overall two-electron transfer to give a cationic intermediate.

A comparison of the anodic oxidation reactions of phenylacetic acid (76) and 1-methylcyclohexane acetic acid (77) at platinum and carbon electrodes was made by Ross and Finkelstein.[112] At platinum, products arising from both free radical and cationic intermediates were observed, with the products arising from free radical precursors predominating. However, at carbon, almost all the products were considered to result from the generation of carbonium ions at the anode. It was suggested that the ability of a carbon anode to promote the generation of cations was due to the presence, within carbon, of numerous paramagnetic centres[113] which were capable of binding anodically generated radicals, impeding their desorption and hence promoting a second electron transfer.



(76)

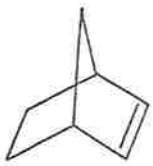


(77)

That foreign anions can alter the mechanism of the anodic oxidation process has been demonstrated by Coleman, Utley, and Weedon.[114]

It was found that the addition of only 1.0% sodium perchlorate caused the electrolysis of sodium phenylacetate to switch over completely to a cationic mechanism.

Analysis, and therefore rationalisation of products from anodic oxidation reactions may be complicated by secondary reaction of the products under the conditions of the electrolysis. Hydrocarbons may be oxidised at platinum electrodes.[115] The dimethoxylation of some olefins by electrolysis has also been observed.[116] For example, reaction of norbornene (23) at platinum electrodes in methanolic sodium methoxide produces mainly exo-syn-2,7-dimethoxynorbornane (78) and some exo-2-methoxynorbornane (79).



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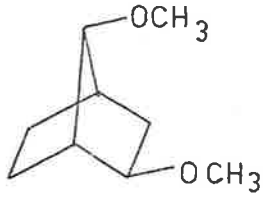

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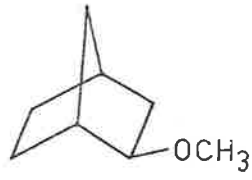


(79)

Primary alcohols may react at the anode, presumably through the carboxylic acid, to give products of the nor-radical or nor-carbonium ion. As an example, the results of the electrolysis of 1-pentanol are shown in Table 6.[117]

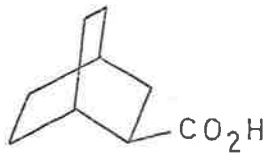
The oxidation of secondary alcohols to ketones may become an important reaction if the alcohols are soluble in the solution being electrolysed. The possibility that ketones may be formed from the

TABLE 6.

Electrolysis of 1-pentanol in 20% aqueous potassium hydroxide solution.

n-butane	32%
1-butene	50
trans-2-butene	9
cis-2-butene	8

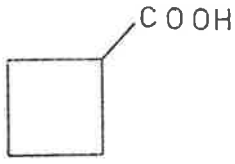
reaction between alkyl radicals and oxygen has also been investigated.[110] In a study of the electrolysis of 2-carboxybicyclo[2,2,2]octane (80) and endo-2-carboxybicyclo[3,2,1]octane (75b) in aqueous solution, Pleyps[110] observed both alcoholic and ketonic products. However, the ketones obtained were shown not to be derived from the alcoholic products. It was also noted that as the base concentration was increased, the amount of ketone produced also increased (from 10% at pH 7 to 90% at a concentration of 6.6N). Since at higher base concentrations in water, greater amounts of oxygen are evolved, it was suggested that reaction of the alkyl radical with oxygen was likely to be a significant reaction. The fact that ketones were not formed in non-aqueous solvents would appear to support this hypothesis.



(80)

One of the most important aspects of carbonium ion chemistry has been the recognition that the properties of the cation are dependent on its mode of generation. Thus, cations generated by deamination or deoxidation have been found to be highly energetic, reactive species which appear to be poorly solvated. On the other hand, cations generated by solvolytic processes seem to be less energetic, better solvated, and more selective in their subsequent reactions. With the demonstration that cations are involved in the anodic oxidation of carboxylic acids, it is then of particular interest to determine whether these cations have properties which resemble those observed for cations generated by deamination, deoxidation, or solvolysis.

Keating and Skell[118] found that the product distributions from each of cyclobutanecarboxylic acid (56), cyclopropaneacetic acid (81), and allylacetic acid (82), on oxidation at platinum electrodes, were very similar to those formed by deamination of the corresponding amines. Reichenbacher and Skell[119] generated the 3,3-dimethyl-1-butyl cation by anodic oxidation and deoxidation and found that the cations produced in each case were very similar. Koehl[111] has suggested that cations generated at carbon electrodes are more energetic than those produced in solution by deamination or deoxidation. The anodic oxidation of cycloalkyl carboxylic acids has been reported by Traynham[102,120] to produce high energy, poorly solvated carbonium ions. On the other hand, Gassman[103] found that when either cis- and or trans-3-carboxybicyclo-[3,1,0]hexane (69) or (70), was electrolysed at platinum electrodes, the product mixtures obtained were quite different from those produced



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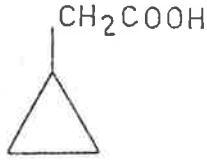

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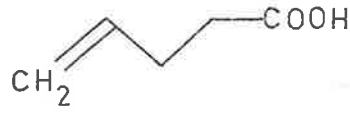
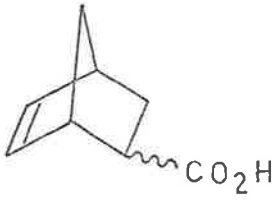


(82)

by deamination and solvolysis.

That relatively stable cations, similar to those generated by solvolytic methods, may be produced on anodic oxidation of carboxylic acids, has been demonstrated by Corey and coworkers.[109] Anodic oxidation of exo- or endo-2-carboxynorbornane (60) or (61), in methanol at platinum electrodes produced exo-norbornyl methyl ether (79) in 35-40% yield and only a very small amount of norbornanone (22); no endo-norbornyl methyl ether could be detected in the reaction. When optically active endo acid (61) was used, the resulting exo methyl ether (79) was racemic. Similarly, electrolysis of either exo- or endo-2-carboxynorborn-5-ene (83) afforded only 3-methoxynortricyclene (84).



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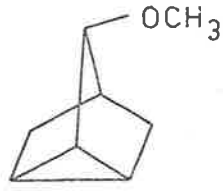


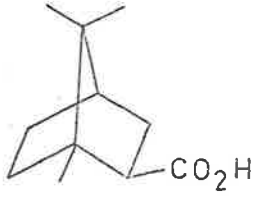
(84)

The products observed in the above reactions were found to closely correlate with the products obtained in the corresponding solvolytic reactions.[18,121] In order to account for the nature of products formed from the decarboxylation of the exo and endo norbornyl acids (60) and (61) Corey postulated that the non-classical norbornyl cation (3) was an intermediate in the reaction.

In view of the apparently different types of cation which may be generated electrolytically, and the influence that is exerted on the mechanism of the reaction by the nature of the electrode, it was considered highly desirable to examine the anodic oxidation of the carboxylic acids (85-89) at both carbon and platinum electrodes.

4. Aims of project.

From the foregoing Introduction, it is clear that the mechanism of the oxidative decarboxylation of carboxylic acids is far from clear-cut. In fact a broad spectrum of mechanistic interpretation has appeared in the literature. In some systems, purely free radical precursors have been postulated, while in other systems, only products arising from cationic intermediates have been detected. It was considered that the series of acids, (85), (86), (87), (88), and (89) would serve as a sensitive mechanistic probe in an examination of the oxidative decarboxylation reaction. The great propensity for rearrangement in cationic reactions involving isobornyl, bornyl, camphenehydro, and methylcamphenilyl derivatives (e.g. 85, 86, 87, and 88 respectively), suggested that the above compounds would be ideally suited to detect cationic intermediates in these reactions. Also, since α-campholenyl derivatives solvolyse to give intermediates having properties very similar to those formed from solvolysis of isobornyl, bornyl, camphene-hydro, and methylcamphenilyl derivatives, it was considered of interest to determine the nature of the oxidative decarboxylation reaction of β-(2,2,3-trimethylcyclopent-3-enyl)propionic acid (89), especially if the acids (85), (86), (87), and (88) gave the same intermediate on decarboxylation (Scheme 8). Furthermore, it was thought that an investigation of the effect of added copper II salts may provide further insight into the mechanism of the oxidative decarboxylation process.



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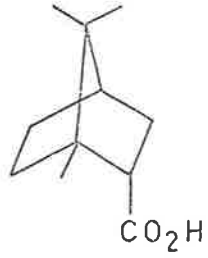

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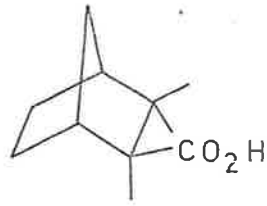

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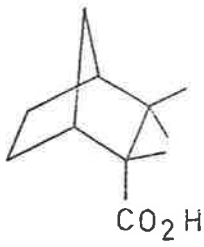

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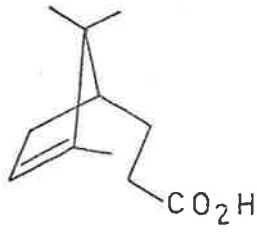

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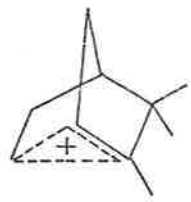
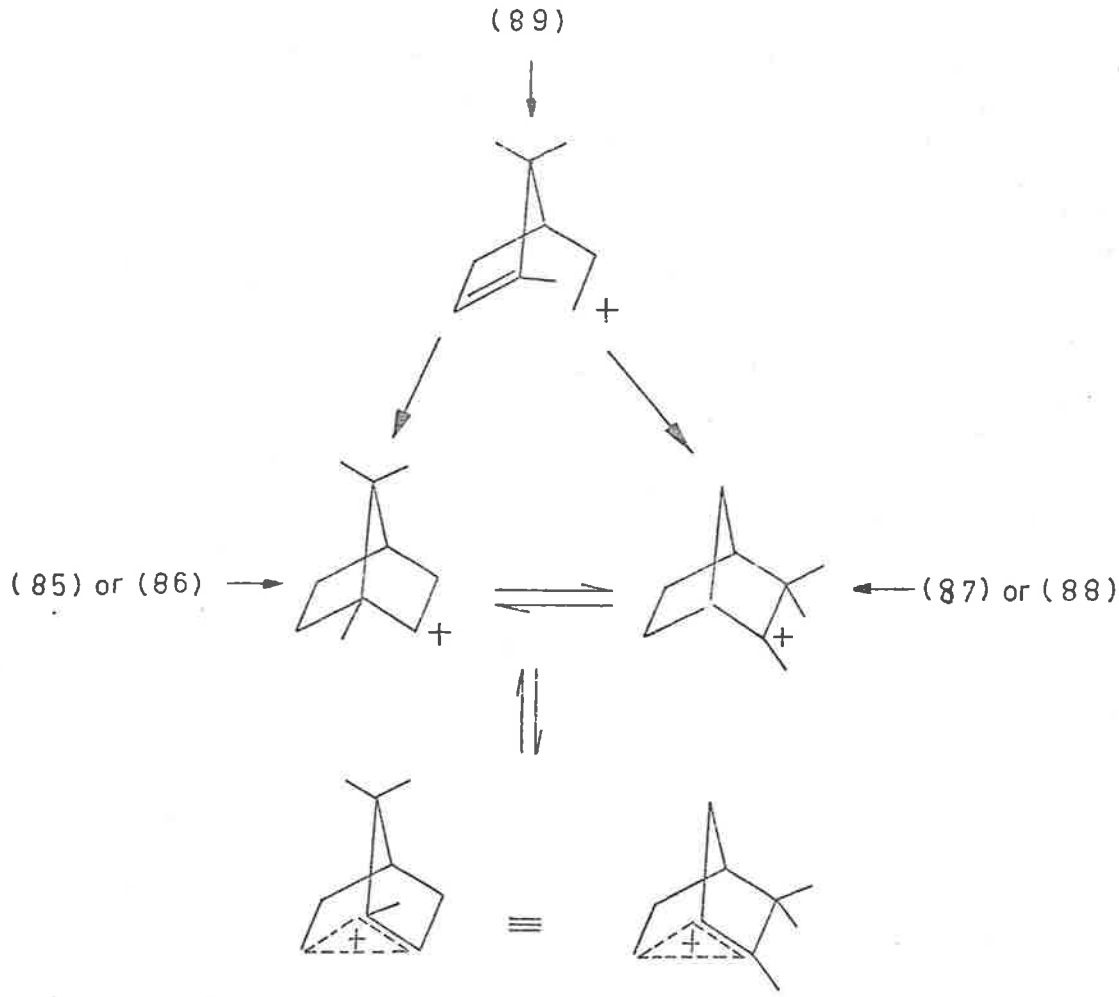


(68)

The continuing interest in the structure of the norbornyl and substituted norbornyl cations, and the possibility that decarboxylation of the acids (85), (86), (87), (88), and (89) may produce a common cationic intermediate [e.g. the supposed non-classical camphenehydroisobornyl cation (68)], further promoted interest in these reactions.

In a preliminary study of the oxidative decarboxylation of the acids (85) and (86) by Gream and Wege[78] relatively large quantities (1-2 g) of the acids were used in each determination of the products of the reaction. It was considered, however, highly desirable to develop a procedure involving the use of a small quantity (c. 50 mg) of the acid



Scheme 8.

for each determination, especially as preliminary work[123] had indicated that large quantities of the acids (87) and (88) might not have been readily obtainable.

A similar dichotomy of mechanism to that observed in the oxidative decarboxylation of acids has been associated with the anodic

oxidation of carboxylic acids. The partitioning of products between those derived from radical and cationic precursors has been shown to be dependent both on the structure of the acid and the nature of the anode. A cationic mechanism has been found to increase in importance on going from a primary to a tertiary acid, and on changing from a platinum to a carbon electrode.

For the same reasons as cited above for the oxidative decarboxylation reactions it was hoped that a study of the anodic oxidation of the acids (85), (86), (87), (88), and (89) would further elucidate the mechanism of the electrolytic process.

Hence, in view of the above objectives:

(1) a synthesis of exo- and endo-2-carboxy-2,3,3-trimethylnorbornane, (87) and (88) respectively was undertaken;

(2) the oxidative decarboxylation of the acids (85), (86), (87), (88), and (89) was studied in the presence and absence of copper II salts, in benzene and dimethylsulphoxide as solvent;

(3) the anodic oxidation of the acids (85), (86), (87), (88), and (89) was carried out in methanolic sodium methoxide at both platinum and carbon electrodes;

(4) procedures were developed for the quantitative analysis of products obtained from the oxidative decarboxylation reactions, and the anodic oxidations, involving the use of relatively small amounts (c. 50 mg) of acid for each determination.

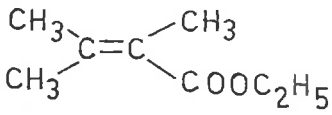
RESULTS AND DISCUSSION.

1. Synthetic work.

(i) Exo- and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88).

Several approaches to the synthesis of the exo and endo isomers of 2-carboxy-2,3,3-trimethylnorbornane were envisaged. Successful as well as several unsuccessful routes to the synthesis of the acids are described in the following discussion.

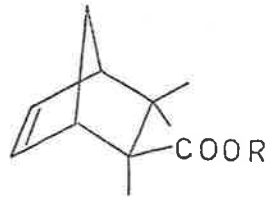
In a previous study[123] it was considered that the most obvious and convenient route to the two acids (87) and (88) involved the Diels-Alder reaction between cyclopentadiene and ethyl 2,3-dimethylbut-2-enoate (90) to give the two adducts (91) and (92). Subsequent alkaline



(90)

(91, R = C_2H_5)

(93, R = H



(92, R = C_2H_5)

(94, R = H)

hydrolysis of the two adducts was expected to give a mixture of the two acids (93) and (94) which should be readily separable by conversion of endo-acid (93) into its iodolactone. Thereafter, it was considered that the preparation of the two pure acids (87) and (88) would be achieved without difficulty by sequences previously described for the preparation of pure exo- and endo-2-carboxynorbornane from cyclopentadiene and acrylic acid.[122] However, previous work[123] showed that adduct formation

between cyclopentadiene and ethyl 2,3-dimethylbut-2-enoate (90) could not be effected under a variety of reaction conditions. It was considered that the failure of adduct formation to occur was due to the adverse electronic and steric effects of the three methyl groups in the dienophile. That the introduction of methyl groups about the double bond in acrylic acid and its derivatives does have an adverse cumulative effect is evident from the fact that the yields of adducts from cyclopentadiene and methyl acrylate,[121] α-methylacrylic acid,[124] α,β-dimethylacrylyl chloride,[125] and β,β-dimethylacrylic acid[126] are 90, 68, 57, and c. 5% respectively.

Considerable attention was given to the possibility that the acids (87) and (88) could be prepared by sequences involving the conjugate addition of a methyl group to suitable α,β-unsaturated carbonyl derivatives.

In the earlier investigation[123] it was shown that 8-carbomethoxycamphene (95, R = CO_2CH_3), on treatment with methylmagnesium iodide in the presence of cuprous chloride, gave none of the desired compound (96) (since exo addition of a methyl group was anticipated*). 1,2-Addition, rather than the desired conjugate (1,4-addition[127] occurred since the only products isolated were the tertiary alcohol (97) and probably the compound (98) and polymeric material derived from it. The diene (98)

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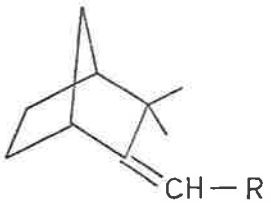
* In the absence of a bulky substituent at the 7-syn position, reactions of norbornyl derivatives occur preferentially from the exo side.[128-130] An exception to this general rule occurs in the catalytic hydrogenation of the unsaturated alcohol (125) (see later).

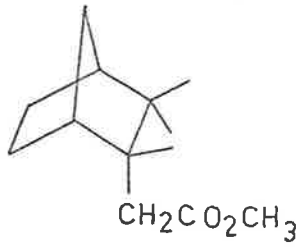


(95, R = CO_2CH_3)

(99, R = CO_2H)

(100, R = $COCH_3$)

(101, R = CHO)



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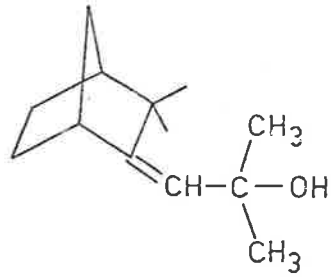

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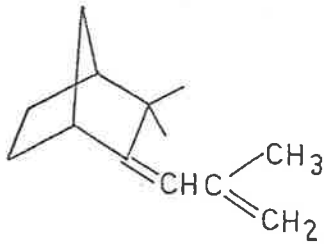

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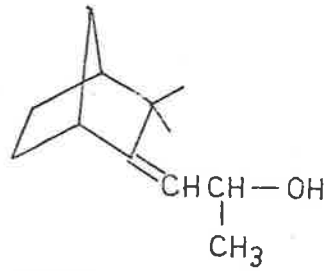


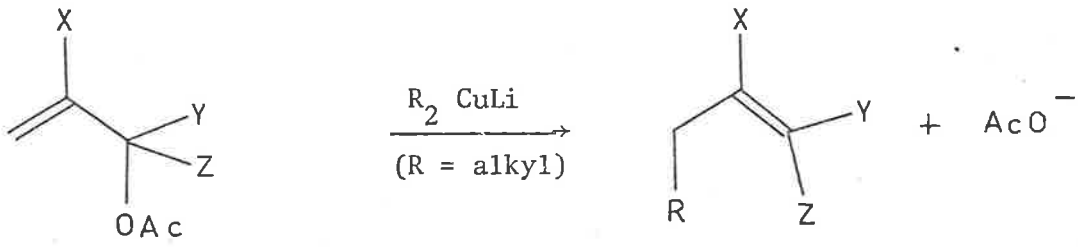
(102)

was probably formed from the alcohol (97) by acid catalysed dehydration under the strongly acidic conditions of the work-up procedure.

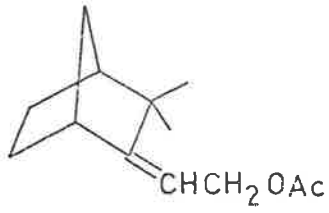
Dimethylcopperlithium has been shown to add a methyl group in a specific 1,4 manner to α,β-unsaturated ketones.[131] When 8-acetylcamphene (100, R = $COCH_3$), prepared by the reaction of methyllithium with 8-carboxycamphene (99, R = CO_2H), was treated with the above reagent, the tertiary alcohol (97) resulting from 1,2-addition was the only product isolated. A similar result was also observed when 8-formylcamphene (101, R = CHO) was allowed to react with dimethylcopperlithium,

since the secondary alcohol (102) was the only product that could be isolated from the reaction mixture.

It has been reported[132] that dialkylcopperlithium reagents may react with allylic acetates to give products resulting from allylic rearrangements followed by acetate displacement. It was hoped therefore



that treatment of the allylic acetate (103) with dimethylcopperlithium would give endo-2-vinyl-2,3,3-trimethylnorbornane (104) (assuming that the methyl group is introduced from the exo direction[128-130]) which should be readily oxidised to the endo acid (88). However, the only products isolated from the reaction mixture were 8-ethylcamphene (105, 35%), the unsaturated alcohol (106, 30%), and unchanged starting material (103, 11%). Since 8-ethylcamphene had not been previously reported, an authentic sample was prepared by a Wittig reaction between camphenilone (107), n-propyltriphenylphosphonium iodide, and potassium t-butoxide in light petroleum. The formation of 8-ethylcamphene (105) was assumed to result from a direct displacement of the acetoxy group in (103) by a methyl group from the dimethylcopperlithium reagent. The unsaturated alcohol (106) was presumed to arise from the hemi-ketal (108) [resulting from 1,2-addition of the reagent to the carbonyl group of (103)], during the working-up process.



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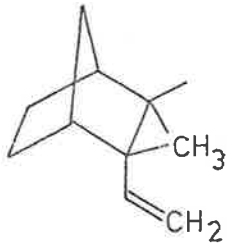

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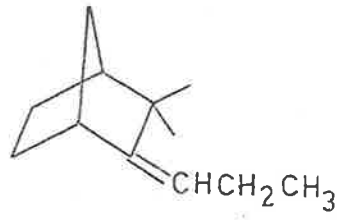

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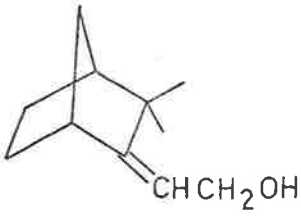

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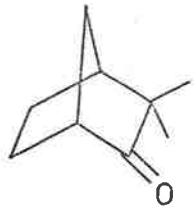

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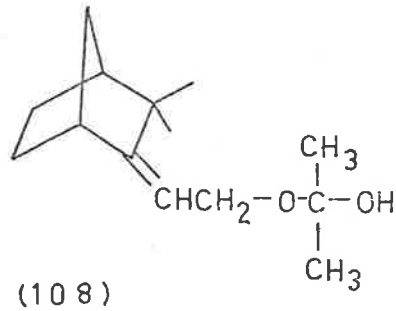
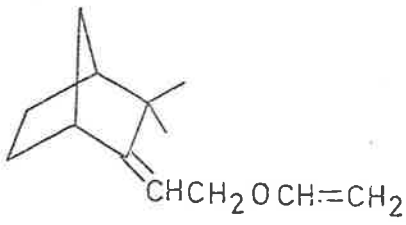


(108)

It would appear that the failure of both the Grignard and dimethylcopperlithium reagents to undergo the desired reactions described above must be due to steric crowding around the required sites of attack such that 1,2-addition and direct displacement become the favoured reactions.

Another route investigated for the preparation of the endo acid (88) involved a Claisen rearrangement. Treatment of the allylic alcohol (106) with ethylvinyl ether in the presence of mercuric acetate afforded a good yield of the vinyl ether (109). On being heated at 220° for 4 hours in a sealed tube under nitrogen, (109) was converted into an unsaturated aldehyde which was assigned the structure (110) on the basis

that the transition state for the Claisen rearrangement would be formed by reaction proceeding from the exo rather than the endo side.[128-130]*



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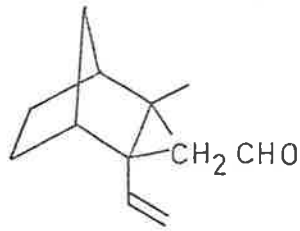

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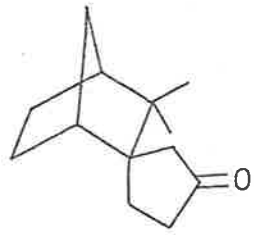
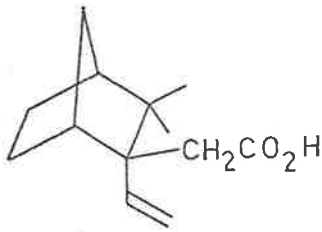
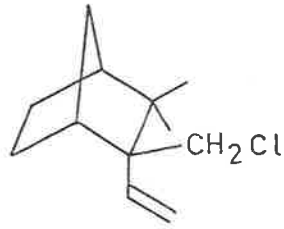


(111)



(112)



(113)

Several possibilities seemed to exist for the conversion of (110), a γ,δ-unsaturated aldehyde into the required endo acid (88).

The decarbonylation of a γ,δ-unsaturated aldehyde with tris-triphenylphosphine rhodium chloride to introduce an angular methyl group into a molecule has been reported.[134] Treatment of the aldehyde (110)

---

* Although the product appeared to be homogeneous, Corey and Schulman[133] have reported that a thio-Claisen rearrangement involving norbornan-2-one gives a 3:2 mixture of epimers (configurations not determi

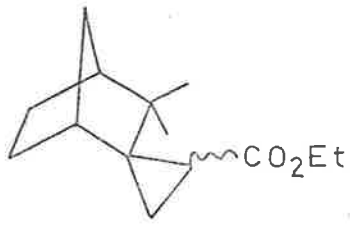
with the above rhodium complex in benzonitrile at 160° for 12 hours gave none of the required endo-2-vinyl-2,3,3-trimethylnorbornane (104). However, there was obtained a compound (54%), $C_{13}H_{20}O$ whose infrared spectrum showed a strong absorption at 1742 cm^{-1}. The combined spectral properties (mass, infrared, and n.m.r.) (see Experimental) were consistent with the structure being (111). At the time, this reaction provided a new method of preparing cyclopentanone derivatives. Very recently, however, Sakai and coworkers[135] have reported similar examples of the cyclisation of γ,δ-unsaturated aldehydes to cyclopentanone derivatives and have shown it to be a reaction of potential synthetic utility.

The unsaturated acid (112), formed from the aldehyde (110) by oxidation with silver oxide was considered as a potential precursor to the endo acid (88). Attempts to prepare the endo-2-vinyl-2,3,3-trimethylnorbornane (104) by heating the acid (112) with copper powder in quinoline at 265° were unsuccessful and only unchanged acid (112) was recovered.

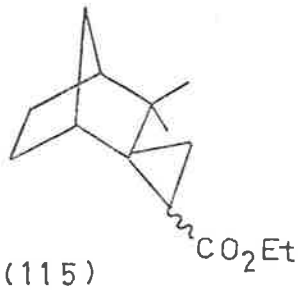
Another approach involved heating the acid (112) with lead tetraacetate and lithium chloride in benzene[136] in the hope that the unsaturated chloride (113) would be formed. Subsequent conversion of the chloride (113) into the olefin (104) did not appear to offer any real difficulty. However, treatment of the unsaturated acid (112), with the above reagent gave none of the desired chloride (113). Instead, a complex mixture whose infrared spectrum indicated the presence of lactonic material and from which no pure compounds could be isolated

was formed. An analogy for the formation of lactones when γ,δ-unsaturated acids are treated with lead tetraacetate in the presence or absence of lithium chloride is provided by the work of Moriarty and coworkers[137] with exo- and endo-2-carboxynorborn-5-ene (83).

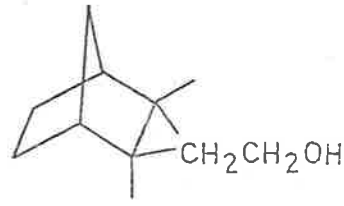
The possibility that the two acids (87) and (88) might be formed in sequences involving reduction of the cyclopropyl esters (114) and (115), respectively, was also investigated. It was considered that the Birch reductions of (114) and (115) may lead to the alcohols (116) and (117) respectively, which could be converted by standard procedures into the exo and endo acids (87) and (88) respectively. Alternatively, catalytic hydrogenolysis of the two cyclopropyl esters might lead to the two esters (118) and (119) which would be equally useful for conversion into (87) and (88).



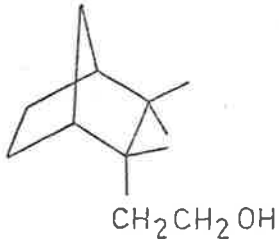
(114)



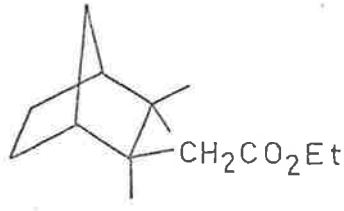
(115)



(116)



(117)



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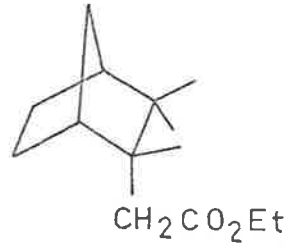
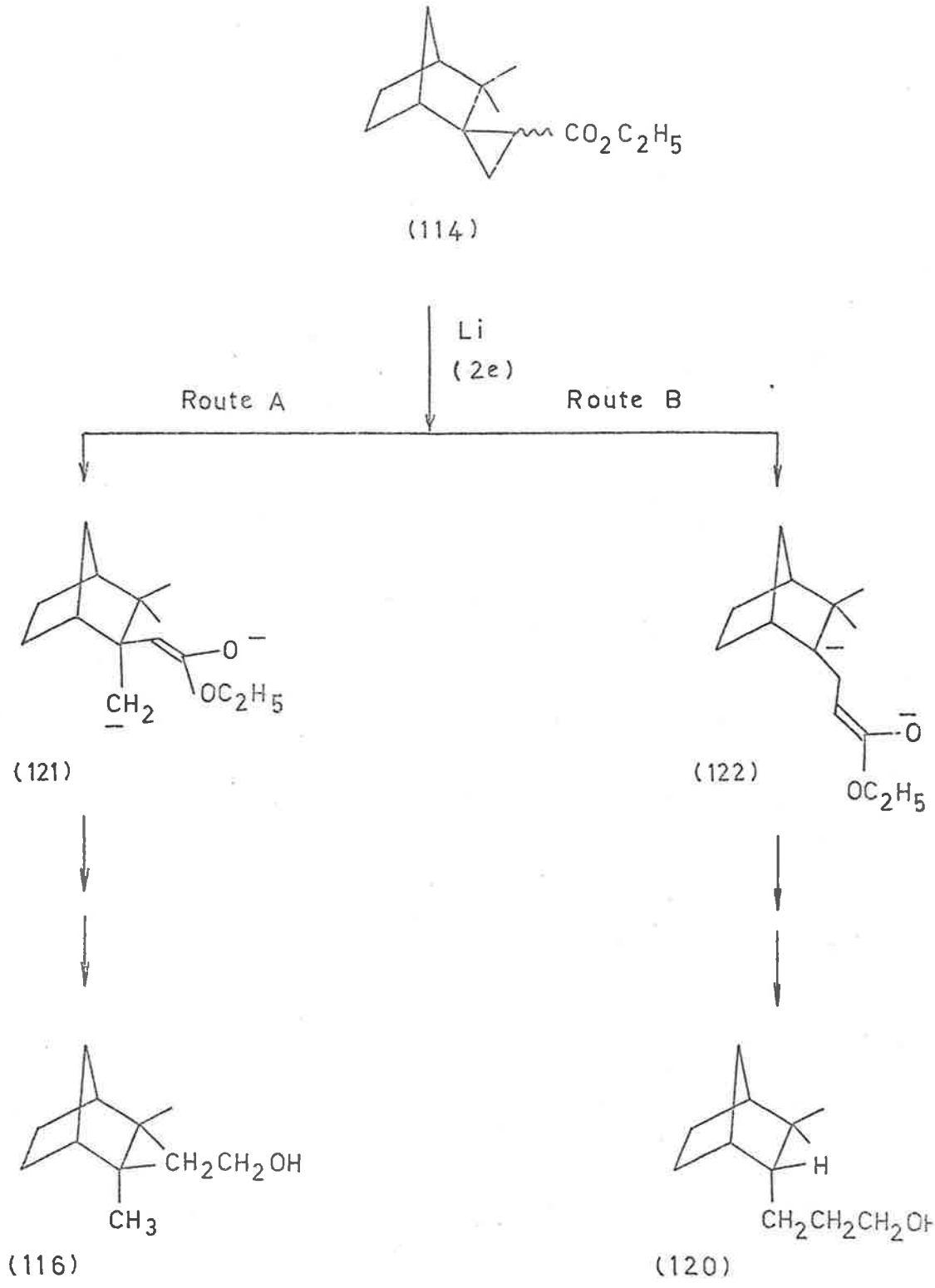


(119)

At the time that this approach to the synthesis of (87) and (88) was investigated, it was known that the direction of ring cleavage in the Birch reduction of certain rigid α-cyclopropyl carbonyl derivatives could be predicted on the basis of a stereoelectronic requirement,[138] viz. the bond that is cleaved is the one having the greater overlap with the π-system of the carbonyl group. However, in the case of the cyclopropyl esters (114) and (115) this requirement cannot be applied because the carbonyl group can rotate to the same extent over both bonds of the cyclopropane ring. Assuming that a carbanionic mechanism[139] would be operative during the reductive cleavage of the cyclopropane ring, it was reasoned that for the two modes of ring opening in the cyclopropyl ester (114), route A (Scheme 9) would be preferred. The alcohol (116) rather than (120) (it was assumed that protonation of the precursor tertiary carbanion in the reduction sequence would occur mainly from the exo direction[128-130*]) might have been the expected major product on the basis of thermodynamic stability that the primary carbanion (121) would be formed in preference to the tertiary carbanion (122).

---

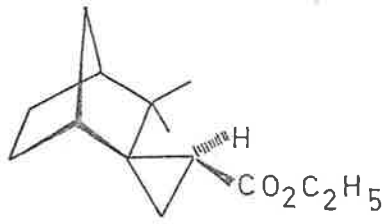
* Very recently however, it has been shown[140] that a high degree of inversion can occur at the β-carbon in the reduction of a conjugated cyclopropyl ketone by an alkali metal in liquid ammonia. Lower temperature (-78^{o} instead of -33^{o}) as well as the absence of an alcohol as a proton source increased the extent of inversion.



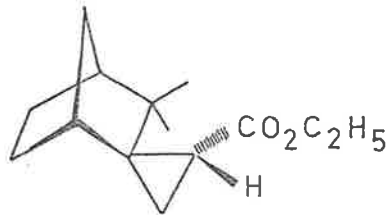
Possible modes of Birch reduction of the cyclopropyl ester (114).

Scheme 9.

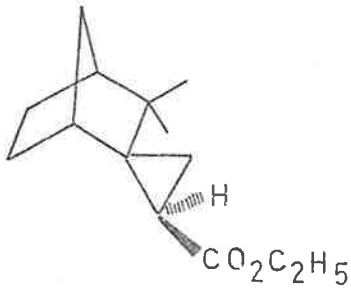
Treatment of camphene (123) with ethyldiazoacetate and copper sulphate in refluxing cyclohexane gave a mixture (80%) which was shown by g.l.c. to contain at least three [isomers A (55%), B (25%), and C (20%)] of the four possible stereoisomers corresponding to the two cyclopropyl esters i.e. (114a), (114b), (115a), and (115b). Preparative g.l.c. afforded a complete separation of isomer C and partial separation of A and B. Assignment of stereochemistry to the isomers was not possible; it can be assumed however, that the addition of the carbethoxy-carbene generated from ethyl diazoacetate should occur predominantly from the <u>exo</u> direction[128-130] of camphene to give (114) as the major product. Although it was realised that the removal by base of the



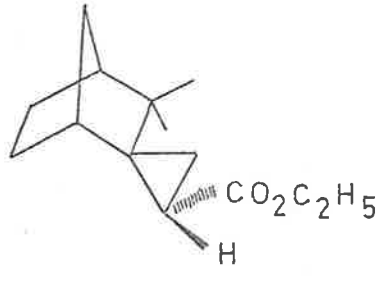
(114a)



(114b)



(115a)

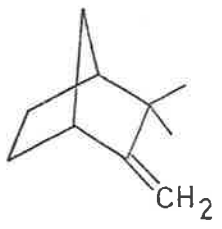


(115b)

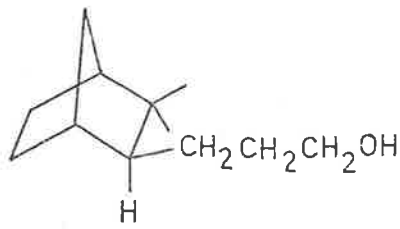
α-hydrogen atom in α-cyclopropyl esters may, or may not be a favourable process,[141] an attempt was made to resolve the stereochemistry of the components of the mixture by equilibration with sodium ethoxide in ethanol. It was considered that the more stable of the two stereoisomers of the exo ester (114) would be the one in which the carbethoxy group is directed away from the gem-dimethyl group (i.e. 114a) and it was hoped that prolonged reaction of the mixture with sodium ethoxide would increase the proportion of this isomer (114a). However, the composition of the mixture remained unchanged after treatment with sodium ethoxide solution (0.5M) in boiling ethanol for 43 hours.

Although the stereochemistry of the various components (i.e. isomers A, B, and C) of the mixture of esters (114) and (115) was unknown, both the isomer C and the mixture of A and B were subjected to Birch reductions with lithium and liquid ammonia containing t-butanol. In both cases, the same mixture (1:9) of the exo and endo alcohols (124) and (120) respectively, was obtained. Initially, an attempt to assign the configuration of the two alcohols formed by the reduction of the cyclopropyl esters was based on a comparison with the alcohols formed by catalytic hydrogenation of the unsaturated alcohol (125). In the reduction of the unsaturated alcohol (125) under one atmosphere of hydrogen in the presence of platinum, two alcohols in the ratio of 7:3 were formed. The major product was initially believed to be the alcohol (120) on the grounds that the addition of hydrogen to the double bond in (125) should occur preferentially from the exo direction.[128-130] In the catalytic hydrogenation of camphene (123) it has been reported[142]

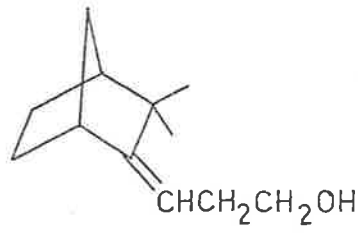
that exo to endo addition of hydrogen occurs in the ratio of 3:1. However, if the major product formed by hydrogenation of (125) was the endo alcohol (120), then the predominant product formed by the Birch reduction of the cyclopropyl esters would have been the exo alcohol (124). This assignment of stereochemistry seemed doubtful however, as it would have required protonation of the precursor tertiary carbanion (122) in the reduction sequence to have occurred predominantly from the endo direction. Hence it was considered that further proof was required to determine whether the major product formed by catalytic hydrogenation of the alcohol (125) was in fact (120) and not (124).



(123)



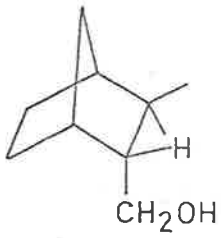
(124)



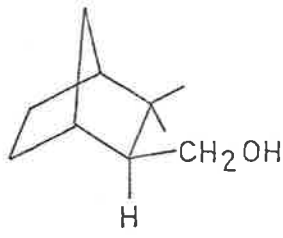
(125)

The problem of assignment of configuration to the two alcohols formed by the reduction of the cyclopropyl esters was overcome in the following way. Oxidative hydroboration of camphene (123) gives a 9:1 mixture of the endo and exo alcohols (126) and (127) respectively.[143] Hence it would be expected that hydroboration of camphene followed by reaction of the resulting organoboranes with ethyl bromoacetate in the presence of potassium t-butoxide[144] would give a mixture (c. 9:1) of

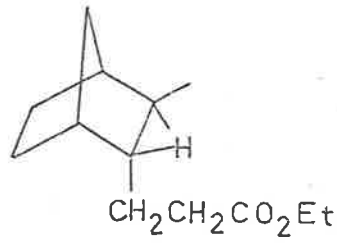
the endo and exo esters (128) and (129) respectively. Subsequent reduction of the mixture of esters with lithium aluminium hydride should lead to a mixture (c. 9:1) of the required endo and exo alcohols (120) and (124) respectively. When the sequence of reactions outlined above was carried out with camphene, there was indeed obtained a mixture of two alcohols in the ratio of 9:1. The product obtained from the above sequence was identical to the alcohols formed from the cyclopropyl esters and from the hydrogenation of (125). However, the major component corresponded to the minor one obtained by catalytic hydrogenation of (125). Since the configurations of the two alcohols obtained by the route involving the organoboranes can be assigned unambiguously, the catalytic hydrogenation of the unsaturated alcohol (125) appears to represent the first clear-cut example of a reaction occurring predominantly from the endo direction in a norbornyl derivative not bearing a bulky substituent at the 7-syn position. The formation of the exo alcohol (124) may be due, at least in part to hydrogen exchange and scrambling reactions,[128] although the hydroxyl group in the substrate might well have played a role, especially as camphene[142] under the same conditions of hydrogenation added hydrogen predominantly from the exo direction. It should be noted that the cyclopropyl alcohols (130) and (131), were not present in the mixture of products formed by the Birch reduction of the cyclopropyl esters (114) and (115). The cyclopropyl alcohols (130) and (131) were prepared by reduction of the corresponding cyclopropyl esters (114) and (115) with lithium aluminium hydride.



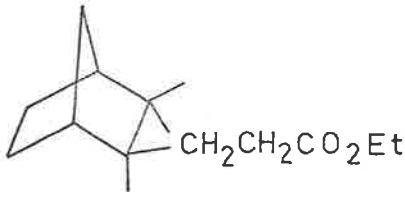
(126)



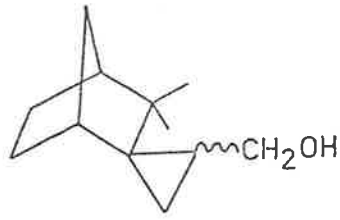
(127)



(128)



(129)



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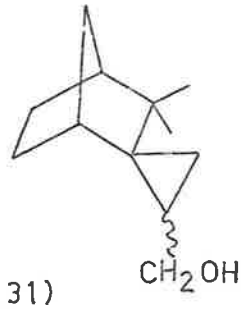


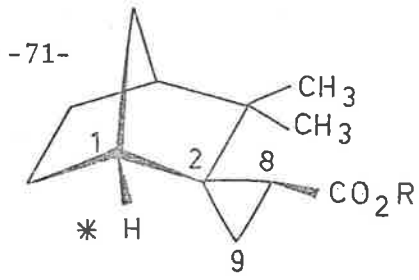
(131)

A consideration of the reasons for the formation of the alcohols (120) and (124) (the formation of the latter indicates that protonation of the carbanion (122) (Scheme 9) did not occur exclusively from the exo direction) in the Birch reduction of the cyclopropyl esters (114) and (115) would now appear to be in order. Initially it was considered unlikely that (120) (and hence also 124) would be formed since it required the intermediacy of the thermodynamically less stable tertiary carbanion (122) rather than the more stable primary species (121) (Scheme 9). Since the completion of this aspect of the work, Dauben and Wolf[145] have reported that the direction of ring cleavage

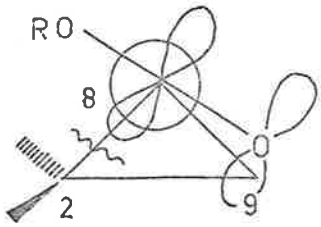
in the Birch reduction of conformationally mobile conjugated cyclopropyl ketones was subject to steric factors; it was only in the absence of such factors that cleavage of the cyclopropyl ring bond gave the thermodynamically more stable carbanion.

An examination of models of the cyclopropyl esters (114) and (115) clearly indicates that such steric factors should control the direction of cleavage of the cyclopropyl ring in the Birch reductions and that the products should indeed be the alcohols (120) and (124). To predict the direction of ring cleavage in the isomer of the exo ester in which the carbethoxy group is directed away from the gem-dimethyl group at C_3 (i.e. 114a) it is necessary to consider the two conformations A and B (for this type of representation, see[145]) of the cyclopropyl ester portion. It should be noted that only conformations which allow overlap of the carbonyl π-system with one of the cyclopropane bonds can be considered[145] (Scheme 10). In B, steric interaction between the oxygen atom of the carbonyl group and the bridgehead hydrogen atom at C_1 occurs.

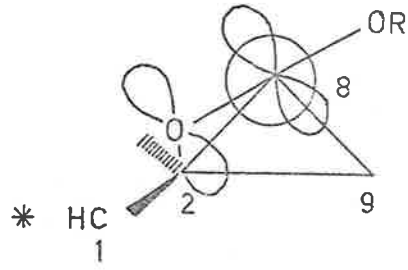
The absence of such an interaction in A, results in reduction taking place through this conformation with a resultant cleavage of the C_2-C_8 bond leading to the formation of the alcohols (120) and (124). If the carbethoxy group is directed towards the gem-dimethyl group at C_3, i.e. (114b), the two conformations C and D of the cyclopropyl ester moiety must be considered if reduction is to occur (Scheme 11). In D, there is a severe steric interaction between the oxygen atom of the carbonyl function and the exo-methyl group at C_3. The absence of such an interaction in C, results in reduction occurring through this



(114 a)

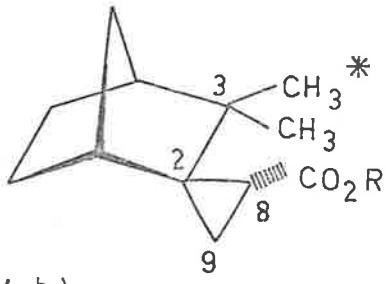


A

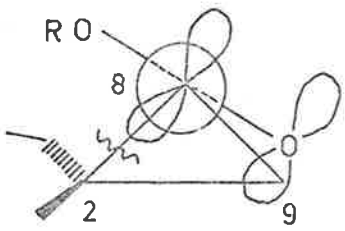


B

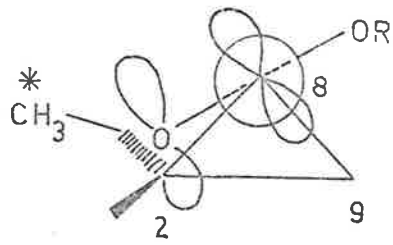
Scheme 10.



(114 b)



C



D

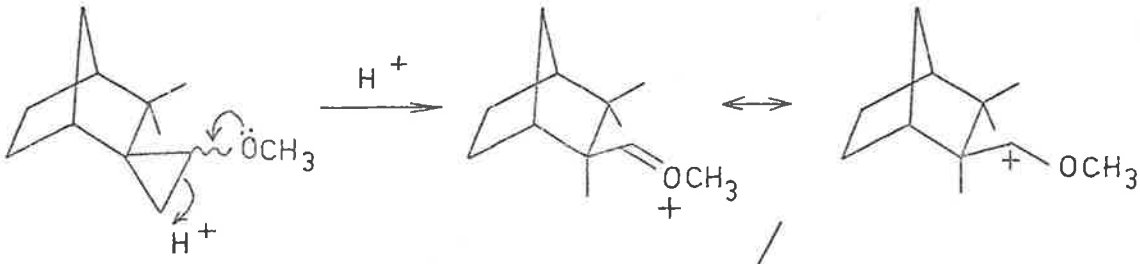
Scheme 11.

conformation with a resultant cleavage of the C_2-C_8 bond leading again to the alcohols (120) and (124). If a similar assessment of the steric factors involved in the various conformations capable of undergoing reduction for the two isomers corresponding to the endo ester (115) is made, it can be deduced that the alcohols (120) and (124) should once again be the preferred products.

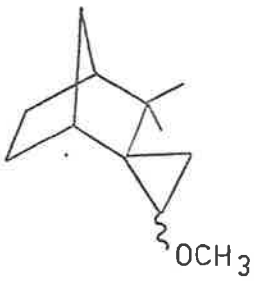
An attempt to cleave the cyclopropyl ring in the esters (114) and (115) by the action of hydrogen in the presence of platinum in acetic acid at 50° and 6 atmospheres[146] was unsuccessful.

The potential of the methoxycyclopropane derivatives (132) and (133) as possible precursors to the required acids (87) and (88) was also investigated. It has been demonstrated in recent years[147] that angular methyl groups may be introduced into compounds by the acid catalysed ring opening of methoxycyclopropane derivatives. Bond cleavage of the cyclopropyl ring occurs towards the least substituted carbon atom of the ring to form the most stable carbonium ion. In the case of (132), both these conditions are satisfied by ring opening proceeding as shown. In the presence of water, either under the conditions of the reaction or in the working-up process, the product would be the exo aldehyde (134). Similarly, acid catalysed ring opening of the endo methoxy-cyclopropane (133) would yield the endo aldehyde (135).

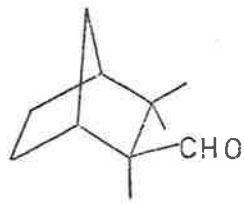
Mixtures of (132) and (133) were formed from camphene (123) using two different methods for generating methoxycarbene, the required addend. Atwell[148] has reported that the heating of dimethoxymethyl-trimethoxysilane (136) at 125° is a convenient method for the generation



(132)



(133)



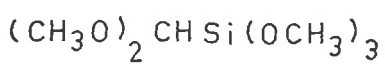
(134)

(135)

of methoxycarbene. When camphene was heated at 125° for 16 hours with the silane (136), there was obtained a mixture (72%) which consisted (by g.l.c.) of four components, presumably the four stereoisomers corresponding to (132) and (133). Preparative g.l.c. afforded complete separation of the major component (60% of the mixture) and partial separation of the other three. Because of the preference for <u>exo</u> addition[128-130] to the double bond of camphene, the major component was assumed to be one of the stereoisomers, preferably (132a) for steric reasons, corresponding to (132).

The other method employed for the preparation of a mixture of the methoxycyclopropane derivatives (132) and (133) involved generation

of the required methoxycarbene from the reaction between methyllithium and methyldichloromethyl ether.[149] The reaction between camphene and the methoxycarbene generated by this procedure proceeded smoothly at 25° to give the same four compounds (70%) as were formed using the silane derivative (136); however, the major component now amounted to 75%, rather than 60% of the mixture. The greater stereoselectivity in this case may be attributed to the much lower temperature at which the reaction was carried out.



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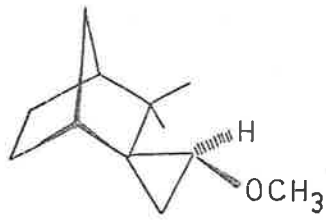
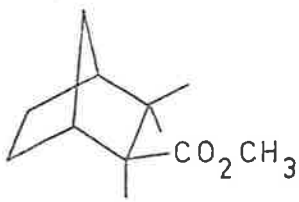
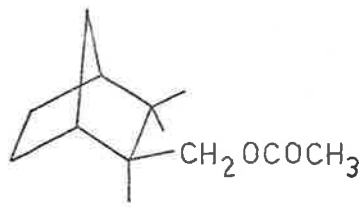


(132a)



(137)



(138)

Treatment of the pure isomer, assumed to be (132a), with hydrochloric acid in boiling methanol, followed by oxidation of the

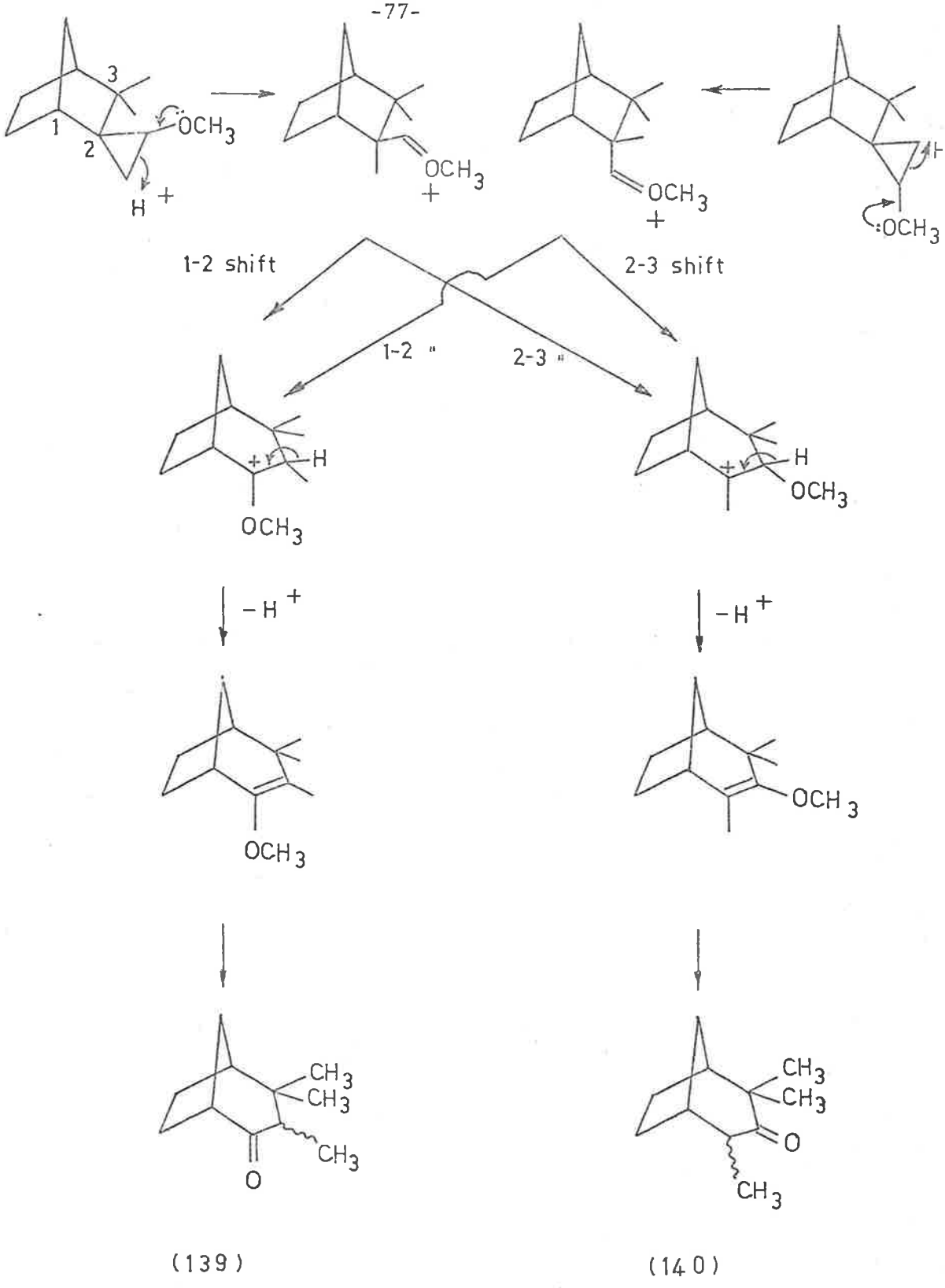
crude product with Jones reagent, gave a crystalline acidic product, $C_{11}H_{18}O_2$ in varying yields (14-37%). Its spectral characteristics, particularly those of the n.m.r. spectrum which showed resonances at δ0.99, 1,07, and 1.17 corresponding to the presence of three tertiary methyl groups, were consistent with the compound being the required exo-2-carboxy-2,3,3-trimethylnorbornane (87). In an attempt to prove that the material was not contaminated by the epimeric endo acid (88), its methyl ester (137) and the acetyl derivative (138) of the alcohol obtained by reduction of the methyl ester with lithium aluminium hydride were subjected to exhaustive g.l.c. analysis. In all cases, the samples appeared to be homogeneous.

Although successful, the above route to exo-2-carboxy-2,3,3-trimethylnorbornane (87) had the following disadvantages: (i) because the difference in retention times of the components in the mixture was small, separation of the isomer (132a) by preparative g.l.c. was extremely tedious, (ii) the conversion of (132a) into the required acid occurred in low yield, and (iii) the stereochemistry of the final acid, though based on the sound premise that exo attack[128-130] would be the expected mode of addition of methoxycarbene to camphene, had not been rigorously established.

In a preliminary study, the product from the reaction between camphene (123) and dimethoxymethyltrimethoxysilane (136) was treated with 70% perchloric acid in glacial acetic acid at 115° for 20 minutes. The product, a mixture (4:1) of two components, was separated by preparative g.l.c. The two products, both $C_{11}H_{18}O$, exhibited almost

identical infrared spectra showing a strong carbonyl absorption at 1705 cm^{-1}. The n.m.r. spectra of both compounds indicated the presence of three methyl groups. No aldehydic material was detected in the reaction mixture. On the basis of microanalytical and spectral data, the two products were believed to be 3,4,4-trimethylbicyclo[3,2,1]octan-2-one (139) and 2,4,4-trimethylbicyclo[3,2,1]octan-3-one (140). Attempts to synthesise the two compounds by treatment of camphenilone (107) with diazoethane in the presence of born trifluoride were unsuccessful; starting material only was recovered. The ring expansion of cycloalkanones with diazoalkanes in the present of a Lewis acid is markedly dependent on steric factors[150] and it would seem that the failure of camphenilone (107) to undergo the reaction with diazoethane is the result of the substituents at the α-carbon atoms. Although successful syntheses of the bicyclic ketones (139) and (140) were highly desirable, no further attempts were made in the present work. The formation of the two ketones by the action of perchloric acid on the methoxycyclopropane derivatives (132) and (133) can be readily explained by the sequences shown in Scheme 12.

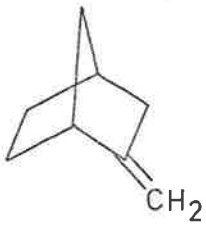
In order to test whether a specific bond of the bicyclo[2,2,1]-heptyl skeleton (i.e. either the 1-2, or the 2-3 bond) was involved in the ring expansion reaction, the chromatographically pure methoxycyclopropane (132a) was treated under the same conditions to those described above for the ring expansion of the mixture of isomers (132) and (133). The product obtained however, consisted of a mixture of the same two products [presumably (139) and (140)] in a ratio of 7:3 (cf. with the


3
1
2
OCH3
H +
OCH3
+
OCH3
+
:OCH3
1-2 shift
2-3 shift
1-2 "
2-3 "
H
OCH3
H
OCH3
-H+
-H+
OCH3
OCH3
CH3
CH3
CH3
O
O
CH3
(139)
(140)

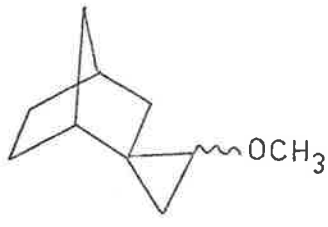
Scheme 12.

ratio of 4:1 for the mixture). This would appear to indicate that either the 1-2 or the 2-3 bond of the bicyclo[2,2,1]heptyl skeleton may participate in the ring expansion reaction.

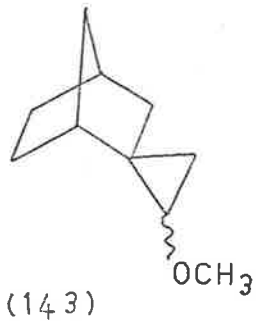
In order to test the generality of the ring expansion reaction of bicyclo[2,2,1]heptyl derivatives to the corresponding bicyclo[3,2,1]-octanones, another example was chosen. 2-Methylenenorbornane (141) was prepared by a Wittig reaction between norbornan-2-one (22), methyltriphenylphosphonium iodide and potassium t-butoxide in ether. Subsequent treatment of the olefin (141) with methyllithium and dichloromethyl methyl ether[149] gave a mixture (78%) which was shown (by g.l.c.) to contain three components. The major product which constituted 90% of the reaction mixture was separated by preparative g.l.c. and its spectral properties were characteristic of the methoxycyclopropane derivative (142). It should be noted that an estimation of the isomeric purity of the product was not possible because the corresponding endo epimer (143) was unknown; however it was assumed that the product consisted mainly of the exo isomer (142) because of the preference of attack of reagents from the exo direction[128-130] in the reactions of norbornyl derivatives.



(141)

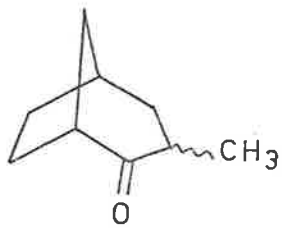


(142)



(143)

Treatment of the separated methoxycyclopropane (142) with perchloric and acetic acid using identical conditions to those employed in the ring expansion of the substituted methoxycyclopropane derivatives (132) and (133) gave three products, i.e. A (10%), B (87%), and C (3%). The reaction mixture, $C_9H_{14}O$ showed a strong infrared absorption at 1705 cm^{-1} and the n.m.r. spectrum showed a doublet resonance at δ0.95, indicating the presence of a secondary methyl group. The spectral data was consistent with the structures of A, B, and C being either (144) or (145). In an attempt to deduce the correct structure of the three



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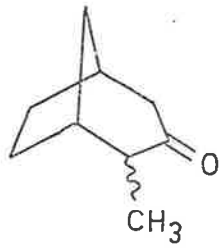

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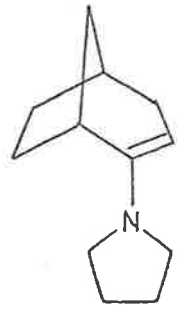


(146)

components A, B, and C of the mixture, the pyrrolidine enamine of bicyclo[3,2,1]octan-2-one, i.e. (146) was treated with an excess of methyl iodide in refluxing benzene. Alkylation of the enamine (146) would be expected to produce only exo- and endo-3-methylbicyclo[3,2,1]-octan-2-one (144). In fact two products corresponding to the compounds B and C, in the ratio of 4:1, respectively, were obtained as well as

a large amount (c. 70% of the reaction mixture) of bicyclo[3,2,1]octan-2-one. Preparative g.l.c. afforded a sample of the mixture (assumed to be B and C), the spectral properties and g.l.c. characteristics of which were virtually identical to those observed for the product arising from the acid catalysed ring expansion of the methoxycyclopropane (142). Examination of a model of the enamine (146) indicates that the exo side of the molecule is more accessible to attack by the alkyl halide and hence the major component (i.e. B), was assumed to be exo-3-methylbicyclo-[3,2,1]octan-2-one, while C was believed to be the corresponding endo epimer, i.e. endo-3-methylbicyclo[3,2,1]octan-2-one. Thus the other product, i.e. compound A, was considered to be either exo- or endo-2-methylbicyclo[3,2,1]octan-3-one (145). Unfortunately, time did not allow an independent synthesis of the epimeric 2-methylbicyclo[3,2,1]octan-3-ones (145), and hence an unambiguous assignment of structure to the products obtained from the acid catalysed ring expansion of the methoxycyclopropane (142) was not possible. In the light of the above results it would appear that treatment of a suitably substituted bicyclo[2,2,1]-heptyl derivative under the conditions described above, may be of synthetic value in the preparation of substituted bicyclo[3,2,1]octanone derivatives.

In view of the disadvantages mentioned previously for the preparation of exo-2-carboxy-2,3,3-trimethylnorbornane (87) by the acid catalysed ring opening of the methoxycyclopropane (132a), attention was turned to the possibility that the two acids, (87) and (88), could be synthesised by routes involving the hydrogenolysis of suitable cyclopropanated precursors. Synthetic routes involving the exo and endo

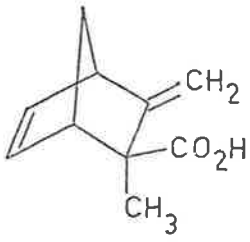
isomers of 2-carboxy-2-methyl-3-methylenenorborn-5-ene (147) and (148), respectively, seemed to be attractive.

The Diels-Alder reaction between cyclopentadiene and 2-methyl-but-2,3-dienoic acid (149) gave a mixture (3:2, 94%) of the exo and endo adducts (147) and (148), respectively.[151] The exo acid (147) was conveniently separated from the mixture by conversion of the endo acid (148) into the iodolactone (150) with iodine and potassium iodide in sodium bicarbonate solution. Conversion of the exo acid (147) to its methyl ester and subsequent reduction with lithium aluminium hydride gave exo-2-hydroxymethyl-2-methyl-3-methylenenorborn-5-ene (151) (98%). Taking advantage of the fact that the double bonds in homoallylic alcohols have enhanced rates of reaction with the Simmons-Smith reagent,[152] the compound (151) was treated with three equivalents of the reagent to give the required product (152) (90%) together with unchanged starting material (5%) and a compound (5%) assumed to be the dicyclopropanated derivative (153) on the basis of its g.l.c. behaviour and the fact that it was formed in 50% yield when (151) was treated with six equivalents of the Simmons-Smith reagent. Since the product could not be purified by recrystallisation, a pure sample of (152) was obtained by preparative g.l.c.

However, the necessity to obtain a large quantity of pure (152) was avoided by use of the following procedure to prepare exo-2-carboxy-2,3,3-trimethylnorbornane (87). The crude mixture of alcohols (151), (152), and (153), obtained from the Simmons-Smith reaction, was reduced with hydrogen (6 atmospheres) in the presence of platinum in acetic acid

at c. 50°[146] to give a product which, since it contained some acetyl derivative(s) (detected by infrared and n.m.r. spectra), was treated with lithium aluminium hydride in ether. Unexpectedly, the product of reduction was invariably (154) in which the cyclopropyl moiety had been left intact. However, in a preliminary experiment, when a sample of pure (152) was subjected to the same hydrogenation conditions described above, hydrogenolysis of the cyclopropyl ring, as well as reduction of the double bond occurred. Oxidation of the alcohol (154) with Jones reagent followed by hydrogenolysis of the derived cyclopropyl acid (155) gave the required exo acid (87) [57% from (151)]. The acid obtained from this route was identical to that formed via the methoxycyclopropyl derivative (132a), thus confirming the assignment of exo configuration previously made.

Because of the success realised in the synthesis of the exo acid (87) from exo-2-carboxy-2-methyl-3-methylenenorborn-5-ene (147) it would appear logical to attempt a synthesis of the endo acid (88) from the epimeric endo-2-carboxy-2-methyl-3-methylenenorborn-5-ene (148). This was not done, however, as Vaughan and coworkers[153] have described a convenient six-stage synthesis of endo-2-hydroxymethyl-2-methyl-3-methylenenorbornane (156). This compound seemed to offer a simple and convenient route to the required endo acid (88). Simmons-Smith methylenation of the unsaturated alcohol (156) afforded an excellent yield (88%) of the cyclopropanated derivative (157). Subsequent hydrogenolysis of (157) with platinum in acetic acid gave endo-2-acetoxymethyl-2,3,3-trimethylnorbornane (158) (16%) as well as the required endo-2-hydroxy-



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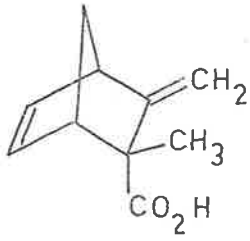

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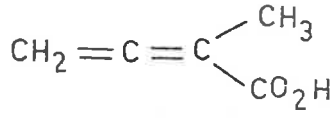

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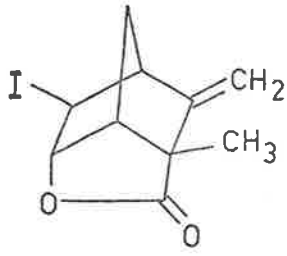

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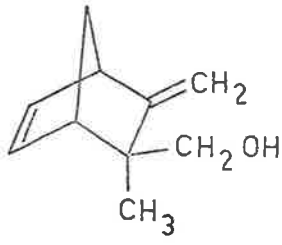

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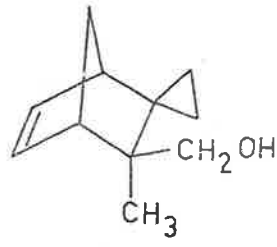

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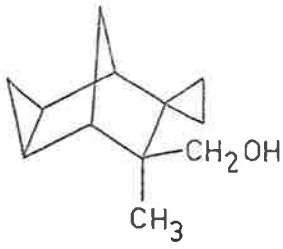

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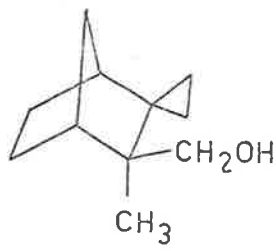
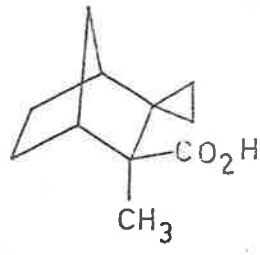
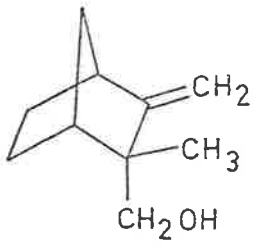


(154)

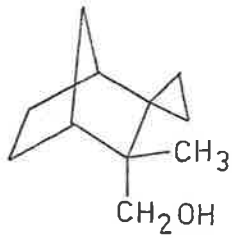


(155)

methyl-2,3,3-trimethylnorbornane (159). Oxidation of the last mentioned compound with Jones reagent gave the required endo-2-carboxy-2,3,3-trimethylnorbornane (88). An improved procedure, which avoided the undesired formation of acetyl derivative(s) under the conditions of the hydrogenolysis reaction, involved a quantitative conversion of the cyclopropyl alcohol (157) into the corresponding acid (160) by treatment with Jones reagent. Subsequent hydrogenolysis of (160) with platinum in glacial acetic acid gave the required endo acid (88) (> 90%).



(156)



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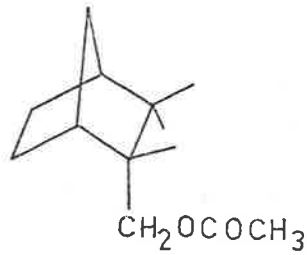

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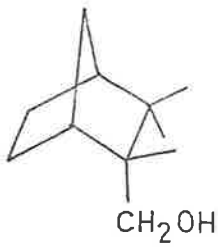
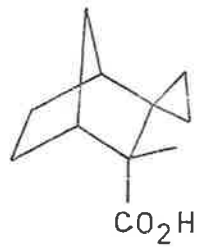


(159)



(160)

G.l.c. analysis of samples of exo- and endo-2-carboxy-2,3,3-trimethylnorbornane, obtained by the synthetic routes described above indicated that the two acids were different and neither sample was

contaminated by the other epimer. The n.m.r. spectra of the two acids showed that the chemical shifts of the three tertiary methyl groups were significantly different for each acid (Table 7).

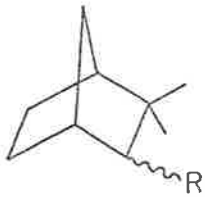
TABLE 7.

Chemical shifts (δ) of the methyl groups of exo- and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88) respectively.

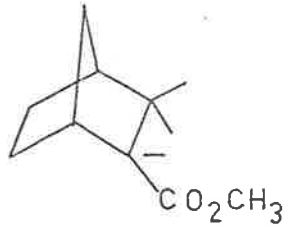
exo acid (87)	endo acid (88)
0.99	1.03
1.07	1.10
1.17	1.30

Before successful syntheses of the exo and endo acids (87) and (88) had been achieved, methylation at C_2 in 2-carbomethoxy-3,3-dimethylnorbornane (161) had been investigated as a possible route to the endo acid (88). Oxidative hydroboration[143] of camphene (123) afforded a mixture (1:9) of exo- and endo-2-hydroxymethyl-3,3-dimethylnorbornane (127) and (126) respectively, which on oxidation with Jones reagent gave a mixture (1:9) of the corresponding exo- and endo-2-carboxy-3,3-dimethylnorbornanes (162). The required 2-carbomethoxy-3,3-dimethylnorbornane (161) was readily prepared by methylation of the mixture of epimers of (162) with diazomethane. No attempt was made during the synthesis of (161) to separate the exo and endo isomers because the formation of a carbanion from either of the two epimers of the ester (161) would lead to the same species (163). Methylation of the anion should lead to

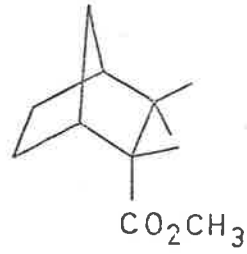
almost exclusive exo substitution[128-130] forming endo-2-carbomethoxy-2,3,3-trimethylnorbornane (164).



(161, R = CO_2CH_3)
(162, R = CO_2H)



(163)



(164)

Earlier investigation[123] indicated that the proposed methylation of (161) with methyl iodide in both 1,2-dimethoxyethane and N,N-dimethylformamide using sodium hydride[154] as base did not proceed; quantitative recoveries of starting material were obtained. Similarly, initial experiments using sodium triphenylmethylide[155] in ether as base and methyl iodide as the alkylating agent, were unsuccessful in the preparation of the required ester (164). However, evidence for the formation of the anion (163) was obtained by the addition of deuterium oxide, instead of methyl iodide, to the mixture formed from (161) and excess of sodium triphenylmethylide in ether after being refluxed for 24 hours. Mass spectrometry showed that deuterium had been incorporated into the ester (161) to an extent of c.75% under these conditions.

An attempt was also made to methylate the acid (162) at C_2. The successful alkylation of carboxylic acids in the α-position in tetrahydrofuran-hexamethylphosphoramide solution using lithium diiso-

propylamide as base has been reported.[156] When 2-carboxy-3,3-dimethylnorbornane (162) was treated with this base, followed by methyl iodide, starting material (98%) was recovered.

After having successfully synthesised the acids (87) and (88) by the routes already described, it was decided to reinvestigate the methylation of the ester (161). That deuterium was incorporated into the ester (161) under the conditions previously described suggested that successful methylation of (161) should be possible and this was indeed found to be the case. Treatment of the ester (161) with an excess of sodium triphenylmethylide followed by methyl iodide under somewhat prolonged conditions (see Experimental), gave a neutral fraction consisting of triphenylmethane, unchanged starting material (161), the required endo ester (164), its epimer (137), and impurities together with an acidic fraction (54%). The latter was identified as 2-carboxy-3,3-dimethylnorbornane (162) and was presumably formed from its ester (161) by the action of sodium triphenylmethylide in a $B_{AL}2$[157] reaction. A ready separation of the components of the neutral fraction was achieved by taking advantage of the relative ease of hydrolysis of the esters of secondary and tertiary carboxylic acids. When the neutral fraction was refluxed with dilute sodium hydroxide in aqueous methanol for 18 hours, 2-carboxy-3,3-dimethylnorbornane (162) (16%) and endo-2-carboxy-2,3,3-trimethylnorbornane (88) (0.5%) were obtained. The resultant neutral fraction was then heated with sodium hydroxide (0.5N) in 85% aqueous dimethylsulphoxide[158] for 19 hours at 87° to give a mixture of the endo acid (88) (19%) and the epimeric exo acid (87) (1%). However, as

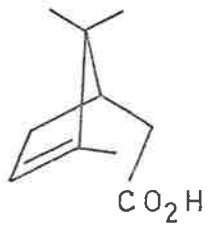
recrystallisation of the mixture resulted in only an inefficient removal of the minor component, preparation of the endo acid (88) by this method, especially when a pure sample was required, was considered far from satisfactory.

(ii) Exo- and endo-2-carboxybornane (85) and (86).

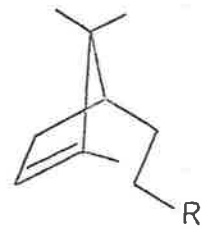
The exo and endo isomers of 2-carboxybornane may be prepared by methods outlined by Gream and Wege.[78]

(iii) β-(2,2,3-Trimethylcyclopent-3-enyl)propionic acid (89).

The unsaturated acid (89) was prepared from α-campholenic acid (165)[159] in the following manner. Reduction of the acid (165) with lithium aluminium hydride gave a good yield of the alcohol (166). Conversion of α-campholenol (166) into the corresponding p-nitrobenzenesulphonate (167)[160] followed by reaction with sodium cyanide in dimethylformamide afforded the corresponding nitrile (168). Alkaline hydrolysis of the crude nitrile (168) produced the required acid (89).



(165)



(166, R = OH)

(167, R = $OSO_2C_6H_4NO_2$)

(168, R = CN)

(89, R = CO_2H)

A sample of the methyl ester (89, CH_3 in place of H), prepared by treatment of the acid (89) with diazomethane, was examined by g.l.c. and was found to be essentially homogeneous. Of special importance was the absence of the methyl esters of *exo*- or *endo*-2-carboxybornane. There was, however, a trace (*c.* 1%) of impurity detected. It should be noted that the method outlined above for the preparation of the unsaturated acid (89) is almost identical to that described by Wege,[163] except that in the present work the α-campholenic acid (165) was reduced directly to give α-campholenol (166), while Wege reduced the methyl ester of the acid (165) to produce the alcohol (166).

2. Oxidative decarboxylation of carboxylic acids with lead tetraacetate.

The acids (85), (86), (87), (88), and (89) were treated with lead tetraacetate (c. 1.48 equivalents) in either benzene or dimethylsulphoxide, containing pyridine in the presence or absence of cupric acetate monohydrate at 92.5 - 93.5° for 4 hours. The results are summarised in Tables 8-12. For convenience, the decarboxylation reactions will be discussed in four parts:

(1) decarboxylation of exo- and endo-2-carboxybornane (85) and (86),

(2) decarboxylation of exo- and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88),

(3) decarboxylation of β-(2,2,3-trimethylcyclopent-3-enyl)propionic acid (89), and

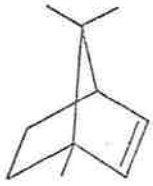
(4) correlation of results of the oxidative decarboxylation of the acids (85), (86), (87), and (88).

(1) Oxidative decarboxylation of exo- and endo-2-carboxybornane (85) and (86).

The products formed when the exo and endo isomers of 2-carboxybornane, i.e. (85) and (86) respectively, were treated under the conditions described above, included bornylene (31), tricyclene (169), camphene (123), 8-methylcamphene (170), bornyl acetate (64), isobornyl acetate (63), camphene hydrate acetate (171), a mixture of three acetates (i.e. A, B, and C), camphor (25), acetoxydimethylsulphoxide (173), and

a product which could not be identified. The results are summarised in Tables 8 and 9. The products 8-methylcamphene (170) and the acetates A, B, and C were found by Gream and Wege[78] to be formed when camphene was treated with lead tetraacetate in benzene, and were therefore due to secondary reactions. The results of studies of the action of lead tetra-acetate on camphene in acetic acid by several workers[161,162] led Wege[163] to postulate that one of the acetates (i.e. A, B, or C) was the ring expanded enol-acetate (172). The identification of camphor (25) and acetoxydimethylsulphoxide (173) will be discussed later. It should be noted that the results of the study of the uncatalysed oxidative decarboxylation of the bornyl acids (85) and (86), carried out by Wege[78] (Table 5) are in close agreement with the results obtained in the present work (Tables 8 and 9).

The significant result to be noted in the decarboxylation of exo- and endo-2-carboxybornane (85) and (86), is that in the presence of added copper II salts, there is a dramatic decrease in the amount of rearranged products. In the absence of copper II salts, the major product formed from the decarboxylation of (85) or (86) was camphene (123) (56-59% in benzene). However, on the addition of cupric acetate, the unrearranged olefin, bornylene (31) became the major product; the yield increasing from c. 0.5% in the uncatalysed reaction to 59-70% in the presence of copper II acetate. The oxidative decarboxylation of acids in the presence of copper II salts has also been reported by Kochi[66] and Cross[79] to result in the formation of increased amounts of unrearranged olefins at the expense of rearranged products. The above workers have



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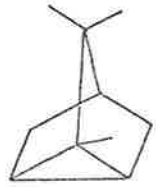

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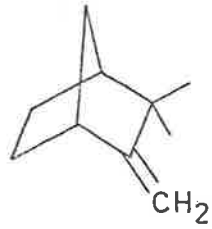

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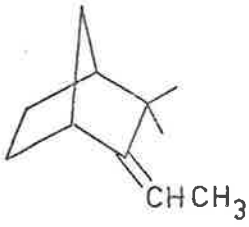

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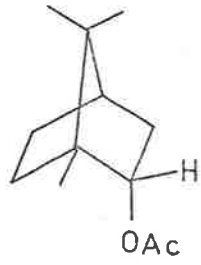

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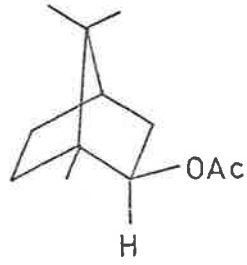
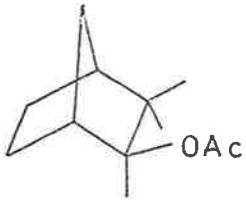


(63)



(171)

(172)

suggested that the formation of olefins involved copper alkyl intermediates which decomposed via a cyclic transition state in which cationic character was not well developed (Fig. 5). Kochi[66] has suggested that the formation of olefins by this process may be favoured by synergic bonding between the olefin and the copper I salt formed.[164]

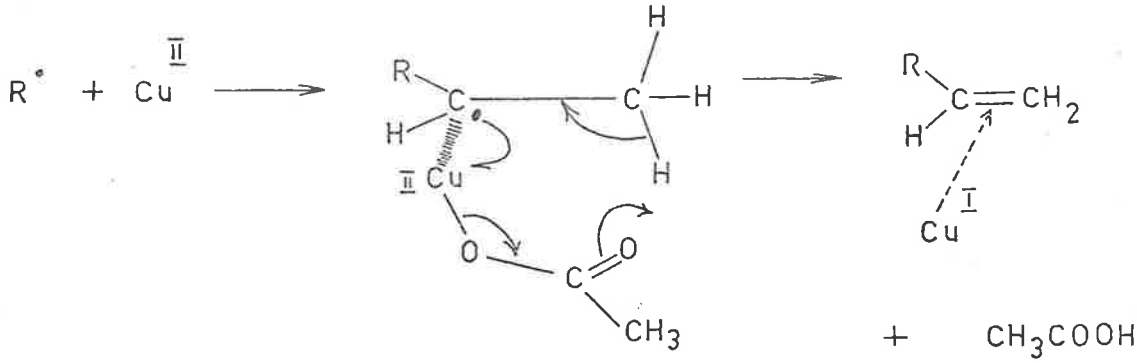


Fig. 5.

The decrease in the yield of rearranged products in the copper II catalysed decarboxylation of (85) and (86) suggests that cationic intermediates may not be formed initially, but may be possibly derived from lead alkyl species. That the free bornyl radical (66) was an intermediate in these reactions was extremely unlikely as Berson and coworkers[165] have shown that, in the temperature range of the above reactions, the bornyl radical does not undergo skeletal rearrangement. Hence the presence of substantial amounts of rearranged products demonstrates that free radical intermediates are not directly involved in the reaction.* It has also been shown[165,166] that the main product in

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* The formation of camphor (25) in small amounts (c. 2%) may involve the intermediacy of the bornyl radical; however, this reaction will be discussed in more detail later.

reactions of the bornyl radical (66) is bornane (65); this product was not detected in the above reactions even though the analytical conditions were such that 0.1% of the compound could have been detected.

As a result of both kinetic and product studies carried out by Cross[79] on the cupric ion oxidation of the heptyl, 3,3-dimethyl-2-butyl, 2,3-dimethyl-2-butyl, and 1- and 2-adamantyl radicals, generated by the action of lead tetraacetate on the corresponding carboxylic acids, it was postulated that the oxidation of alkyl radicals by lead carboxylates involved two distinct mechanisms.

(i) Oxidation by lead IV involving an electron transfer reaction forming a cation and a lead III carboxylate. This is exactly the same as equation 4, Scheme 6 in Kochi's proposed mechanism (see Introduction).

i.e. $Pb^{IV} + R^{\cdot} \rightarrow Pb^{III} + R^{+}$

(ii) Oxidation by lead III involving the formation of a lead IV alkyl which may decompose via a cyclic S_Ni mechanism* yielding acetates (Fig. 6) or by a cyclic cis-elimination giving olefins (Fig. 7).

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* Criegee[167] has postulated that in the reaction of certain olefins with lead tetraacetate, decomposition of lead alkyl intermediates may occur via a cyclic mechanism to form acetates in a similar manner to that described above.

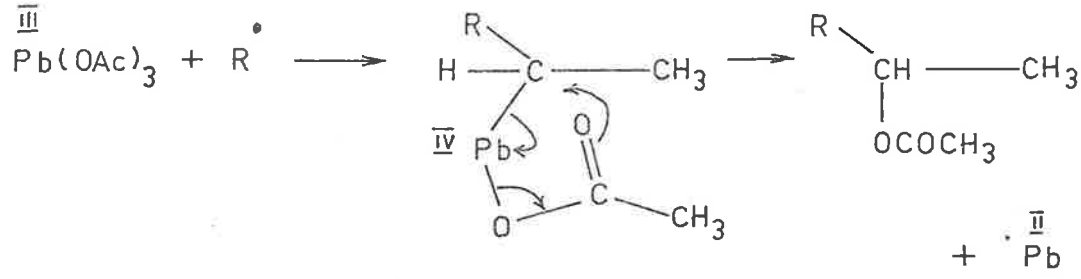


Fig. 6.

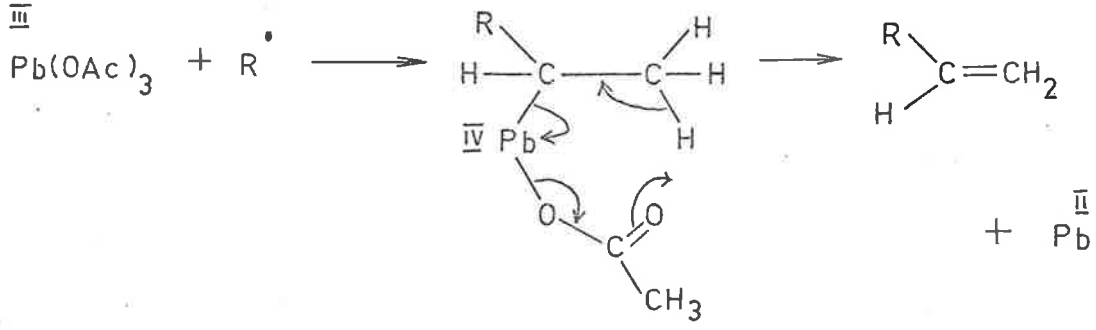
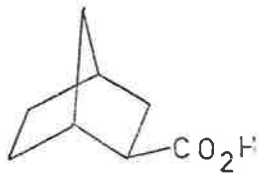


Fig. 7.

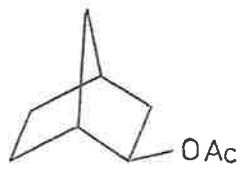
Such a duality of mechanism provides an alternative explanation for the results of Corey and Casanova.[77] The above workers found that oxidative decarboxylation of optically active exo- or endo-2-carboxy-norbornane, i.e. (60) or (61), gave only the exo acetate (62) which had a 43% retention of optical activity when benzene was used as solvent. The classical norbornyl cation (4) was proposed as an intermediate in

the reaction. However, the above results may be explained on the basis of free radical intermediates which may be oxidised by either lead III or lead IV as described above. On this basis 43% of the exo acetate (62) arises via a cyclic S_Ni mechanism, which results in retention of optical identity. The remainder of the product reacts with lead IV and possibly lead III by an electron transfer mechanism, yielding racemic products via cationic intermediates.

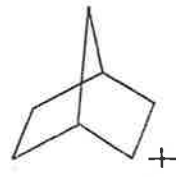


(60)

(61)



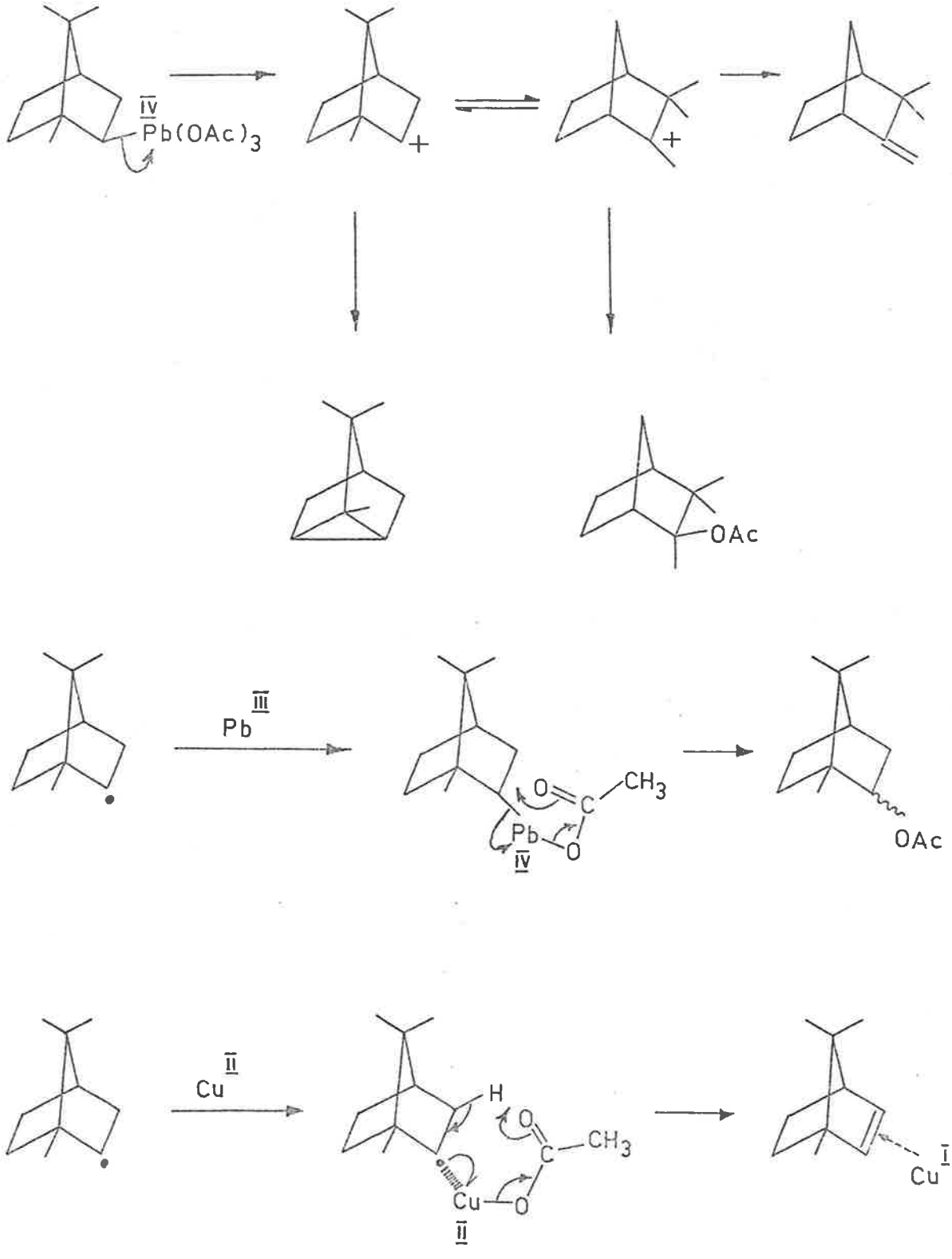
(62)



(4)

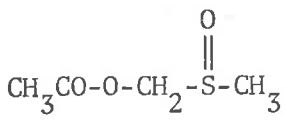
Formation of the observed products from the oxidative decarboxylation of exo- and endo-2-carboxybornane (85) and (86), may also be rationalised in terms of either lead IV alkyl intermediates or direct electron transfer involving oxidation by lead IV to produce cations directly. Possible routes to some of the products are depicted in Scheme 13. The formation of bornylene (31) in the copper II catalysed decarboxylation of the acids (85) and (86) may be explained in terms of a copper alkyl intermediate which may decompose by a cyclic cis elimination as has been proposed by Kochi[66] and Cross[79] (Scheme 13).

In an attempt to identify some of the minor products which were formed in the oxidative decarboxylation of the bornyl acids, a 75:25

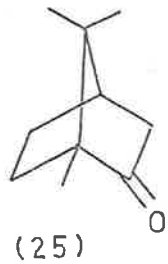


Scheme 13.

mixture of exo:endo 2-carboxybornane i.e. (85) and (86), was treated with lead tetraacetate in dimethylsulphoxide containing pyridine. Treatment of either of the acids under the conditions described above was shown in the quantitative work to produce a mixture of three products, whose structures were unknown. Preparative g.l.c. afforded a complete separation of the three unknown components formed from the large scale (c. 1 g of acid) reaction of the 75:25 mixture of acids. Two of the products were readily identified as camphor (25) and acetoxydimethylsulphoxide (173) (see Experimental). The third product appeared to be a mixture and could not be identified on the basis of its spectral characteristics. Since only very small quantities of the product were available, this compound was not further investigated.



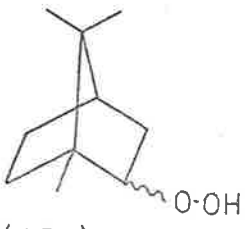
(173)



(25)

Acetoxydimethylsulphoxide (173) was found to be present in all the oxidative decarboxylation reactions in which dimethylsulphoxide was used as a solvent, and was assumed to result from the reaction of lead tetraacetate with the solvent. Camphor (25) was observed as a product when the bornyl carboxylic acids (85) and (86) were treated with lead tetraacetate in either benzene or dimethylsulphoxide as solvent, and in the presence or absence of copper II acetate. It was considered that the camphor may have been produced by a scavenging of the bornyl radical (66)

by traces of oxygen present in the reaction medium. In order to test this hypothesis, the oxidative decarboxylation reaction was carried out in an atmosphere of oxygen for varying lengths of time. In the presence of supposedly oxygen-free nitrogen, treatment of the mixture of acids under the conditions described above afforded c. 2% camphor (25). However, in an atmosphere of dry oxygen, similar treatment for six hours gave a 9% yield of camphor, while the yield was increased to 13% after 48 hours. These results would appear to indicate that oxygen is involved in the formation of camphor and the detection of camphor in the oxidative decarboxylation reactions of exo- and endo-2-carboxybornane (85) and (86) may provide some evidence for the intermediacy of the bornyl radical (66) in these reactions. A possible route to camphor (25) may involve initial formation of the hydroperoxide (174) by reaction of the bornyl radical with oxygen. Subsequent breakdown of the hydroperoxide under the reaction conditions, followed by oxidation of the alcohol (175) by lead tetraacetate may have produced the camphor. Treatment of isoborneol (175, exo-OH) with lead tetraacetate, under the conditions described for the oxidative decarboxylation of the acids (85) and (86) in dimethylsulphoxide gave camphor (25) almost exclusively. Another possible source of the alcohol (175) may involve a trapping of the bornyl cation (67) by traces of water in the reaction medium.



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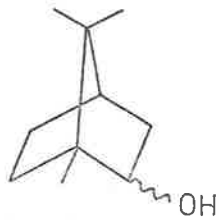


(175)

TABLE 8.

Product composition of the oxidative decarboxylation of exo-2-carboxybornane (85).

	$Pb(OAc)_4$ benz/py -	$Pb(OAc)_4$ benz/py Cu^{++}	$Pb(OAc)_4$ DMSO/py -	$Pb(OAc)_4$ DMSO/py Cu^{++}
Bornylene (31)	0.6	58.9	0.1	30.9
Tricyclene (169)	2.4	0.5	0.1	trace
Camphene (123)	58.5	35.3	63.9	49.4
8-Methylcamphene (170)	3.1	-	3.5	-
Bornyl acetate (64)	2.4	0.2	1.7	0.4
Isobornyl acetate (63)	5.1	0.7	1.6	0.4
Camphene hydrate Acetate (171)	10.5	2.6	1.8	0.9
Acetates A, B, and C (Secondary products)	3.5	0.7	-	-
Camphor (25)	2.0	0.5	2.0	1.8
Acetoxydimethylsulphoxide (173)	-	-	2.0	0.9
Unknown	5.5	4.3	2.0	3.7
Ratio of (64) : (63)	32:68	20:80	53:47	48:52
Equivalents of $Pb(OAc)_4$	1.48	1.39	1.45	1.45
(average of 2 reactions)	1.50	1.44	1.46	1.46
Total % yield*	93.6	103.7	78.7	88.4

* The yields expressed above are absolute % yields based on the amount of acid which underwent reaction.

TABLE 9.

Product composition of the oxidative decarboxylation of endo-2-carboxybornane (86).

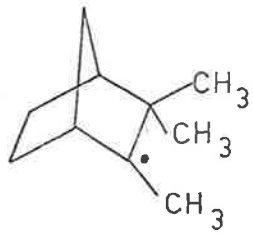
	$Pb(OAc)_4$ benz/py -	$Pb(OAc)_4$ benz/py Cu^{++}	$Pb(OAc)_4$ DMSO/py -	$Pb(OAc)_4$ DMSO/py Cu^{++}
Bornylene (31)	0.4	70.1	0.1	27.5
Tricyclene (169)	2.4	0.5	0.1	trace
Camphene (123)	55.7	21.3	52.9	38.1
8-Methylcamphene (170)	2.2	-	4.2	-
Bornyl acetate (64)	2.3	0.4	1.6	0.4
Isobornyl acetate (63)	5.0	1.0	1.5	0.5
Camphene hydrate Acetate (171)	10.1	2.3	1.6	0.7
Acetates A, B, and C (secondary products)	6.2	0.3	-	-
Camphor (25)	0.5	0.6	2.1	0.8
Acetoxydimethylsulphoxide(173)	-	-	2.2	0.9
Unknown	6.1	5.1	2.1	3.6
Ratio of (64) : (63)	32:68	26:74	53:47	46:54
Equivalents of $Pb(OAc)_4$	1.48	1.45	1.47	1.46
(average of 2 reactions)	1.52	1.48	1.47	1.46
Total % yield	90.9	101.6	68.4	72.5

(2) Oxidative decarboxylation of exo and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88).

The oxidative decarboxylation of the above acids, i.e. (87) and (88), gave similar but not identical product distributions to those observed for the decarboxylation (in the absence of copper II salts) of exo- and endo-2-carboxybornane (85) and (86). The results are summarised in Tables 10 and 11. The acids (87) and (88) afforded slightly higher yields of camphene (123) than did the corresponding bornyl carboxylic acids (85) and (86). The addition of copper II acetate did not produce the dramatic changes in product distribution observed in the decarboxylation of the bornyl carboxylic acids; however, there was a small increase in the yield of camphene (123) in the presence of copper II salts (c. 65% yield for the decarboxylation of the endo acid (88) in the absence of copper to c. 78% in the copper catalysed reaction). The relatively small changes observed in the copper catalysed decarboxylation of the tertiary acids (87) and (88) are not surprising, since, in this case, the only β-hydrogen atoms available to participate in a cyclic elimination reaction as postulated in the decarboxylation of the bornyl acids (85) and (86) are the bridgehead hydrogen at C_1, and the hydrogen atoms on the C_2 methyl group. Elimination from the bridgehead position would be an unfavourable process on the basis of Bredt's Rule[168] and elimination of one of the hydrogen atoms on the C_2 methyl group would give camphene (123).

The similarity in product distribution between the uncatalysed and copper catalysed decarboxylation reactions of the acids (87) and (88)

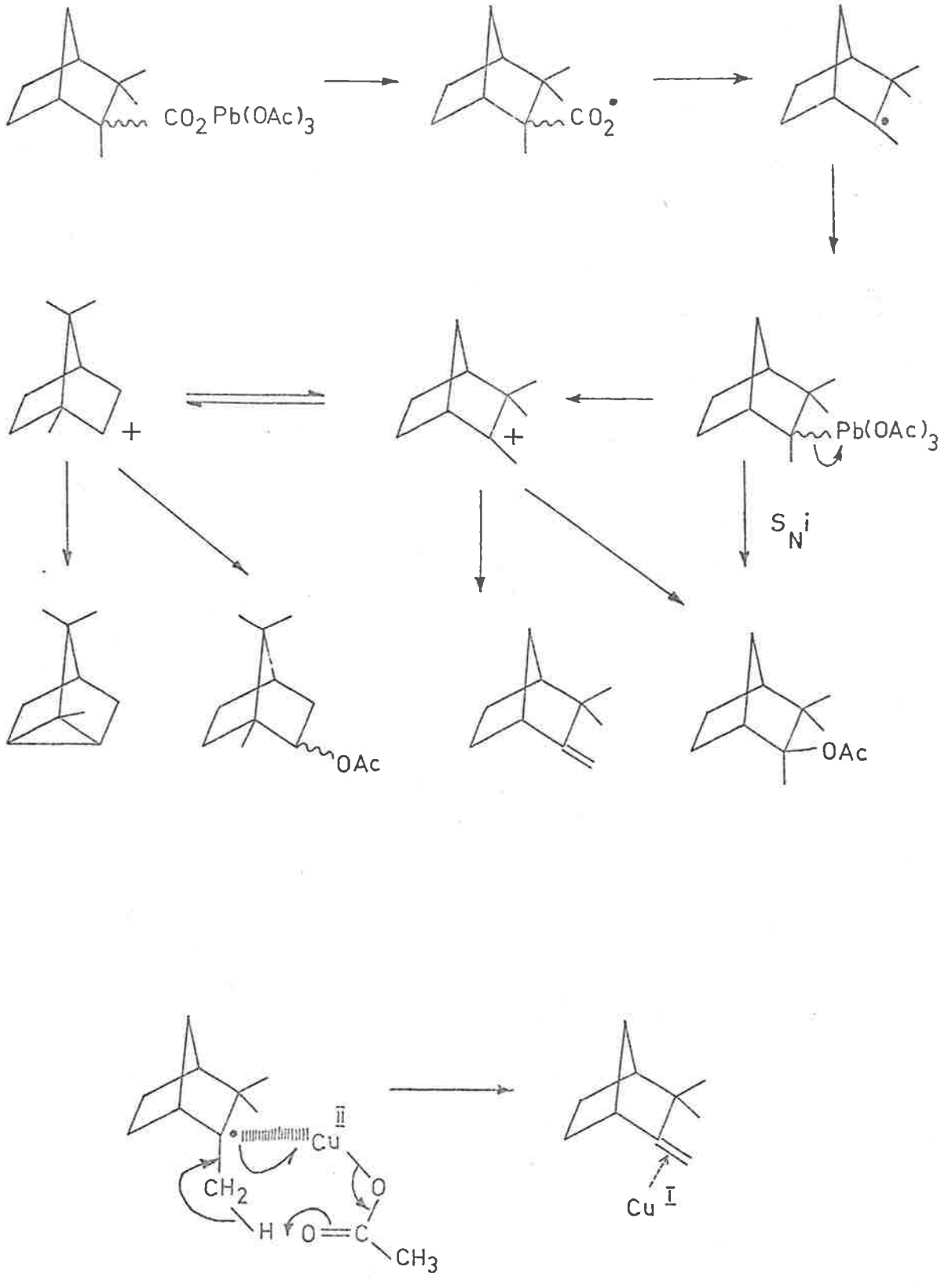
suggests that, in the case of tertiary alkyl radicals, lead IV and lead III species are competing effectively with the copper II salts in product formation. This would appear to be borne out by the fact that the addition of copper II salts, on decarboxylation of the secondary bornyl carboxylic acids produces an increase (c. 10%) in the overall yield of the reaction (Tables 8 and 9). In the case of the tertiary carboxylic acids however, no appreciable increase in the overall yield of products in the reactions is observed on the addition of cupric acetate (Tables 10 and 11). It should also be noted that decarboxylation of the tertiary acids (87) and (88), produced no products which were directly attributable to the free 2,3,3-trimethylnorbornyl radical (176).



(176)

Possible routes to the products observed in the decarboxylation of the tertiary acids (87) and (88) are depicted in Scheme 14.

The oxidative decarboxylation reactions of (85), (86), (87), and (88) were also carried out in dimethylsulphoxide as solvent. It was considered that such a typical dipolar aprotic solvent may provide further insight into the mechanism of the oxidative decarboxylation reaction. Dimethylsulphoxide has been reported[169] in certain cases to



Scheme 14.

facilitate the oxidative decarboxylation reaction. Chapman and co-workers[169] have reported that oxidative bisdecarboxylation reactions which proceed only slowly in refluxing benzene occur readily in dimethylsulphoxide at room temperature. Dramatic changes in product compositions were however, not found when dimethylsulphoxide was used instead of benzene in the oxidative decarboxylation reactions of the acids (85), (86), (87), and (88). There was observed, however, a general increase in the yield of camphene (123) at the expense of tricyclene (169) and the bicyclic acetates.

The formation of small amounts (c. 2%) of camphor (25) on decarboxylation of the acids (87) and (88) in dimethylsulphoxide as solvent was surprising, since the bornyl radical (66) [i.e. the proposed precursor to the camphor which was formed on decarboxylation of the acids (85) and (86)] was not expected to be an intermediate in these reactions. That camphor (25) could have resulted from a secondary reaction of one of the products of the reaction with lead tetraacetate was also investigated. Treatment of isobornyl acetate (63), camphene hydrate acetate (171), and camphene hydrate (171, H in place of Ac) with lead tetraacetate under the conditions of the decarboxylation reaction, resulted in the formation of very small amounts (< 0.5%) of camphor from each of the above compounds. Camphene hydrate was considered to be a possible intermediate in the decarboxylation of (87) and (88) if either (i) the 2,3,3-trimethylnorbornyl radical (176) was trapped by traces of oxygen in the reaction mixture in an analagous process to that described for the bornyl radical (66), or (ii) the 2,3,3-trimethylnorbornyl cation

TABLE 10.

Product composition of the oxidative decarboxylation of exo-2-carboxy-2,3,3-trimethylnorbornane (87).

	$Pb(OAc)_4$ benz/py -	$Pb(OAc)_4$ benz/py Cu^{++}	$Pb(OAc)_4$ DMSO/py -	$Pb(OAc)_4$ DMSO/py Cu^{++}
Bornylene (31)	-	-	-	-
Tricyclene (169)	1.6	1.6	0.1	0.1
Camphene (123)	66.9	77.4	76.2	75.9
8-Methylcamphene (170)	0.5	-	2.3	-
Bornyl acetate (64)	-	-	0.2	<0.1
Isobornyl acetate (63)	1.1	1.1	0.6	0.8
Camphene hydrate acetate (171)	9.7	7.8	2.2	1.6
Methylcamphenilyl acetate (186)	-	0.6	-	0.2
Acetates A, B, and C (secondary products)	7.1	2.1	-	-
Camphor (25)	-	-	1.7	1.4
Acetoxydimethylsulphoxide (173)	-	-	1.6	0.7
Unknown	5.4	3.6	-	-
Ratio of (64) : (63)	0:100	0:100	22:78	5:95
Ratio of (186) : (171)	0:100	7:93	0:100	10:90
Equivalents of $Pb(OAc)_4$	1.48	1.48	1.48	1.48
(average of 2 reactions)	1.49	1.48	1.48	1.49
Total % yield	92.3	94.2	84.9	80.7

TABLE 11.

Product composition of the oxidative decarboxylation of endo-2-carboxy-2,3,3-trimethylnorbornane (88).

	$Pb(OAc)_4$ benz/py -	$Pb(OAc)_4$ benz/py Cu^{++}	$Pb(OAc)_4$ DMSO/py -	$Pb(OAc)_4$ DMSO/py Cu^{++}
Bornylene (31)	-	-	-	-
Tricyclene (169)	1.2	1.4	trace	0.1
Camphene (123)	64.7	77.7	73.9	78.7
8-Methylcamphene (170)	0.1	-	2.8	-
Bornyl acetate (64)	-	-	0.2	-
Isobornyl acetate (63)	1.2	1.0	0.6	0.8
Camphene hydrate acetate (171)	10.7	8.9	2.3	2.1
Methylcamphenilyl acetate (186)	-	0.3	-	trace
Acetates A, B, and C (secondary products)	9.2	3.5	-	-
Camphor (25)	-	-	2.0	1.5
Acetoxydimethylsulphoxide(173)	-	-	0.9	0.5
Unknown	6.8	4.4	-	-
Ratio of (64) : (63)	0:100	0:100	20:80	0:100
Ratio of (186) : (171)	0:100	3:97	0:100	1:99
Equivalents of $Pb(OAc)_4$	1.48	1.48	1.48	1.48
(average of 2 reactions)	1.50	1.48	1.48	1.49
Total % yield	93.9	97.2	82.7	83.7

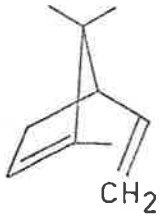
(182) was trapped by traces of moisture in the reaction medium. No further attempts were made, however, to determine the precise origin of the camphor in this work.

(3) Oxidative decarboxylation of β-(2,2,3-trimethylcyclopent-3-enyl)-propionic acid (89).

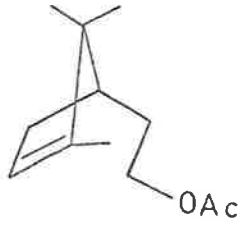
Preliminary studies of the oxidative decarboxylation reaction of β-(2,2,3-trimethylcyclopent-3-enyl)propionic acid (89) by Wege[163] indicated that similar products to those obtained from the decarboxylation of the bornyl carboxylic acids (85) and (86) were formed; i.e. tricyclene (169), camphene (123), 8-methylcamphene (170), and bicyclic acetates. It was suggested by Wege[163] that the low yield (c. 10%) of decarboxylation products might be increased by the addition of cupric acetate which, he envisaged, would increase the efficiency of oxidation of possible alkyl radical intermediates to carbonium ions. Since there was some doubt as to the homogeneity of the material used by Wege, the oxidative decarboxylation reaction of the unsaturated acid (89) was re-examined and extended to include an examination of the effects of copper II salts and to study the effect of change of solvent. The results of these studies are summarised in Table 12.

The products formed when the unsaturated acid (89) was treated with lead tetraacetate in benzene containing pyridine included the diene (177, trace), the olefin (178, 1.5%), tricyclene (169, 1.5%), camphene (123, 21%), 8-methylcamphene (170, 1%), isobornyl acetate (63, 1%), camphene hydrate acetate (171, 3%), the acetates A, B, and C, and

possibly a trace of α-campholenyl acetate (179).



(177)



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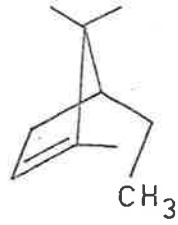

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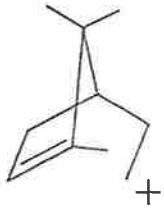

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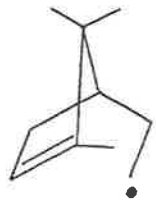


(181)

The overall yield of products in the uncatalysed reaction was c. 33%. However, on the addition of cupric acetate to the decarboxylation reaction, the yield was increased to c. 68%. An even more dramatic increase in yield was achieved when dimethylsulphoxide was used as solvent. In this case the yield was increased from c. 6% in the uncatalysed reaction to c. 36% in the presence of copper II salts. The generally lower yields found on decarboxylation of the unsaturated acid (89) in comparison with those found for the acids (85), (86), (87), and (88) may be attributed, at least in part, to the lower reactivity of a primary carboxylic acid towards lead tetraacetate[62] and to the susceptibility of the double bond in (89) to attack by lead tetraacetate. Kochi[62] and

Cross[79] have reported that the addition of copper II salts markedly increases the rate of decarboxylation of primary carboxylic acids. Thus the increased rate of decarboxylation (and hence cyclisation) of the unsaturated acid (89) may result in a decrease in the amount of by-products formed by attack on the double bond of the acid (89) by lead tetraacetate. Hence an overall increase in the yield of identifiable products might be expected.

Of particular significance in the product distribution of the above reaction was the virtual absence of the diene (177) in the uncatalysed reaction, and the formation of this compound as the major product (33%) in the copper catalysed reaction. The fact that only trace amounts of the diene (177) and α-campholenyl acetate (179) were formed in the uncatalysed reaction suggested that the α-campholenyl cation (180) was an unlikely intermediate in the reaction. According to Kochi's mechanism[62-66] for the decarboxylation of acids by lead tetraacetate, one of the intermediates expected in the decarboxylation of the unsaturated acid (89) would be the α-campholenyl radical (181). Formation of the diene (177) may be postulated to involve trapping of the α-campholenyl radical (181) by a copper II species, with subsequent elimination via a cyclic copper-acetate-substrate transition state (Fig. 8), by a similar process to that suggested for the copper catalysed decarboxylation of the bornyl carboxylic acids (85) and (86). The olefin (178) must have arisen from the α-campholenyl radical (181) by a hydrogen abstraction reaction.

The formation of cyclised products (camphene, tricyclene,

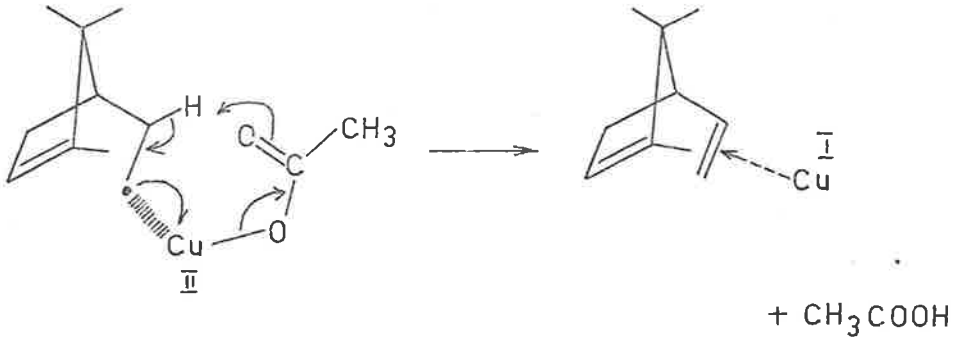
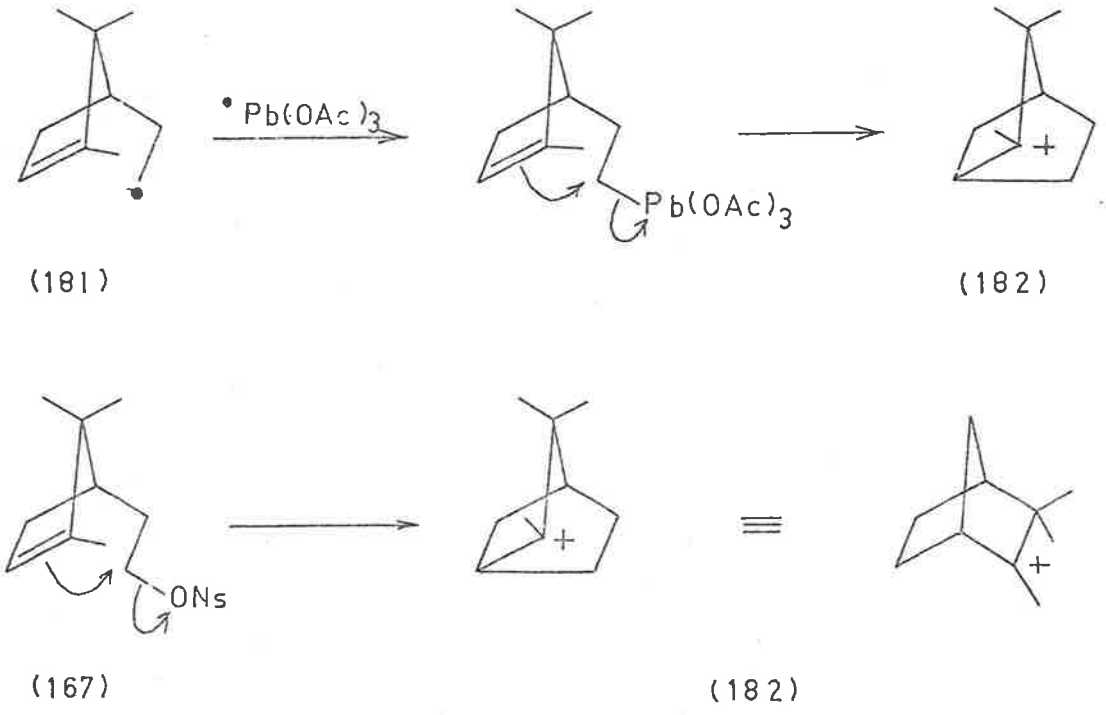


Fig. 8.

8-methylcamphene, isobornyl acetate, and camphene hydrate acetate) raises several important questions. Both the rate of cyclisation and the mode of cyclisation will be significant factors in determining the product distribution of the reaction. Because of the proposed intermediacy of the α-campholenyl radical (181) in the oxidative decarboxylation of the unsaturated acid (89), it was considered necessary to generate the radical under conditions where formation of metal alkyl species and subsequent oxidative processes were not possible. The results of this study are described in a subsequent section (Results and Discussion, part 3).

The possibility that cationic intermediates may be involved in the oxidative decarboxylation of the unsaturated acid (89) prompts a comparison of the products found in the above reactions, with those obtained on solvolysis of the p-nitrobenzenesulphonate of α-campholenol

i.e. (167). The products observed by Gream and Wege[160] on acetolysis of the sulphonate (167) for 5 hours at 100° in the presence of excess of sodium acetate included camphene (123, 73%), tricyclene (169, 2%), isobornyl acetate (63, 14%), and α-campholenyl acetate (179, 8%). The marked similarity between the products observed on solvolysis of (167) and those obtained from the uncatalysed decarboxylation of (89), (see Table 12) suggests that similar intermediates may be involved in the two reactions (e.g. the 2,3,3-trimethylnorbornyl cation (182), see Scheme 15).



Scheme 15.

TABLE 12.

Product composition of the oxidative decarboxylation of β-(2,2,3-trimethyl-cyclopent-3-enyl)propionic acid (89).

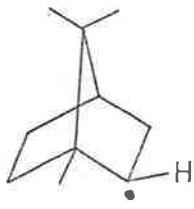
	$Pb(OAc)_4$ benz/py -	$Pb(OAc)_4$ benz/py Cu^{++}	$Pb(OAc)_4$ DMSO/py -	$Pb(OAc)_4$ DMSO/py Cu^{++}
Diene (177)	trace	33.0	-	28.6
Olefin (178)	1.6	-	0.1	-
Tricyclene (169)	1.6	1.2	-	-
Camphene (123)	20.9	27.4	2.2	3.7
8-Methylcamphene (170)	0.9	-	-	-
Bornyl acetate (64)	-	0.3	-	-
Isobornyl acetate (63)	1.3	0.7	-	-
Camphene hydrate acetate (171)	3.0	2.0	-	-
Methylcamphenilyl acetate(186)	-	-	-	-
α-Campholenyl acetate (179)	trace	-	-	-
Acetates A, B, and C (secondary products)	3.3	trace	-	-
Unknown	-	3.3	3.9	3.2
Ratio of (64) : (63)	0:100	30:70	-	-
Ratio of (186) : (171)	0:100	0:100	-	-
Equivalents of $Pb(OAc)_4$	1.45	1.47	1.46	1.46
(average of 2 reactions)	1.47	1.48	1.47	1.46
Total % yield	32.6	67.9	6.2	35.5

(4) Correlation of results of the oxidative decarboxylation of the acids (85), (86), (87), and (88).

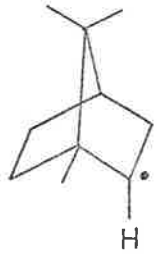
The fact that a given epimeric pair of carboxylic acids, i.e. (85) and (86) or (87) and (88) gives essentially the same product distribution on decarboxylation suggests that the initially formed radical intermediate (assuming Kochi's mechanism is correct) undergoes rapid equilibration before being trapped by either a lead III or a copper II species. Hence subsequent decomposition of the resultant lead or copper alkyl species gives the same product distribution for either epimeric acid.

Of interest is the ratio of bornyl:isobornyl acetates (ie. endo:exo) formed in the various decarboxylation reactions (Table 13). The formation of bornyl and isobornyl acetates (64) and (63) may arise either by a cyclic S_Ni mechanism involving a lead IV or copper II alkyl intermediate, as has been suggested by Kochi[66] and Cross,[79] or by direct acetate attack on a cationic intermediate produced by an electron transfer reaction between a lead IV or lead III species and the alkyl radical. The ratio of bornyl:isobornyl acetate formed by an cyclic S_Ni reaction should be influenced by the ratio of bornyl:isobornyl radicals, i.e. (66a) and (66b), in the equilibrium mixture, or, if the radical is planar, the relative amounts of exo:endo attack by the lead or copper species. That equilibrium mixtures may be formed on treatment of epimeric carboxylic acids with lead tetraacetate has been demonstrated by Elakovich and Traynham.[170] These workers found that treatment of either

cis- or trans-4-t-butylcyclohexanecarboxylic acid, (183) or (184) respectively, with lead tetraacetate in the presence of lithium chloride gave the same mixture of epimeric chlorides (185).



(66a)



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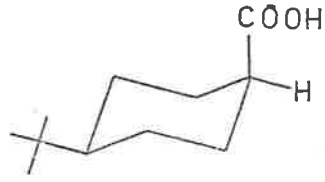

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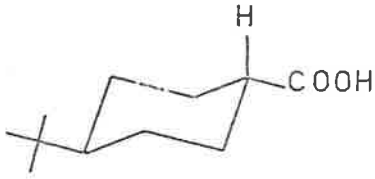

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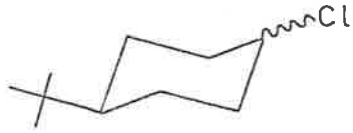


(185)

In the cationic pathway to acetate formation, the factors influencing the ratio of bornyl:isobornyl acetate may include the properties of the solvent and the nature of the attacking nucleophile.

The formation of appreciable amounts of endo acetate, i.e. bornyl acetate (64) on oxidative decarboxylation of the bornyl carboxylic acids (85) and (86) may be a result of the bulky 7-syn methyl group hindering to some extent, the approach of a large lead species from the

TABLE 13.

Ratio of bornyl (64) : isobornyl (63) acetates formed from the oxidative decarboxylation of the acids (85),(86),(87), and (88).

Substrate	$Pb(OAc)_4$ benz/py -	$Pb(OAc)_4$ benz/py Cu^{++}	$Pb(OAc)_4$ DMSO/py -	$Pb(OAc)_4$ DMSO/py Cu^{++}
(85)	32:68	20:80	53:47	48:52
(86)	32:68	26:74	53:47	46:54
(87)	0:100	0:100	22:78	5:95
(88)	0:100	0:100	20:80	0:100

exo side of the molecule. The small decreases in the proportion of endo acetate produced when copper II salts were present in the reaction may be a result of the less bulky copper species being more able to approach the bornyl radical (66) from the exo side of the molecule. When dimethylsulphoxide was used as solvent, a substantial increase in the proportion of bornyl acetate (64) resulted. This may be due to increased solvation of the bornyl cation (67) by dimethylsulphoxide from the exo side of the molecule, resulting in the increased possibility of attack from the endo direction by the relatively unsolvated acetate anion.

In the case of the decarboxylation of exo- and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88) in benzene as solvent, only the exo acetate, i.e. isobornyl acetate (63) was formed. This result is not surprising since formation of the rearranged isobornyl acetate must

have involved a cationic precursor. That cations generated by solvolysis of isobornyl derivatives produce exclusively exo substituted products has been well documented.[12] However, decarboxylation of either exo- or endo-2-carboxy-2,3,3-trimethylnorbornane (87) or (88) in dimethylsulphoxide as solvent in the absence of copper II salts gave a mixture of endo:exo acetates in the ratio of 20:80 respectively. A similar increase in the proportion of endo acetate was observed on decarboxylation of the bornyl carboxylic acids (85) and (86) in dimethylsulphoxide. This may be a result of increased solvation of the bornyl cation (67) by dimethylsulphoxide from the exo side of the molecule rendering endo attack by the acetate anion more likely. The almost exclusive formation of exo acetate from the copper catalysed decarboxylation of the acids (87) and (88) in dimethylsulphoxide appears anomalous and a further study of these reactions, in a variety of solvents and in the presence and absence of copper, would appear to be necessary in order to further elucidate the mechanism of the oxidative decarboxylation process.

Also of interest was the fact that the exo acetate, camphene hydrate acetate (171), formed by decarboxylation of the tertiary acids (87) and (88) in benzene or dimethylsulphoxide in the presence of added copper II salts (Table 10 and 11), was contaminated by small amounts (1-10%) of the corresponding endo acetate, i.e. methylcamphenilyl acetate (186). The endo acetate (186) was not detected in the products of the decarboxylation of the corresponding bornyl carboxylic acids (85) and (86) under any of the reaction conditions studied. Formation of the tertiary endo acetate (186) may be a result of endo attack on the 2,3,3-

trimethylnorbornyl radical (176) by cupric acetate. Subsequent decomposition of the copper alkyl intermediate by a cyclic S_Ni mechanism may be postulated to rationalise the product observed (Fig. 9).

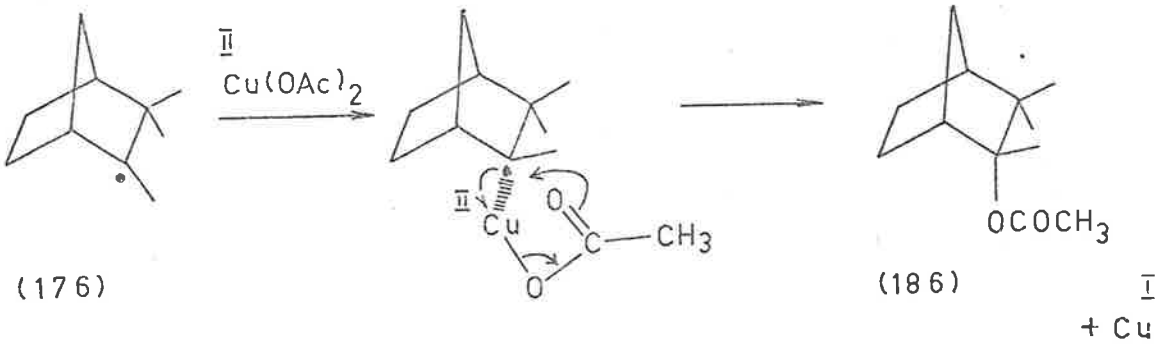
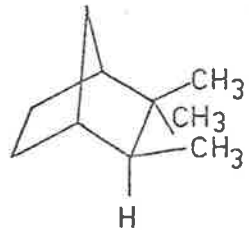


Fig. 9.

The absence of methylcamphenilyl acetate (186) when lead IV was the only oxidant present in the reaction may be a result of the greater bulk of the lead species precluding attack from the endo side of the molecule. The observation that endo attack on the 2,3,3-trimethylnorbornyl radical (176) formed in the copper catalysed decarboxylation of the tertiary acids (87) and (88), can occur to an extent of no more than 10%, would appear to be consistent with the observation that generation of the 2,3,3-trimethylnorbornyl radical (176) under non-oxidative conditions (see Results and Discussion, part 3), results in 4-6% endo hydrogen abstraction producing the hydrocarbon

(187), i.e. 2,3,3-trimethylnorbornane (exo isocamphane).

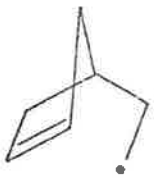


(187)

An attempt was also made in the present work to study the oxidative decarboxylation reactions in acetic acid as solvent. It was found however, that treatment of the acids (85), (86), and (89) with lead tetraacetate in acetic acid as solvent gave no observable products.

3. Cyclisation of the α-campholenyl radical (181).

Because of the proposed intermediacy of the α-campholenyl radical (181) and the formation of cyclised products in the oxidative decarboxylation of β-(2,2,3-trimethylcyclopent-3-enyl)propionic acid (89) it was considered necessary to generate the radical (181) under conditions where formation of possible lead or copper alkyl species, and subsequent oxidative processes were not possible. The process developed by Menapace and Kuivila[68] involving treatment of the appropriate halide with tri-n-butyltin hydride appeared to provide the ideal non-oxidative method required to study the behaviour of the α-campholenyl radical (181). A similar study of the 2-(cyclopent-3-enyl)ethyl radical (188) has been reported by Wilt, Massie, and Dabek.[171] The radical (188) was found to undergo cyclisation to form norbornane (21) as well as hydrogen abstraction to give 2-(cyclopent-3-enyl)ethane (189).



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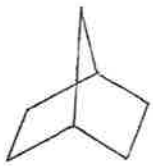
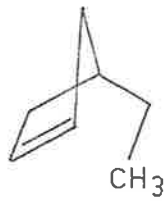


(21)



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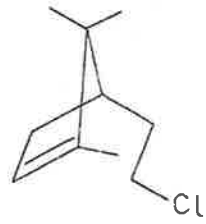
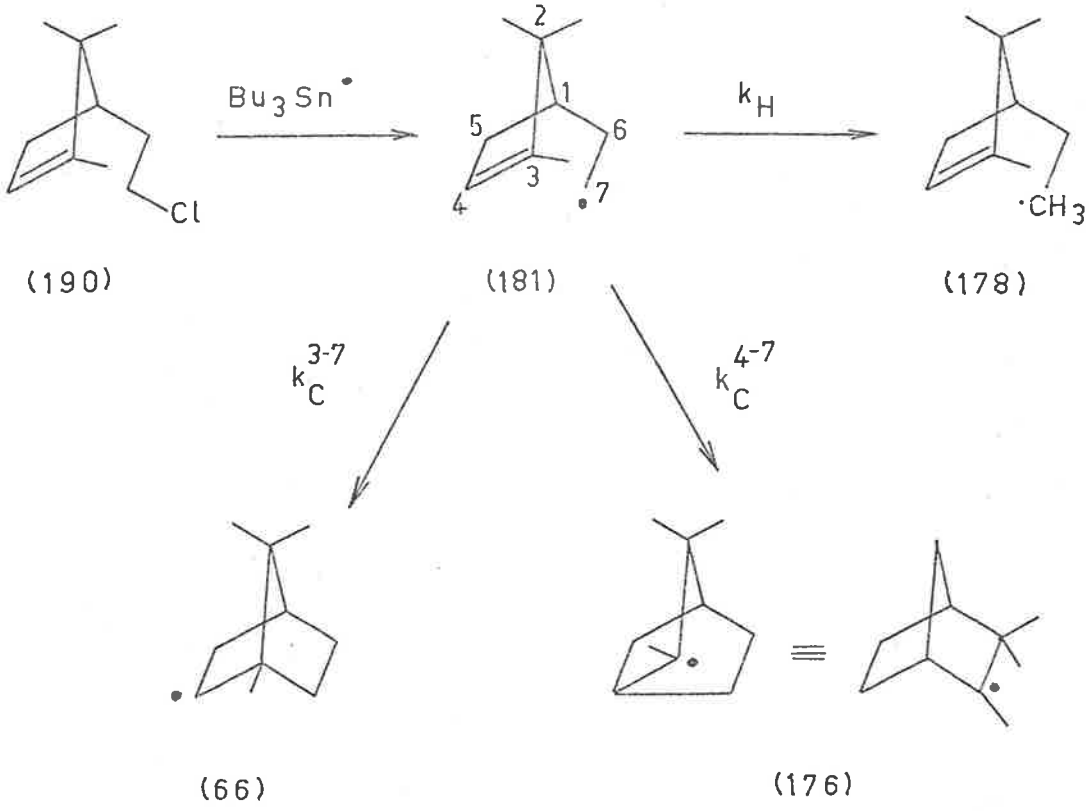


(190)

Theoretically, the α-campholenyl radical may cyclise in two ways; (i) cyclisation may either occur at the 4-position of the cyclo-

pentene ring to produce the 2,3,3-trimethylnorbornyl radical (176), or, (ii) at the 3-position giving rise to the bornyl radical (66), (Scheme 16).



Scheme 16.

The required chloride (190) was prepared by the method of Wege,[163] from the corresponding p-nitrobenzenesulphonate (167) by treatment with pyridine hydrochloride in dry N,N-dimethylformamide as solvent. The reaction with tri-n-butyltin hydride and the unsaturated chloride (190) was carried out in sealed tubes with degassed benzene as solvent using azobisisobutyronitrile (AIBN) initiator at 93° and

di-t-butyl peroxide (DTBP) at 130°. In all cases an approximately one molar excess of the unsaturated chloride (190) was used and the reaction time was 21 hours. The results of the above reactions are summarised in Table 14.

It can be seen from these results that cyclisation of the α-campholenyl radical (181) does indeed occur, the thermodynamically more stable 2,3,3-trimethylnorbornyl radical (176) being formed preferentially. This result is in accord with the observation that camphene (123) constitutes a substantial proportion of the product from the oxidative decarboxylation of the unsaturated acid (89). Also of interest is the fact that bornane (65) and bornylene (31), which could presumably arise from the bornyl radical (66), were not detected in the oxidative decarboxylation of the unsaturated acid (89).

In the case of the α-campholenyl radical generated from the stannane reaction, it is obvious that the rate of the hydrogen abstraction reaction, producing the olefin (178), is much greater than the rate of cyclisation of the primary radical (181). However, when the unsaturated acid (89) was treated under conditions of oxidative decarboxylation, in either benzene or dimethylsulphoxide, in the absence of copper II salts, the products identified were almost exclusively those of cyclisation. This was not surprising as there was no efficient hydrogen donor (e.g. tri-n-butyltin hydride) present in the decarboxylation reactions. However, in the copper II catalysed decarboxylation reaction of the unsaturated acid (89), the predominance of the uncyclised diene (177) suggests that the α-campholenyl radical (181) is being trapped

TABLE 14.

Products from the reaction of the unsaturated chloride (190) with tri-n-butyltin hydride.

[n Bu_3SnH]	Temp ^oC	Product (178)	Composition % (65)	(191)	Conversion
.10022	93[a]	92.5	trace	7.5[c]	39
.05011	93	86.4	0.2	13.4[d]	38
.02505	93	77.5	0.4	22.1[e]	35
.10022	130[b]	78.9	1.4	19.7[f]	39
.05011	130	71.2	0.7	28.0[g]	41
.02505	130	57.7	2.7	39.6[h]	38

a AIBN (azobisisobutyronitrile) used as initiator.

b DTBP (di-t-butylperoxide) used as initiator.

c only a trace of the exo isomer (187)

d c. 4% exo isomer (187)

e c. 4% exo isomer (187)

f c. 6% exo isomer (187)

g c. 5% exo isomer (187)

h c. 5% exo isomer (187)

by a copper II species at a comparable rate to that of cyclisation. An estimation was made of the rate constants of 4-7 cyclisation (k_c^{4-7}) and 3-7 cyclisation (k_c^{3-7}) employing the expression used by Wilt et al.[171] and Beckwith et al.[172a] (equation 11). The results are summarised in Table 15.

$$\frac{[\text{cyclised products}]}{[\text{H-abstraction product}]} = \frac{k_c^{3-7} + k_c^{4-7}}{k_H} \cdot \frac{1}{\text{av.}[Bu_3SuH]} \quad (11)$$

TABLE 15.

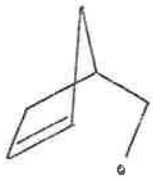
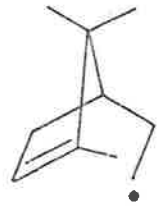
Estimated* rate constants for cyclisation of the α-campholenyl radical (181).

	Temp.	k sec^{-1}
k_c^{3-7}	93	$.09 \times 10^4$
	130	8.8×10^4
k_c^{4-7}	93	5.09×10^4
	130	13.0×10^4

* based on $k_H^{93^\circ} \sim 8.68 \times 10^6\ M^{-1}\ sec^{-1}$; $k_H^{130^\circ} \sim 9.6 \times 10^6\ M^{-1}\ sec^{-1}$.

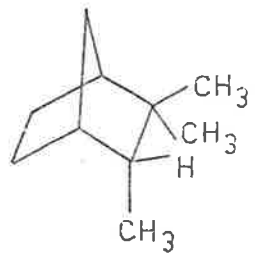
It is interesting to compare the rates of radical cyclisation observed by Wilt[171] in the case of the 2-(cyclopent-3-enyl)ethyl radical (188) with those in the case of the α-campholenyl radical (181) (Table 16).

TABLE 16.

			
k_c/k_H	7.3×10^{-3} (93°) 19×10^{-3} (130°)	k_c^{3-7}/k_H	0.1×10^{-3} (93°) 9.5×10^{-3} (130°)
		k_c^{4-7}/k_H	5.8×10^{-3} (93°) 14×10^{-3} (130°)

It can be seen in the case of the substituted α-campholenyl radical (181) that the presence of an extra methyl group at the site of radical attack markedly retards the rate of cyclisation. An examination of a model of the α-campholenyl radical (181) indicates that the methyl group at C-2 (see Scheme 16 for the numbering system) which is cis to the ethyl group bearing the radical centre may also hinder attack at the C-3 position. This is especially so if cyclisation occurs by the mechanism proposed by Struble, Beckwith, and Gream,[172b] namely, by an interaction of the radical centre with the π*-orbital of the double bond, in the plane of the π-system and along a line perpendicular to one of the olefinic carbon atoms. The direction of cyclisation appears to be influenced both by steric factors (as mentioned above) and thermodynamic considerations;

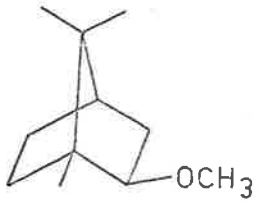
the thermodynamically more stable tertiary radical, i.e. the 2,3,3-trimethylnorbornyl radical (176) being formed in preference to the secondary bornyl radical (66). Also of interest is the fact that the endo isomer of 2,3,3-trimethylnorbornane (191) is formed to an extent of greater than 95% (Table 14). This observation is in accord with the fact that the preferred direction of reaction of norbornyl derivatives (in the absence of a bulky substituent at the 7-syn position) is from the exo side of the molecule.[128-30] However, the formation of a small amount (c. 5%) of product resulting from endo attack on the 2,3,3-trimethylradical (176) in the stannane reaction is consistent with the fact that in the copper catalysed decarboxylation of the epimeric 2-carboxy-2,3,3-trimethylnorbornanes (87) and (88), trapping of the intermediate 2,3,3-trimethylnorbornyl radical (176) by a copper II species proceeded to an extent of up to 10% from the endo side of the molecule; i.e. the exo acetate, camphene hydrate acetate (171), was contaminated with the corresponding endo acetate, methylcamphenilyl acetate (186) (up to 10%) (Tables 10 and 11).



(191)

4. Anodic oxidation of carboxylic acids.

The study of the anodic oxidation of the carboxylic acids (85), (86), (87), (88), and (89) in methanol containing sodium methoxide necessitated the synthesis of probable products from these reactions. exo- and endo-2-Methoxybornane (isobornyl and bornyl methyl ether, respectively), i.e. (192) and (193), exo- and endo-2-methoxy-2,3,3-trimethylnorbornane (camphene hydrate methyl ether and methylcamphenilyl methyl ether, respectively), i.e. (194) and (195) and α-campholenyl methyl ether (196) were considered likely products if cationic intermediates were involved in the electrolytic process. Treatment of the corresponding alcohols in dry N,N-dimethylformamide, with sodium hydride



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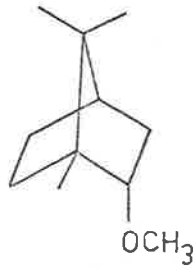

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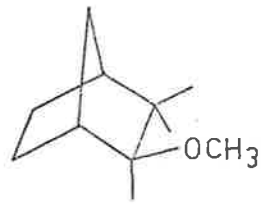

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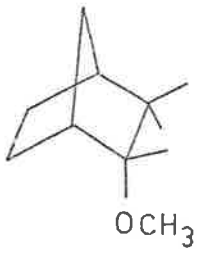

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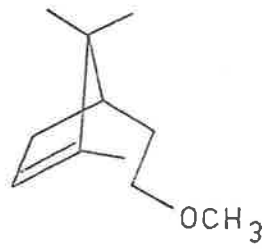

(196)

at 100-110°, in the presence of a catalytic amount of methanol, followed by methyl iodide and further heating for c. 3 hours afforded good yields of all five methyl ethers. In order that trace amounts of any of the five ethers could be detected, a gas-liquid chromatographic separation of all five products was required. However, resolution of exo- and endo-2-methoxy-2,3,3-trimethylnorbornane (194) and (195) respectively, proved to be extremely difficult. Of a very wide range of conventional and Golay columns investigated, only one (a 300' x .01" Golay column coated with liquid methylsilicone, i.e. SE 30) gave a satisfactory separation of the two ethers. The separation afforded using this column was such that less than 0.5% of the endo epimer could be detected. Separation of the other methyl ethers was readily achieved using a conventional column (15' 5% Apiezon).

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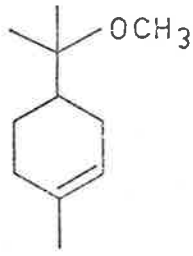
Because of the possibility that "hot" cationic intermediates may be involved in the anodic oxidation of the above acids, preparation of α-terpinyl methyl ether (197) was considered necessary. Treatment of α-terpineol (198) with sodium hydride in N,N-dimethylformamide, followed by methyl iodide as described above for the preparation of the ethers (192-196) unexpectedly gave a complex mixture of products. Oxymercuration-demercuration of limonene (199) with one equivalent of mercuric acetate in aqueous tetrahydrofuran has been reported[173] to produce mainly α-terpineol (198, 70%) together with a small amount of the terpin hydrate (200, 7%). When limonene was treated with one equivalent of mercuric acetate in anhydrous methanol followed by alkaline sodium borohydride, there was obtained a mixture consisting of unchanged starting material

(39%), α-terpinyl methyl ether (33%), and the dimethyl ether (201, 28%). The required ether (197) was readily obtained from the mixture by preparative gas-liquid chromatography.



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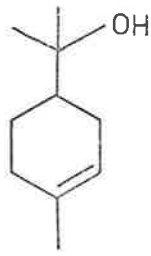

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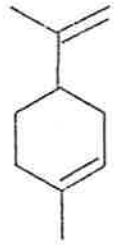

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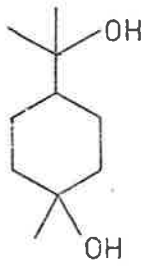

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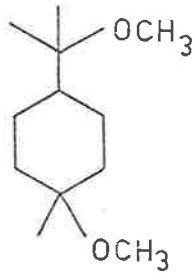
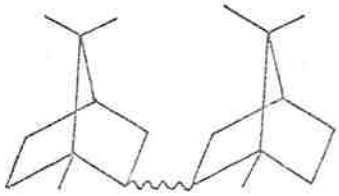


(201)

Although the Kolbe dimers (202), (203), and (204) were not prepared in this work, it was considered that the presence of bornane (65), 2,3,3-trimethylnorbornane (187) or (191), and 4-ethyl-2,3,3-trimethylcyclopentene (178) in the products would provide unequivocal evidence for the presence of the bornyl (66), 2,3,3-trimethylnorbornyl (176), and α-campholenyl (181) radicals in the reactions under investigation.

As far as could be ascertained, previous investigations on



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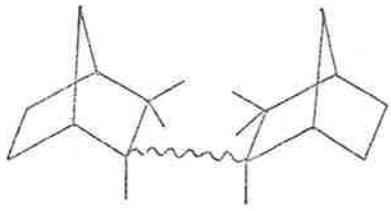

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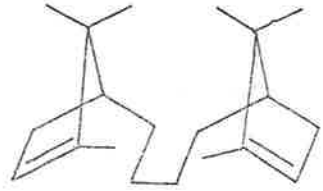


(204)

anodic oxidations of carboxylic acids have been carried out on relatively large amounts (at least 500 mg) of compound. Since large amounts of all the acids (85), (86), (87), (88), and (89) were not readily available, an electrolysis apparatus (see Experimental) was devised which required the use of only 50 mg of acid for each run. The electrolyses were carried out in methanolic sodium methoxide (c. 0.04M) using both platinum and carbon electrodes. In each case, a potential of 10 volts was maintained across the electrodes and the current was c. 50-60 mA.

When exo- and endo-2-carboxybornane (85) and (86) respectively, and exo and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88), respectively were electrolysed in methanol for 2 hours at room temperature, each gave the same products and in very similar proportions (Table 17). In all cases, the yields of the neutral products formed in the electrolyses were consistently 90 ± 5%.

The absence of bornane (65) and 2,3,3-trimethylnorbornane (191) in the mixtures obtained from the acids (85), (86), (87), and (88) indicates that none of the products are formed directly from the bornyl

TABLE 17.

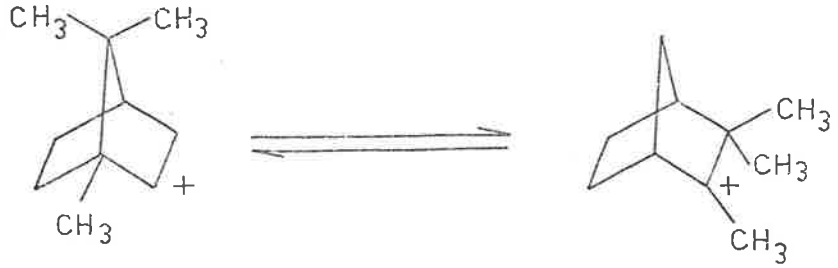
Products from anodic oxidation of exo- and endo-2-carboxybornane (85) and (86) respectively, and exo- and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88), respectively, in methanol containing sodium methoxide (0.04M).

Substrate	Products[a]							
	tricyclene (169)		camphene (123)		isobornyl methyl ether (192)		camphene hydrate methyl ether (194)	
	Pt	C	Pt	C	Pt	C	Pt	C
(85)	trace	-	19.7	19.5	1.1	0.8	79.2	79.6
(86)	trace	-	17.8	19.6	1.1	1.2	81.8	79.2
(87)	trace	-	18.3	23.3	0.7	0.9	81.0	75.8
(88)	trace	-	21.7	25.1	1.2	1.2	77.1	73.7

a The yields at platinum (Pt) and carbon (C) electrodes have been normalised to 100%.

and 2,3,3-trimethylnorbornyl radicals, (66) and (176) respectively. On the other hand, the composition of the mixtures shows that cationic intermediates are the precursors of each of the products. These intermediates could either be derived from an acyloxonium ion (route B, Scheme 7) or by oxidation of a radical intermediate (route A, Scheme 7).

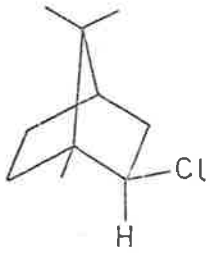
If the operative pathway to cationic intermediates is the latter, the initially formed carbonium ion in the case of the acids (85) and (86) must be the bornyl cation (67) since Berson[165] has shown that the bornyl radical does not undergo skeletal rearrangement at relatively low temperatures. Camphene (123) and camphene hydrate methyl ether (194), the rearranged products from (85) and (86), could thus have been derived only from the 2,3,3-trimethylnorborn-2-yl cation (182) formed by a 1,2-shift in the initially formed bornyl cation (67). Likewise, provided that the 2,3,3-trimethylnorbornyl radical (176) does not undergo skeletal change, the first formed carbonium ion from the acids (87) and (88) must be the 2,3,3-trimethylnorborn-2-yl cation (182). Isobornyl methyl ether (192), the only rearranged product from (87) and (88) must have been derived from the bornyl cation (67) formed from (182) by a subsequent 1,2-shift. The fact that all four acids produce mixtures of very similar composition (see Table 17) indicates that the overall reaction for each involves the same set of intermediate carbonium ions. It would thus seem reasonable to assume that each acid gives the bornyl (67) and 2,3,3-trimethylnorbornyl (182) cations which have essentially reached equilibrium before conversion to products. It was also found



(67) (182)

that exclusive exo substitution occurred during the reactions, i.e. the isobornyl methyl ether (192) and camphene hydrate methyl ether (194) were uncontaminated by their corresponding endo isomers.

These results are in close agreement with the findings of Bunton[174]. Solvolysis of isobornyl chloride (205), bornyl chloride (206), and camphene hydrochloride (18) in methanolic sodium methoxide afforded only camphene (123), camphene hydrate methyl ether (194), and possibly a very small amount (< 1%) of isobornyl methyl ether (192). The product composition was found to be independent of the substrate, but the amount of elimination was found to increase both with increasing methoxide ion concentration and with increases in temperature. The results are summarised in Table 18.



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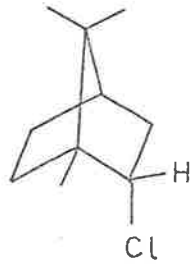

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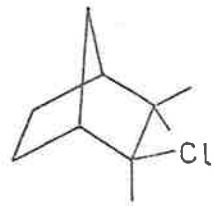


(18)

Although the concentrations of methoxide used by Bunton are somewhat higher than those employed in the anodic oxidation reactions (0.2M in solvolysis vs. c. 0.04M used in the electrolysis reactions), extrapolation of Bunton's results back to a concentration of c. 0.04 molar indicates that solvolysis of camphene hydrochloride (18) at 25.3° might be expected to yield c. 20% camphene. Similarly at 25.3° isobornyl

TABLE 18.

Product composition from the methanolysis of isobornyl chloride (205), bornyl chloride (206), and camphene hydrochloride (18).

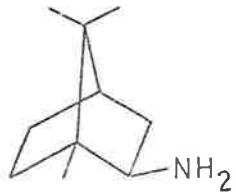
Substrate	Temp (°C)	$[NaOCH_3]$(M)	Products (%)	
			camphene (123)	camphene hydrate methyl ether (194)
(18)	25.3	0.2	22	78
(18)	25.3	1.5	55	45
(18)	25.3	3.0	87	13
(205)	25.3	0.2	25	75
(205)	25.3	1.5	55	45
(205)	25.3	3.0	85	15
(205)	100.0	0.2	61	39
(206)	100.0	0.2	61	39

chloride would be predicted to afford an approximate yield of 24% camphene.

It should also be noted that the hydrocarbons tricyclene (169) and bornylene (31) were not formed during the solvolysis of the chlorides (18), (205), and (206). A similar result was obtained on electrolysis of the acids (85), (86), (87), and (88), where only a trace amount (if any) of tricyclene (169) was detected.

That the anodic oxidation of some carboxylic acids has given

products which are very similar to those obtained by deamination of the corresponding amines[118] (i.e. by a route which may give rise to a "hot" cationic intermediate) prompted a comparison of the products obtained by electrolytic oxidation of the acids (85), (86), (87), and (88), with those reported for the deamination of the corresponding exo- and endo-bornylamines, (207) and (208) respectively. Hückel[175] has reported that



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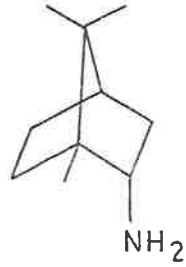


(208)

the deamination of exo- and endo-bornylamine in aqueous nitrous acid at 45° gave different product distributions for each epimer. endo-Bornylamine (208) was found to give c. 40% of monocyclic, ring opened products [i.e. α-terpineol (198) (34%) and limonene (199) (5%)]. Deamination of exo-bornylamine gave only a very small amount (c. 1% α-terpineol) of ring opened products (Table 19).

Kirmse[176] has recently reported that the photolytic decomposition of camphor benzenesulphonylhydrazone (209) in methanolic sodium methoxide, followed by loss of nitrogen from the resultant bornyl diazonium salt (210), afforded a complex mixture of products. At a concentration of 0.2M sodium methoxide, bornyl derivatives (including

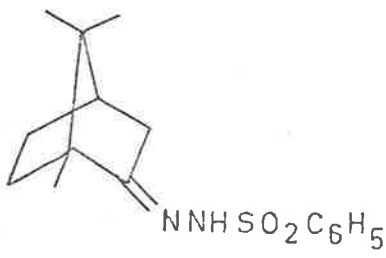
TABLE 19.

Product composition from the deamination of exo- and endo-bornylamine (207) and (208).

	endo-bornylamine (208)	exo-bornylamine (207)
Camphene	10*	19
Camphene hydrate	44	61
Tricyclene	1	6
α-Terpineol	34	1
Limonene	5	0
Borneol	2	) 10
Isoborneol	1	)

* % yields

camphene (123) and camphene hydrate methyl ether (194)] were formed to an extent of c. 82%; pinane derivatives (c. 11%) and monocyclic products (c. 7%) were also detected.



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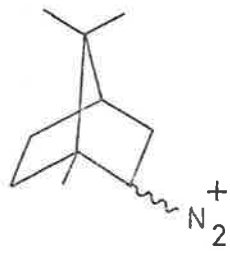


(210)

The absence of ring opened products and the very similar product distribution between a given exo, endo pair of carboxylic acids, e.g. (85 and 86) or (87 and 88) observed in the anodic oxidation of exo- and endo-2-carboxybornane (85) and (86), and exo- and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88), would appear to preclude the intermediacy of a "hot", high energy, partially desolvated cationic intermediate. The close similarity between products obtained from electrolysis and those observed by Bunton[174] for the methanolysis of the corresponding chlorides (18), (205), and (206) is strongly suggestive of a common cationic intermediate for both the solvolytic and electrolytic routes.

These results appear to be in accord with those reported by Corey[109] for the anodic oxidation of exo- and endo-2-carboxynorbornane (60) and (61). Anodic oxidation of either the exo or endo carboxylic acid at platinum electrodes in methanol, produced only exo-2-methoxynorbornane (79) and a very small amount of norcamphor (22) as the only volatile products. The methyl ether (79) obtained from optically active endo-2-carboxynorbornane (61) was found to be racemic. The products obtained by Corey were found to be very similar to those obtained by solvolysis[18] of suitable norbornyl derivatives. To account for the nature of the products, Corey postulated that the "non-classical" norbornyl cation (3) was involved.

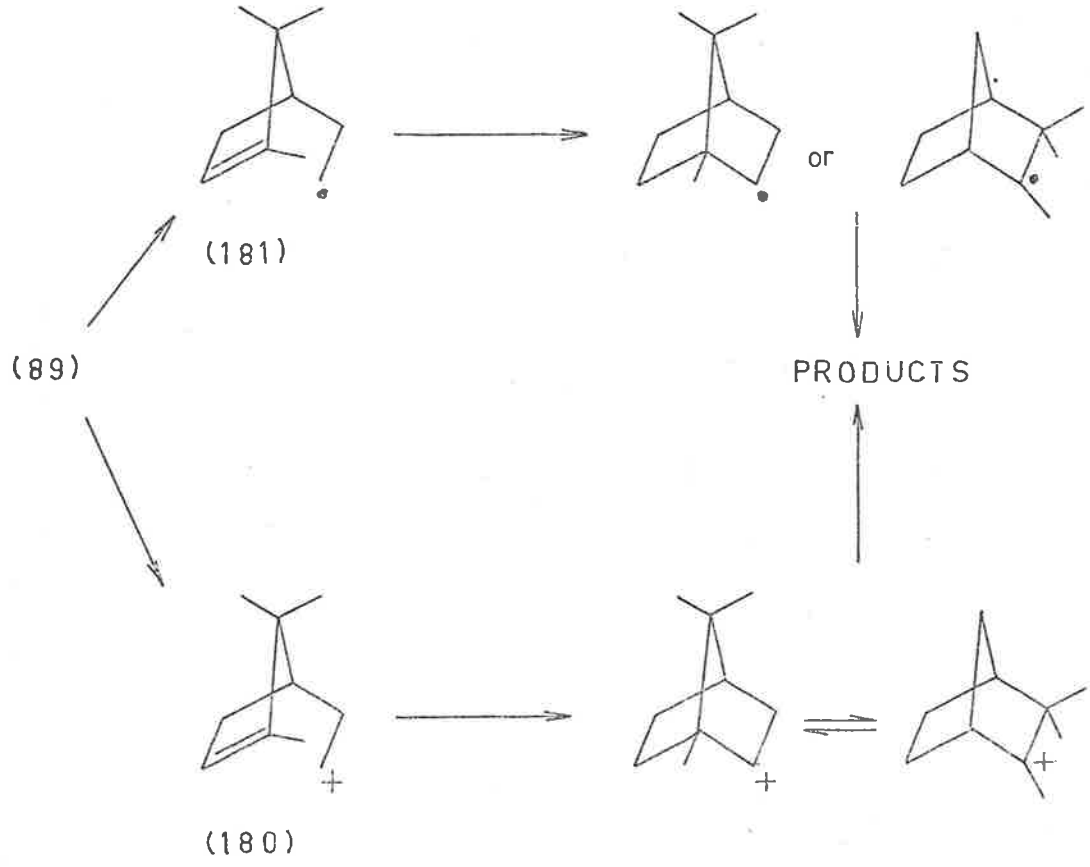
That a dichotomy of mechanisms may operate during the anodic oxidation of carboxylic acids has been well documented.[111,112] The electrode material appears to play a significant role, with carbon elec-

trodes apparently promoting the formation of cationic interemdiates, while at platinum electrodes, a radical mechanism would appear to predominate. However, electrolysis of exo- and endo-2-carboxybornane (85) and (86), and exo- and endo-2-carboxy-2,3,3-trimethylnorbornane (87) and (88) at platinum electrodes appears to proceed via cationic intermediates and the substitution of carbon electrodes has very little, if any, effect on the observed product distribution (Table 17).

To conclude this section on the electrolysis of the four acids (85), (86), (87), and (88), mention must be made of the fact that, at platinum but not at carbon electrodes, all four acids gave products which contained small quantities (ranging from barely detectable traces to 0.2%) of camphor (25). Corey[109] also found that the electrolysis of exo- and endo-2-carboxynorbornane (60) and (61), respectively, in methanol at a platinum anode yielded the corresponding ketone, norcamphor (22) in "a very small amount". The formation of ketones in anodic oxidations of carboxylic acids has been ascribed[90] to the reaction of intermediate radicals with oxygen in the medium and to oxidation of secondary alcohols which can be formed in aqueous media. In the present work, the amounts of camphor formed are so small that it is possible that both traces of oxygen and water in the medium may have been responsible for its formation.

The anodic oxidation of β-(2,2,3-trimethylcyclopent-3-enyl)-propionic acid (89) was also studied in methanolic sodium methoxide solution (c. 0.04M) using both platinum and carbon electrodes. This system was considered of interest because of the possibility of cyclisation of either the monocyclic radical (181) or cation (180), to form

similar intermediates to those which may have been expected for the anodic oxidation of the epimeric 2-carboxybornanes (85) and (86) and the epimeric 2-carboxy-2,3,3-trimethylnorbornanes (87) and (88). These processes are outlined in Scheme 17.



Scheme 17.

When the unsaturated acid (89) was electrolysed under the same conditions used for the four acids (85), (86), (87), and (88), only low yields of identifiable products were obtained (Table 20). Unlike the

TABLE 20.

Products from anodic oxidation of β-(2,2,3-trimethylcyclopent-3-enyl)-propionic acid (89) in methanol containing sodium methoxide (0.04M).

Anode	Products (%)[a]					
	(123)	(177)	(178)	(192)	(194)	(196)
Platinum	1.7	4.5	2.7	trace	2.4	1.2
Carbon	0.7	-	-	0.2	4.4	0.3

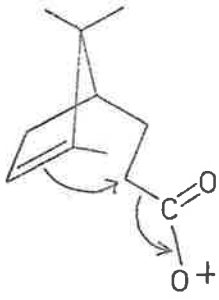
a Absolute yields based on amount of acid consumed.

four acids already discussed, the nature of the products from (89) was highly dependent on the electrode used.

In the case of electrolysis of the acid (89) at a platinum electrode, it is clear that both radicals and cations are directly involved in product formation. 4-Ethyl-2,3,3-trimethylcyclopentene (178) must have arisen as a result of hydrogen abstraction from the α-campholenyl radical (181) while part of the 2,3,3-trimethyl-4-vinylcyclopentene (177) could well have arisen as a result of a disproportionation reaction involving the α-campholenyl radical (181). The absence of 2,3,3-trimethyl-norbornane (191) in the product shows that camphene (123) must have been derived from a cationic precursor. α-Campholenyl methyl ether (196) and camphene hydrate methyl ether (194) must also have been derived from cationic precursors since radical reactions in methanol give the hydroxy-

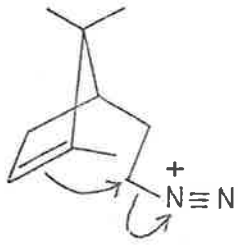
methyl ($.CH_2OH$) and not the methoxy ($CH_3O.$) radical.[177] The α-campholenyl methyl ether (196) and that portion of the 2,3,3-trimethyl-4-vinylcyclopentene (177) not derived from a disproportionation reaction involving the radical (181) must have been formed from the α-campholenyl cation (180). The formation of camphene and camphene hydrate methyl ether could be rationalised in three ways: (i) cyclisation of the α-campholenyl radical (181) to form the 2,3,3-trimethylnorbornyl radical (176) which is rapidly oxidised to the corresponding cation (182) before it has time to undergo typical radical reactions, (ii) cyclisation of the α-campholenyl cation (180) to form the 2,3,3-trimethylnorbornyl cation (182) directly, or (iii) by π-participation in the acyloxonium ion (211) (see Scheme 7, route B) to give once again the cation (182). It is, however, not possible to make a distinction between these three possibilities on the available information. That low yields of cyclised products can result, however, from a "hot" α-campholenyl cation (180) and/or by π-participation in the diazonium ion (212) has been shown for the deamination of α-campholenyl-N-nitrosourea (213) in methanol containing sodium methoxide[178] and of α-campholenylamine (214) in acetic acid.[179]

The results of the anodic oxidation of the unsaturated acid (89) at carbon electrodes indicate that only cationic intermediates are involved. In this case only products arising from either the α-campholeny cation (180) or the 2,3,3-trimethylnorbornyl cation (182) (see Scheme 17) were identified. This is in accord with the reported[111,112] tendency of carbon electrodes to promote the formation of cationic intermediates in the anodic oxidation of carboxylic acids.



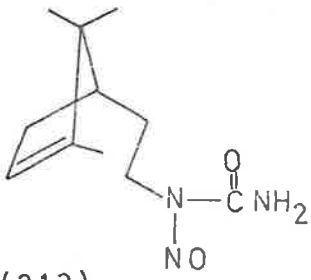
(211)

(182) + CO_2

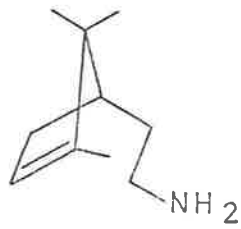


(212)

(182) + N_2



(213)



(214)

It should be noted that in the anodic oxidation reactions of the unsaturated acid (89), substantial amounts of a complex mixture of products were obtained. The infrared spectrum indicated that the material was possibly lactonic in composition; however, the nature of these products was not further investigated. The possibility that the

yield of identifiable products formed in the anodic oxidation of the acid (89) may have been increased with increasing reaction time was also investigated. Electrolysis at platinum electrodes for 2 hour gave c. 12.5% overall yield of identifiable products (Table 20), with c. 69% of the acid (89) being recovered unchanged. Prolonged electrolysis (21 hour) at platinum electrodes, however, gave only 4.5% overall yield of products with only 5% of the acid being recovered unchanged. Thus it would appear that the olefinic products were being consumed in secondary reactions.

EXPERIMENTAL.

General.

All melting points (determined in Pyrex capillaries using an electrically heated Gallenkamp apparatus) and boiling points are uncorrected. Infrared spectra were recorded with either a Perkin-Elmer 237 grating spectrophotometer or a Unicam SP.200 spectrophotometer. The characteristics of the infrared bands are expressed in the text as follows: s, strong; m, medium; w, weak; vw, very weak; b, broad. N.m.r. spectra were determined with a Varian DP60 or T60 spectrometer operating at 60 MHz, using tetramethylsilane as the internal standard, and unless stated otherwise, carbon tetrachloride as the solvent; data are reported in the order: value, integral, multiplicity, coupling constant. Mass spectra were recorded with a Hitachi Perkin-Elmer RMU-6D spectrometer operating at 70 eV. Microanalyses were carried out by the Australian Microanalytical Service, Melbourne.

Low-boiling light petroleum and light petroleum refer to the fractions having b.p. 30-40°, and 40-60°, respectively. Unless stated otherwise, all organic solvent extracts were dried over anhydrous sodium sulphate.

Analytical (both qualitative and quantitative) gas-liquid chromatography (g.l.c.) was carried out with a Perkin-Elmer 881 gas chromatograph which was fitted with a Perkin-Elmer 194B printing integrator. Preparative g.l.c. was carried out with an Aerograph Autoprep 705 instrument. Both instruments were equipped with flame ionisation detectors and nitrogen was used as the carrier gas. The following columns were used:

(A) 5% FFAP on Varaport 30 (100-120 mesh), 12 ft by 1/12 in.

(B) 5% Apiezon M on Varaport 30 (100-120 mesh), 15 ft by 1/12 in.

(C) 5% FFAP on Varaport 30 (100-120 mesh), 6½ ft by 1/12 in.

(D) 5% UCON 50-LB-550-X on Varaport 30 (100-120 mesh), 6 ft by 1/12 in

(E) 5% UCON 50-LB-550-X on Varaport 30 (100-120 mesh), 11ft by 1/12 in

(F) 10% Carbowax 20M on Chromosorb W (80-100 mesh) which had been treated with cold 10% aqueous sodium hydroxide for 10 min, washed with distilled water to pH8, and dried at 130° for 15 hr, 12 ft by 1/12 in.

(G) 15% FFAP on Gaschrom A (40-60 mesh) which had been treated with base as described for (F), 10 ft by 1/6 in.

(H) 5% Apiezon M on Varaport 30 (100-120 mesh), 10 ft by 1/8 in.

(I) 5% FFAP on Varaport 30 (100-120 mesh), 10 ft by 1/8 in.

(J) UCON LB-550-X Capillary, 300 ft by 0.01 in.

(K) Apiezon Q Capillary, 150 ft by 0.01 in.

(L) Butanediol Succinate (BDS) Capillary, 150 ft by 0.02 in.

(M) SE-30 Silicone Capillary, 150 ft by 0.01 in.

(N) 30% FFAP on Chromosorb A (80-100 mesh), 20 ft by 3/8 in.

(O) 20% Apiezon L on Chromosorb W (60-80 mesh), 5 ft by 3/8 in.

The columns A-G were constructed of Pyrex glass, H-M of stainless steel, and N and O of aluminium. For the analytical columns A-F, H & I, the flow rate of the carrier gas (nitrogen) was 30 ml/min, while for the capillary columns J-M it was 2 ml/min. The flow rates of the carrier gas (nitrogen) for the preparative columns G, N, and O are given in the text.

For the quantitative analyses, the responses (to the detector in the g.l.c. apparatus) of the authentic compounds with respect to the internal standard (i.e. 1,3,5-trimethylbenzene for the oxidative decarboxylation and anodic oxidation reactions and 1-methyl-4-*i*-propyl-benzene for the radical cyclisation reactions) were determined by running accurately weighed samples of the authentic compound (*c* 5-20 mg) and the internal standard (*c*. 20 mg) in ether (*c*. 1 ml) under the conditions of the analysis. The areas of peaks were determined with a Perkin-Elmer 194B printing integrator and with the use of response factors, the absolute yields (by weight) and hence the percentage yields of each of the products were determined. Each product analysis was the average of at least 2 g.l.c. determinations and was carried out in duplicate.

Qualitative identifications of products were made initially by comparing the retention times of the components with those of authentic samples and then by peak enhancement ("spiking").

Work described in part 1.

8-Carbomethoxycamphene (95).

Treatment of 8-carboxycamphene[180] (99) with excess of ethereal diazomethane gave 8-carbomethoxycamphene as a colourless oil, b.p. 118-122°/14 mm (lit.[181] 94°/4 mm). ν_{max} 1710 s, 1655 m cm^{-1}; n.m.r.:δ5.34 (1H, singlet), 3.97 (1H, broad), 3.58 (3H, singlet), 2.0-1.1 (7H, complex), 1.06 (6H, singlet).

8-Acetylcamphene (100).

A solution of methyllithium in ether (5 ml, 9.0 mmol) was added dropwise to a solution of 8-carboxycamphene (99) (730 mg, 4.1 mmol) in ether (10 ml) at 0°. After the mixture had been stirred at 0° under N_2 for 30 min, it was treated with saturated ammonium chloride solution (10 ml). The organic layer was separated, washed with 10% sodium hydroxide solution (2 ml) and water (3 x 5 ml), and dried. Removal of the solvent gave a pale yellow liquid which was distilled to give 8-acetylcamphene (100) (700 mg, 97%) as a colourless liquid, b.p. 84-86°/15 mm. (Found: C, 81.0; H, 10.4. $C_{12}H_{18}O$ requires C, 80.9; H, 10.2%). ν_{max} 1690 s, 1625 s cm^{-1}; n.m.r. : δ5.78 (1H, singlet), 3.97 (1H, broad singlet), 2.08 (3H, singlet), 2.0-1.1 (7H, complex), 1.07 (6H, singlet); mass spectrum: m/e 178 (61%), 163 (46%), 108 (63%), 43 (100%).

Treatment of 8-Acetylcamphene (100) with Dimethylcopperlithium.

A solution of 8-acetylcamphene (100) (306 mg, 1.7 mmol) in ether (3 ml) was added dropwise to a stirred solution of dimethylcopper-

lithium[182] in ether (33 ml, 8.3 mmol) under N_2 at 0°. After the reaction mixture had been stirred at 0° for 1 hr and then at room temperature for 3 hr, the excess of reagent was destroyed at 0° by the dropwise addition of saturated ammonium chloride solution (c. 20 ml). The organic phase was separated, the aqueous phase was washed with ether (10 ml), and the combined organic extracts were washed with saturated sodium chloride solution (2 x 10 ml) and water (10 ml). Concentration of the extract gave a yellow liquid (304 mg) which was chromatographed on neutral alumina (10 g). Elution with 5% ether in light petroleum gave unchanged starting material (194 mg, 63%), identified by its infrared and n.m.r. spectra, and by g.l.c. (column A, 142°). Further elution with ether gave the unsaturated tertiary alcohol (97) (80 mg, 24%) identified by its infrared and n.m.r. spectra, and by g.l.c. (column A, 142°).

Treatment of 8-Formylcamphene (101) with Dimethylcopperlithium.

A solution of 8-formylcamphene[183] (101) (246 mg, 1.5 mmol) in ether (3 ml) was added dropwise to a solution of dimethylcopperlithium in ether (15 ml, 8.0 mmol) maintained under N_2 at 0°. After the mixture had been stirred at 0° for 4 hr, it was worked-up as described for the corresponding reaction with 8-acetylcamphene to give a yellow oil (302 mg) whose infrared spectrum exhibited absorptions at 3350 (strong) and 1675-1680 cm^{-1} (weak). Preparative plate chromatography (silica gel, 5% ether in light petroleum) afforded the alcohol (102), (193 mg, 43%) which was obtained as a colourless liquid, b.p. 60-80° (block)/2 mm. (Found: C, 79.6; H, 10.8. $C_{12}H_{20}O$ requires C, 79.9; H, 11.2%). ν_{max} 3300 s,

1673 w, 1060 s, 795 s cm^{-1}; n.m.r. : δ4.93 (1H, doublet J 8Hz), 4.37 (1H, quintet J 6Hz), 3.00 (1H, broad singlet), 2.0-1.0 (14H, complex), 1.15 (3H, doublet J 6Hz); mass spectrum: m/e 180 (2%), 162 (100%). Oxidation of a portion of the alcohol with Jones reagent[184] gave 8-acetylcamphene (100), identified by its spectral properties and by g.l.c. (column D, 155°).

Reaction of the Unsaturated Acetate (103) with Dimethylcopperlithium.

The unsaturated acetate (103) (91%), b.p. 76-78°/0.8 mm (lit.[185] 72-73°/0.45 mm) was prepared from the unsaturated alcohol[185] (106) by the conventional acetic anhydride/pyridine method.

To a solution of dimethylcopperlithium in ether (20 ml, 11 mmol) under N_2 at 0° was added dropwise a solution of the unsaturated acetate (103) (420 mg, 2.02 mmol) in ether (3 ml). After the mixture had been stirred at 0° for 1½ hr and then at room temperature for ½ hr, it was worked-up in the usual manner to give an oil (332 mg). A portion (300 mg) of the product was chromatographed on silica gel (10 g). Elution with light petroleum gave 8-ethylcamphene (105) (117 mg, 35%) as a colourless liquid, b.p. 80-100° (block)/45 mm. (Found: C, 88.0; H, 12.1. $C_{12}H_{20}$ requires C, 87.7; H, 12.3%). ν_{max} 1670 vw, 1380 w, 1360 w cm^{-1}; n.m.r. : δ4.83 (1H, triplet J 8 Hz), 2.92 (1H, broad singlet); 1.97 (2H, quintet J 8Hz); 2.0-1.0 (7H, complex); 1.00, 0.97, and 0.90 (triplet J 8Hz) (total 9H); mass spectrum: m/e 164 (60%), 149 (100%), 135 (89%), 121 (80%), 107 (92%), 93 (75%). Elution with 10% ether in

light petroleum gave a liquid (47 mg, 11%) which was identified as unchanged starting material on the basis of its infrared spectrum. Further elution with 20% ether in light petroleum yielded the unsaturated alcohol[185] (106) which was identified by its spectral and g.l.c. properties.

8-Ethylcamphene (105).

Potassium t-butoxide (1.79 g, 0.016 mol) was added to a stirred suspension of n-propyltriphenylphosphonium iodide (6.9 g, 0.016 mol) in dry light petroleum (b.p. 60-80°; 60 ml) under nitrogen. After the mixture had been stirred at room temperature for 30 min, camphenilone[186] (107) (2.21 g, 0.016 mol) in light petroleum (b.p. 60-80°, 20 ml) was added dropwise to it; stirring was continued for 1 hr at room temperature and then for 20 hr with the mixture under reflux. On being cooled, the solution was washed successively with 80% aqueous methanol (3 x 20 ml) and water (20 ml) and dried. Removal of the solvent afforded a residue (1.67 g) which was chromatographed on silica gel (50 g). Elution with light petroleum gave 8-ethylcamphene (168 mg, 11%) having spectral (mass, infrared, and n.m.r.) properties and g.l.c. characteristics (column B, 115°) identical with those of the material isolated from the reaction between the compound (103) and dimethylcopperlithium. Further elution with 5% ether in light petroleum gave unchanged camphenilone (940 mg, 43%).

The Vinyl Ether (109).

A solution of 8-hydroxymethylcamphene[185] (106) (39.6 g, 0.238

mol) and mercuric acetate (64 g) in ethyl vinyl ether (1000 ml, distilled from sodium) (for methods of preparing vinyl ethers, see ref. 187) was heated under reflux (N_2) for 49 hr. After most of the excess of ethyl vinyl ether had been removed from it by distillation, the mixture was cooled, diluted with ether (600 ml), and then stirred for 2 hr at room temperature after glacial acetic acid (3.4 ml) had been added to it. After further dilution with ether (400 ml), the solution was successively washed with potassium hydroxide solution (5%, 500 ml), and water (2 x 500 ml) and dried (potassium carbonate). Removal of the solvent gave a residue which was fractionated to give the required vinyl ether (109) (35.2 g, 77%) as a colourless liquid, b.p. 114-117°/15 mm. (Found: C, 81.0; H, 10.8. $C_{13}H_{20}O$ requires C, 81.2; H, 10.5%). ν_{max} 1603 s, 1198 s, 810 m cm^{-1}; n.m.r. : δ6.32 (1H, centre of X part of an ABX system, J_{AX} 14Hz, J_{BX} 7Hz), 5.07 (1H, triplet J 7Hz), 4.22-3.75 (4H, overlapping doublet J 7Hz at 4.11 and AB part of the ABX system with J_{AB} c. 2Hz), 2.95 (1H, broad singlet), 2.00-1.00 (7H, broad), 1.05 and 1.02 (6H, 2 overlapping singlets of equal intensity).

The Unsaturated Aldehyde (110).

The vinyl ether (109) (9.9 g, 0.051 mol) was heated in a sealed tube under nitrogen at 220° for 4 hr. Distillation of the product gave the aldehyde (110) (7.6 g, 78%) as a colourless liquid, b.p. 132-134°/12 mm which solidified on cooling. Although satisfactory microanalytical data could not be obtained [presumably due to ready oxidation to the acid (112)], the spectral data were in complete agreement with the assigned structure. ν_{max} 3060 w, 2720 w, 1720 s, 1610 w cm^{-1}; n.m.r. : δ9.68

(1H, triplet J 2.5Hz), 6.33-4.67 (3H, ABC system with C part centred at 6.08, J_{AC} 17Hz, J_{BC} 11Hz, and $J_{AB} \leq$ 1.5Hz), 2.43 (2H, overlapping doublets J 2.5Hz), 2.33-1.00 (8H, broad and complex), 0.97 and 0.94 (6H, 2 overlapping singlets of equal intensity).

exo-2-Carboxymethyl-2-vinyl-3,3-dimethylnorbornane (112).

A solution of sodium hydroxide (0.94 g, 23 mmol) in water (38 ml) was added dropwise to a well-stirred mixture of the unsaturated aldehyde (110) (1.0 g, 5.4 mmol) and ethanol (25 ml).[188] After the mixture had been stirred at room temperature for 20 hr, it was filtered and the filtrate was washed with ether, acidified with concentrated hydrochloric acid, and extracted with ether. The dried ether extract was concentrated to give a pale yellow solid (0.92 g, 85%) which, after a recrystallisation from low boiling light petroleum followed by distillation at 100-110° (bath)/12 mm, gave exo-2-carboxymethyl-2-vinyl-3,3-dimethylnorbornane (112) as a colourless crystalline solid, m.p. 102-104° (sealed capillary). (Found: C, 74.6; H, 9.6. $C_{13}H_{20}O_2$ requires C, 75.0; H, 9.7%). ν_{max} 3300-2500 br, 1705 s, 1635 m cm^{-1}; n.m.r. ($CDCl_3$) : δ9.83 (1H, broad), 6.25 - 4.07 (3H, AMX system with X, M, and A parts centred at 6.03, 4.98, and 4.67 respectively; J_{AX} 17Hz, J_{MX} 11Hz, and J_{AM} 1.5Hz), 2.55 (2H, singlet), 2.1-1.0 (8H, broad and complex), 0.97 and 0.92 (6H, 2 overlapping singlets of equal intensity).

Attempted Decarbonylation of exo-2-Formylmethyl-2-vinyl-3,3-dimethylnorbornane (110).

A solution of the unsaturated aldehyde (110) (486 mg, 2.53

mmol) and tris-triphenylphosphine rhodium chloride (1.94 g, 2.1 mmol) in dry benzonitrile (7 ml) was stirred under nitrogen at 160° for 12 hr.* Distillation of the mixture gave two factions. The first having b.p. 20-180° (bath)/22 mm was shown by g.l.c. (column I, 95°) to consist of benzonitrile only. A portion (327 mg) of the second fraction (363 mg), b.p. 20-180° (bath)/0.05 mm, was chromatographed on silica gel (15 g). Elution with 5% ether in light petroleum gave the cyclopentanone derivative (111) (235 mg, 54%) as a colourless liquid, b.p. 80-90° (block)/1.5 mm which was shown to be homogeneous by g.l.c. (column F, 150°) (Found: C, 81.0; H, 10.5. $C_{13}H_{20}O$ requires C, 81.2; H, 10.5%). ν_{max} 1742 s cm^{-1}; n.m.r.: δ2.2-1.1 (complex) and 0.97 (singlet) in ratio of approximately 7:3; mass spectrum: m/e 192 (57%), 149 (51%), 109 (100%), 96 (62%), 83 (87%), 69 (93%), 67 (75%), 55 (53%), 41 (72%).

The exo- and endo-Cyclopropyl Esters (114) and (115) respectively.

A solution of ethyl diazoacetate[191] (70 g, 0.61 mol) in cyclohexane (430 ml) was added dropwise over a period of 3 hr to a refluxing

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* The conditions used by Sakai and coworkers[135] to form cyclopentanone derivatives from γ,δ-unsaturated aldehydes were much milder than those in the present work. The reason for these vigorous conditions,[189] which are probably not necessary, arose indirectly. Earlier reactions carried out under milder conditions were not investigated further since the burgundy colour of the complex did not change to yellow as was expected if decarbonylation had taken place.[190]

mixture of camphene (123) (21 g, 0.15 mol) and anhydrous copper sulphate (12.5 g) in cyclohexane (63 ml). After the mixture had been stirred under reflux for a further 7 hr, it was cooled, filtered, and the solvent was removed under reduced pressure. Fractionation of the residue gave a fraction (26.9 g, 79%), b.p. 84-88°/1 mm (lit.[192] 128-136°/14 mm) which was shown by g.l.c. (column I, 165°) to contain at least three components (in increasing order of retention times) A (55%), B (25%) (these two were only partially separated), and C (20%). (Found - for mixture: C, 75.5; H, 9.8. $C_{14}H_{22}O_2$ requires C, 75.6; H, 10.0%). Preparative g.l.c. (column N, 187°, N_2 125 ml/min) afforded a complete separation of isomer C but only partial separation of isomers A and B. The infrared and mass spectra of the three samples and of the original mixture were identical. Isomer C (Found: C, 75.3; H, 9.9. $C_{14}H_{22}O_2$ requires C, 75.6; H, 10.0%) exhibited the following spectral properties: ν_{max} 1720 s, 1170 vs cm^{-1}; n.m.r. : δ3.98 (2H, quartet J 7Hz), 2.2-0.6 (11H, complex), 1.20 (3H, triplet J 7Hz), 0.91 and 0.86 (6H, 2 overlapping singlets of equal intensity); mass spectrum: m/e 222.

Birch Reduction of Cyclopropyl Ester (C).

A solution of isomer C (140 mg, 0.63 mmol) (obtained by preparative g.l.c.) in dry tetrahydrofuran (1.5 ml) and t-butanol (0.5 ml) was added dropwise to a stirred solution of lithium (80 mg, 11.4 mg-atom) in liquid ammonia (15 ml). After 2 hr, solid ammonium chloride was added to the mixture and the ammonia was allowed to evaporate. A solution of the residue in ether was washed successively with 10% hydro-

chloric acid and dilute sodium chloride solution and dried. Removal of the solvent gave a colourless oil (120 mg) which was distilled to give a mixture, b.p. 80-85° (block)/0.05 mm, shown by g.l.c. (Column I, 165°) to consist of the endo- and exo-alcohols (120) and (124), respectively, in the ratio of 9:1. ν_{max} 3350 s, 1050 s cm^{-1}; n.m.r. : δ3.52 (2H, poorly resolved triplet), 2.88 (1H, broad singlet), 2.11 (1H, broad singlet), 1.8-1.0 (13H, broad and complex), 0.93 and 0.81 (each 3H, singlets). In addition, two small singlets (approximately 1/10 the intensity of the previous two signals) were present at 0.96 and 0.88.

When the mixture of isomers A and B was subjected to the same reduction conditions as described above, a mixture of alcohols (120) and (124) of the same composition as from isomer C was obtained.

exo- and endo-3(3-Hydroxypropyl)-2,2-dimethylnorbornane (124) and (120) respectively.

(a) A solution of the alcohol[130] (125) (0.50 g) in ethanol (10 ml) was shaken with hydrogen in the presence of platinum oxide at room temperature and pressure for 1 hr. After the mixture had been filtered, the ethanol was removed under reduced pressure to give a liquid which was distilled to give a mixture (7:3) as shown by g.l.c. (column I, 165°) of the exo- and endo-alcohols (124) and (120) respectively, b.p. 65° (block)/0.05 mm (Found: C, 79.2; H, 12.3. $C_{12}H_{22}O$ requires C, 79.1; H, 12.2%). ν_{max} 3320 s, 1050 s cm^{-1}; n.m.r. : δ3.62 (2H, triplet J 6Hz), 2.82 (1H, singlet), 2.2-0.9 (13H, broad and complex), 0.96, 0.93, 0.88, and 0.81 (c. 6H, singlets in approximate ratio of 3:1:3:1).

(b) (i) A stirred solution of the organoborane[143] formed from camphene (11.8 g, 0.05 mol) and diborane in tetrahydrofuran (80 ml) was treated dropwise at 0° with a solution of ethyl α-bromoacetate (8.35 g, 0.05 mol) in dry t-butanol (25 ml) followed by a solution of potassium t-butoxide (5.60 g, 0.05 mol) in t-butanol (50 ml). After being stirred at room temperature for 17 hr, the solution was diluted with water (50 ml) and extracted with ether (3 x 60 ml). The combined ether extract was washed thoroughly with water, dried, and concentrated to give a yellow liquid (19.5 g) which was fractionally distilled to give the crude esters (128 and 129) (2.75 g), b.p. 89-100°/1 mm. Since analytical g.l.c. (column A, 140°) showed that the esters were contaminated with impurities (c. 15%), the overall yield approximated 36% since only 1/3 of the camphene is converted into the required product.[144] Preparative g.l.c. (column N, 200°, N_2 150 ml/min) gave a pure sample of the esters (Found: C, 75.2; H, 11.0. $C_{14}H_{24}O_2$ requires C, 75.0; H, 10.8%). ν_{max} 1730 s, 1175 s, 780 s cm^{-1}; n.m.r. : δ4.03 (2H, quartet J 7Hz), 2.12 (2H, broad singlet), 1.9-1.0 (20H, includes a triplet J 7Hz at 1.23 and 2 singlets each of 3H at 0.93 and 0.83); mass spectrum: m/e 224 (2%), 109 (100%).

(ii) A mixture of the esters (128 and 129) (purified by preparative g.l.c.) was reduced with lithium aluminium hydride in ether in the usual way to give a mixture (> 90%) of the alcohols (120) and (124) in the ratio of 9:1 as shown by g.l.c. (column I, 165°). The infrared and n.m.r. spectra of this mixture and those from the Birch reductions of the cyclopropyl esters (114) and (115) were identical.

Preparation of the Alcohols (130) and (131).

(a) When a mixture (208 mg, 7:3) of the isomers A and B of the cyclopropyl esters (31) and/or (32) was heated under reflux with lithium aluminium hydride (50 mg) in ether (5 ml) for 1 hr, the usual working-up procedure gave a mixture (155 mg, 92%), b.p. 65° (block)/0.1 mm of the alcohols (130) and/or (131). (Found: C, 79.8; H, 11.1. $C_{12}H_{20}O$ requires C, 79.9; H, 11.2%). ν_{max} 3320 s, 3040 w, 1010 s cm^{-1}; n.m.r. : δ3.8-3.15 (2H, AB part of ABX system with A and B centred at 3.62 and 3.32 with J_{AB} 11.5Hz, J_{AX} c. 8Hz, and J_{BX} c. 6.5Hz), 2.44 (1H, broad singlet), 2.0-1.0 (8H, broad), 1.0-0.35 (9H, including two very prominent singlets at 0.85 and 0.72, and two smaller ones at 0.80 and 0.76) g.l.c. (column I, 165°) showed that the mixture contained 2 components in the ratio of 7:3.

(b) Reduction of the isomer C obtained from the mixture of cyclopropyl esters (114) and (115) with lithium aluminium hydride as described in (a) gave a single product (column I, 165°). ν_{max} 3320 s, 3045 w, 1020 cm^{-1}; n.m.r. : δ3.8-3.15 (2H, AB part of ABX system with A and B centred at 3.55 and 3.32, J_{AB} 11Hz, J_{AX} c. 8Hz, and J_{BX} c. 6Hz), 2.1-1.0 (9H, complex), 0.98 and 0.65 (6H, 2 singlets of equal intensity), 0.6-0.15 (2H, complex); mass spectrum: m/e 180 (4%), 94 (100%).

Preparation of the Methoxycyclopropyl Derivatives (132) and (133).

(a) A mixture of camphene (1.0 g, 7.4 mmol) and dimethoxymethyltrimethoxysilane[148] (1.1 g, 5.6 mmol) was heated in a sealed tube under

nitrogen at 125° for 16 hr and then chromatographed on silica gel (50 g). Elution with light petroleum gave camphene (100 mg). Further elution with light petroleum containing ether (2%) gave a mixture of the methoxycyclopropyl derivatives (132) and (133) (860 mg, 72%), b.p. 100° (block)/1.2 mm as a colourless liquid (Found: C, 80.3; H, 11.0. $C_{12}H_{20}O$ requires C, 79.9; H, 11.2%). G.l.c. analysis (column B, 135°) showed that the mixture contained four components (in order of increasing retention times) in the proportion of 4, 14, 22, and 60%. Preparative g.l.c. (column N, 170°, N_2, 120 ml/min) gave the major component (132a) as a homogeneous liquid. ν_{max} 3060 w, 1125 m, 1105 w, 1095 w, 1066 s, 1025 w cm^{-1}; n.m.r. : δ3.27 (3H, singlet), 2.92 (1H, X part of ABX system with J_{AX} and J_{BX} 10.5Hz), 2.0-1.0 (8H, broad and complex), 0.86 and 0.67 (each 3H, 2 singlets of equal intensity), 0.5-0.2 (2H, complex); mass spectrum: m/e 180 (11%), 97 (100%).

(b) An ethereal solution of methyllithium (50 ml, 1.4N, 70 mmol) was added dropwise to a stirred solution of camphene (1.0 g, 7.4 mmol) and methyldichloromethyl ether (4.05 g, 35.2 mmol) under nitrogen at 0°. After the mixture had been stirred at room temperature for 24 hr, excess of methyllithium was destroyed by the cautious addition of water, and the ether layer was separated. After having been washed with saturated sodium thiosulphate solution and water, the dried ether extract was concentrated to give a residue which was chromatographed on silica gel (60 g). Elution with light petroleum gave camphene (300 mg). Further elution with light petroleum containing ether (2%) gave a mixture (650 mg, 70%) of the methoxycyclopropyl derivatives (132) and (133). G.l.c.

(column B, 135°) showed that the mixture contained the four components as in (a) above but in the proportion of 2, 15, 8, and 75%.

Conversion of the Methoxycyclopropyl Derivative (132a) into exo-2-Carboxy-2,3,3-trimethylnorbornane (87).

A mixture of (132a) (566 mg), concentrated hydrochloric acid (0.7 ml) and sufficient methanol (c. 10 ml) to produce homogeneity was heated under reflux under nitrogen for 70 hr. On being cooled, the mixture was diluted with water and extracted with ether. After having been washed successively with saturated sodium chloride solution, water, saturated sodium bicarbonate solution and water, the dried ether extract was concentrated to give a residue which was dissolved in acetone (12 ml) and treated with excess of Jones reagent at room temperature for 2 hr. The excess of oxidant was then destroyed with ethanol and the solution was diluted with water and extracted with ether. Work-up in the usual manner (with extraction with 10% sodium hydroxide) gave an acidic fraction (190 mg, 37% overall) which on sublimation at 110°/11 mm gave exo-2-carboxy-2,3,3-trimethylnorbornane (87) as colourless crystals, m.p. 200-210° (sealed capillary). (Found: C, 72.4; H, 10.0. $C_{11}H_{18}O_2$ requires C, 72.5; H, 10.0%). ν_{max} 3400-2500 br, 1690 s cm^{-1}; n.m.r. : δ11.6 (1H, broad), 2.5-1.2 (8H, complex), 1.17, 1.07, and 0.99 (9H, 3 singlets of equal intensity); mass spectrum: m/e 182 (12%), 139 (36%), 83 (100%). G.l.c. analysis (column A, 190°) indicated that the compound was homogeneous.

Treatment of the acid (87) with excess of ethereal diazomethane gave exo-2-carbomethoxy-2,3,3-trimethylnorbornane (137) as a colourless liquid, b.p. 100° (block)/11 mm, which on cooling solidified. (Found: C, 73.5; H, 10.1. $C_{12}H_{20}O_2$ requires C, 73.4; H, 10.3%). $\nu_{max}^{CCl_4}$ 1720 s, 1255 s, 1115 s cm^{-1}; n.m.r. : δ3.57 (3H, singlet), 2.5-1.0 (8H, complex), 1.10, 0.95, and 0.90 (9H, 3 singlets of equal intensity); mass spectrum: m/e 196 (34%), 181 (7%), 83 (100%). Analysis by g.l.c. (columns B, 130°; C, 105°; J, 150°) indicated that the compound was homogeneous.

When the ester (137) (60 mg) was reduced with lithium aluminium hydride in ether, the resulting alcohol (34 mg) was treated with acetic anhydride (2 ml) and pyridine (2 ml) at room temperature for 68 hr. After work-up in the usual manner, there was obtained exo-2-acetoxymethyl-2,3,3-trimethylnorbornane (138) as a colourless liquid, b.p. 120° (block)/11 mm; ν_{max} 1732 s, 1245 s, and 795 s cm^{-1}; n.m.r. : δ3.87 (2H, singlet), 1.97 (3H, singlet), 2.0-1.0 (c. 8H, complex), 1.00 and 0.90 (9H, 2 singlets in 1:2 ratio); mass spectrum: m/e 210 (absent), 168 (6%), 150 (38%), 137 (81%), 107 (100%). Analysis by g.l.c. (columns B, 140°; D, 150°; D, 135°; J, 150°; K, 150°; L, 125°; M, 105°) indicated that the compound was homogeneous.

Acid catalysed ring expansion of (132) and (133).

The material used in this reaction was the mixture of isomers (132) and (133) of the methoxycyclopropane formed by the reaction of camphene (123) with the silane (136).

A solution of the methoxycyclopropanes (310 mg) in glacial

acetic acid (3 ml) and perchloric acid (70%, 1.8 ml) was sealed in a glass tube under nitrogen and heated at 115° for 20 minutes. The reaction mixture, on being cooled, was diluted with ether (5 ml) and washed with saturated sodium bicarbonate solution until no more effervescence occurred. The ethereal layer was separated, dried, and then concentrated to give an oil (240 mg) which on distillation afforded a colourless liquid, b.p. 110-120° (block)/12 mm. G.l.c. analysis (column I, 133°) showed the product to be a mixture of two compounds in the ratio of 4:1. Preparative g.l.c. (column N, 177°, N_2 200 ml/min) afforded an excellent separation of the two compounds. Samples of the major product (82 mg, 82%) and the minor product (17.5 mg, 18%) were collected and found to be pure by analytical g.l.c. On the basis of the combined spectral and microanalytical data, the two products were believed to be 3,4,4-trimethylbicyclo[3,2,1]octan-2-one (139) and 2,4,4-trimethylbicyclo[3,2,1]-octan-3-one (140); however, an assessment of which product was which was not possible. The major fraction was obtained as a colourless liquid, (Found: C, 79.7; H, 11.1. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%). ν_{max} 2960 s, 2910 s, 2865 s, and 1705 s cm^{-1}; n.m.r. : δ2.8-1.1 (9H, complex), 1.07 (3H, singlet), and 0.91 (6H, singlet); mass spectrum : m/e 166 (43%), 109 (100%), 108 (75%), 95 (80%), and 69 (43%).

The minor fraction was also a colourless liquid, (Found: C, 79.6; H, 11.2. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%). ν_{max} 2950 s, 2865 s, and 1705 s cm^{-1}; n.m.r. : δ2.8-1.1 (9H, complex), 1.04 (3H, singlet), and 0.88 (6H, singlet); mass spectrum: m/e 166 (43%), 119 (97%), 117 (100%), 97 (76%), 67 (52%), and 55 (42%).

2-Methylenenorbornane (141).

Potassium t-butoxide (10.1 g, 0.090 mol) was added to a stirred suspension of methyltriphenylphosphonium iodide (36.8 g, 0.091 mol) in dry ether (200 ml) under nitrogen. After the mixture had been heated under reflux for 30 min, it was cooled to -78° and a solution of norbornan-2-one (5.0 g, 0.046 mol) in dry ether (15 ml) was added dropwise to it. The mixture was then allowed to warm up slowly to room temperature overnight (c 9 hr), and finally heated under reflux for 1 hr. Careful distillation of the ether from the reaction mixture afforded a crude product to which was added 80% aqueous methanol (100 ml) and low boiling light petroleum (100 ml). On separation of the upper phase, the methanolic extract was washed with low boiling light petroleum (4 x 50 ml). The combined light petroleum extracts were washed with water (3 x 50 ml) and dried. Careful removal of the solvent by fractional distillation gave a crude product (7.7 g) which on distillation gave the required 2-methylenenorbornane (141) (2.4 g, 49%) as a colourless liquid, b.p. 120-122°/760 mm (lit.[193] b.p. 121-122°/760 mm). G.l.c. analysis (column B, 80°) indicated the product was homogeneous.

Preparation of the methoxycyclopropane derivatives (142) and (143).

To a stirred solution of 2-methylenenorbornane (2.0 g, 0.019 mol) and methyldichloromethyl ether (10.6 g, 0.093 mol) maintained under nitrogen at 0°, was added dropwise an ethereal solution of methyllithium (60 ml of a 1.67M solution, i.e. c. 0.100 mol). The resultant yellow suspension was stirred at room temperature for 24 hr. and then

water (100 ml) was carefully added to the solution to destroy any excess of methyllithium. Following the addition of ether (50 ml), the organic layer was separated and the aqueous extract was washed with ether (1 x 50 ml). The combined ethereal extracts were washed with saturated sodium thiosulphate solution (3 x 50 ml) and water (2 x 50 ml) and dried. Removal of the solvent afforded the crude product which was chromatographed on silica gel (50 g). Elution with low boiling petroleum ether containing 2% ether gave a pale yellow liquid (2.2 g, 78%) which was shown by g.l.c. (column H, 90°) to contain three components. Preparative g.l.c. (column G, 115°, N_2 85 ml/min) gave a pure sample of the major component (c. 90% of the reaction mixture) as a colourless liquid, b.p. 65-70° (block)/45 mm, (Found: C, 79.3; H, 10.8. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%). ν_{max} 3065 w, 2945 s, 2860 s, 2815 m, 1445 m, 1370 m, 1220 m, 1190 m, 1145 m, 1125 m, 1085 m, and 980 m cm^{-1}; n.m.r. : δ3.26 (3H, singlet), 2.83 (1H, X part of ABX system with J_{AX} + J_{BX} 9.5Hz), 2.5-0.7 (10H, broad and complex), and 0.7-0.1 (2H, complex); mass spectrum : m/e 152 (20%) and 79 (100%).

Acid catalysed ring expansion of (142).

The methoxycyclopropane derivative used was the component (142) which was purified by preparative g.l.c. in the previous experiment.

A solution of the methoxycyclopropane (142) (274 mg) in glacial acetic acid (3 ml) and perchloric acid (70%, 1.8 ml) was sealed in a glass ampoule under nitrogen and heated at 115-118° for 20 min. On being cooled, the solution was diluted with ether (20 ml) and washed with

saturated sodium bicarbonate solution until the washings were basic. The ethereal layer was washed with water (2 x 10 ml) and dried. Removal of the ether gave a crude product (186 mg) which on distillation afforded a colourless liquid (159 mg, 64%), b.p. 100-110° (block)/30 mm. G.l.c. analysis (column B, 120°) indicated that the product consisted of three products, i.e. A (10%), B (87%), and C (3%); (Found: C, 78.6; H, 10.2. $C_9H_{14}O$ requires C, 78.2; H, 10.2%). ν_{max} 2935 s, 2865 s, 1705 s, 1445 m, 1050 m, and 910 m cm^{-1}; n.m.r. : δ2.8-1.1 (11H, complex) and 0.95 (3H, doublet J 6.5Hz); mass spectrum : m/e 138 (38%), 80 (100%), and 67 (68%).

2-N-Pyrrolidinobicyclo[3,2,1]oct-2-ene (146).

A solution of bicyclo[3,2,1]octan-2-one (1.00 g, 0.0081 mol) and pyrrolidine (0.60 g, 0.0085 mol) in dry toluene (20 ml) was refluxed under nitrogen with a catalytic amount of p-toluenesulphonic acid (water being separated with a Dean-Stark trap) for 16 hr. Removal of the solvent at atmospheric pressure, followed by distillation of the residue gave the following fractions: (i) b.p. 90-100° (block)/0.5 mm (0.21 g); (ii) b.p. 100-120° (block)/0.1 mm (0.60 g); and (iii) b.p. 120-130° (block)/0.1 mm (0.16 g). Fraction (ii) appeared to contain only a very small amount of starting material and its infrared spectrum was consistent with that expected for the enamine (146); ν_{max} 1630 s cm^{-1}.

3-Methylbicyclo[3,2,1]octan-2-one (144).

The enamine (146) used was portion of fraction (ii), b.p. 100-

120°/0.1 mm obtained in the previous experiment.

A mixture of the enamine (0.54 g, 0.003 mol) and methyl iodide (1.70 g, 0.012 mol) in dry benzene (5 ml) was heated under reflux under nitrogen for 15 hr. Then water (2 ml) was added to the mixture which was heated under reflux for a further 30 min. Ether (15 ml) was added to the cooled mixture which was washed with water (1 x 5 ml), dilute sulphuric acid (10%, 3 x 5 ml), and water (2 x 5 ml). Removal of the solvent from the dried extract gave a pale yellow liquid (215 mg) which on g.l.c. analysis (column B, 120° and column A, 110°), appeared to contain mainly bicyclo[3,2,1]octan-2-one (c. 70% of the reaction mixture) and a mixture (4:1) of the compounds corresponding to the products B and C respectively, which were obtained from the acid catalysed ring expansion of (142). Preparative g.l.c. (column O, 110°, 90 ml N_2/min) separated the mixture of B and C from the bicyclo[3,2,1]octan-2-one. The spectral characteristics (i.e. i.r., n.m.r., and mass spectrum) of the mixture (i.e. B and C) were identical to those observed for the product of the acid catalysed ring expansion of (142).

exo-2-Carboxy-2-methyl-3-methylenenorborn-5-ene (147).

(Although the synthesis of the acid (147) has been reported,[151] full experimental details were not available for the present work.)

2-Methylbut-2,3-dienoic acid (149), m.p. 69-70° (from low boiling light petroleum) was obtained by heating under reflux ethyl 2-methylbut-2,3-dienoate[194] with 2N ethanolic sodium hydroxide for 1 hr.

A solution of the acid (149) (7.9 g, 0.081 mol) and freshly

distilled cyclopentadiene (26.7 g, 0.405 mol) in carbon tetrachloride (30 ml) was heated under reflux under nitrogen for 7 hr. On being cooled, the solution was diluted with ether (100 ml) and extracted with 10% sodium hydroxide solution (3 x 30 ml) and water (30 ml). Acidification of the combined sodium hydroxide and water extracts with 10% hydrochloric acid followed by extraction with ether gave a mixture (3:2; 12.4 g, 94%) of the exo- and endo-adducts (147) and (148) respectively.

A solution of iodine (9.0 g, 0.036 mol) and potassium iodide (26.5 g, 0.16 mol) in water (80 ml) was added to the above mixture (12.4 g) (which contained c. 5.2 g (i.e. 0.032 mol) of the endo-adduct (148) as determined by n.m.r. spectroscopy) which was dissolved in sodium bicarbonate solution (0.5N, 200 ml). After the solution had been stirred in the dark at room temperature for 44 hr, it was extracted with ether (3 x 100 ml) and the combined ether extracts were washed with saturated sodium thiosulphate solution (50 ml) and water (2 x 50 ml), and dried. Removal of the ether gave the crude iodolactone (150) (8.8 g, 96%) which was recrystallised from ether and low boiling light petroleum as a white crystalline solid, m.p. 100-102°. ν_{max} 1780 s, 1770 s cm^{-1}; n.m.r. : δ5.25 (1H, singlet), 5.08 (2H, singlet with shoulder), 3.90 (1H, broad singlet), 3.12 (1H, broad singlet), 2.87 (1H, poorly resolved doublet J 5Hz), 2.6-1.8 (2H, AB quartet centred at 2.40 and 1.93, J_{AB} 12Hz), 1.23 (3H, singlet). The aqueous sodium bicarbonate extract was acidified with 10% hydrochloric acid and extracted with ether (3 x 100 ml). After being washed with saturated sodium thiosulphate solution (50 ml) and water (2 x 50 ml) and dried, the combined ether extract was concentrated

to give a white solid (5.65 g) which was sublimed at 110-120°/15 mm to give exo-2-carboxy-2-methyl-3-methylenenorborn-5-ene (147) (4.6 g, 60%), m.p. 122-123°. ν_{max} 3400-2400 br, 1690 s cm^{-1}; n.m.r. : δ12.13 (1H, broad singlet), 6.15 [2H, multiplet (very fine splitting)], 5.07 (1H, singlet), 5.00 (1H, singlet), 3.17 [2H, multiplet (very fine splitting)], 2.0-1.6 (2H, complex), 1.27 (3H, singlet); mass spectrum: m/e 164 (27%), 66 (100%). [Barnett and McKenna[151] have reported that (147) has a variable m.p. The n.m.r. spectral properties quoted[151] for the compound are however very similar to those listed above.]

exo-2-Hydroxymethyl-2-methyl-3-methylenenorborn-5-ene (151).

Treatment of exo-2-carboxy-2-methyl-3-methylenenorborn-5-ene (147) (4.6 g) with excess of ethereal diazomethane afforded a quantitative yield of the corresponding methyl ester as a colourless liquid. ν_{max} 3060 w, 1720 s, 1650 w, 1240 s, 1110 s, 895 s, cm^{-1}; n.m.r. : δ6.13 (2H, multiplet with very fine splitting), 5.02 (1H, singlet), 4.93 (1H, singlet), 3.67 (3H, singlet), 3.13 (2H, multiplet with very fine splitting), 1.68 (2H, broad singlet), 1.20 (3H, singlet); mass spectrum: m/e 178 (24%), 66 (100%). A solution of the ester (5.0 g, 0.028 mol) in ether (10 ml) was added dropwise to a slurry of lithium aluminium hydride (1.10 g, 0.029 mol) in ether (100 ml) in a nitrogen atmosphere at room temperature. After it had been heated under reflux for 1½ hr, the mixture was worked-up in the usual manner to give exo-2-hydroxymethyl-2-methyl-3-methylenenorborn-5-ene (151) as a colourless solid (4.16 g, 98%), m.p. 67-68°. (Found: C, 80.0; H, 9.2. $C_{10}H_{14}O$ requires C, 80.0;

H, 9.4%). ν_{max} 3360 s, 3060 w, 1655 m, 1020 s, 870 s cm^{-1}; n.m.r. : δ6.13 (2H, broad singlet), 4.90 (1H, singlet), 4.57 (1H, singlet), 3.50 (2H, singlet), 3.13 (1H, broad singlet), 2.77 (1H, broad singlet), 2.13 (1H, broad singlet), 1.67 (2H, complex multiplet), 1.00 (3H, singlet); mass spectrum: m/e 182 (5%), 83 (100%). G.l.c. (column A, 142°) showed that the compound was homogeneous.

Preparation of Compound (152).

Methylene iodide (16.1 g, 0.060 mol) was added dropwise, with caution, to a mixture of exo-2-hydroxymethyl-2-methyl-3-methylenenorborn-5-ene (151) (2.55 g, 0.017 mol) and zinc-copper couple[195] (0.051 mol) in refluxing dry ether (50 ml). After the mixture had been heated under reflux for 5 hr (after which time monitoring by g.l.c. (column A, 142-180°) showed that the mixture contained starting material (5%), the required product (90%) and a component (5%) having a much longer retention time), it was cooled and the excess of reagent was destroyed by the dropwise addition of saturated ammonium chloride solution. Ether extraction and work-up in the usual manner gave the crude product (9.75 g) as a yellow oil which was chromatographed on neutral alumina (Woelm, 200 g). Elution with 20% ether in light petroleum gave unchanged methylene iodide while elution with ether gave a mixture of the three components detected by g.l.c. Preparative g.l.c. (column F, 175°, N_2 160 ml/min) afforded the major component which was sublimed at 90-100°/75 mm to give the alcohol (152) as a white solid, m.p. 137-139° (sealed capillary). (Found: C, 80.4; H, 9.4. $C_{11}H_{16}O$ requires C, 80.4; H, 9.8%). ν_{max}

3320 s, 3060 w, cm^{-1}; n.m.r. ($CDCl_3$) : δ6.27 (2H, multiplet with very fine splitting), 3.79 and 3.19 (2H, AB quartet J_{AB} 11Hz), 2.87 (1H, broad singlet), 1.93 (2H, broad), 1.43 (2H, broad), 0.73 (3H, singlet), 0.27 (4H, singlet); mass spectrum: m/e 164 (absent), 146 (3%), 92 (100%).

Preparation of the Acid (155).

A mixture (2.0 g) of the alcohols obtained from the above Simmons-Smith reaction was shaken with platinum oxide (606 mg) in glacial acetic acid (25 ml) under hydrogen (6 atm) for 7 hr at 50°. On being coole the reaction mixture was diluted with water (200 ml) and extracted with ether (3 x 30 ml). After the combined ether extracts had been washed with water until the washings were neutral, they were dried, and concentrated to give a crude product (2.02 g). Since its n.m.r. and infrared spectra indicated the presence of the acetyl derivative (16%), the crude product was stirred overnight at room temperature with a slurry of lithium aluminium hydride (0.5 g) in ether (100 ml). Work-up in the usual manner gave crude (154) (1.88 g); ν_{max} 3360 s, 3060 w, 1020 s cm^{-1}; n.m.r. : δ3.37 and 3.02 (2H, AB quartet J 10.5Hz), 2.3-1.0 (c. 9H, complex), 0.80 (3H, singlet), 0.6-0.1 (4H, complex), which was dissolved in acetone (100 ml) and treated with excess of Jones reagent at room temperature. After the mixture had been stirred at room temperature for 4 hr, it was worked-up in the standard way to give an acidic fraction (1.68 g) as a white solid which was sublimed at 80-100°/11 mm to give the acid (155) (1.16 g, 57%), m.p. 140-142° (sealed capillary). (Found: C, 73.0; H, 9.0. $C_{11}H_{16}O_2$ requires C, 73.3; H, 9.0%). ν_{max} 3300-

2500 br, 1690 s cm^{-1}; n.m.r. ($CDCl_3$) : δ10.9 (1H, very broad singlet), 2.6-1.1 (8H, broad and complex), 1.10 (3H, singlet), 0.8-0.3 (4H, complex); mass spectrum: m/e 180 (2%), 135 (90%), 93 (100%).

exo-2-Carboxy-2,3,3-trimethylnorbornane (87).

A mixture of the acid (155) (1.11 g) and platinum oxide (300 mg) in glacial acetic acid was shaken with hydrogen at 50° and 6 atmospheres pressure for 8 hr. On being cooled, the mixture was diluted with ether (70 ml) and washed with water (10 x 50 ml) until the washings were neutral. After the organic extract had been dried, it was concentrated to give the crude acid (87) (1.12 g) which was shown by g.l.c. (column A, 190°) to contain an impurity (6%) having the same retention time as the starting material (155). Two recrystallisations of the product from low boiling light petroleum followed by sublimation at 100-120°/12 mm gave pure exo-2-carboxy-2,3,3-trimethylnorbornane (87) as a colourless solid m.p. 202-210° (sealed capillary) having spectral properties (infrared, n.m.r., and mass) and g.l.c. behaviour (column A, 190°) identical to those of the material prepared from the methoxycyclopropyl derivative (132a).

Preparation of the alcohol (157).

Methylene iodide (50.9 g, 0.190 mol) was added dropwise to a mixture of endo-2-hydroxymethyl-2-methyl-3-methylenenorbornane[153] (156) (4.7 g, 0.031 mol) and zinc-copper couple[195] (0.187 mol) in refluxing ether (65 ml) under nitrogen. After being heated under reflux for 21 hr, the mixture was cooled and saturated ammonium chloride solution (50 ml)

was added carefully to it. The ether layer was separated and the aqueous layer was washed with ether (30 ml). The combined ether extracts were washed with water (2 x 30 ml), dried, and concentrated to give a yellow liquid which was chromatographed on neutral alumina (100 g). Elution with 40% ether in light petroleum gave the alcohol (157) as a colourless solid (4.5 g, 88%) which was homogeneous as judged by g.l.c. (column A, 142°). The product was sublimed at 80-90°/30 mm and then recrystallised from low boiling light petroleum at -78° to give (157), m.p. 169.5-171.5° (sealed capillary). (Found: C, 79.4; H, 10.8. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%). ν_{max} 3310 s, 3065 w, 1045 m, 1020 s, 1005 cm^{-1}; n.m.r. : δ3.45 and 3.00 (2H, AB quartet J_{AB} 11Hz), 2.2-1.0 (8H, broad), 0.90 (3H, singlet), 0.40 (2H, broad singlet), 0.23 (2H, broad singlet); mass spectrum: m/e 166 (3%), 135 (100%).

endo-2-Hydroxymethyl-2,3,3-trimethylnorbornane (159).

A mixture of the alcohol (157) (153 mg) and platinum oxide (27 mg) in glacial acetic acid (4 ml) was shaken with hydrogen (6 atm) at 50° for 9.5 hr. On being cooled, the reaction mixture was diluted with ether (15 ml) and washed successively with water (2 x 10 ml), saturated sodium bicarbonate solution (5 ml) and water (2 x 10 ml), and dried. Removal of the ether gave a residue (144 mg) which was shown by g.l.c. (column A, 142°) to consist of the required alcohol (83%) and its acetyl derivative (17%). The crude mixture was chromatographed on silica gel (8 g). Elution with 5% ether in light petroleum gave a colourless liquid (22 mg) whose infrared spectrum and g.l.c. behaviour was identical with

that of endo-2-acetoxymethyl-2,3,3-trimethylnorbornane (158) prepared by acetylation of (159) with acetic anhydride in pyridine. Further elution with 20% ether in light petroleum gave endo-2-hydroxymethyl-2,3,3-trimethylnorbornane (115 mg). Sublimation at 80-90°/20 mm gave the alcohol as a white solid, m.p. 191-192° (sealed capillary). (Found: C, 78.7; H, 11.7. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%). ν_{max} 3320 s, 1018 m, 1000 m cm^{-1}; n.m.r. : δ3.57 and 3.40 (2H, AB quartet J_{AB} 11Hz), 2.0-1.0 (8H, broad and complex), 0.98 and 0.95 (each 3H, overlapping singlets); mass spectrum: m/e 168 (absent), 150 (10%), 107 (100%).

Preparation of the Acid (160).

A solution of the alcohol (157) (4.15 g) in pure acetone (100 ml) was treated dropwise at 0° with Jones reagent until the colour of the reagent persisted. After the mixture had been stirred at room temperature for 30 min, it was treated dropwise with isopropyl alcohol (10 drops) to destroy the excess of oxidising agent, then diluted with water (1000 ml) and extracted with ether (4 x 100 ml). The combined ether extracts were washed with 10% sodium hydroxide solution (3 x 50 ml) and water (3 x 50 ml). Acidification of the basic extract with 10% hydrochloric acid followed by ether extraction gave the required acid (160) (4.5 g, 100%). Sublimation at 100-105°/12 mm gave the acid as a colourless solid, m.p. 203-205° (sealed capillary). (Found: C, 73.2; H, 9.1. $C_{11}H_{16}O_2$ requires C, 73.3; H, 9.0%). $\nu_{max}^{CCl_4}$ 3400-2500 br, 1690 s; n.m.r. : δ11.7 (1H, broad), 2.33 (1H, broad singlet), 2.0-1.1 (7H, complex), 1.20 (3H, singlet), 0.7-0.2 (4H, complex); mass spectrum: m/e 180 (15%), 107 (100%).

endo-2-Carboxy-2,3,3-trimethylnorbornane (88).

A mixture of the acid (160) (1.64 g) and platinum oxide (160 mg) in glacial acetic acid (15 ml) was shaken with hydrogen (6 atm) at 48° for 7 hr. On being cooled, the reaction mixture was diluted with ether (50 ml) and washed with water (7 x 100 ml), dried, and concentrated to give the crude acid (1.62 g, 95%). Recrystallisation from light petroleum (b.p. 30-40°) followed by sublimation at 110-120°/12 mm gave endo-2-carboxy-2,3,3-trimethylnorbornane as a colourless solid, m.p. 244-245° (sealed capillary). (Found: C, 72.6; H, 10.1. $C_{11}H_{18}O_2$ requires C, 72.5; H, 10.0%). $\nu_{max}^{CCl_4}$ 3400-2500 br, 1690 s cm^{-1}; n.m.r. : δ11.8 (1H, broad singlet), 2.2-1.0 (c. 8H, complex), 1.30, 1.10, and 1.03 (each 3H, singlets); mass spectrum: m/e 182 (5%), 139 (32%), 83 (100%).

2-Carbomethoxy-3,3-dimethylnorbornane (161).

A mixture (5.5 g), m.p. 80-82°, of endo- and exo-2-hydroxymethyl-3,3-dimethylnorbornane (126) and (127) respectively, which was prepared from camphene (123) by oxidative hydroboration,[143] was oxidised with Jones reagent to give 2-carboxy-3,3-dimethylnorbornane (162) (4.9 g, 82%), m.p. 64-65° (for various literature melting points, see Wolinski[196]). Treatment of the acid (4.9 g) with excess of ethereal diazomethane gave 2-carbomethoxy-3,3-dimethylnorbornane (161) (4.5 g, 86%), b.p. 74-76°/3 mm. (Found: C, 72.6; H, 9.7. $C_{11}H_{18}O_2$ requires C, 72.5; H, 10.0%). ν_{max} 1730 s, 1190 s, 1160 s, 1065 m, 1035 m cm^{-1}; n.m.r. : δ3.53 (3H, singlet), 2.4-1.0 (9H, broad and complex), 1.07 and 0.9 (c. 5H, 2 singlets of equal intensity). As well, 2 singlets of equal intensity accounting

for c. 1H were present at δ1.10 and 0.85. Although the compound appeared to be homogeneous as judged by g.l.c., the presence of the two possible isomers was shown by the presence of the 4 singlets in the methyl region of the n.m.r. spectrum.

C-Methylation of 2-Carbomethoxy-3,3-dimethylnorbornane (161).

After a solution of 2-carbomethoxy-3,3,-dimethylnorbornane (161) (592 mg, 3.25 mmol) in ethereal sodium triphenylmethylide[197] (31 ml, 16.25 mmol) had been heated under reflux under nitrogen for 17½ hr, methyl iodide (2.31 g, 16.25 mmol) was added dropwise to it. The mixture was then heated under reflux for a further 28 hr, cooled, and treated carefully with water (20 ml). The organic layer was separated, washed with water, and the combined aqueous extracts were acidified with 10% hydrochloric acid and extracted with ether. Concentration of this extract (after being dried) gave 2-carboxy-3,3-dimethylnorbornane (162) (295 mg, 54%) identified by its m.p. and infrared spectrum and by the g.l.c. behaviour (column E, 142°) of its methyl ester (from diazomethane). The dried neutral extract was concentrated to give an orange oil (7.5 g) which has shown by g.l.c. (column E, 142°) to contain unchanged starting material (161) and endo- and exo-2-carbomethoxy-2,3,3-trimethylnorbornane (164) and (137) respectively, - the three compounds being in the ratio of 45:51:4. After a solution of the crude neutral fraction in methanol (41 ml) containing 10% aqueous sodium hydroxide (27 ml) had been heated under reflux for 18 hr, it was cooled, diluted with water (250 ml), and extracted with ether (4 x 50 ml). The dried ether extract was concen-

trated to give an orange solid (7.4 g) which was shown by g.l.c. (column E, 142°) to contain endo- and exo-2-carbomethoxy-2,3,3-trimethylnorbornane in the ratio of 96:4, and no starting material (161). The aqueous extract was acidified with concentrated hydrochloric acid, and extracted with ether which, after being dried, yielded 2-carboxy-3,3,-dimethylnorbornane (162) (87 mg, 16%) whose methyl ester (diazomethane) revealed the presence of endo-2-carbomethoxy-2,3,3-trimethylnorbornane (164) (3%) (column E, 142°). A solution of the neutral fraction in 85% aqueous dimethylsulphoxide (50 ml) containing sodium hydroxide (1.05 g) was heated at 87° under nitrogen for 19 hr. On being cooled, the solution was diluted with water (70 ml) and extracted with ether (7 x 50 ml). After being acidified with concentrated hydrochloric acid, the aqueous extract was worked-up in the usual manner to give a pale yellow solid (111 mg, 19% overall) whose spectral properties (infrared and n.m.r.) were identical to those of endo-2-carboxy-2,3,3-trimethylnorbornane (88) prepared by a method already described. G.l.c. analysis of the acid (column A, 190°) and its methyl ester (diazomethane) (column A, 130°) showed the presence of the exo-epimer (6-7%). After sublimation at 100-120°/11 mm, the product (90 mg) was recrystallised from low boiling light petroleum at -70° to give colourless crystals (30 mg), m.p. 244-245° (sealed capillary) which contained the exo-acid (87) (3%) (column A, 190°; column A, 130° for the methyl ester).

α—Campholenic acid (165).

The acid was prepared[198] by the alkaline fusion of D-camphor-

10-sulphonic acid as a colourless liquid, b.p. 104-106°/0.9 mm (lit.[198] b.p. 95.5°/0.54 mm - 97.5°/0.65 mm.

α-Campholenol (166).

α-Campholenic acid (10.0 g, 0.60 mol) in dry tetrahydrofuran (25 ml) was added dropwise to a stirred slurry of lithium aluminium hydride (3.4 g, 0.9 mol) in tetrahydrofuran (25 ml) under an atmosphere of nitrogen. The mixture was heated under reflux for 18 hr and worked-up in the usual manner to give the alcohol (166) (7.7 g, 85%) as a colourless liquid, b.p. 120-122°/21 mm (lit.[163] b.p. 119-121°/21 mm).

α-Campholenyl p-nitrobenzenesulphonate (167).

p-Nitrobenzenesulphonyl chloride (13.35 g, 0.059 mol) was added to an ice-cold solution of α-campholenol (7.52 g, 0.048 mol) in dry pyridine (75 ml). The mixture was stirred at 0° for 2 hr, diluted with ice-cold water, and the precipitated product was collected and dried (13.8 g, 83%). Recrystallisation from a low boiling light petroleum-ether mixture at -78° yielded the sulphonate as pale yellow crystals (10.4 g, 63%), m.p. 82-83° (lit.[163] m.p. 86-87° - dependent on rate of heating).

β-(2,2,3-Trimethylcyclopent-3-enyl)propionic acid (89).

Powdered sodium cyanide (13.0 g, 0.27 mol) was added to a cold solution of α-campholenyl p-nitrobenzenesulphonate (10.4 g, 0.03 mol) in dimethylformamide (85 ml). The reaction mixture was stirred at room temperature overnight and then poured into water. Subsequent ether

extraction, drying, and removal of the ether gave the crude nitrile (168) as a pale yellow oil (4.9 g), which showed an infrared absorption at 2240 cm^{-1} and no sulphonate bands. The crude nitrile was heated under reflux with a solution of sodium hydroxide (35 g) in water (87 ml) for 18 hr. The cooled solution was washed with ether and the aqueous layer was acidified with dilute hydrochloric acid. The carboxylic acid was extracted into ether, and the ether extract was washed with water and dried. Removal of the ether afforded the crude acid (89) (4.2 g, 76%), which on distillation gave a colourless liquid, b.p. 147-148°/6 mm which solidified on cooling. The solid was recrystallised from low boiling light petroleum as colourless needles, m.p. 46-48° (lit.[163] m.p. 43-45°). ν_{max} 3500-2400 br, 1700 s cm^{-1}; n.m.r. : δ11.5 (1H, broad singlet), 5.20 (1H, broad singlet), 2.7-1.4 (10H, complex), 1.00 (3H, singlet), and 0.80 (3H, singlet).

Work described in part 2.

Camphene (123).

Camphene was prepared[199] by the dehydration of (±)-isoborneol with zinc chloride in benzene as a colourless liquid, b.p. 159-160° (lit.[200] b.p. 159-160°), which solidified on cooling.

Tricyclene (169).

Tricyclene was prepared by the oxidation of camphor hydrazone with mercuric oxide[201] and had physical constants in agreement with literature values.

Bornylene (31).

The olefin was prepared by the method of Shapiro[202] by treatment of camphor tosylhydrazone[203] with a solution of butyllithium in hexane. Bornylene was obtained as a colourless liquid, b.p. 149-150° (lit.[204] b.p. 150-151°), which solidified on cooling.

Bornane (65).

A mixture of camphor hydrazone (5.0 g,0.030 mol), potassium hydroxide (2.0 g, 0.036 mol) and diethylene glycol (30 ml) was heated under reflux for 2 hr. During this period a considerable amount of white material sublimed into the condenser. The material was washed out with ether; the vessel was set for distillation, and c. 15 ml of diethylene glycol was distilled from the mixture. The combined distillate and ether solution was washed with water and dried. Removal of the

ether and distillation of the residue gave a colourless solid (3.5 g), b.p. 155-170°. Recrystallisation from methanol afforded pure bornane (1.5 g, 36%) as a colourless crystalline solid, m.p. 155-156° (sealed capillary), (lit.[205] m.p. 156-157°).

8-Methylcamphene (170).

A mixture of sodium hydride (1.68 g, 0.070 mol) and ethyltriphenylphosphonium bromide (16.5 g, 0.043 mol) in dry tetrahydrofuran (45 ml) was heated under reflux under nitrogen for 2 hr. A solution of camphenilone (107) (5.52 g, 0.040 mol) was then added dropwise to the mixture which was heated under reflux for a further 19 hr. The cooled solution was diluted with water (300 ml) and extracted with ether. The ether extract was washed thoroughly with water and dried. Subsequent removal of the solvent gave a crude product (19.2 g), which was extracted with low boiling light petroleum (100 ml). Undissolved triphenylphosphine oxide was removed from the mixture by filtration. Thorough washing of the filtrate with 80% aqueous methanol, followed by water, completed removal of the oxide. After being dried, the solvent was removed to give a pale yellow liquid (6.3 g) which was chromatographed on silica gel (150 g). Elution with light petroleum afforded 8-methylcamphene as a colourless liquid (3.7 g, 73%), b.p. 76-78°/22 mm. G.l.c. analysis (column B, 100°) indicated that the product consisted of two components in the ratio of 77:23. According to Wege[163] the two components are the Z- and E- isomers respectively of 8-methylcamphene. Preparative g.l.c. (column N, 120°, N_2 120 ml/min) afforded a complete separation of the two isomers (rechecked on column B).

The major product was obtained as a colourless liquid; n.m.r. : δ5.10 (1H, quartet J 7Hz), 2.5 (1H, broad singlet), 1.60 (3H, doublet J 7Hz), 2.0-1.0 (7H, complex), 1.15 and 1.05 (each 3H, singlets); mass spectrum: m/e 150 (23%), 107 (100%).

The minor fraction was also a colourless liquid, n.m.r. : δ4.90 (1H, quartet J 7Hz), 2.90 (1H, broad singlet), 1.55 (3H, doublet J 7Hz), 2.0-1.0 (7H, complex), 1.00 and 0.99 (each 3H, singlets); mass spectrum: m/e 150 (5%), 57 (100%).

Attempts to obtain satisfactory microanalytical data for the two isomers of 8-methylcamphene resulted in consistently low carbon values. A similar difficulty in obtaining analytically pure 8-methylcamphene was encountered by Wege.[163]

Bornyl acetate (64).

The acetate was prepared by the standard acetic anhydride-pyridine acetylation of pure borneol.

Isobornyl acetate (63).

The acetate was prepared by the same method employed above, by the acetylation of pure isoborneol.

Camphene hydrate.

The alcohol was prepared by the method of Coxon, Hartshorn, and Lewis[206] by the oxymercuration-demercuration of camphene. The product was recrystallised from low boiling light petroleum as colourless crystals, m.p. 150-151° (sealed capillary, lit.[206] m.p. 150-151°).

Camphene hydrate acetate (171).

The acetate was prepared by the method of Wege[163] by the treatment of a cold solution of camphene hydrate in N,N-dimethylformamide with acetyl chloride. The tertiary acetate was obtained as a colourless liquid, b.p. 65° (block)/0.5 mm. G.l.c. analysis (column F, 130°) indicated the product was homogeneous.

Methylcamphenilol.

Methylcamphenilol was prepared by the addition of methylmagnesium iodide to camphenilone (107).[207,208] Low temperature recrystallisation from low boiling light petroleum afforded the alcohol as colourless crystals, m.p. 117-118° (lit.[208] m.p. 118-119°).

Methylcamphenilyl acetate (186).

The acetate was prepared by the method of Wege,[163] following a similar procedure to that employed for the preparation of camphene hydrate acetate. The acetate was obtained as a colourless liquid, b.p. 60° (block)/0.7 mm. G.l.c. analysis (column F, 130°) showed the acetate was homogeneous.

α-Campholenyl acetate (179).

The acetate was prepared from α-campholenol (166) by the usual acetic anhydride-pyridine method, as a colourless liquid, b.p. 119-120°/16-17 mm (lit.[198] b.p. 74-76°/1.9 mm). ν_{max} 2950 s, 1740 s, 1460 m, 1370 m, 1250 s, and 1045 s cm^{-1}; n.m.r. ($CDCl_3$) : δ5.25 (1H, broad singlet), 4.10 (2H, triplet J 7Hz), 2.03 (3H, singlet), 2.5-1.3 (8H,

complex), 0.97 and 0.76 (each 3H, singlets); mass spectrum: m/e 196 (4%), 121 (100%).

4-Ethyl-2,3,3-trimethylcyclopentene (178).

Treatment of α-campholenol (166) (1.92 g, 0.013 mol) with p-toluenesulphonyl chloride (5.15 g, 0.025 mol) at 0° in dry pyridine, followed by stirring at room temperature for 10 hr gave, after work-up, the crude tosylate as a pale yellow oil (2.92 g). ν_{max} 2930 s, 1650 w, 1595 w, 1370 s, 1185 s, 965 s, 930 s, and 820 s cm^{-1}; n.m.r. ($CDCl_3$): δ7.78 and 7.30 (4H, "A_2B_2" system consisting of two doublets "J_{AB}" ∿ 8Hz), 5.18 (1H, broad singlet), 4.10 (2H, poorly resolved triplet J 6Hz), 2.45 (3H, singlet), 2.4-1.0 (8H, complex), 0.95 and 0.72 (each 3H, singlets).

A solution of the crude p-toluenesulphonate (2.92 g, 0.010 mol) in dry tetrahydrofuran (10 ml) was added dropwise to a slurry of lithium aluminium hydride (1.44 g, 0.038 mol) in tetrahydrofuran (20 ml). The mixture was then heated under reflux for 24 hr under nitrogen. The usual work-up procedure gave the crude product (0.80 g) which was chromatographed on silica gel (50 g). Elution with light petroleum, followed by distillation gave the required olefin as a colourless liquid (0.44 g, 24%), b.p. 68-75° (block)/45 mm (lit.[166] b.p. 70.5-71°/45 mm), which appeared to be pure by g.l.c. (column B, 100°). ν_{max} 2950 s, 1655 w, 1470 s, 1385 m, 1360 m, 1015 w, and 810 m cm^{-1}; n.m.r. ($CDCl_3$): δ5.25 (1H, broad singlet), 2.7-1.0 (8H, complex), 0.99 (6H, singlet with broad base), 0.75 (3H, singlet); mass spectrum: m/e 138 (17%), 123 (100%).

2,3,3-Trimethyl-4-vinylcyclopentene (177).

The diene was prepared by the modified method of Goldsmith and Cheer.[209] α-Campholenyl acetate (179) was heated to 250° at a pressure of 120 mm, and passed through a silica glass column (330 mm x 25 mm) packed with silica glass helices; the column being maintained at 450-470°. The product was collected in traps cooled to -78°. The product was then diluted with ether, washed with saturated sodium bicarbonate solution and water, and dried. The ether was removed to give the product which contained a mixture of unreacted acetate and the required diene (177). Distillation afforded a hydrocarbon fraction (b.p. up to 130°/760 mm) which was shown by g.l.c. analysis (column H, 80°) to contain two products in the ratio of 9:1. Preparative g.l.c. (column O, 120°, N_2 120 ml/min) afforded a pure sample of the diene (177). ν_{max} 2950 s, 1635 m, 1460 s, 1005 s, 915 s, and 810 s cm^{-1}; n.m.r. ($CDCl_3$) : δ6.2-5.5 (1H, complex multiplet), 5.3-4.7 (3H, complex), 2.6-1.2 (6H, complex), 0.98 and 0.77 (each 3H, singlets); mass spectrum: m/e 136 (28%), 93 (100%).

2,3,3-Trimethylnorbornane (187) or (191) (Isocamphane).

The hydrocarbon was prepared by the catalytic hydrogenation of camphene[142] as a mixture (3:1) of the endo- and exo-isocamphanes (191) and (187) respectively.

Oxidative decarboxylation of the acids (85), (86), (87), (88), and (89) in benzene.

The following procedure is typical:

A mixture of the acid (58.50 mg, 0.321 mmol), pyridine (23.4 mg, 0.296 mmol), lead tetraacetate (206.5 mg, 0.446 mmol), and cupric acetate monohydrate (21.6 mg, 0.108 mmol) in pure, dry benzene (1.0 ml) was thoroughly flushed with dry, oxygen-free nitrogen and sealed in a Pyrex tube (c. 80 mm x 15 mm) containing a small, teflon-coated magnetic stirrer bar. The reaction mixture was stirred at 92.5-93.5° for 4 hr and then cooled to -78°. To the opened tube was added ice-cold aqueous nitric acid (10% V/V, 6 ml) and low-boiling light petroleum (6 ml). At this stage an accurately weighed amount of internal standard (1,3,5-trimethylbenzene, 20-25 mg) in low-boiling light petroleum (3 ml) was quantitatively transferred to the reaction mixture. The aqueous layer was separated and washed with low-boiling light petroleum (c. 2 ml). The combined organic extracts were washed with water (3 ml).

Unchanged acid was recovered by washing the organic extracts with ice-cold 10% sodium hydroxide solution (3 ml) and water (2 x 3 ml). Subsequent acidification with dilute hydrochloric acid and ether extraction afforded any unchanged acid. The light petroleum extract, after treatment with 10% sodium hydroxide solution and water to remove the acidic material, was dried and concentrated by distilling most of the light petroleum through a column (100 mm) packed with glass helices while the temperature of the bath was maintained at 50-55°. The final concentrate [after cooling of the flask in ice (to facilitate drainage of solvent held in the column) and washing the column with a small quantity of low-boiling light petroleum (2-3 ml) to ensure that none of the material to be analysed was held in the column] was analysed by g.l.c.

as follows:

Quantitative hydrocarbon analysis: The hydrocarbons were analysed using column B, which was maintained at 100°. After all the hydrocarbons had been eluted, the column was programmed to 130° at 24°/min to elute the acetates and determine a given ratio of bornyl:isobornyl acetate. On this column it was found that camphene hydrate acetate decomposed, but this did not interfere with the analysis of any of the other products.

Quantitative acetate analysis: Acetates were analysed using column F which was maintained at 90° in order to elute the hydrocarbons and the internal standard. Then the column was programmed to 130° at 24°/min to elute the acetates. It should be noted that column F did not resolve a given mixture of bornyl and isobornyl acetates, while column B did provide a good separation of the two products. Hence column B was used to determine a given ratio of bornyl:isobornyl acetate, and column F was used to determine quantitatively the amount of the combined bornyl and isobornyl acetates.

Each product analysis was the average of 2 g.l.c. determinations and each reaction was carried out in duplicate.

Oxidative decarboxylation of the acids (85), (86), (87), (88), and (89) in dimethylsulphoxide.

The following procedure is typical:

A mixture of the acid (49.80 mg, 0.274 mmol), pyridine (24.00 mg, 0.304 mmol), lead tetraacetate (177.5 mg, 0.401 mmol), and cupric acetate monohydrate (25.3 mg, 0.127 mmol) in pure dry dimethylsulphoxide (1.0 ml) was thoroughly degassed with dry, oxygen-free nitrogen and sealed in a glass ampoule as described previously. After the mixture was stirred at 92.5-93.5° for 4 hr, the tube was cooled to -78° and opened. To the opened tube was added low-boiling light petroleum (6 ml), water (5 ml), and an accurately weighed amount of internal standard (1,3,5-trimethylbenzene, 20-25 mg) in low-boiling light petroleum (c. 2 ml). After the addition of more water (10 ml), the aqueous phase was separated and the organic layer was washed with water (5 x 5 ml). The method of separation of the neutral from the acidic material was identical to that described for the oxidative decarboxylation reactions in benzene. The conditions of analysis of the products were also identical to those described previously.

Preparative scale decarboxylation of a mixture (75:25) of exo- and endo-2-carboxybornane (85) and (86).

A mixture of the acids (1.53 g, 8.4 mmol), lead tetraacetate (5.44 g, 12.3 mmol), and pyridine (0.73 g, 9.3 mmol) in dry, degassed dimethylsulphoxide (30 ml) was stirred at 92.5-93.5° for 4 hr under nitrogen. Water (100 ml) was then added to the cooled solution which was transferred to a separating funnel with low-boiling light petroleum (50 ml). After the addition of a further 100 ml of water, the organic layer was separated and washed thoroughly with water (5 x 50 ml).

Unchanged acid was removed by washing with 10% sodium hydroxide solution (2 x 10 ml) and water (2 x 10 ml). Acidification with dilute hydrochloric acid, followed by ether extraction, gave the unchanged acid (0.33 g, 22%). After being dried, the solvent was removed from the neutral portion of the reaction mixture. Distillation of the residue afforded a mixture of hydrocarbons and acetates, b.p. up to 130° (bath)/ 0.01 mm, which were collected in a trap cooled to -78°.

The mixture was submitted to preparative g.l.c. (column G, 110°, N_2, 120 ml/min) in an attempt to isolate and determine the structure of three components of the mixture which had not previously been identified. Two of the products were identified as camphor (25) and acetoxydimethylsulphoxide (173); the other product could not be identified on the basis of its spectral characteristics (i.e. infrared, n.m.r., and mass spectrum). Camphor was obtained as a white solid whose infrared and n.m.r. spectra were identical to those of an authentic sample of camphor. Acetoxydimethylsulphoxide (173) was obtained as a colourless liquid. ν_{max} 2930 w, 1740 m, 1440 w, 1375 w, 1215 m, 1020 w, and 960 w cm^{-1}; n.m.r. : δ5.06 (2H, singlet), 2.24 (3H, singlet), and 2.06 (3H, singlet); mass spectrum: m/e 120 (36%), 90 (13%), 73 (18%), 61 (24%), 43 (100%). The unknown compound had the following spectral characteristics: ν_{max} 2950 s, 1735 w, 1460 m, 1395 m, 1375 m, 1310 w, and 1100 w cm^{-1}; n.m.r. : δ4.3-3.9 (complex), 2.7-1.1 (complex), and 1.0-0.9 (at least three very close singlets), the ratio of the three groups of absorptions was c. 1:9:9 respectively; mass spectrum: m/e 159 (5%), 157 (13%), 136 (25%), 121 (17%), 119 (38%), 117 (39%), 110 (39%), 95 (100%), 93 (25%), 81 (23%), 41 (14%).

Work described in part 3.

α-Campholenyl chloride (190).

The chloride was obtained by treatment of the p-nitrobenzenesulphonate of α-campholenol (167) with pyridine hydrochloride in N,N-dimethylformamide at room temperature for 20 hr according to the method of Wege.[163] Distillation gave the chloride as a colourless liquid, b.p. 92-94°/15 mm, which was shown to be homogeneous by g.l.c. (column B, 100°). The chloride exhibited the following spectral properties: ν_{max} 3035 m, 2950 br, 1640 w, 1435 m, 1355 m, 1110 m, 850 m, 795 m, 740 m, and 680 m cm^{-1}; n.m.r. : δ5.20 (1H, broad singlet), 3.5 (2H, multiplet), 2.6-1.3 (8H, complex), 1.00 and 0.76 (each 3H, singlets).

General procedure for the reaction of α-campholenyl chloride (190) with tri-n-butyltin hydride.

Solutions of tri-n-butyltin hydride[210] in dry, deoxygenated benzene were prepared in the concentrations given in Table 14.

A solution of tri-n-butyltin hydride in benzene (43.75 mg, 0.15 mmol, i.e. either 1.5 ml of a 0.10022M solution, 3.0 ml of a 0.05011M solution, or 6.0 ml of a 0.02505M solution), α-campholenyl chloride (50.00 mg, 0.29 mmol) and either azobisisobutyronitrile (AIBN, c. 2 mg) or di-t-butyl peroxide (DTBP, c 2 mg) was thoroughly flushed with dry, oxygen-free nitrogen and sealed in a Pyrex tube (c. 80 mm x 15 mm). After being heated at either 93° or 130° for 21 hr the ampoule was cooled to -78° and opened. An accurately weighed amount of internal

standard (1-methyl-4-i-propylbenzene, c 6 mg) in low-boiling light petroleum (c 2 ml) was quantitatively added to the reaction mixture which was analysed by g.l.c. as follows:

The products were analysed using column B, which was maintained at 100°. After the hydrocarbons and internal standard had been eluted, the column was programmed to 160° at 48°/min to elute any unchanged α-campholenyl chloride.

Each product analysis was the average of 2 g.l.c. determinations and each reaction was carried out in duplicate.

Work described in part 4.

General procedure for the preparation of the methyl ethers, (192), (193), (194), (195), and (196).

To a stirred mixture of the alcohol (1.00 g, 0.0065 mol), sodium hydride (0.40 g, 0.0165 mol), and N,N-dimethylformamide (10 ml), maintained under nitrogen at 100-110°, was added methanol (3 drops) followed by methyl iodide (1.85 g, 0.013 mol). After being stirred at 100-110° for 3 hr, the mixture was cooled, diluted with water (10 ml), and extracted with ether. The dried ether extract was concentrated to give an oil which was chromatographed on silica gel (50 g). Elution with light petroleum containing 5% ether gave the required ether which was obtained as a colourless liquid in yields of 60-70% after distillation at 80° (block)/15 mm. In this way the following methyl ethers were prepared:

exo-2-Methoxybornane (isobornyl methyl ether) (192):

ν_{max} 2950 s, 2870 s, 2810 m, 1110 s, and 1085 s cm^{-1}; n.m.r. : δ3.20 (3H, singlet), 3.10 (1H, complex), 2.5-1.0 (7H, complex), and 0.90, 0.85, and 0.80 (each 3H, singlets); mass spectrum: m/e 168 (6%), 95 (100%). The n.m.r. spectrum was in accord with that reported in the literature,[211] as was the boiling point, (lit.[212] b.p. 78°/17 mm).

endo-2-Methoxybornane (bornyl methyl ether) (193) :

ν_{max} 2980 s, 2950 s, 2870 s, 2810 m, 1120 s, and 1090 s cm^{-1}; n.m.r. :

δ3.40 (1H, complex), 3.25 (3H, singlet), 2.3-1.0 (7H, complex), and 0.85 (9H, singlet); mass spectrum: m/e 168 (6%), 95 (100%). The n.m.r. spectrum was in accord with that reported in the literature,[211] as was the boiling point, (lit.[211] b.p. 74-75°/12 mm).

exo-2-Methoxy-2,3,3-trimethylnorbornane (camphene hydrate methyl ether) (194):

ν_{max} 2950 b,s, 2820 s, 1110 s, 1085 s, and 1055 s cm^{-1}; n.m.r. : δ3.10 (3H, singlet), 2.3-1.0 (8H, complex), and 1.07, 0.90, and 0.87 (each 3H, singlets); mass spectrum: m/e 168 (3%), 85 (100%); (Found: C, 78.6; H, 11.9. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%).

endo-2-Methoxy-2,3,3-trimethylnorbornane (methylcamphenilyl methyl ether) (195):

ν_{max} 2930 b,s, 2825 s, 1130 s, 1095 s, and 1060 s cm^{-1}; n.m.r. : δ3.10 (3H, singlet), 2.3-1.0 (8H, complex), and 1.10, 0.90, and 0.85 (each 3H, singlets); mass spectrum: m/e 168 (4%), 85 (100%); (Found: C, 78.3; H, 11.7. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%).

α-Campholenyl methyl ether (196):

ν_{max} 3040 w, 2960 s, 2930 s, 2870 s, and 1115 s cm^{-1}; n.m.r. : δ5.22 (1H, broad singlet), 3.30 (2H, triplet J 6.5Hz), 3.25 (3H, singlet), 2.6-1.2 (5H, complex), 1.60 (3H, broad singlet), and 0.98 and 0.80 (each 3H, singlets); mass spectrum: m/e 168 (7%), 121 (55%), 108 (48%), 95 (100%), and 93 (50%); b.p. 104-107°/39 mm; (Found: C, 78.2; H, 11.9.

$C_{11}H_{20}O$ requires C, 78.5; H, 12.0%).

α-Terpinyl methyl ether (197).

Limonene (5.0 g, 36.8 mmol) was added to a rapidly stirred suspension of mercuric acetate (11.7 g, 36.8 mmol) in anhydrous methanol (36 ml) at room temperature. After being stirred for 10 min, the mixture was treated with 3N sodium hydroxide (36 ml) followed by a solution of sodium borohydride (0.68 g) in 3N sodium hydroxide (36 ml). The mixture was then stirred at room temperature for 30 min, diluted with water (300 ml), and extracted with ether (3 x 70 ml). The combined ether extracts were washed with water (4 x 50 ml), dried, and concentrated to give a colourless oil (7.2 g) which was shown by g.l.c. (column B, 120°) to consist of limonene (39%), α-terpinyl methyl ether (33%), and the dimethyl ether (201, 28%). The three components were readily separated by preparative g.l.c. (column O, 145°, 130 ml N_2/min). α-Terpinyl methyl ether (197) was obtained as a colourless liquid, b.p. 80-90° (block)/12 mm. (Found: C, 78.6; H, 12.1. $C_{11}H_{20}O$ requires C, 78.5; H, 12.0%). ν_{max} 2970 s, 2930 s, 2830 s, 1435 m, 1375 m, 1360 m, and 1080 s cm^{-1}; n.m.r. : δ5.35 (1H, broad singlet), 3.10 (3H, singlet), 2.4-1.2 (10H, complex), and 1.05 (6H, singlet); mass spectrum: m/e 168 (trace), 73 (100%).

The dimethyl ether (201) was obtained as a colourless oil, b.p. 90-100° (block)/12 mm. (Found: C, 71.9; H, 12.2. $C_{12}H_{24}O_2$ requires C, 72.0; H, 12.1%). ν_{max} 2970 s, 2940 s, 2825 m, 1460 m, 1375 m, 1360 m, and 1080 s cm^{-1}; n.m.r. : δ3.10 (6H, singlet), 2.2-1.1 (9H, complex),

and 1.02 (9H, singlet); mass spectrum: m/e 200 (trace), 73 (100%).

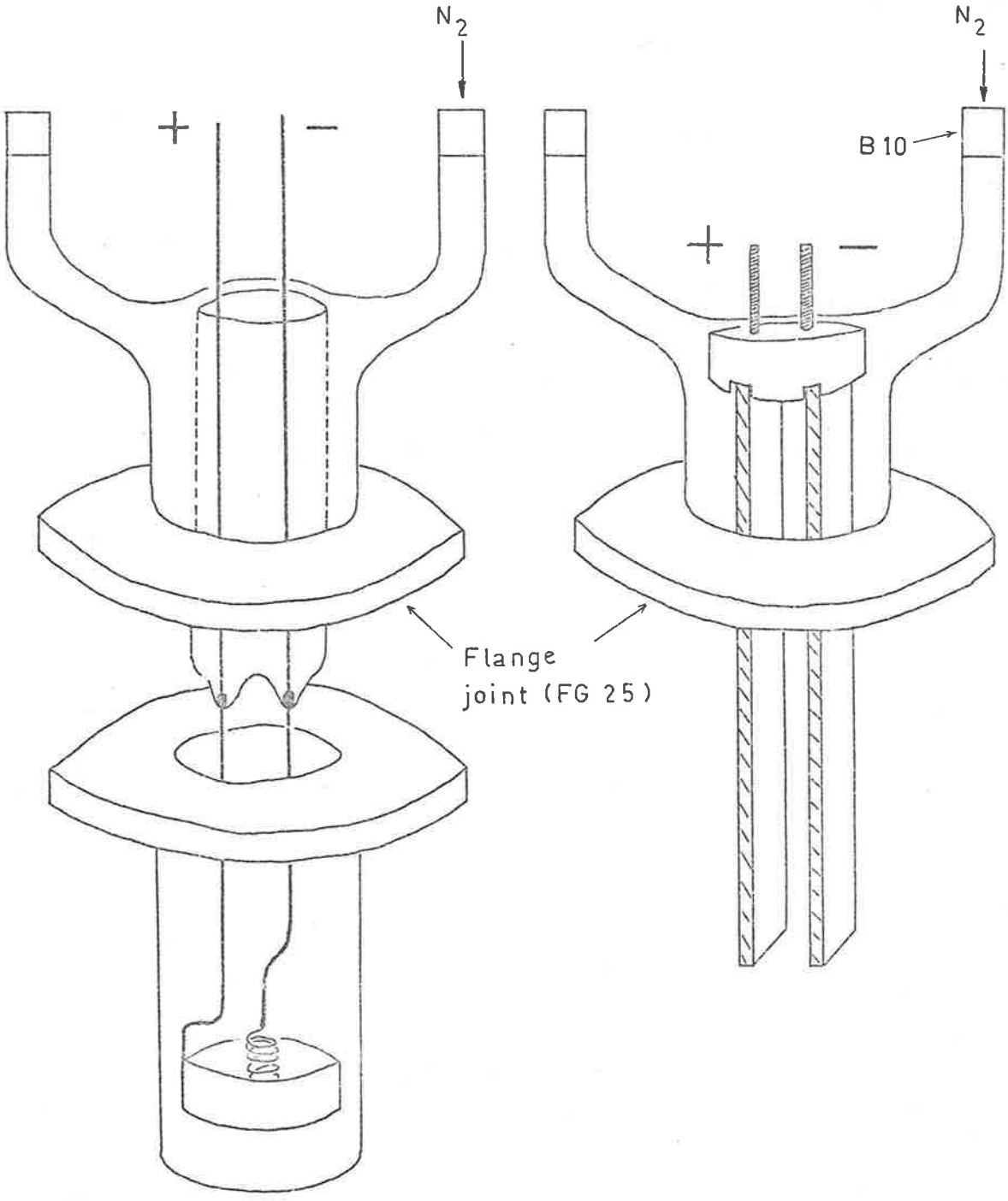
DESCRIPTION OF ELECTROLYSIS CELLS:

The electrolysis cell used consisted of a cylindrical glass vessel (60 mm deep x 24 mm diameter), the contents of which could be stirred magnetically. Into this vessel was placed either the platinum or graphite electrode assembly (Fig. 10). The platinum electrode assembly consisted of an outer circular anode of platinum foil (63 mm x 10 mm x 0.13 mm) and an inner cathode which consisted of a tightly wound coil of platinum wire. The distance between the two electrodes was 6-7 mm.

The graphite electrode assembly consisted of two parallel strips of graphite (75 mm x 18 mm x 2 mm) which were separated by a distance of 6 mm by a glass spacer. A regulated D.C. power supply provided a potential between the two electrodes which could be adjusted to supply a constant potential of 10 volts. During all the electrolyses a current of 50-60 mA was maintained.

General procedure for anodic oxidation:

To an accurately weighed sample of the acid (c. 50.00 mg, 0.275 mmol) in the electrolysis vessel, was added a solution of methanolic sodium methoxide (10 ml, 0.0396M i.e. 0.396 mmol). After fitting of the appropriate electrode assembly and flushing with dry nitrogen, a potential of 10.0 volts was maintained across the electrodes for two hours. During the anodic oxidation the electrolyte was stirred magneti-



Platinum Electrode Assembly

Graphite Electrode Assembly

Fig. 10.

cally. On completion of the electrolysis the electrodes were removed and washed with low-boiling light petroleum (7 ml). The reaction mixture was then transferred quantitatively, with the aid of low-boiling light petroleum (c.3 ml), to a separating funnel containing saturated sodium chloride solution (10 ml), and an accurately weighed sample of 1,3,5-trimethylbenzene (c. 20.00 mg) in low-boiling light petroleum (3 ml) was added to the mixture. The organic layer was separated and the aqueous portion was washed with low-boiling light petroleum (1 x 10 ml). The combined organic extracts were washed with water (2 x 5 ml) and dried (Na_2SO_4). The solution was then carefully concentrated by distillation of most of the petroleum ether through a column (100 mm x 15 mm) packed with glass helices; the temperature of the bath being maintained at 50-55°. After cooling in ice and washing of the column with low-boiling light petroleum (1-2 ml) the final concentrate (c. 5 ml) was analysed by g.l.c.

Unchanged acid was recovered by acidification of the aqueous alkaline extract with dilute hydrochloric acid. Subsequent extraction of the aqueous extract with low-boiling light petroleum (2 x 10 ml), washing with water (1 x 5 ml), and drying (Na_2SO_4), followed by removal of the solvent gave any unchanged carboxylic acid.

QUANTITATIVE ANALYSIS: The product was analysed on column B, maintained at a temperature of 100°. After all the hydrocarbons had been eluted (c. 11 min), the column was programmed to 120° at 48°/min to elute the methyl ethers. To establish whether the exo-2-methoxy-2,3,3-trimethyl-

norbornane (194) contained any of the endo epimer (195), the reaction mixture was also analysed on a Golay column (300' x 0.01") which was coated with liquid methylsilicone (SE-30). The column was maintained at a temperature of 125° with a pressure of 13.75 psi of nitrogen and the methyl ether (194) was eluted after c. 35 min.

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