A Thesis Entitled

"PYROLYTIC STUDIES IN THE ALICYCLIC SERIES"

Submitted for the Degree of Doctor of Philosophy

to the Faculty of Science of the

University of Glasgow

by

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September 1973

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To

Mag

Jamie

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and

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SUMMARY

of a Ph. D. Thesis Entitled

PYROLYTIC STUDIES IN THE ALICYCLIC SERIES

submitted by JAMES BOYD

to the Faculty of Science

of the University of Glasgow

October 1973.

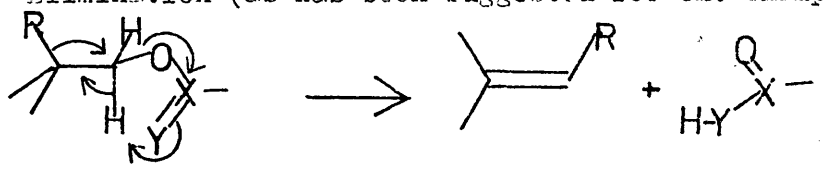
The thesis, concerned largely with pyrolytic elimination of esters through mechanisms other than the normal[1,2,3,4] 1,2-route, is in three main parts : I Introduction, II Adamantanoid Series, and III Cyclohexylcarbinyl and Decalyl Series.

The Introduction first reviews a variety of mechanistic rationalisations advanced to explain data on 1,2- eliminations. In particular the Quasi-Heterolytic[5,6] and Concerted[1,7] mechanisms are critically compared. The author favours the latter, noting that ester pyrolysis can be related to the general Retro-Ene reaction.[3]

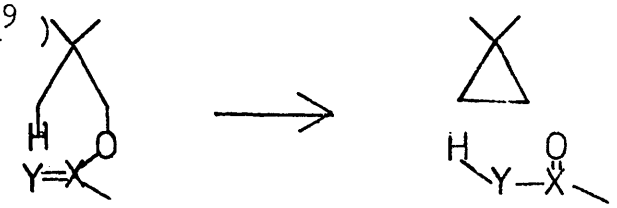
A literature survey (1900- 1971) is made and twenty-two examples of reports of anomalous product formation on ester pyrolysis are recorded. Each is discussed.

It appears that all recorded examples, other than those carried out under conditions likely to cause acid or surface catalysed rearrangement, may be explained by extensions of three mechanisms namely :-

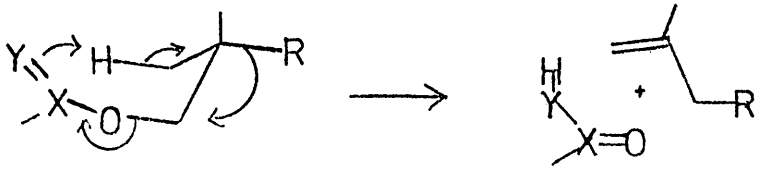
(a) - Elimination (as has been suggested for one example by Kwart[8]



(b) 1,3- Elimination with cyclopropyl formation (suggested on poor evidence by Bunton[9])



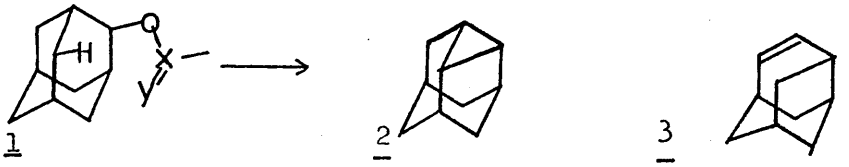
(c) 1,3- Elimination with 2-alkyl migration (suggested on good evidence by Bunton[9], though for one example only.)



The thesis which follows investigates aspects of the latter two mechanisms (a and b above) and structures derived by their application to model systems.

II Adamantanoid Series

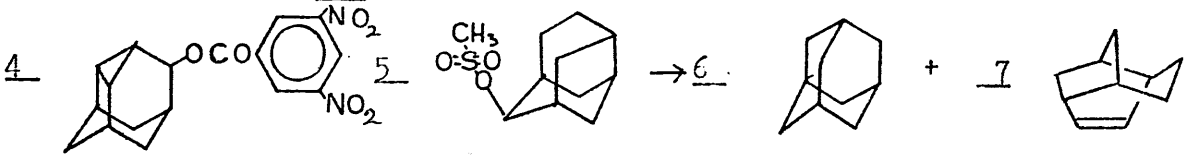
2- Adamantyl esters (i.e. tetracyclo-(3,3,1,$1^{3,7}$)-decyl-) e.g. 1 were chosen as a model.



1 2 3

Pyrolysis of the acetate was unsuccessful, but the -S-methyl xanthate, toluene p-sulphonate, and methane sulphonate gave the products 2,4 - dehydroadamantane 2 and protoadamantene 3, predicted from mechanisms a and b above. (Yields and ratios varied, but maximum was 95% of 2 and 3 in the ratio 60; 40) Possible mechanisms are discussed.

Other esters pyrolysed were 2- (8,9-dehydroadamantyl)-3,5-dinitro-benzoate 4 (the corresponding alcohol was produced by ozone treatment of 2,4-dehydroadamantane 2) and 10-protoadamantyl methanesulphonate 5.



4 5 6 7

The former though eliminating ester failed to give identifiable products. The latter gave adamantane 6 and an olefin thought to be 7

A series of reactions was carried out on protoadamantene 3 , namely epoxidation (and hydride reduction of the epoxides), hydroboration (and oxidation) and oxymercuration. The stereochemistry of 3 and its effect on the course of the above reactions is discussed.

The europium shifted n.m.r. spectra of all four 4- and 5-protoadamantanols , the 4- and 5-protoadamantanones, 4exo- and 4endo-methyl-protoadamantanols and 4endo-phenyl protoadamantanol are recorded and discussed. Configuration, conformation and C-C bond angle strain are among topics discussed in relation to information derived from the spectra.

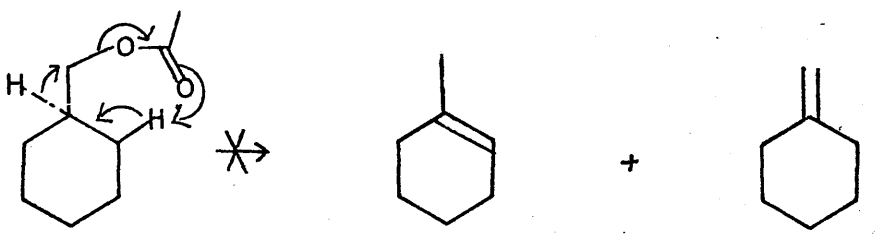
III Cyclohexylcarbinyl and Decalyl Series

It had been hoped that a modification of the 1,3-elimination mechanism c above might explain the observation of (a) the reported[10] formation of 1-methyl cyclohexene on pyrolysis of cyclohexylcarbinyl acetate 8 and (b) apparent anti-elimination in some esters of cyclic alcohols e.g. 1-decalyl 11 (ref. 11)

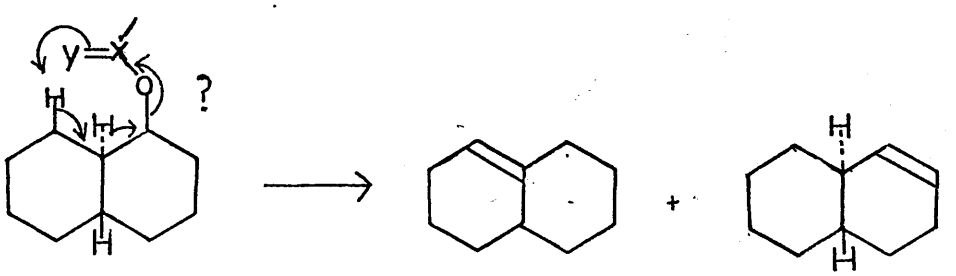
(see 8 and 11 with arrows over)

The pyrolysis of 8 was, however, found to occur with formation of methylenecyclohexane 10 only, the product 9 only appearing through subsequent contact of 10 with acid.

Pyrolysis of esters such as 11 did give $\Delta^{1,9}$-octalin 12 but not by a 1,3-mechanism, since C_9-deuterium was eliminated. The anti-elimination product 12 does not appear to arise through isomerisation of ester or of the normal product t-$\Delta^{1,2}$-octalin. Various mechanisms are considered.



8 9 10



11 12

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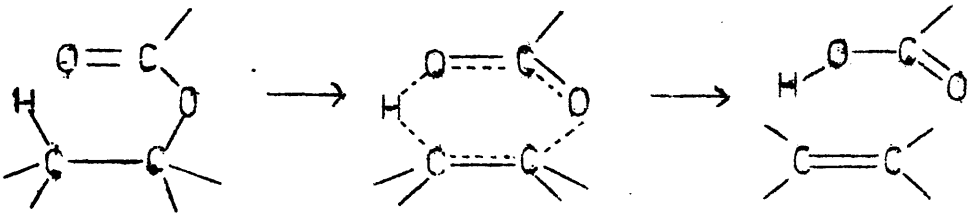
INTRODUCTION.

This thesis is largely concerned with the scope and application of pyrolytic eliminations of esters through pathways other than that of normal 1,2 - elimination. Before proceeding with a discussion of the evidence for such pathways it is perhaps advisable to consider the normal mode of pyrolytic elimination in some detail.

The pyrolytic 1, 2 - elimination of esters is a well established synthetic tool of long standing and several reviews [1,2,3,4,5,6] on different aspects of the reaction are available.

The most usual description of the mechanism is the "concerted" route first proposed by Hurd and Blunk.[7] In this mechanism the bonds are formed and broken simultaneously and without separation of charges, the transition state being represented by structure 2 of fig. 1.

Fig. 1.

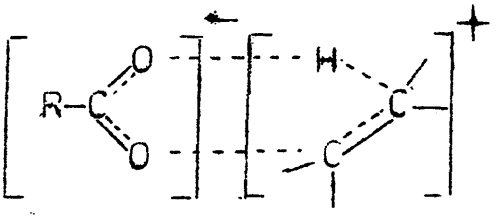


1 2 3

This mechanism is attractive since it expresses (a) that the reaction is homogeneous and unimolecular as has been found on kinetic investigation [1,2,4,5] and (b) that it proceeds by loss of cis - β - hydrogen atom [1,2]. In addition it is compatible with the observation of (c) large deuterium isotope effects [1,8], of cis - β - β - deuterated esters and (d) negative activation entropies [1,5,12].

Some authors, notably Kooyman [5] and Maccoll [4,6,8] consider that the concerted mechanism is not satisfactory in that it does not account for rate increases due to (a) electron with-drawing groups on the ester [1,13,14,15] (b) α alkylation [4,5] (i.e. rate tertiary > secondary > primary esters) and (c) electron withdrawing substitution α to the removed hydrogen. [4,5] These latter authors have suggested a "quasi heterolytic" [4,5,8] mechanism represented by the transition state [4]

Fig.2



with varying degrees of dissociation. The activation energies observed for pyrolyses (30 - 48 Kcal/mole) preclude the formation of separate ions since this would require too high an energy (220 Kcal/mole[16]). Instead a close ion pair is suggested. Thus if the charges are separated by 2Å, coulombic energy is around 170 K/cal/mole[5] leaving an activation energy of ca. 50 kcal./mole. The possibility of forming such an ion pair where the distance of separation approaches covalent bond length has never been established in theory or practice. It should be noted that in solution (as distinct from the gas phase) where solvation may occur and the medium is of high dielectric constant a greater separation of ions, without a corresponding increase in energy, is possible.

It is possible to account for the effects of substitution α to removed hydrogen or its substitution by deuterium by postulating [4,5] a two stage reaction scheme comprising a rapid ionic equilibrium stage followed by a slow hydrogen removal stage:-

$$RCO_2R' \underset{k_2}{\overset{k_1}{\rightleftharpoons}} (RCO_2^-) + (R'^+)$$

$$(RCO_2^-) + (R'^+) \xrightarrow{k_3} RCO_2H + \text{olefin}$$

If k_3 is the slow step:-

$$k_{obs} = \frac{k_1 k_3}{k_2 + k_3}$$

and if $k_3 \ll k_1$

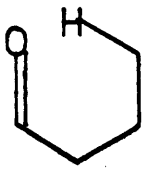
$$k_{obs} \approx \frac{k_1 k_3}{k_2}$$

Thus, for example, a deuterium isotope effect on k_3 produces the same effect on k_{obs}, while factors affecting ease of hetrolysis also affect k_{obs}.

While the quasi hetrolytic mechanism goes a long way in explaining relative kinetic data [4,5] De Puy[1] has pointed out as Kooyman[5] in part agrees, that (a) the magnitude of the rate enhancement effects of α- substitution are too small to account for substantial involvement of hetrolysis in the reaction pathway, while (b) the effects of β- substitution [1,5] are too small to support the concept of the E_2 type removal of the β- hydrogen by the acyl anion and (c) when carried out in solution, rates show little variation with solvent polarity[1].

What is required at this stage is an attempt to explain the observed facts by application of a more sophisticated view of the concerted reaction, taking into account the effect of electron withdrawing groups at α- and β - positions. Though this is difficult since the influence of polarity in concerted reactions is not fully understood, a reconsideration of the concerted mechanism may prove fruitful.

FIG 5



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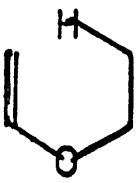

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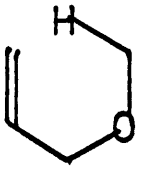

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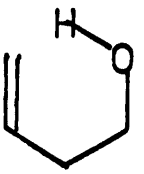

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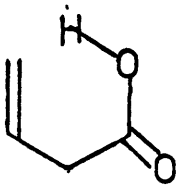

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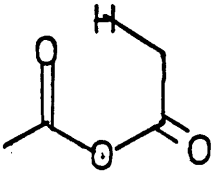

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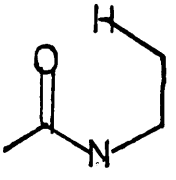

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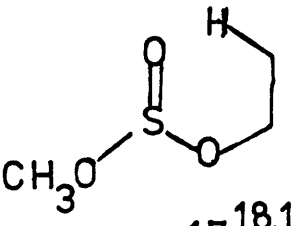

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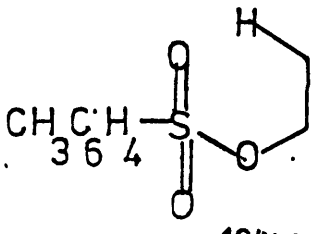
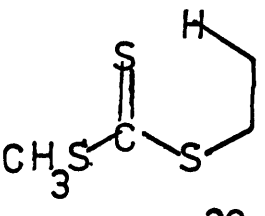


18 (this thesis)



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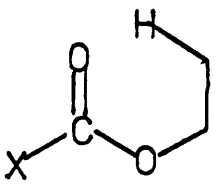


20 1,4,5 X = alkyl or phenyl

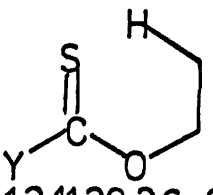
21 1,20,22 X = OR

22 23 X = NSO$_2$C$_6$H$_4$CH$_3$

23 24 X = Cl

24 20,25 X = NHCH

25 26 X = SR

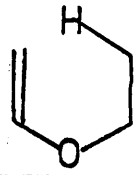
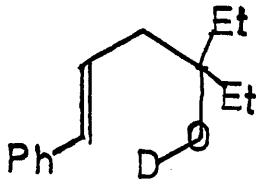


26 1,2,11,20,26-29 Y = alkyl or phenyl RS-

27 26 Y = OR

28 30 Y = N(CH$_3$)$_2$

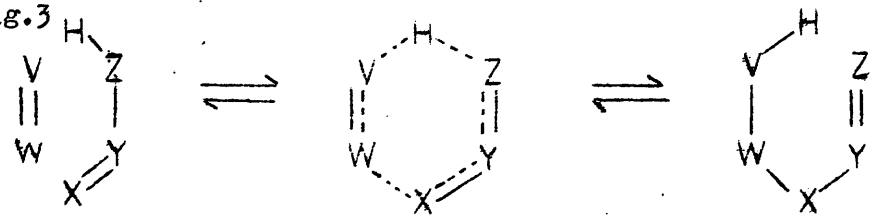
TABLE 1

Substrate	E_A Kcal.mole^{-1}	ΔS cal.deg^{-1}	Ref.
	43.8	- 10.2	31,3
	41.8	-4.8	32,3
$CH_3CO_2CH_2CH_3$	48		1
Ar-$CO_2CH_2CH_3$	38.1		1
3β-cholesteryl acetate	44.1	-3.6	1,20
3β-cholesteryl Me-xanthate	32.9	-4.7	1,2
3β-cholesteryl Et-carbonate	41	-4.3	1,20
3β-cholestanyl Me-xanthate	33.8	-5	1,2

H.M.R. Hoffmann[3] in his recent review on the "ene" reaction very briefly suggests that ester pyrolysis may be related to the "retro-ene" reaction.

The "ene" reaction in its most general sense is the addition of a double bond species (normally called the enophile[3]) to a doubly bonded species containing an allylic hydrogen (the "ene"[3]).

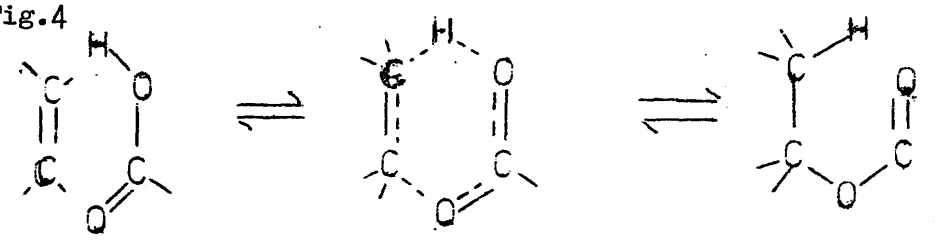
Fig.3



It can be seen that while the reaction normally refers to largely carbocyclic systems, carboxylic ester pyrolysis represents a particular "retro" case where Z = O, Y = C, X = O and W = V = C

or

Fig.4



In fig.5 are listed some examples of species known to undergo thermal fragmentation in a manner consistent with the reaction scheme depicted in fig. 3 above.

Table 1 lists some activation energies and entropies observed for known "retro-ene" and ester pyrolysis reactions.

Consideration of table 1 and other available data[1,2,3,4,5,6], shows that ester pyrolysis has activation parameters closely similar to accepted concerted reactions of the ene type, and shows similar deuterium isotope effects.[1,3]

Consideration of transition state theory [33] suggests that the rate/energy relationship is of the form:-

$$k = \frac{ekt}{h} \; e^{\frac{\Delta S^*}{k}} \; e^{\frac{-\Delta H^*}{kt}} \qquad \text{EQN.1}$$

Thus reaction rates can be compared in terms of activation entropy ΔS^* and activation enthalpy ΔH^*

$$\text{ie} \quad \frac{k_1}{k_2} = e^{\frac{\delta(\Delta S^*)}{k}} \; e^{\frac{-\delta(\Delta H^*)}{kT}} \qquad \text{EQN.2}$$

Let us assume for the moment that the ΔS^* values of a series of pyrolyses of different esters of the same alcohol are identical. This is not too serious an assumption, since ΔS^* values observed normally fall into a fairly narrow range (ca - 3 to -5 e.u.) and variation appears [1,20,4] to depend more on the nature of the alcohol residue than the acid function.

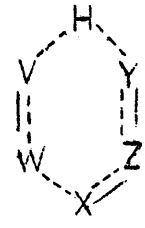
Then

$$\frac{k_1}{k_2} = e^{\frac{-\delta(\Delta H^*)}{kT}} \qquad \text{EQN.3}$$

$$\text{or} \quad \ln \frac{k_2}{k_1} \propto \delta(\Delta H^*) \qquad \text{EQN.4}$$

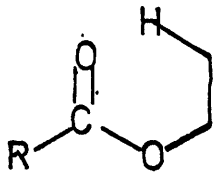
If we consider that in the transition state of the "retro ene" reaction (fig.6. 5.)

Fig.6



bond breaking and bond making have proceeded to an equal extent, then the enthalpy of activation ΔH^* will reflect the energy required to break the relevant bonds less terms for energy gained in forming the relevant bonds.

SCHEME 1



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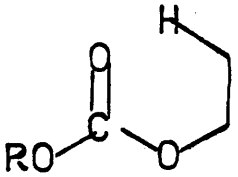

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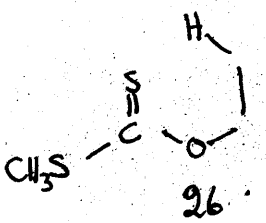
BOND ENERGY EXPENDED	GAINED	BOND ENERGY EXPENDED	GAINED
D_{C-H}	D_{O-H}	D_{C-H}	D_{O-H}
D_{CO}	$D_{\pi CC}$	D_{CO}	$D_{\pi CC}$
$D_{\pi CO}$	$D_{\pi CO}$	$D_{\pi CO}$	$D_{\pi CO}$

$\Delta H = D_{CH} + D_{CO} + D_{\pi CO} - D_{OH} - D_{\pi CO} - D_{\pi CC}$

$= D_{C-H} - D_{\pi C=c} - D_{O-H} + D_{CO}$



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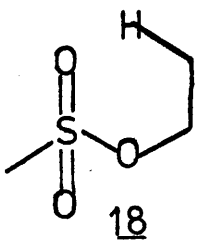
SCHEME 2



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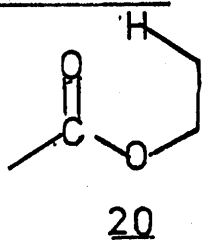

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BOND ENERGY EXPENDED	GAINED	BOND ENERGY EXPENDED	GAINED
D_{CH}	D_{SO_2-H}	D_{CH}	D_{CO_2-H}
D_{SO_2-C}	$D_{\pi CC}$	D_{CO_2-C}	$D_{\pi CC}$
$D_{\pi SO}$	$D_{\pi SO}$	$D_{\pi CO}$	$D_{\pi CO}$

$H = D_{CH} + D_{SO_2-C} - D_{SO_3-H} - D_{\pi CC}$

$H = D_{CH} + D_{CO_2-C} - D_{CO_2-H} - D_{\pi CC}$

To use this theory one must then make the drastic assumption that the energy required to "half break" and "half make" the bonds is proportional to the energy required to completely break and completely make the same bonds.

Or. $\delta(\Delta H^*) \propto \delta(\Delta H)$

hence from EQN.3. $\ln \frac{k_1}{k_2} \propto \delta(\Delta H)$ EQN.4

Enthalpy (Δ H) values can be found by subtracting dissociation energy of bonds formed from dissociation energy of bonds broken. Hoffman[3] outlines a similar argument and conclusion in his review.

For example, comparing carboxylic ester (Scheme 1,20) and alkyl carbonate (Scheme 1,21) pyrolyses, the same bonds (to a first approximation) are broken and made in each case. These pyrolyses might then be expected to proceed at similar rates and with similar activation energies, as is in fact observed (see table 1).

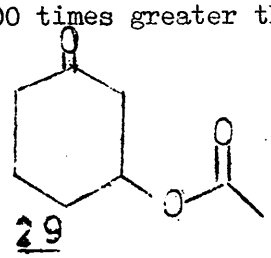
If, in comparing the pyrolysis of xanthate (Scheme 1 26) and carbonate (Scheme 1 21), we assume C-O bonds of equal strength, it can be seen that the main differences in activation enthalpy are two fold. The formation of a relatively weaker SH bond (ca. 90 Kcal/mole [34]) in the xanthate case and a stronger OH bond (ca. 112 Kcal/mole [34]) in carbonate case should favour carbonate pyrolysis, however this is probably outweighed by the breaking of the much weaker C = S bond in xanthate compared with the C = O bond broken in carbonate pyrolysis (D π C = S = 67, D π CO = 107 Kcal.mole [35]) resulting in lower observed[1,2] activation energies for xanthate pyrolysis (see table 1).

Though similar comparison of carboxylic ester and sulphonate pyrolyses (Scheme 2) may not be valid in that Δ S* values may not be comparable, comparison on the basis of Δ H values is interesting.

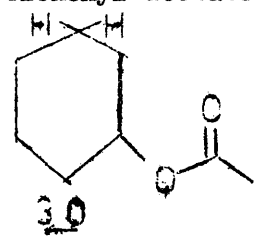
Consideration of Scheme 2 shows that the differences in the two pyrolyses resolve to differences in breaking SO_3 - C and CO_2 - C bonds and in making SO_3 - H and CO_2 - H bonds. If these latter are considered equal (CO_2 - H = 112 K.cal[34] HO_3SO - H = 114 K.cal/mole[35]) then the breaking of the much weaker SO_2 - C bond (60 Kcal/mole[34]) compared with the CO_2 - C bond (85 Kcal/mole[16] n.b. homolytic cleavage) should greatly favour sulphonate pyrolysis. Work described in this thesis and related experiments carried out in these laboratories[36] indicates that sulphonates are pyrolised more readily than the corresponding acetates.

The above approach may explain the affect on pyrolysis rate of α - and β - substitution and of the electron-withdrawing nature of the ester group by their affect on the energies of the bonds broken and made during pyrolysis. Such a study is beyond the scope of this thesis and comment will be confined to one observation which may be relevant to later sections of this thesis.

Pyrolysis of 3-acetoxy-cyclohexanone (29) proceeds at a rate 400 times greater than that of cyclohexyl-acetate 30[1].



29



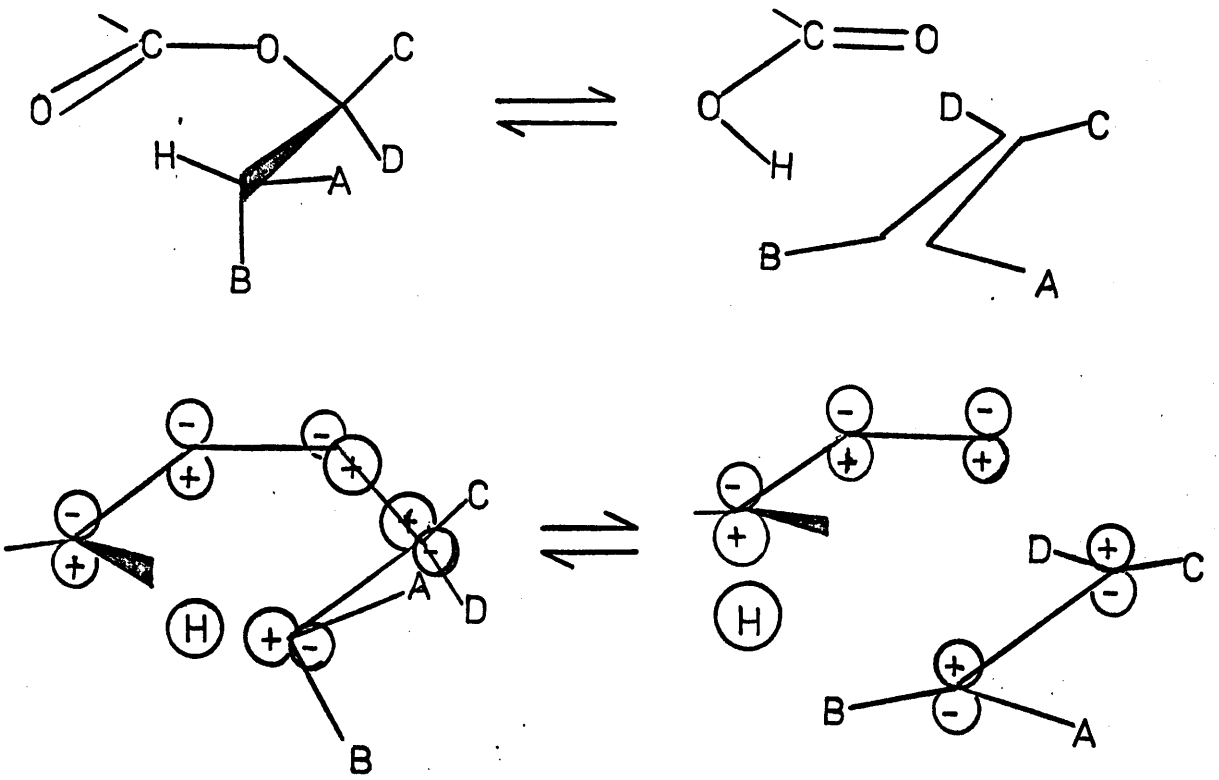
30

While the influence of differing ΔS^* values is impossible to estimate the observed rate enhancement in 29 is consistent with the lower bond energy of COCH - H compared with CH_2 - CH - H.

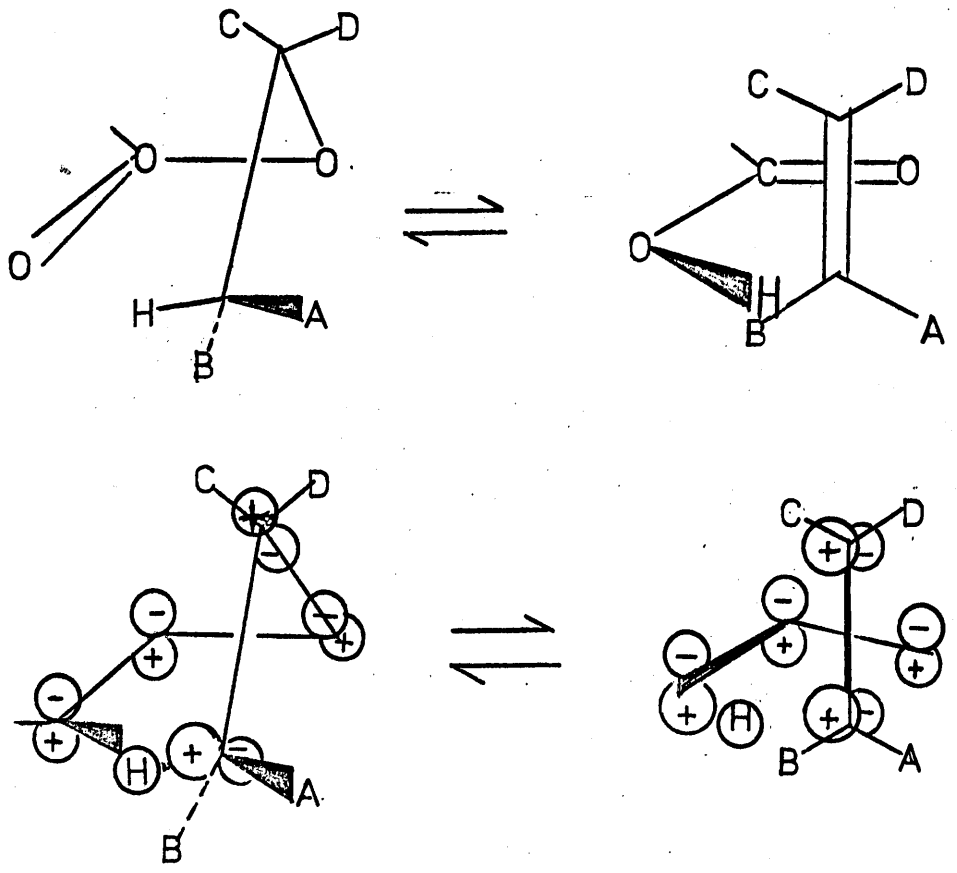
(CH_3COCH_2 - H,92 , CH_3CH_2CH - H,98 Kcal/mole[34]).

and with the formation of a stronger conjugated π bond.

SCHEME 3



SCHEME 4



A consequence of considering ester pyrolyses as fully concerted reactions is that they must obey orbital symmetry rules.[37] Consideration of scheme 3 shows that the accepted mode of ester pyrolysis follows a thermally allowed $\left[2s,2s,2s\right]^{37}$ pathway. Thus, considering the "ene" or condensation direction, the hydrogen is transferred to the same side of the olefin as is involved in forming the new σ -bond and formation of the new π - bond occurs without inversion.

If one now considers scheme 4, it can be seen (as is noted by Hoffman[3]) that there exists an other thermally allowed pathway namely the $\left[2a,2s,2a\right]^{37}$ route where considering the ene or condensation direction, the new π -bond is formed without inversion as before, but opposite sides of the olefin are used in transferring the hydrogen and forming the new σ -bond.

The observable consequences of these different pathways for cleavage should be that the reaction need not follow a <u>syn</u>-course and that the product olefins formed by the two paths are geometrical isomers (See schemes 3 and 4).

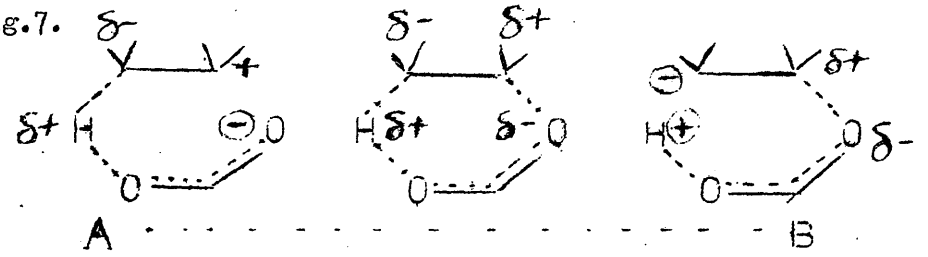
Though the transition state required for the $\left[2a,2s,2a\right]$ pathway is less likely for steric reasons and effective overlap of orbitals may only occur with deformation of the σ-bond skeleton, it is possible that this route accounts for some of the observed <u>anti</u>-pyrolytic eliminations.[1,2,11,21,27,28,29]

This topic is further discussed with regard to the pyrolysis of (1c,9c,10 t) - 1 - decalyl esters.[28,29,38] (page 116)

In a recent paper on ester pyrolyses Tinkleberg Kooyman and Lauw[39] point out that: "Despite the large amount of experimental data there is no general agreement about the mechanism of the reaction./

As yet it seems impossible to accomodate all structure effects known to date in one coherent picture." These authors then go on to consider the mechanism as a "concerted hetrolysis" with both C - O and C - H bonds polarised in the transition state and postulate a range of transition states such as in fig.7.

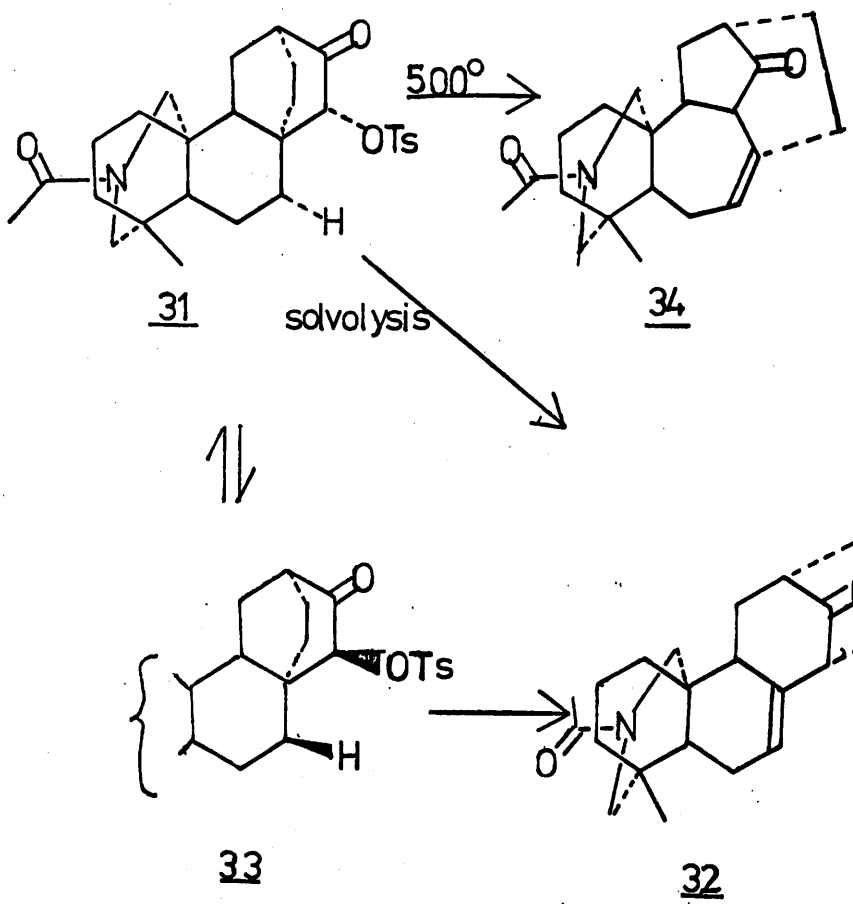
Fig.7.



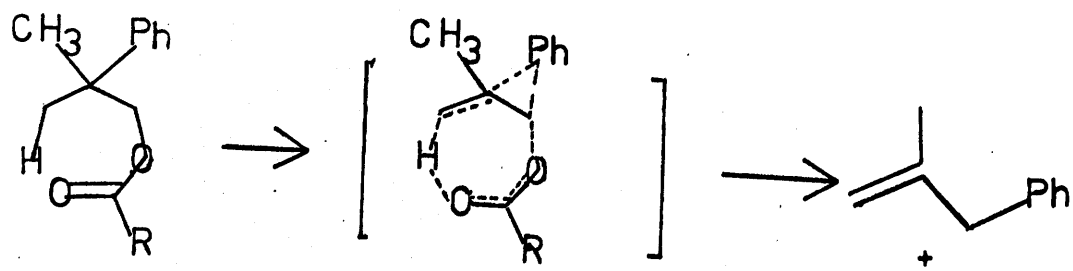
Where, in general, transition state structures will be intermediate and, depending on structure and substitution, will be more or less A - like or B - like.

The authors[39] then claim that all known substituent effects can be accomodated. This is not true since, as they themselves point out in another part of the same paper, elimination of the least acidic β-hydrogen is always preferred and some substituents making the β-hydrogen more acidic (e.g. β-chlorine or β-phenyl -) retard the rate of elimination. These latter facts are not compatible with the suggested range of structures (fig.7) for the transition state and tend to support the idea expressed above (p.7) that the covalent bond strengths of all bonds broken and made must be considered when comparing elimination rate of different ester systems.

Work on anomalous pyrolysis reactions, in this laboratory, first commenced when a means was sought of effecting the conversion of the skeleton of atisane (31) to that of aconane (34). It had been found[36] that solvolysis of the 15α - β-toluene-sulphonate 31 derived from atisine gave olefins of the type 32, the expected product of solvolysis of the epimeric sulphonate 33. It was shown[36] that epimerisation to the more stable 33 was occuring rapidly under solvolysis conditions.



31 34 33 32



35 36 37

At this time a report[40] by Kwart and Hoster appeared in the literature describing a "Wagner-Meerwein" rearrangement occurring during the gas phase pyrolysis of esters of 2-methyl-2-phenyl propanol 35.

These workers obtained low (3 - 9%) yields of 2-methyl-3-phenyl propene 37 and postulated the seven-membered transition state 36 as giving rise to the product.

Accordingly Johnston and Overton[36] pyrolised the alkaloid keto-tosylates 31 and 33 and obtained high (40 - 70%) yields of the corresponding olefins 34 and 32 respectively.

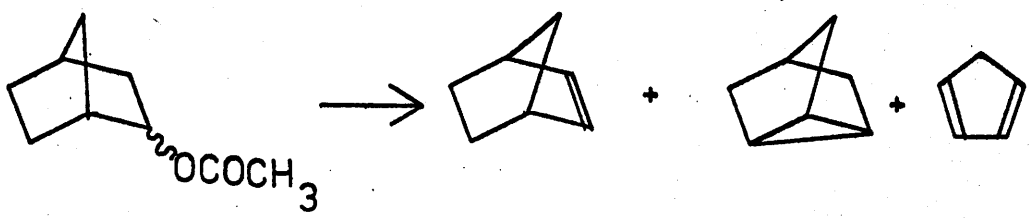
At this point work for this thesis began with an intensive survey of the literature with a view to unearthing previous examples of such rearrangements occurring during ester pyrolysis. This proved a daunting task for a reaction which has been studied for over a century[1]. Examples of such rearrangement were found ranging in publication date from 1900[41] to 1970[58] and these are discussed below (see table 2).

A number of problems arose when searching for and considering inclusion of examples listed (table 2).

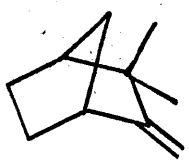
Apparently anomalous products may arise, particularly in examples from the early literature before the advent of t.l.c and g.l.c., through impurities in starting materials. Many of the starting esters are liquids and consequently not readily purified without chromatography.

Many of the product olefins are also liquids and consequently minor products were often missed or inadequately characterised.

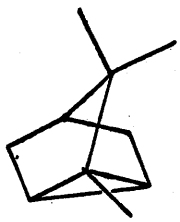
Genuine anomolous products may arise from genuine starting materials but by trivial routes.



38 39 40 41



42



43

Starting material may be isomerised prior to elimination or conditions of pyrolysis or product isolation may isomerise the products of a normal elimination. One must remember that the temperatures experienced during pyrolysis may range from ambient to several hundred degrees and reaction paths insignificant at lower temperatures may become important at higher.

A common reason for omission of examples was the distillation of product out of acid melts or solutions as in the N - p - toluene - sulphonyl carbonate pyrolyses[23] reported by Roach and Daly where the range and nature of the products indicate equilibration of olefins.

Surface-catalysed rearrangements are also possible. A system prone to both acid and surface effects is that of bicyclo - 2,2,1- heptane derivatives. Thus Kwart[12] on pyrolising bicyclo-2,2,1 - heptyl - 2 - acetate 38 obtained, from both exo - and endo - epimers, mixtures of bicyclo heptene 39, nortricyclene 40 and cyclopentadiene 41.

The expected olefin 39 has been shown to undergo facile rearrangement to nortricyclene 40 and some retro "Diels-Alder" decomposition to 41 and ethylene over hot alumina.[42] Vaughan[43] has shown that camphene 42 is readily racemised in contact with pyruvic acid at 156° by a route shown[44] to involve tricyclene 43. The possibility of such rearrangements is discussed in relation to particular examples (Table 2) below.

It is important, as work in this thesis will emphasise, to use methods which will minimise trivial rearrangements. One major improvement in technique is to carry out pyrolyses in flow systems under low pressures of an inert gas. This has a major effect in reducing the likelyhood of bimolecular reactions in condensed phase either in eliminations or in reaction of olefins with the acids produced.

It also reduces surface-catalysed reactions. Problems are still encountered however mainly at the inlet and exit of the system where materials may condense at intermediate temperatures.

There were other difficulties associated with the literature survey. For example, in the many pyrolyses carried out before the days of mechanistic interpretation, anomalies were seldom recognised or recorded as such and are hence difficult to detect.

In much of the recent work cross referencing is poor either through unawareness of previous examples or scepticism of the results obtained.

TABLE 2

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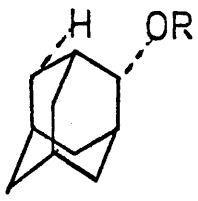
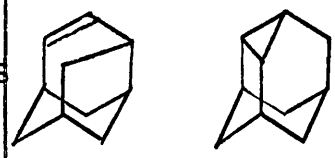
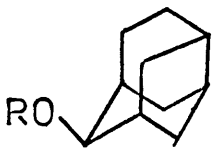
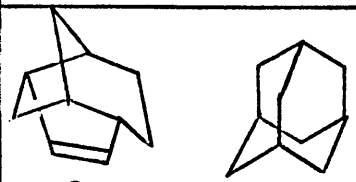
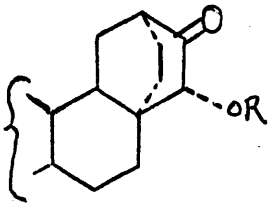
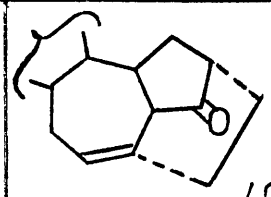
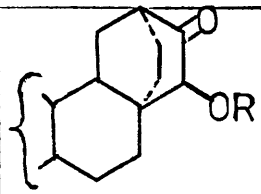
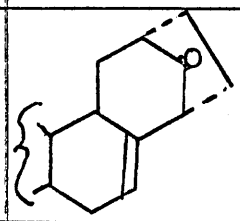
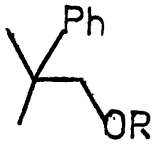
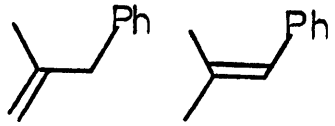
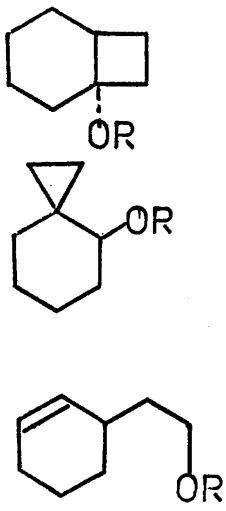
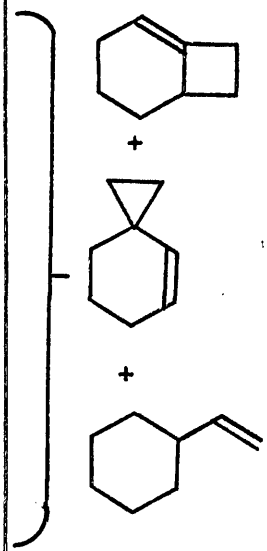
1		$-SO_2\phi CH_3$ $-SO_2CH_3$ $-CS_2CH_3$	this thesis		vapour >500°
2		$-SO_2CH_3$	this th.	 ? 12 % 50-80 %	vap. c. 500°
3		$-SO_2\phi CH_3$	36	 40-70%	vap. 500-600°
4		$-SO_2\phi CH_3$	36		vap. 500-600°
5		$-COCH_3$ $-CO_2CH_3$ $-CS_2CH_3$	40	 3-9 % 2-6 %	vap. 500°
6		$-COCH_3$	45		vap. various

TABLE 2 (cont.)

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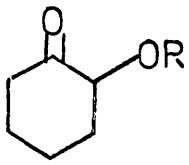
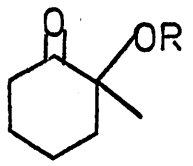
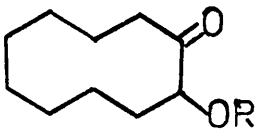
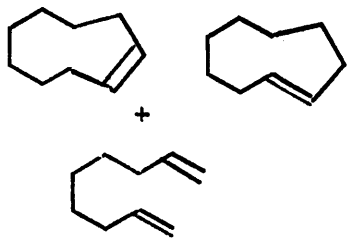
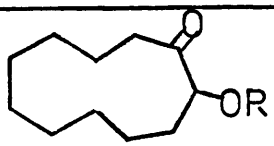
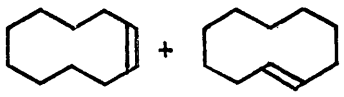
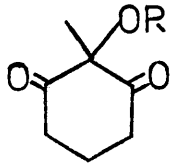
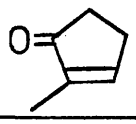
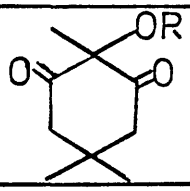
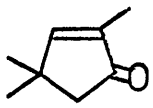
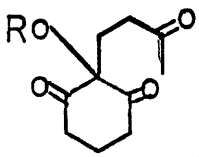
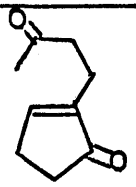
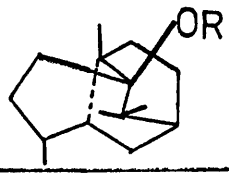
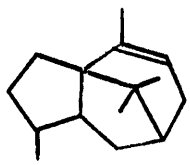
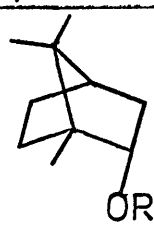
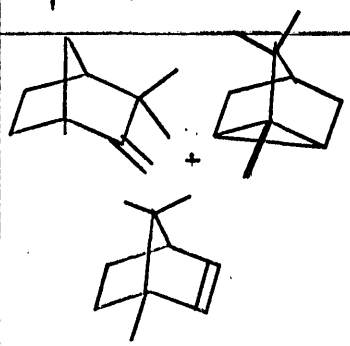
7		$-COCH_3$	46 47	30% 60 % 	liquid
8		$-COCH_3$	46	14% 	liq. 360-400°
9		$-COCH_3$	48		vap. 470°
10		$-COCH_3$	46		liq.
11		$-COCH_3$	49	60-80% 	liq.
12		$-COCH_3$	49	73% 	liq. 220°
13		$-COCH_3$	50	70% 	350°
14		$-COCH_3$	51		liq. 300°
15		$-CS_2CH_3$ $-COCH_2C_6H_5$ $-S(=O)-O-CH_3$ $-COCH_3$	41,52 52 18 53		liq. various liq. " vap. 340°

TABLE 2 (cont.)

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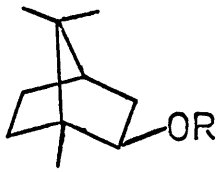
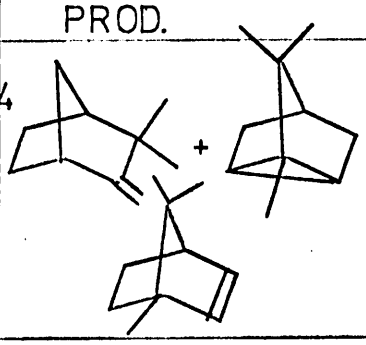
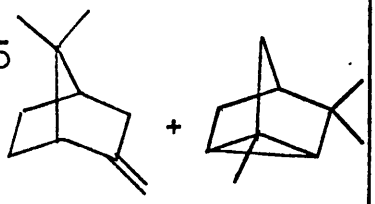
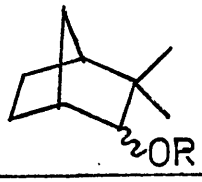
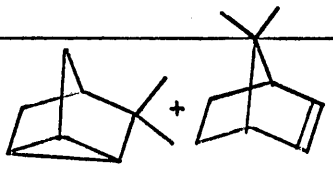
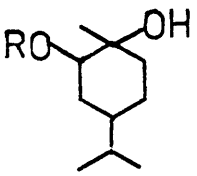
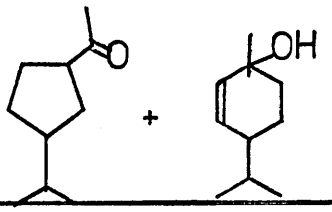
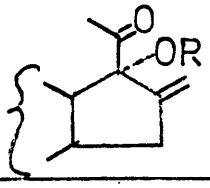
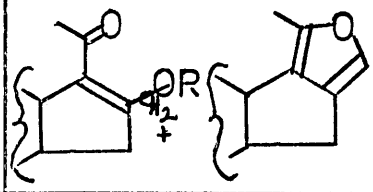
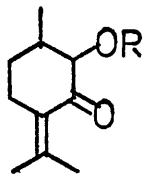
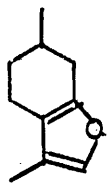
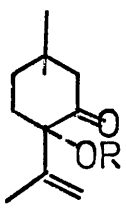
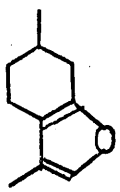
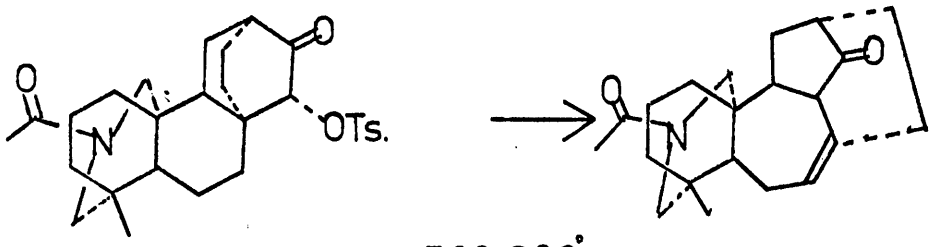
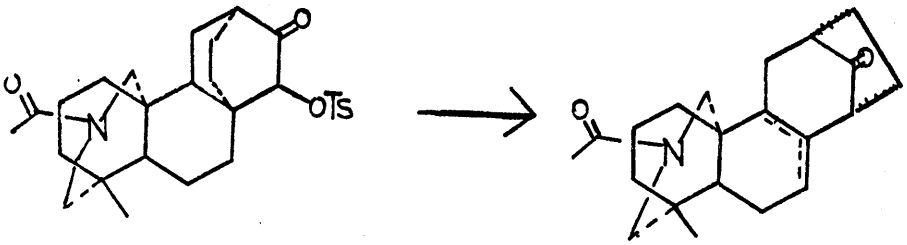
16		$-CS_2CH_3$ $-CONH\phi$ $-COCH_3$	52,54 25 53		liq. " vap.340°
17		$-\overset{S}{C}-S-CH_3$ $-\overset{O}{C}-S-CH_3$ $-\overset{S}{C}-O-CH_3$	26,55 26 26		liq./vap.
18		$-CS_2CH_3$	56		liq.
19		$-COCH_3$	58		liq.
20		$-COCH_3$	59		liq. 360°
21		$-COCH_3$	60		liq.
22		$-COCH_3$	61		liq.

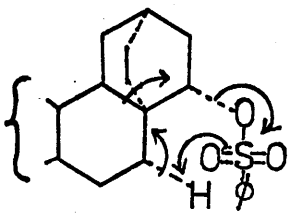
SCHEME 6



31 500-600° 34

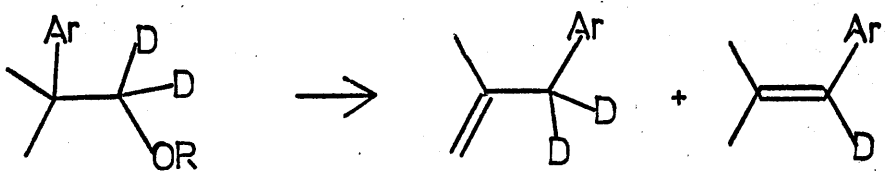


33 32

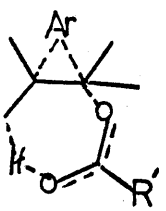


44

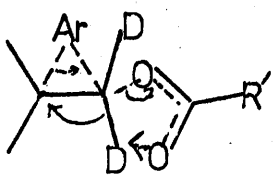
SCHEME 7



35 37 45



46



47

Examples of pyrolysis occurring with rearrangement (see table 2) - discussion

Entries 1 and 2. These entries refer to work reported by us in this thesis and elsewhere[62,63] and are considered in detail in the relevent discussion sections which follow.

Entries 3 and 4. These examples[36] (Scheme 6) have been partly discussed above (p.10). They represent two of the few reported cases of rearrangement occurring during gas phase pyrolysis. The corresponding acetates[36] of tosylates 31 and 33 survive the pyrolysis conditions unchanged.

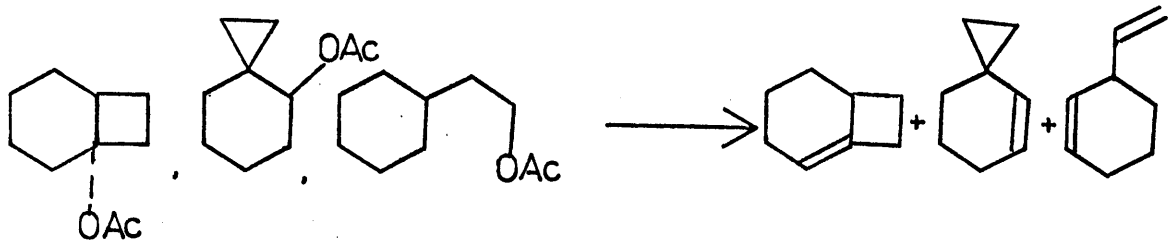
The high yields (75 - 80% by g.l.c.) support the suggestion[36] that the products 34 and 32 arise by a genuine anomalous mechanism. The route suggested[36] involves a cyclic seven membered transition state such as 44.

Entry 5.[40] (Scheme 7) The authors report the formation of 2-methyl-3-phenyl-propene 37 (3-9%) and 1-phenyl-2-methyl-propene 45 (2-6%) on pyrolysis of a series of esters (acetate, methyl-carbonate -, and methyl xanthate-) of 2-phenyl-2-methyl-propanol 35 at a variety of temperatures.

Though the yields are small the authors have taken pains to show that the products do not arise from trivial, thermal cracking, (i.e. radical) routes. The products 37 and 45 are the only ones observed in the case of xanthate pyrolysis.

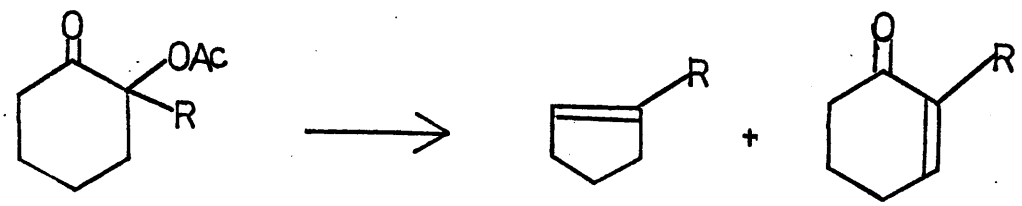
The mechanism advanced to explain the formation of 37 involves a cyclic 7-membered transition state 46, while that explaining the formation of 45 involves α- elimination through a five membered transition state 47.

SCHEME 8



48 49 50 51 52 53

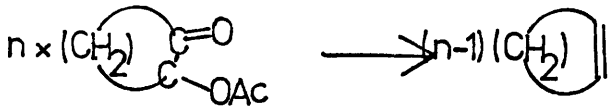
SCHEME 9



54 R=H 56 R=H (30%[46], 62%[47]) 58

55 R=CH_3 57 R=CH_3 (14%)[46] 59

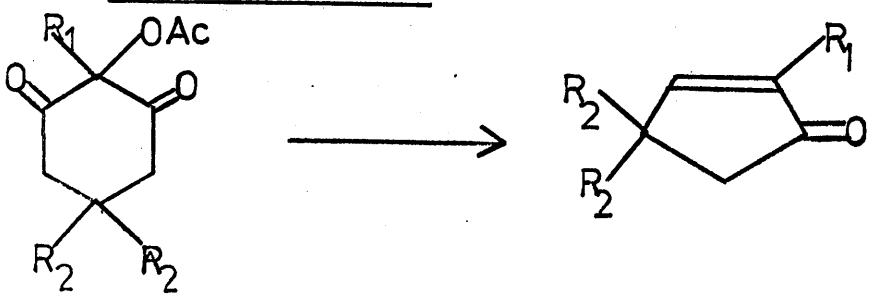
SCHEME 10



60 n=8[48] - - - - - - - -30%

61 n=9[46] - - - -yield "low"

SCHEME 11



64 R_1=CH_3, R_2=H 67 (60–80%)

65 R_1=CH_3 R_2=CH_3 68 (73%)

66 R_1=$CH_2CH_2COCH_3$ R_2=H 69 (70%)

Substantial evidence is adduced for the latter (47), including loss of α - deuterium with a large deuterium isotope effect.

Entry 6[45] (Scheme 8)

Each of the acetates 48, 49 and 50 gives on pyrolysis the expected olefin 51, 52 and 53 respectively plus minor amounts of the other two olefins. The amount of anomalous products varies with temperature and condition of the pyrolysis tube. At lower temperatures and on less contaminated systems the yields of anomalous products are lowest ($< 5\%$). This seems to suggest, as is realised by the authors, that the minor products arise through catalysed isomerisation and not by a novel route.

Entries (7,13)[46 - 50]

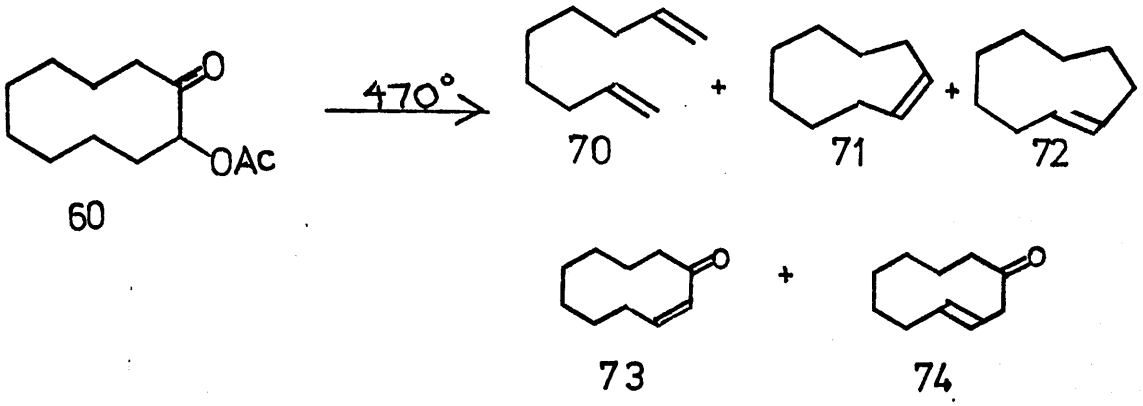
of - cyclohexanone[46,47] (54 scheme 9), - 2 - methyl cyclohexanone[46] of (55 scheme 9), - cyclodecanone[48] (60 scheme 10) and (55- cycloundecanone[46] (61 scheme 10) and of the 2-and 5-substituted - c- 2 - acetoxy - cyclohexane - 1,3 - diones (scheme 11) 64[49] - 265[49] and 66[50].

65[49] and 66[50].

In all of the above cases substantial amounts of ring-contraction product resulting from loss of acetic acid and the ketone function resulted. The respective product structures and yields are shown opposite (schemes 9,10 and 11).

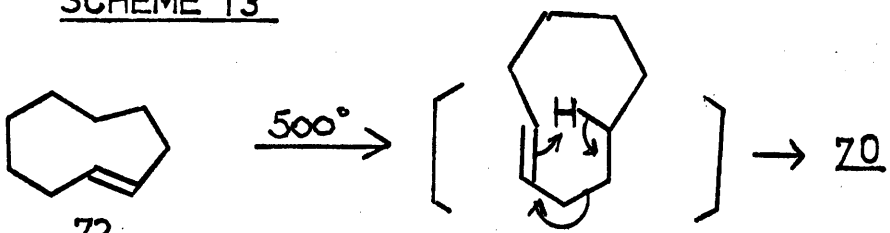
A closer examination[48] of the products of pyrolysis of 2-acetoxy-cyclodecanone 60 (see scheme 12) revealed the presence of the olefins cis-(71) and trans-cyclononene (72) (30% combined) and 1,8 - nonadiene 70 (6%) and the ene-ones, cyclodec-2-ene-one 73 and cyclodec - 3-ene - one 74 (23% combined).

Scheme 12



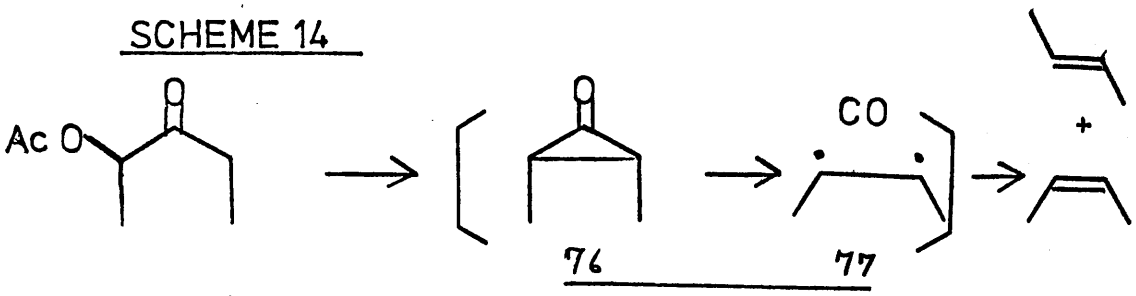
60 70 71 72 73 74

SCHEME 13

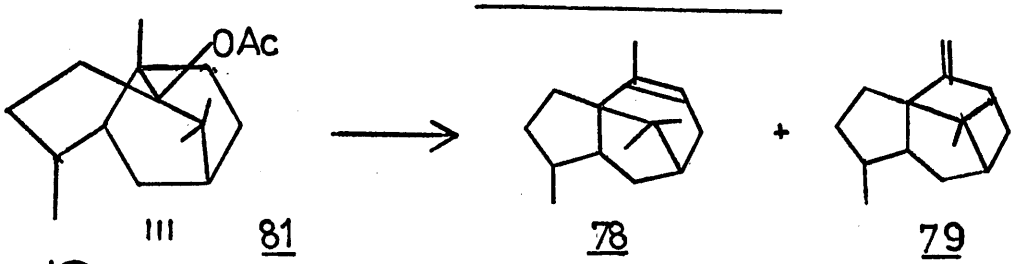


72 75

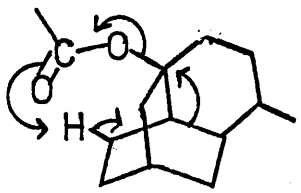
SCHEME 14

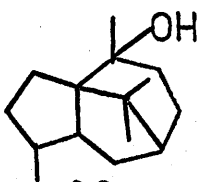


76 77



111 81 78 79





80

The presence of the diene 70 is not unexpected in view of the reported [64] cleavage of trans-cyclononene 72 in 85% yield at 500°. It is interesting to note the suggestion[3] that this also occurs through a "retro-ene" type mechanism (75 scheme 13.)

The presence of the β,γ -ene-one 74 however, suggests that some isomerisation was taking place.

Some mention[48,49] of the variation in results with carbonaceous deposits is made; this however appears to be minor.

The consistency of the ring-contraction reaction over the range of pyrolysis conditions used and the fact that in all cases except one (55 scheme 9) the rearranged product is the major one suggest that this is indeed a genuine anomalous reaction.

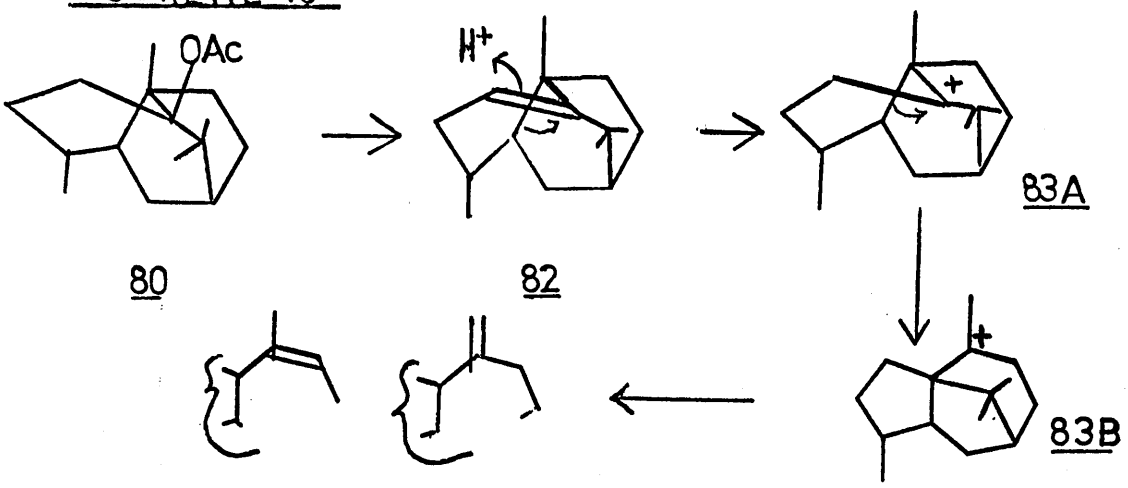
In two reports[48,50] the suggestion is made, though no proof is offered, that the mechanism (scheme 14) may involve abstraction of a proton on the other side of the ketone with formation of a cyclopropanone intermediate 76 which then decomposes via a biradical 77 to give ring contraction products.

Entry 14[51]

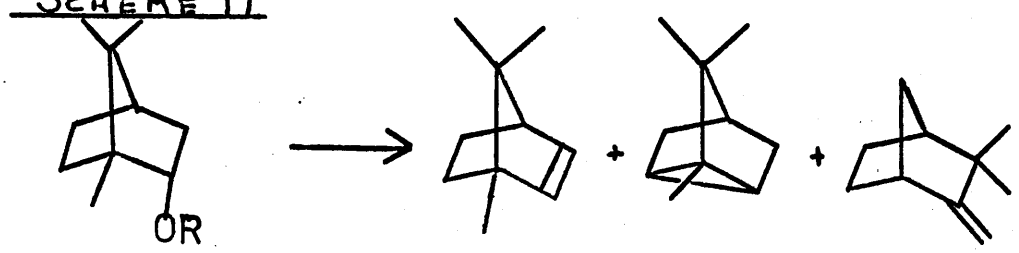
The structure of α -patchoulene 78 derived with its isomer β -patchoulene 79 by pyrolytic elimination of acetic acid from the acetate of naturally occurring patchouli alcohol, had suggested the structure 80 for the alcohol. Subsequent x-ray analysis showed the structure to be in fact 81 and the pyrolysis was described as taking place by an "unprecedented rearrangement". No suggestion of mechanism was offered by the authors.[51]

Three possible mechanisms may be advanced.

SCHEME 16



SCHEME 17



84 R = $-C(=S)-SCH_3$

85 R = $-C(=O)-C_6H_5$

86 R = $-S(=O)-OCH_3$

87 R = $-C(=O)CH_3$

TABLE 3

Figures in parenthesis indicat e % optical purity

Ester	Ref.	bornylene	tricyclene	camphene
xanthate 84	52	70 (97)	13·5	16·5(30)
benzoate 85	52	24·5	21·5	54(30)
sulphite 86	18	minor	minor	major
acetate 87	53	61	23	14·8

(a) The 7-membered transition state with rearrangement (common to entries 1,2,3,4,5,16,18 and 19) is possible, however the pyrolysis conditions (slow distillation of acetic acid from the liquid phase at 300°) are such that acid catalysed processes are highly likely.

(b) The formation of the α, β -elimination product 82 and its isomerisation (scheme 16) is not likely in view of the highly strained nature of the olefin 82 to be formed. The formation of bridgehead double bonds in 3,3,1-bicyclo-nonane systems is not readily accomplished.[65]

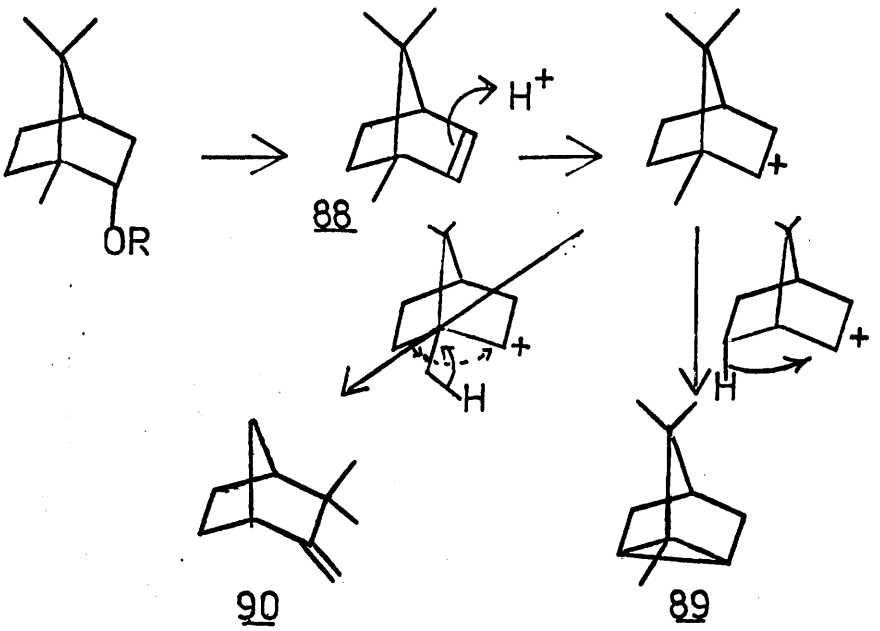
(c) It is more likely that the products 78 and 79 arise through acid-catalysed solvolysis, leading to ion 83A and hence, driven by strain release, to ion 83B and products 78 and 79.

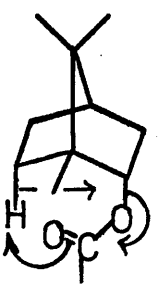
Entry 15

The pyrolyses (scheme 17) are reported of bornyl-methylxanthate 84[41,52], - benzoate 85[52], - methylsulphite 86[18] and -acetate 87[53] giving mixtures of bornylene 88, tricyclene 89 and camphene 90 in the yields and with the degree of optical purity (where these are known)as shown in table 3.

The work of Vaughan[43] and Hirsjarvi[44] which demonstrates the ease of mutual rearrangement of at least two of the products (89 and 90) has already been considered (p.11) and the low optical purity (30%) of the camphene 90 obtained[52] suggests that it and possibly tricyclene 89 have arisen through an ionic (or solvolytic) route or by acid catalysed isomerisation of the α, β -elimination product bornylene 88 as in scheme 18.

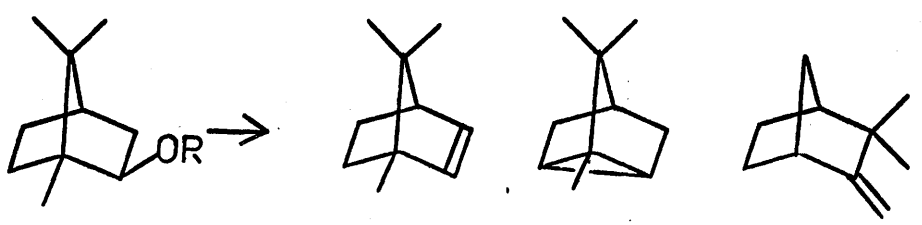
SCHEME 18





91

SCHEME 19



92 R=-$CSCH_3$ 88 89 90

93 R=-COC_6H_5

94 R=-$CONHC_6H_5$

95 R=-$COCH_3$

TABLE 4 Figures in parenthesis indicate % optical purity

Ester	Ref.	Bornylene 88	tricyclene 89	camphene 90
92	52	38·5(92)	—	61·5(100)
93	52	—	13	87 (30)
94	25	?	?	85 (100)
95	53	20	31·5	48·5

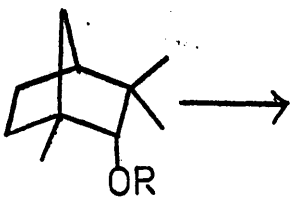
An objection may beraised to the proposal to account for anomalous products as in Scheme 18, in that, where as much as 54% (Table 3) of camphene is produced by isomerisation, the product ratios should show a greater tendency towards equilibrium ratios (i.e. < 5% tricyclene)[43,44] and that the optical activities of camphene (30%) and bornylene (97%) should be lower. This can be argued against on two counts; (a) equilibration studies on the camphene[43,44] and norbornene[42] systems show that the system with the double bond endo - to the 2,2,1 - system (~~norbornene~~ bornylene 88, in this case) is the least stable and hence its conversion to the others (89 and 90) should be faster than their mutual conversion, or their back conversion to norbornene, and (b) Herndon and Mannion[66] have shown that under the conditions required for the pyrolysis of the carboxylic esters 85 and 87 bornylene undergoes retro Diels-Alder fission giving polymeric products undetectable by g.l.c. and hence these authors suggest that bornylene may initially be formed in greater amounts than reported (see table 3).

The seven membered transition state 91 suggested by Bunton[52] is thus not necessarily involved, however stronger evidence for its existence is reported below (see discussion on entry 17).

Entry 16

The pyrolyses (scheme 19) are reported of iso bornyl - methylxanthate 92[52,54] - benzoate 93[52], - N-phenyl carbonate 94[25] and - acetate 95[53] yielding bornylene 88, tricyclene 89 and camphene 85 in the yields and with the degree of optical purity (where these are known) as shown in table 4.

SCHEME 20



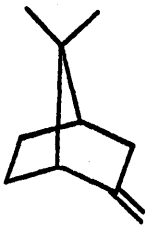
97 R = -C(=S)-S-CH$_3$

98 R = -C(=S)-OCH$_3$

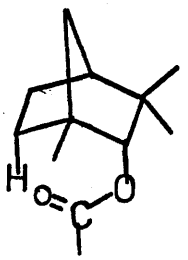
99 R = -C(=O)-SCH$_3$

100 R = -C(=O)-OCH$_3$

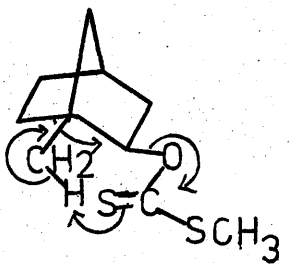
101



102



103



96

The results of the acetate[53] 95 and benzoate[52] 93 pyrolyses may be rationalised on the basis of acid isomerisation of bornylene 88 as in scheme 18 discussed for entry 15, but the high yields of optically pure camphene 90 obtained on pyrolysis of xanthate[52] 92 and N-phenyl carbamate[8] 94 are indicative of a concerted mechanism for its formation. Bunton[52] advances the seven membered transition state 96.

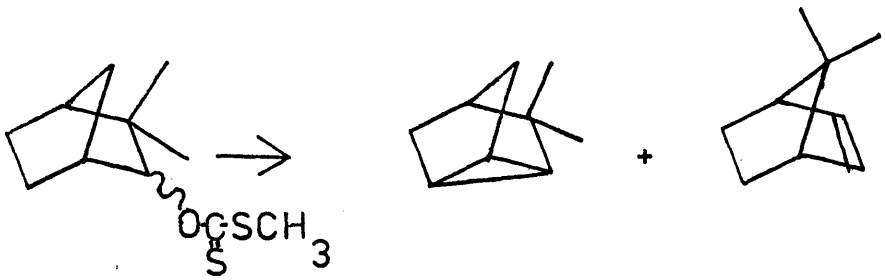
It should be noted that the fragmentation of bornylene under conditions of carboxylic ester pyrolysis reported by Herndon and Mannion[66] (see p.17) is not of major importance in pyrolysis at lower temperatures since Vaughan[25] isolates camphene in > 60% yield from pyrolysis of the N-phenyl carbamate 94 at 220°.

Entry 17

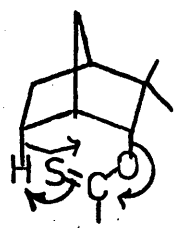
The earliest reference to the pyrolysis of α-fenchyl esters is that of Qvist[55] who in 1918 pyrolised the xanthate 97 claiming to obtain (see scheme 20) cyclofenchene 101 and α-fenchene 102, both of high optical purity. Solomaa[26] in 1959 in a series of thorough experiments on the xanthate 97, thiono-carbonate 98, thiolo-carbonate 99 and carbonate 100, confirmed the production and optical purity (ca. 100%) of cyclofenchene but found only minor amounts of mixed olefins, the exact amount varying with the ester employed and the pyrolysis conditions.

Though no mechanism has been advanced to explain this case, the 7 membered transition state 103 later suggested on poor evidence by Bunton in the case of bornyl ester pyrolysis (entry 15, 91) is plausible and would explain the high yields and optical purities obtained.

SCHEME 21



104 105 106



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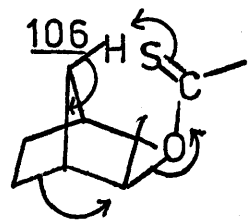

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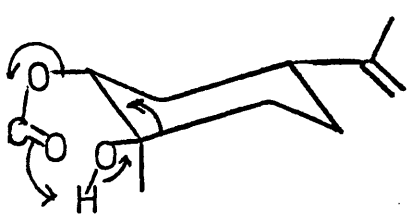

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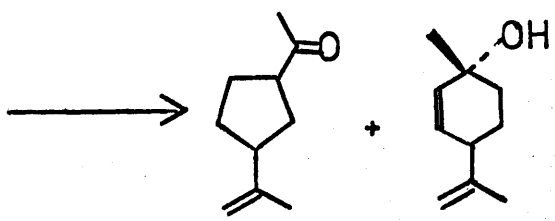
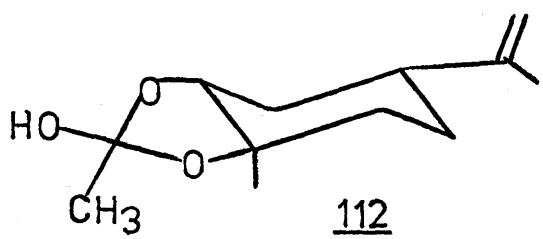


110 111



112

TABLE 5

Acetate :-	Temp.	Alcohol (%)	Ketone(%)
1-hydroxyneocarvomenthyl	449	77	23
1-hydroxy neo-iso-carvomenthyl	480	25	75
4-hydroxyneo menthyl	444	35	65
1-hydroxyneodihydrocarvy	480	70	30
3-hydroxy-4-neocaranyl	420	76	24

Entry 18

Kemppa[56] in 1922 pyrolised (see scheme 21) camphenilyl methyl xanthate 104 claiming to obtain apocyclene 105 and apobornylene 106 in the ratio 6:4.

It is clearly impossible to rationalise the formation of both products from one alcohol in a concerted reaction. However Beckman and Bamberger[57] have suggested that, in all reports prior to 1951 camphenilol must be suspected of being a mixture of endo - and exo - epimers.

It is thus possible to postulated the seven membered transition states of Bunton[52] (see 91,96,103) of the form shown 107 and 108 to account for the observed products.

Entry 19.

Leffingwell and Shackelford[58] on pyrolising a series of trans - α - acetoxy alcohols (eg 1 - hydroxy - neoisocarvomenthyl-acetate 109) obtained products of both normal elimination (e.g. 111) and of a ring contraction process giving methyl ketones (eg 110). Though these workers postulate an ortho-acid intermediate 112 it can be seen[109] that this rearrangement may be an example of the cyclic seven-membered transition state mentioned above, (entries 7,14,16 and 18).

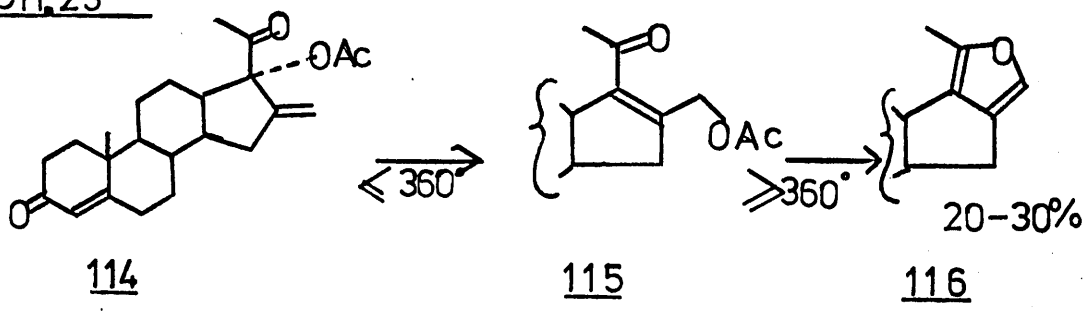
Table 5 list results[58] with similar compounds.

Entries 20,21, and 22

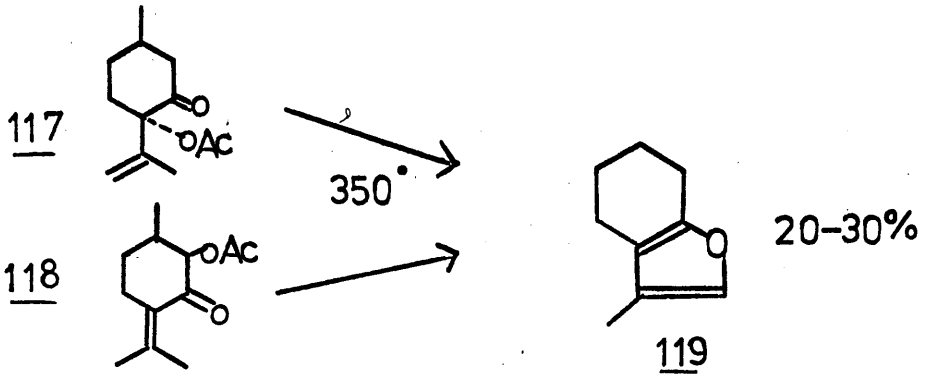
Popper[59] has recently extended the earlier work of Zalkow[60,61] on the pyrolysis of α-acetoxy unsaturated ketones of the pulgeone type 117 and 118 to steroid systems (eg. 114).

The α,β - unsaturated - γ - acetoxy - ketone 115 has been implicated in the latter case (see scheme 23).

SCH.23

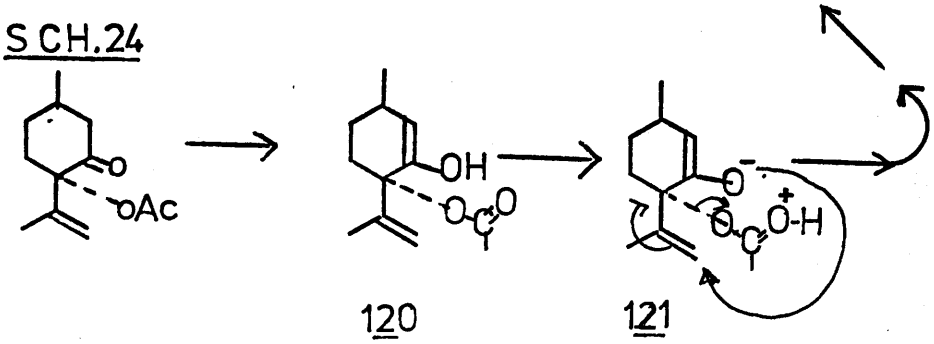


114 115 116



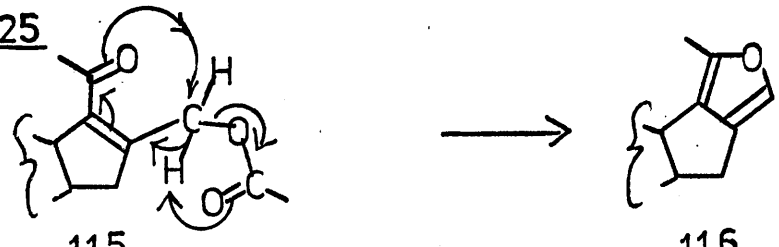
119

SCH.24



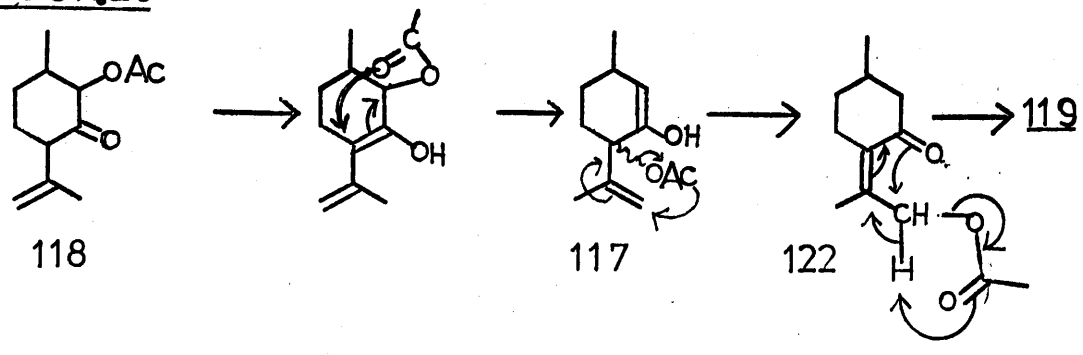
120 121

SCH.25



115 116

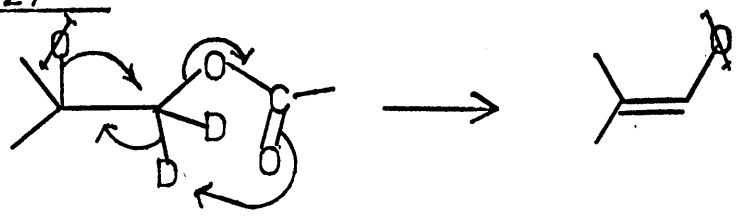
SCH.26



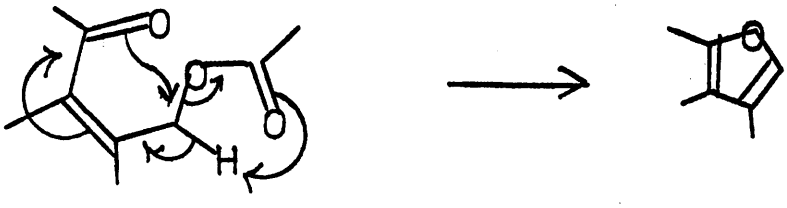
118 117 122

The only mechanism advanced for this rearrangement to the furanoid systems 116 and 119 has been the ionic route (scheme 24) of Zolkow.[60,61] It is possible, however, to rationalise the formation of furanoid structures 116 and 119 through an extension of the 5-membered - α -elimination route of Kwart[40] (see discussion entry 7 scheme 7) as shown in scheme 25 if one allows the possibility of acetate allylic isomerisation[16], as shown in scheme 26.

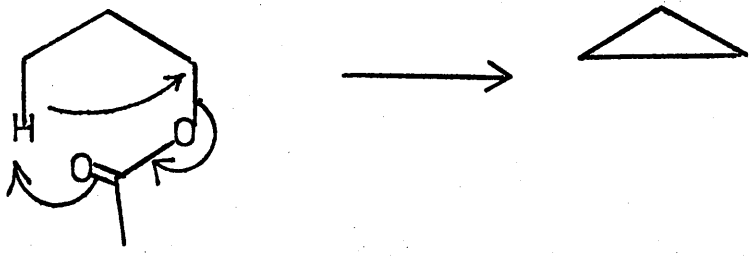
SCH. 27



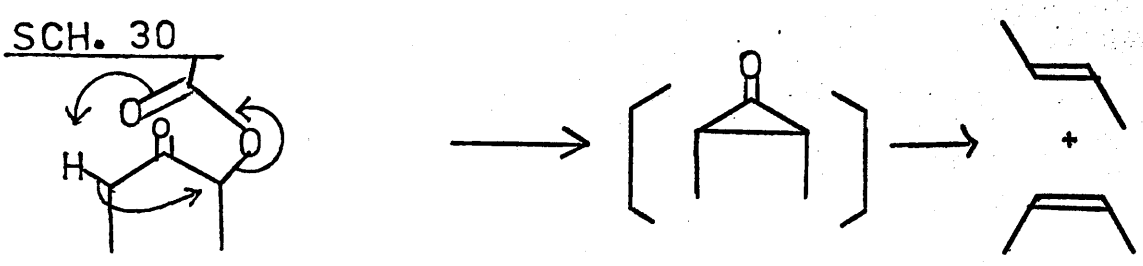
SCH 28



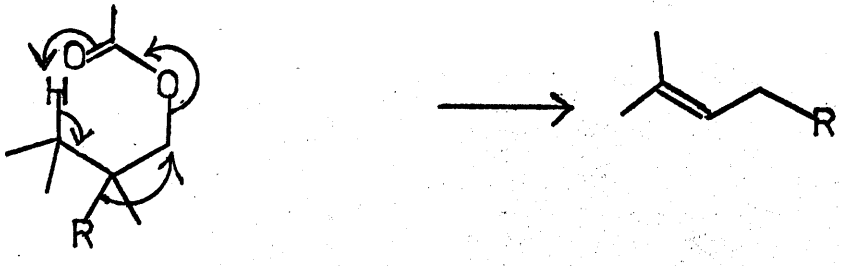
SCH. 29



SCH. 30



SCH. 31



Summary

While the possibility of mechanisms other than those of genuine thermal elimination may account for some of the above examples of rearrangement during esters pyrolysis some strong evidence (see discussion of entries 3,4,5,16 and 17 in particular) remains. All of the more reliable cases can be rationalised on the basis of three mechanisms.

(a) α - elimination

The α - elimination route (scheme 27) soundly established by Kwart[40] (see discussion of entry 7) may also account for the formation of furans on pyrolysis of γ - acetoxy - α,β - unsaturated ketones (scheme 28)

(b) Seven membered - cyclopropyl route.

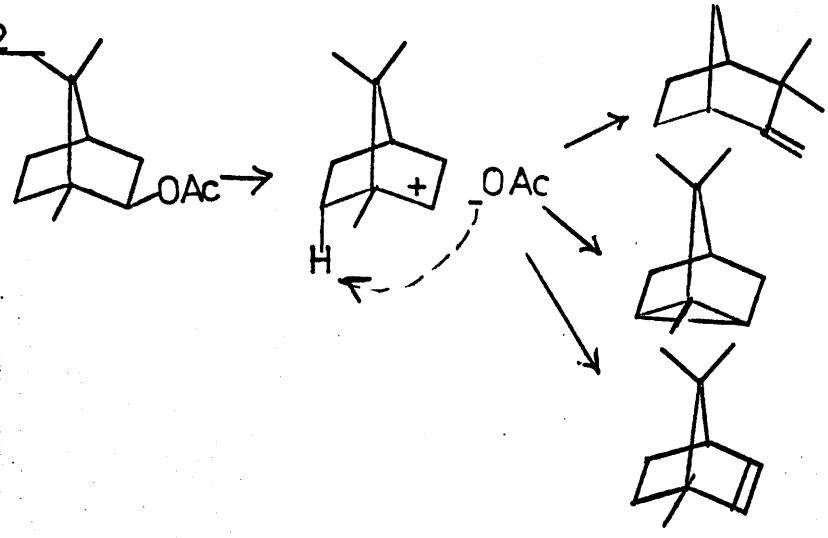
While this route (scheme 29) was originally suggested by Bunton[52] on poor evidence, the better evidence, though not recognised as such, of Salomaa[26] suggests that it is valid (see discussion of entries 15, 17 and 18). It is also possible as has been suggested[48,50] that this mechanism explains the formation of ring contraction products on pyrolysis of α - acetoxyketones (scheme 30) (discussion on entries 7,8,9,10,11,12 and 13).

(c) $\alpha,\delta,-$ elimination with β - alkyl shift.

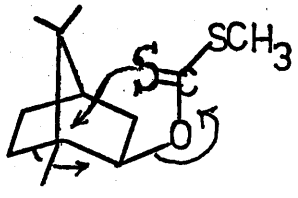
This suggestion (scheme 31) made originally by Bunton[52] would seem to be valid for the pyrolysis of xanthate and N-phenyl carbamate of isoborneol (see discussion of entry 16) and can be applied with varying degrees of confidence to entries 3,4,5,14,18 and 19.

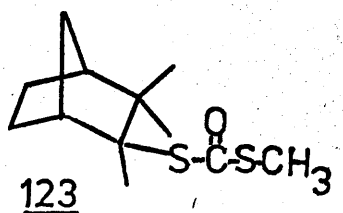
The suggestion[4,8,53] that the pyrolyses of bornyl and isobornyl esters (and chlorides) proceed with "Wagner-Meerwein" rearrangement (see scheme 32.) of the carbonium ion existing/

Sc. 32



SCHEME 34





123

/existing prior to hydrogen abstraction by the acylanion, is not in our view a valid one. It has been suggested (p. 2) that charge separation must not be much greater than the original C - O bond length, if the dissociation energy is not prohibitively to exceed the observed[53] activation energies and it seems to us that such a restriction would rule out the proposed mechanism. The route cannot explain, as has been attempted[4,8,53], the formation, in the gas phase, of tricyclene from isobornyl esters, since this would involve the acyl anion in somehow moving round to the other face of the molecule to abstract the C_6 -endo-proton (scheme 32).

This route would also lead, by internal return, to rearranged esters (scheme 34) and in the case of isobornyl xanthate the more stable dithiolocarbonate[26], which does not pyrolise under the conditions used to pyrolise the xanthate, would surely not have escaped detection.

In the following sections of this thesis an attempt is made to adduce further evidence for and examine the synthetic scope of the "cyclopropyl" (scheme 29) and α, γ - elimination with β - shift (scheme 31) routes and investigate some mechanistic aspects of these reactions.

PART II

ADAMANTANOID SERIES

Nomenclature

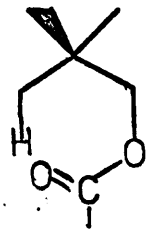
After some thought, it was decided to continue the use of trivial "Adamantanoid" names for:-

adamantane .....(tricyclo-(3,3,1,$1^{3,7}$) - decane)

protoadamantane.....(tricyclo-(4,3,1,$0^{3,8}$) - decane)

and 2,4 - dehydroadamantane...(tetracyclo-(4,3,1,$0^{2,4}$,$0^{3,8}$)-decane.

This was done for reasons of brevity and to avoid confusion over the current[67] use of the trivial names.



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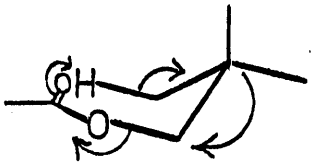
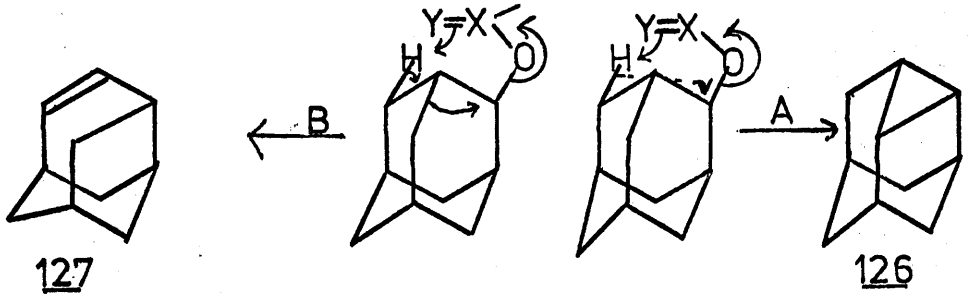


125

SCHEME 35



127

126

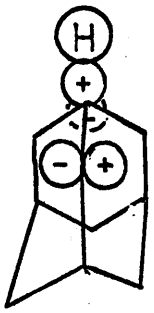


FIG.7

Introduction

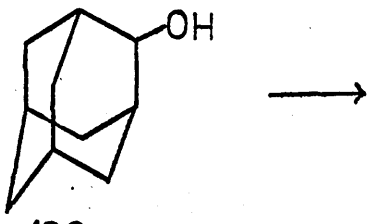
Consideration of the recorded examples (table 2) of anomalous pyrolyses leads one to accept the suggestion of Bunton[52] on the two possible mechanisms involving 1,3 - elimination. The examples appear to have a common steric situation.

In the formation of cyclopropyl compounds the hydrogen abstracted is usually syn-parallel to the C-O bond of the ester function as in 124.

In the case of double bond formation with rearrangement, the abstracted hydrogen and ester C-O bond bear the same relationship as above while the migrating C-C bond is anti-periplanar to both as in 125.

It occurred to us that, if this geometry is optimal, a suitable test case for the general applicability of the reactions should be that of 2-adamantyl esters (scheme 35) where the above steric conditions are rigorously obeyed. The scheme became more attractive when it was seen that the cyclopropyl route (scheme 35A) should, if possible, lead to 2,4 - dehydro-adamantane[68] 126, while the route involving rearrangement (scheme 35B) should produce protoadamantene[69,70] 127. Both of these compounds are known crystalline hydrocarbons whose potential for synthetic and mechanistic exploration interested us.

It should be noted that the complication of 1,2 - elimination should be avoided in this system. Schleyer[71] has pointed out that the orbitals of the C-H bond at position - 1 and the developing vacant - or p-orbital at position - 2 are orthogonal (fig.7) thus minimising the possibility of overlap and making the formation of a double bond between them unlikely. This is, of course, an alternative expression of Bredt's rule[65] on formation of bridgehead double bonds in fused polycycles.



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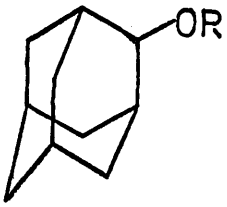
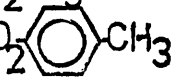
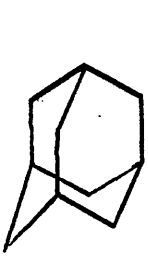


129 R = -COCH$_3$

130 R = -CS$_2$CH$_3$

131 R = -SO$_2$-  -CH$_3$

132 R = -SO$_2$CH$_3$



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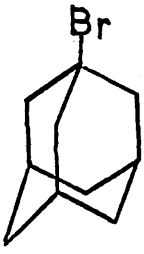

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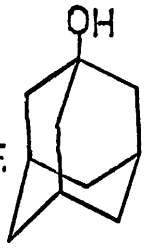

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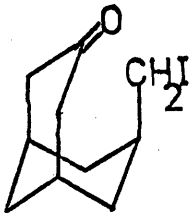

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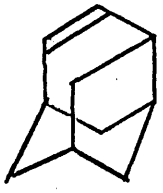

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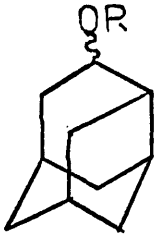
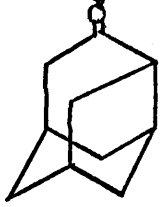


138 R = H

139 R = CS$_2$CH$_3$



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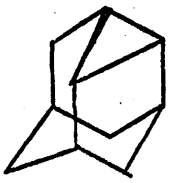

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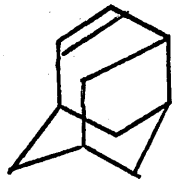

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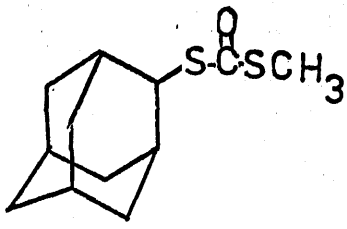


142

Results

2-Adamantanol 128 was prepared[72] from commercially available 2 - adamantanone and its - acetate[73] 129, - S - methylxanthate 130 (m.p. 108 - 109.5°C), -p-toluenesulphonate[74] 131 and -methylsulphonate 132 (m.p. 67 - 68°C) derived by adaptations of standard procedures. All showed the expected physical and spectroscopic characteristics as recorded in the relevant experimental sections below.

1-Bromo-adamantane 134 obtained[75,76] by bromination of commercially available adamantane 133 was hydrolised[72] to give adamantan - 1 - ol 135. The alcohol 135 was treated with leadtetra-acetate and iodine to furnish the iodoketone 136 and hence, without intermediate purification, protoadamantan-4-one 137 by a combination of the methods of Gill[69] and Lunn[77] as described in the experimental section.

Lithium-aluminium-hydride reduction of 137 gave a mixture of epimeric proto-adamantanols (138). Pyrolysis of the unisolated xanthates (139) gave protoadamantene[68] 127.*

The pyrolysis apparatus, described in the Experimental section, consisted of a horizontal, electrically heated (450 - 560°) silica tube lightly packed with glass wool. The substance to be pyrolised was introduced into the tube either as a dispersion in inert solvent (10 - 100 mg) (Method A) or by sublimation (100 - 5000 mg) (Method B) and the products were/

* We are indebted to Dr.R.B. Gill of the University of Nottingham for the gift of a sample of 4-protoadamantanols and his advice on the production of protoadamantene.

collected partly on the cold walls of the tube emerging from the furnace and partly in the cold trap (-196°C) placed in series with it. A foreward flow of helium or nitrogen (0.05 - 0.5 m.m.Hg.) was maintained throughout the experiment.

It was found that the amount (or absence) of glass wool in the pyrolysis tube had very little effect on product ratios and only small effects on yields. This would suggest that the reactions occurring are not of a hetrogeneous or radical chain nature since such reactions are usually extremely sensitive to surface/volume variation[53].

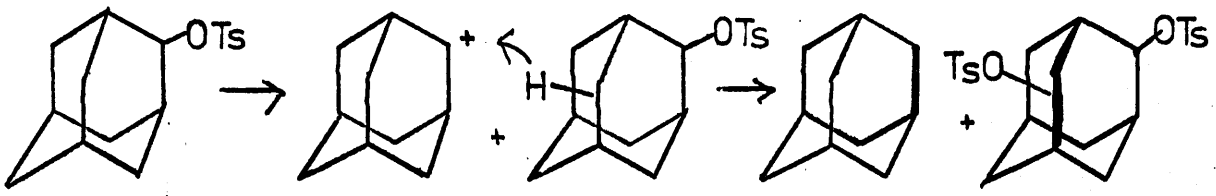
Pyrolysis of 2-adamantylacetate 129 (0.5 mm.Hg., 380°, 500°, 560°C) afforded recovered starting material in $>$ 90% yield. It was considered inadvisable to exceed 560° since skeletal breakdown of adamantane has been observed[79] above 600°.

2-Adamantylxanthate 130 gave (0.5 mm, 550°C) recovered xanthate 130 (50%), -thiolocarbonate 142 (45%, ν_{max}. 1649 and 870 cm^{-1} thiolocarbonate[80]), protoadamantene 127 (2%), dehydroadamantane 126 (2%) and adamantane 133 (1%). A repeat run gave 130 (48%), 142 (45%), 127 (3%), 126 (3%) and 133 (1%).

The thermal rearrangement of alkyl-xanthates to thiolo-carbonates has been previously observed.[26,81]

2-Adamantyl-p-toluenesulphonate 131 and 2-adamantylmethane-sulphonate 132 led to the desired products under the appropriate conditions. Using the injection technique (method A) the tosylate 131 afforded (at 0.5 mm, 550°) more than 90% yield of C10 hydrocarbons, consisting ($\lesssim$ 95%) of protoadamantene 127 and dehydroadamantane 126 in varying proportions (2:3 to 3:1), adamantane ($<$ 5%) and an unidentified hydrocarbon (M^+314) (c. 1%). /

SCHEME 36



/At 760 mm.Hg and 550° the amount of adamantane rose dramatically to 80% of hydrocarbon fraction (c. 50% theoretical yield).

Though no evidence was obtained of the mechanism of formation of adamantane from the sulphonates 131 and 132 it was thought that it might possibly arise through such a means as indicated in scheme 36 by analogy with the disproportionation of 2-adamantanol 128 in sulphuric acid. The proposed di-esters might not be expected to survive the pyrolysis conditions.

Such a disproportionation (scheme 36) should occur to a significant extent only in the hot liquid phase. Adamantane production on pyrolyses was minimal when conditions were used which minimised the extent of condensed phase. (i.e. When lowest pressures were used and where sample was sublimed more rapidly into the system.)

On a larger scale (250mg - 2g) the sample was introduced by sublimation and under these conditions, (0.3 - 0.5 mm.Hg and 520 - 550°) the recovery of hydrocarbon fell to about 50% of theory while the ratio of protoadamantene 127 to dehydro-adamantane 126 rose to 4:1.

On the assumption that the products particularly the dehydroadamantane were being partially destroyed by toluene-p-sulphonic acid formed during the pyrolysis, the inside of the pyrolysis tube and the glass wool at the exit end of the furnace were coated with solid sodium carbonate. This resulted on a 1 - 2g scale, in a better than 95% yield of hydrocarbon consisting of protoadamantene 127, dehydroadamantane 126 (in ratio 2:3) and less than 2% adamantane. The reactivity of the products with methane sulphonic acid was tested. 2,4-Dehydroadamantane (126) was totally converted to 2-adamantyl mesylate 132 in excess neat acid in less than 15 mins. at 20°C while protoadamantene required around 45 mins.

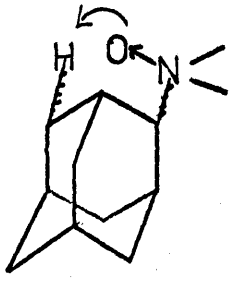
TABLE 6. Pyrolysis of 2-Adamantyl Sulphonates.

RUN	Ester	Method	scale mg	temp. °C	press mmHg	yield† appr.%	126	127	133
1	Tos.	A	20	450	0·5	80	60	37	3
2	"	A	"	550	"	90	50	50	2
3	"	A	"	550	"	90	40	60	2
4	"	A	"	450	760	50	35	20	50
5	"	A	"	550	"	"	10	5	80
6	"	B	100	550	0·3	"	80	13	5
7	"	B	250	520	"	"	70	28	2
8	Mes.	B	150	520	"	40	80	16	2
9	"	B*	1040	520	05	90	40	59	1
10	"	B*	2200	550	0·05	95	40	59	1
11	"	X	20–730	510–530	0·3–0·5		40	60	

* Na_2CO_3 - coated packing and tube.

† Runs 1-5 from t.l.c. ; 6-10 from wt. of crude hydrocarbon.

X Series of runs without glass-wool packing.



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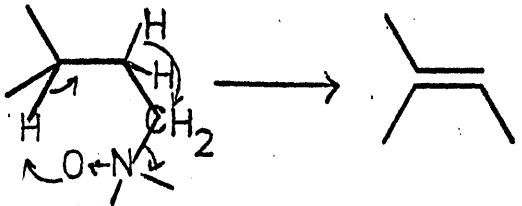


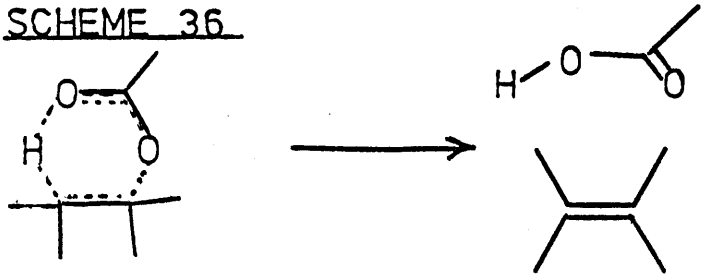
144 145

The pyrolysate recovered with isopentane was filtered through alumina to free it from acid compounds and chromatographed over silver nitrate/alumina (15%) Isopentane eluted dehydroadamantane (57%) m.p. (before recrystallisation) 196 - 199° (lit.[68] 202.5 - 203.5°) and ether eluted protoadamantene (37%) m.p. (before recrystallisation) 179 - 182° (lit.[69] 183 - 185°)

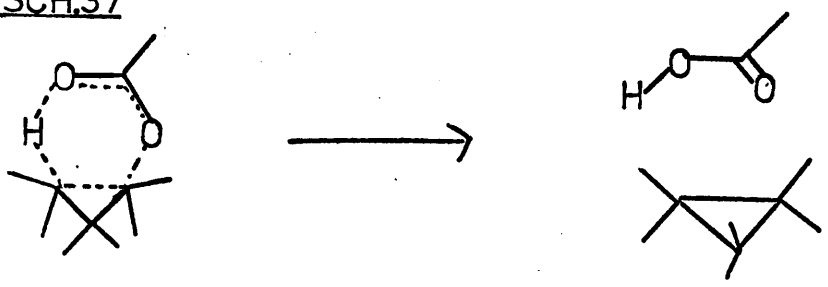
Table (6) lists results of pyrolyses of mesylate and tosylate of 2-adamantanol under a variety of conditions.

At about this time the pyrolysis of 2-adamantyl amine oxides was investigated[83] in this laboratory with a view to establishing the incidence of an analogous reaction proceding through a six rather than a seven membered transition state (143). A relevent precedent exists in the pyrolysis[82] of isoamylamine oxide 144 to give appreciable amounts of 2-methyl but - 2 - ene 145 apparantly by γ -hydrogen abstraction and hydride shift (144 arrows). However pyrolysis of the 2-(dimethyl amine-oxide) of adamantane produced [83] only products typical of Meisenheimer rearrangement[84].

SCHEME 36



SCH.37

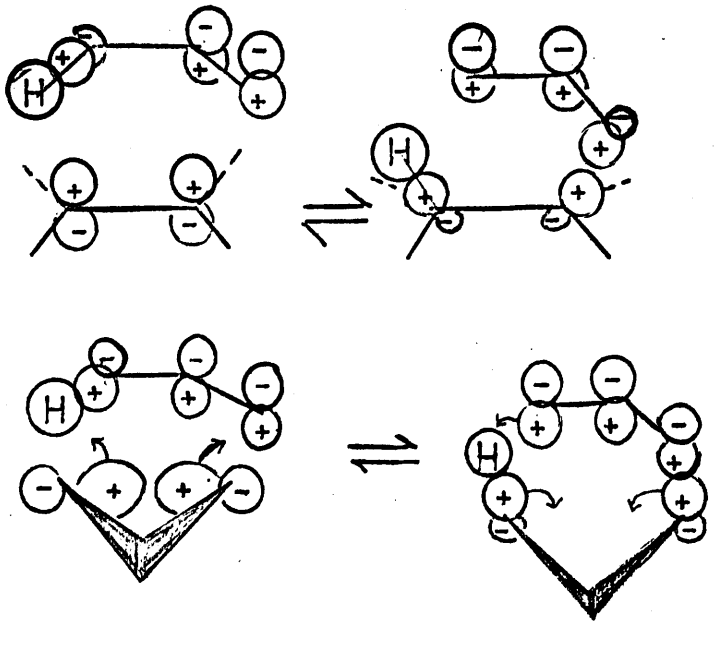


SCHEME 38

A

B

C



Consideration of mechanism of cyclopropyl formation.

The 1,3-elimination leading to cyclopropyl ring formation may be rationalised by analogy with the normal 1,2-elimination. Thus in the anomalous mechanism, the normal formation of a new π bond between two centres (scheme 36) is replaced by formation of a new σ -bond between similar centres (scheme 37).

A comparison of the orbital symmetry implications of the two pathways, best seen by considering the reverse reactions (scheme 38 A and B) shows that both could occur by a thermally allowed $[2s,2s,2s]^{37}$ process. Considering the reverse of the cyclopropyl route (scheme 38B); the cyclopropyl ring is opened in a disrotatory manner (symmetrically-s), new σ bonds are formed on the same face of the cyclopropyl ring (s.) and the new π bond is formed without sign inversion (s).

The possibility of another thermally allowed process should be noted (scheme 38c). In this $[2a,2s,2a]^{37}$ process (again best seen by considering the reverse reaction) the cyclopropyl ring is considered as opening in a conrotatory fashion, new σ-bonds are formed on opposite faces of the cyclopropyl ring and the new π bond is formed as before (scheme 37 A & B). The strain involved in attaining the geometry necessary for this last process may make its observation unlikely and it has, to our knowledge, never been observed.

It would seem that 1,3-elimination to form cyclopropyl ring and 1,2 - elimination to olefin can occur at similar rates. In the pyrolyses of 2-adamantyl esters reported above reaction occurred under conditions similar to those required for 1,2-elimination (see relevent sections dealing with cyclohexyl-carbinyl and 1-decalyl esters below) while Bunton[52] and /

/others[53,54,56] have observed cyclopropyl ring formation in competition with olefin formation in 2,2,1 - bicycloheptane systems (see Introduction, table 2 entries 15 and 18 and discussion p. 16 and p. 19).

As discussed above (p.5) consideration of rate theory leads to a rate expression of the form

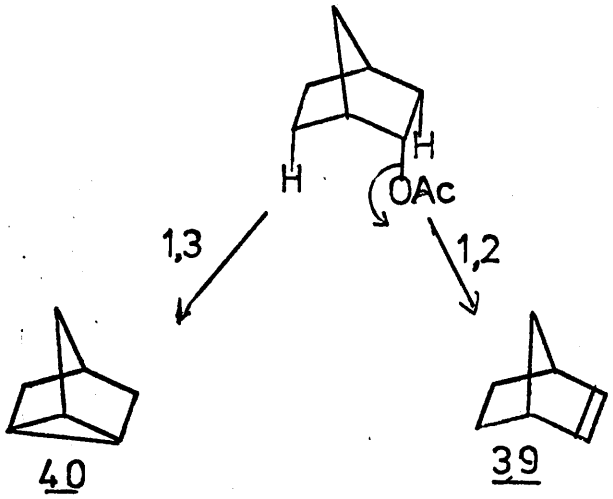
$$k = B\ c\ \frac{\Delta s^*}{k}\ e\ -\frac{\Delta H^*}{kT} \quad \text{- - - EQN. 1}$$

and hence two reactions may be compared and the basis of differences in activation entropy (Δ s*) and activation enthalpy (ΔH^*)

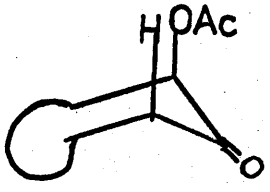
$$\text{i.e.} \quad \frac{k_1}{k_2} = e^{\frac{\delta(\Delta s^*)}{k}}\ e^{\frac{\delta(-\Delta H^*)}{kT}} \qquad \text{EQN.2.}$$

While, in comparing the effect on rate of different ester functions (p. 6), we assumed $\delta(\Delta S^*) = 0$, we cannot do so in comparing the 1,2 -olefin forming and 1,3-cyclopropyl forming routes. It seems reasonable to assume that the 1,3-route will normally have a much more negative activation entropy requirement owing to additional degrees of freedom arising from the additional intervening atom. Since ln(rate) $\propto \Delta S^*$, it is not surprising that all of the recorded examples with the exeption of α-acetoxy ketone cases (see table 2) of the 1,3-route occur in rigid bicyclic systems where lower ground state entropies will minimise the negative, rate reducing, nature of the activation entropy. However, even in these systems, it is likely that ΔS^* values are more negative for 1,3- than for 1,2-elimination and, for the 1,3-route to compete, the ΔH^* values involved must be less than those involved in 1,2 - elimination.

SCHEME 40



40 39



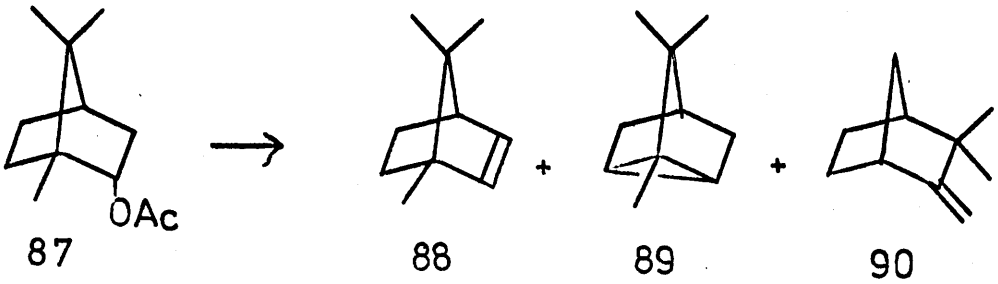
150

If one uses the argument developed above (p. 6), that, for concerted reactions where bond breaking and bond making in the transition state have proceeded to the same extent, one may assume that ΔH^* is proportional to ΔH. Thus the relative ease of two reactions depends on the relative enthalpy changes.

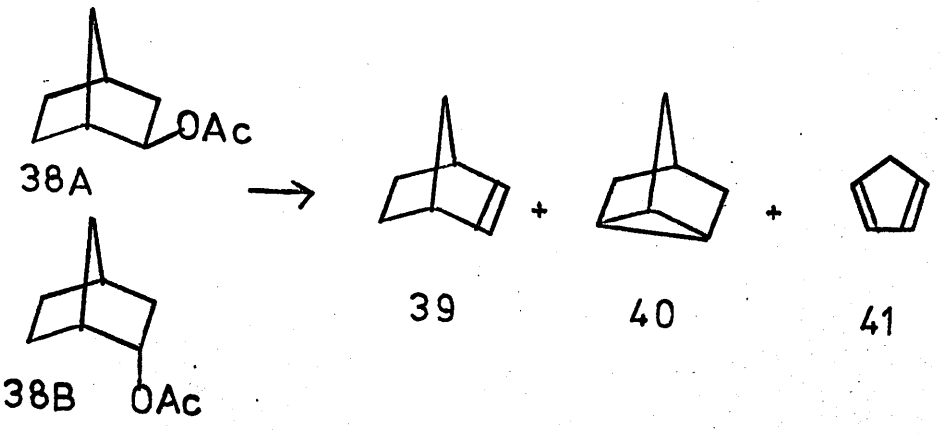
On comparing the 1,3 - and 1,2 -routes in a 2,2,1 - bicycloheptyl system (scheme 40) since both paths occur from the same ester and give the same acid and since there should be negligible difference in the C-H bonds broken, the only factor affecting relative activation enthalpy (ΔH^*) should be enthalpy of formation of the respective products 39 and 40. It has been shown[42] that equilibration of the two structures 39, 40 leads to an excess of nortricyclene 40, (3:1). Thus activation enthalpy for 1,3 - elimination should, in such cases, be less than that for 1,2 -elimination.

In the case of α-acetoxy ketones (table 2, entries 7 - 13), while the negative ΔS^* requirement will be greater than that for the rigid bicyclic systems above, the di-axial conformation 159 is readily accessibles in cyclic ketones. In addition the rate inhibiting effect of the more negative ΔS^* will be offset by the enhancing effects of the carbonyl on (a) the C-H bond to be broken (α-acetoxy ketones[1] and esters[85] are found to react at a rate considerably greater than that of the corresponding alkyl acetates) and (b) the stability of the cyclopropyl ring formed.

It is perhaps significant that no examples have been detected in the literature of the cyclopropanone route occurring in pyrolysis of acyclic keto-acetates. In such species the activation entropy might be expected to be much more negative.



87 88 89 90



38A 38B 39 40 41

While no data on activation parameters exists for authentic and unique cyclopropyl ring formation during pyrolysis two reports are recorded which may be of value.

Emuvon[53] on pyrolysis of bornyl acetate 87, obtained, as determined by g.l.c, bornylene 88 (61%), tricyclene 89 (23.3%) and camphene 90 (14.8%) and derived Arrhenius parameters (330° - 370°) of A 9.96 X 10^{11} and E 45.3 Kcal/mole. While the E value is typical for secondary acetates[4,5], the A value is somewhat low, acetate pyrolyses normally occurring with A of 10^{12} - 10^{13}.[4,5]

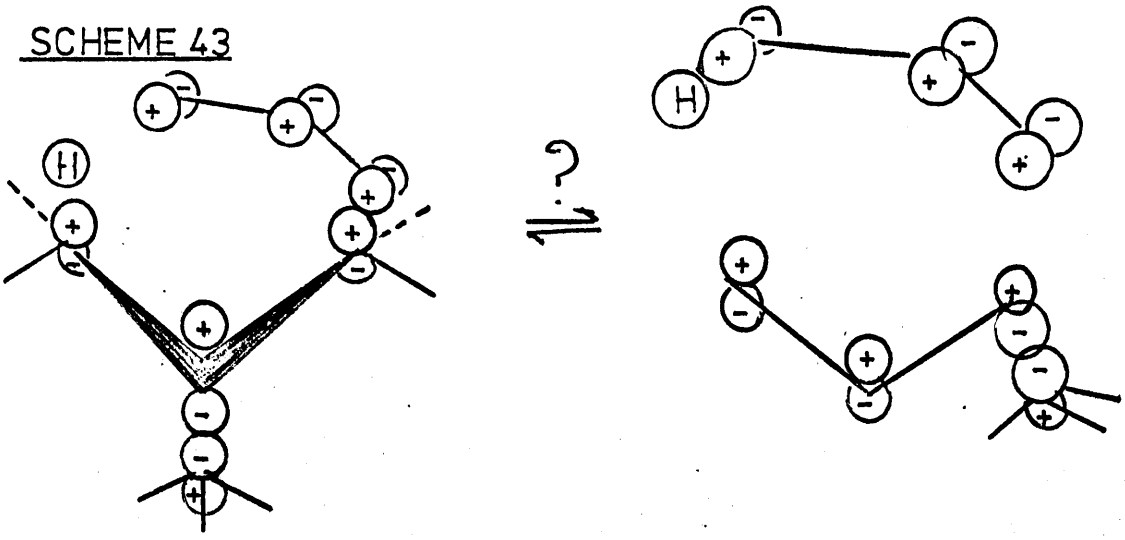
Considerable doubt must exist however on the extent to which these values reflect values for tricyclene 89 formation. Though g.l.c. evidence suggests 23% yield of 89, the work of Herndon and Mannion[66](p. 17) suggests that the yield of tricyclene 89 is much lower, the major product, ~~norbornene~~ bornylene 88 being unstable to reaction conditions and hance undetectable by Emuvon's g.l.c. conditions.

Kwart and Taageperа[12] on pyrolysis of exo-38A and endo-2,2,1 - bicyclohept-2-yl acetate 38B obtained norbornene 39, nortricyclene 40 and cyclopentadiene 41 in varying yields (yield of 41 ranged from 50 - 97%). While the exo-isomer 38A showed activation parameters typical of a rigid ,(-OAc,H) eclipsed, ester (Δ H* 44 Kcal/mole, Δ S* + 1 e.u.) the endo-isomer 38B showed activation enthalpy and entropy lower than the lowest values ever reported[4] (i.e. ΔH* 28 Kcal/mole ΔS* - 33.7 e.u.).

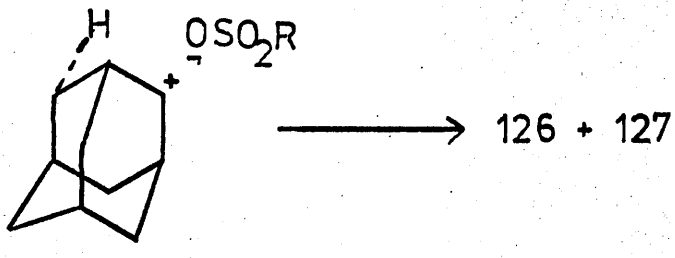
While these values may partly reflect those of the cyclopropyl route, the possibility of surface catalysed reactions [42,66] which the high yields of cyclopentadiene 41 and the very negative activation entropy tend to suggest, cannot be ignored.

The authors[12] try, unconvincingly, to rationalise the results on the basis of differences in 1,2 - elimination in the exo- and endo - cases, the significance of the formation of nortricylene being masked by the formation of significant amounts of the same product on pyrolysis of the exo-isomer presumably through acid or surface catalysed reactions.

SCHEME 43



SCHEME 44



Mechanistic consideration of rearrangement route.

While the mechanism of the cyclopropyl (or homo-retro-ene) route in ester pyrolysis may be discussed by analogy to the normal 1,2 - (or retro-ene) route, this is not possible where 1,3-elimination is accompanied by rearrangement. Thus scheme 41 (p. 29) can be seen to be analagous to scheme 42, but scheme 43 is completely different. While 1,2, - alkyl shifts involving cationic (e.g. Wagner-Weerwein) and anionic (e.g. Stevens) centres have been studied no precedent appears to exist for the concerted 1,2-shift in scheme 43. Consequently, it is difficult to determine whether a concerted thermally allowed pathway is to be expected for this route. A hetrolytic mechanism such as has been suggested by Maccoll[4] and Kooyman[5] might explain the formation of rearranged products (scheme 44).

The rates of (a) 1,3 - elimination with rearrangement and (b) 1,3 - elimination with cyclopropyl ring formation and (c) 1,2- elimination would appear to be of the same order of magnitude. In pyrolysis of 2-adamantyl esters, the products of routes (a) and (b) are formed in similar amounts (protoadamantene :2,4-dehydroadamantane 2:3), while in pyrolysis of isobornyl esters (table 2 entry 16 and p. 17) the products of routes (a) and (c) are also formed in similar amounts (camphene : tricyclene, 3:2).

If we consider all three routes as concerted, that occurring with rearrangement, should (as should the cyclopropyl route discussed above (p 29), have a larger negative activation entropy than the normal 1,2 - elimination, involving as it does an additional intervening atom and rearrangement of an additional bond .

Thus from the expression derived above (p. 30):-

$$\ln \frac{k_1}{k_2} = e^{\frac{\delta(\Delta S^*)}{k}} \; e^{\frac{\delta(-\Delta H^*)}{kT}} \qquad \text{EQN.2.}$$

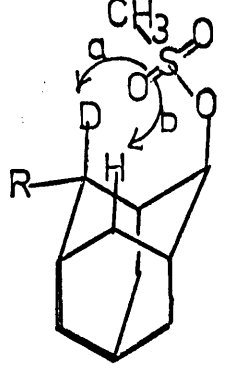
If for the "rearrangement" route ΔS^* values are more negative, the route should only be able to compete where ΔH^* values are lower.

The high (c. 3:2) ratio of camphene to bornylene observed on pyrolysis of isobornyl esters[25,52 - 54] probably reflects the greater stability[42,43] of camphene.

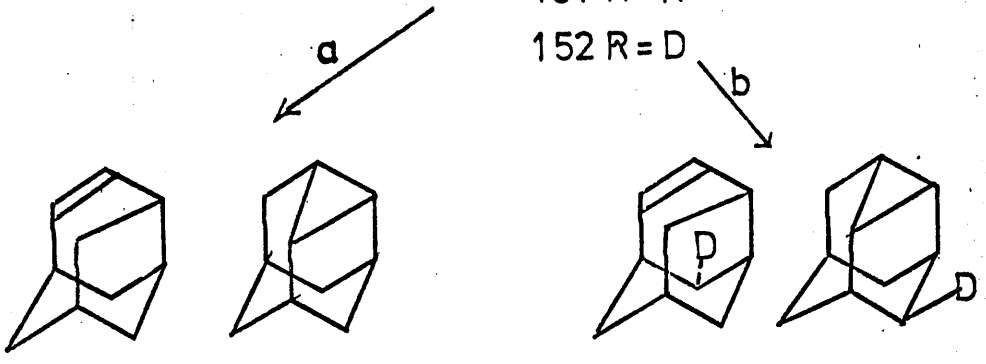
No activation parameters have been reported for authentic 1,3-elimination with rearrangement. The results of Emuvon[53] on isobornyl acetate ($A\ 4.36 \times 10^{11}$ E 42 Kcal) must be regarded as suspect in view of Mannion's[66] suggestion (p.17) that the camphene yield, reported as 48%, is probably much lower and hence the Arrhenius parameters largely reflect the formation of the major product bornylene which arises through a 1,2 - elimination.

One point of mechanistic interest considered, but without success was that of extent of C-H bond breaking in the transition state. It seemed reasonable to attempt to prepare the 4-peri-deuterio-2-adamantyl ester 151 (or its 4-dideuterio- counterpart 152) and study its pyrolysis. It will be noticed (scheme 46) that apart from the deuterium in 151, a plane of symmetry passes through the ester function and between the two possible removable hydrogens. In the absence of a deuterium isotope effect on the rate of either of the elimination reactions observed, both will proceed with equal chance of removal of H or D and the products will both have a deuterium content 50% of that of starting material.

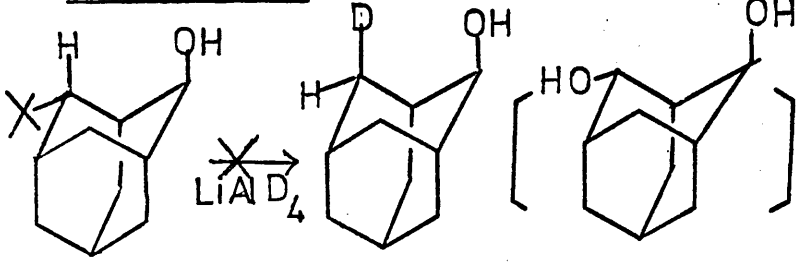
SCHEME 46



151 R=H
152 R=D



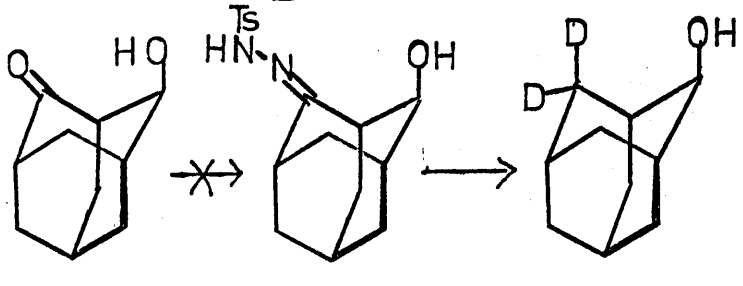
SCHEME 47



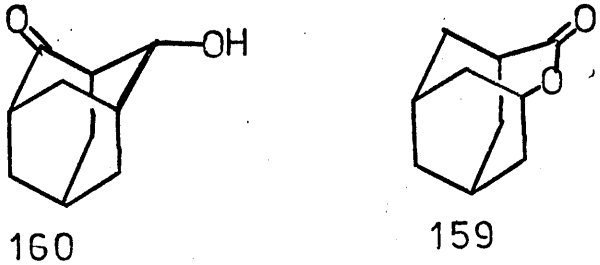
153 X=Cl
154 X=OTs

155

SCHEME 48



156 157 158



160 159

If however there is a kinetic isotope effect on either reaction, the product of that reaction should retain more than 50% of starting deuterium. For example if, for either route k_H/k_D = 2(ca. 100% theoretical maximum at 550° [40]), then there is a 2:1 chance of reaction proceeding with removal of hydrogen rather than deuterium and the product of that route will have a deuterium content 66.7% of that of starting material.

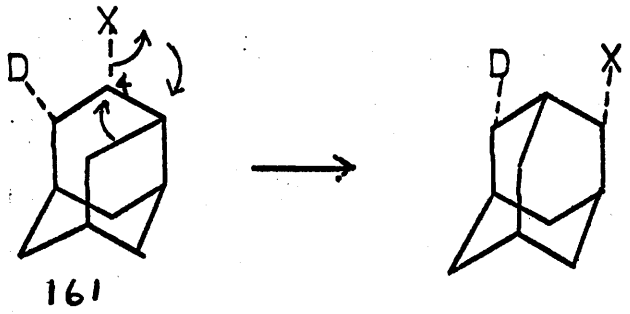
The range of values of deuterium content is fairly small (66.7 → 50% as k_H/k_D max. → zero) and so the method requires highly specific deuteration.

The hydrogenolysis of halide 153 with metal hydride (scheme 47) was ruled out because the stereochemical course of hydrogenolysis is not always specifically that with inversion[86]. In the similar hydrogenolysis of toluene-sulphonate 154 (scheme 47) the product expected is the diol 155 by analogy with the S=O bond attack observed in 2-adamantyl sulphonates[87].

Tosylhydrazone reduction[88] (scheme 48) seemed attractive but in our hands the tosylhydrazone 157 could not be isolated from the reaction of ketol 156 under normal or forcing conditions. Reduction of total product without hydrazone isolation resulted in very poor yields of 2-adamantanol 158.

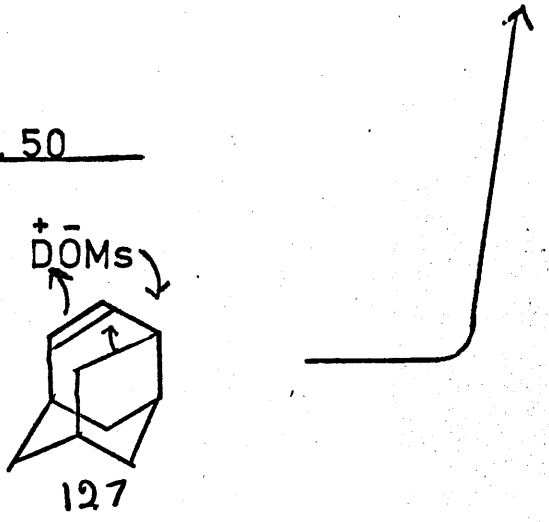
It should be noted that our experiments on preparation of 4-axial-hydroxy-2-adamantanone 156 from the lactone 159 support the recent observations of Sasaki[89] and extend those of McKervey[91] in that treatment of lactone 159 with hot 50% sulphuric acid gives initially the equatorial ketol 160 and that this is then converted to an equilibrium mixture favouring the axial-ketol 156 over a period of several hours.

SCHEME 49



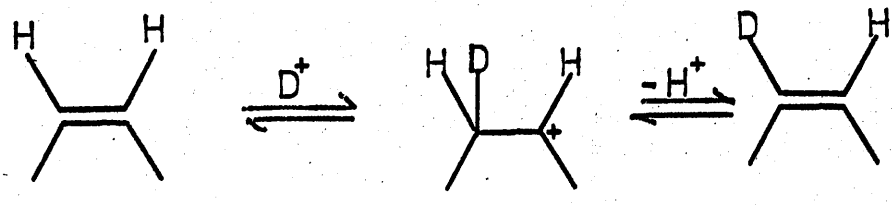
161

SCH. 50



127

SCH. 51



Schemes 49 and 50 rely on the known[67] facile rearrangement of the protoadamantane skeleton (161, 127) to that of adamantane through the C4 - carbonium ion. This would involve a cation system prone to rearrangement and hence scrambling and probably would not lead to sufficiently specific deuteration.

However, since information on the action of methane-sulphonic acid on protoadamantene was required for the pyrolysis work in any case, scheme 50 was attempted.

O-Deuterio-methane-sulphonic acid was prepared by treatment of methane-sulphonyl chloride with D_2O. A solution of anhydrous ethanol in the prepared acid was made in 1:10 molar ratio assuming acid to be water free (i.e. 100%). This showed on n.m.r., methyl singlet of sulphonic acid (δ3.2) and methyl triplet of ethanol (δ1.14) in the integrated ratio of 1:9.7; only possible if the acid is ca. 97% pure. The signal from the acid methyl could then be integrated against that from acid hydrogen. The ratio observed (39:1) compared with that from undeuterated material (39:13) indicated a deuterium content of ca. 93%.

Treatment of protoadamantene with excess deuterio-acid at room temperature for 4 hr. (mixture became homogeneous after 45 min.) gave 2-adamantyl methane sulphonate (78%) m.p. 61-64°. Recrystalisation gave material m.p. 65-66° (mixed with authentic material m.p. was 65-66°).

Mass spectrometry revealed a deuterium content of: 10.1%d_2, 75.5%d_1 and 14.3%d_0 (after correction based on spectrum of unlabeled material). The appearance of some di-deuterio material is to be expected through a rapid protonation-deprotonation mechanism such as in scheme 51.

FIG. 7

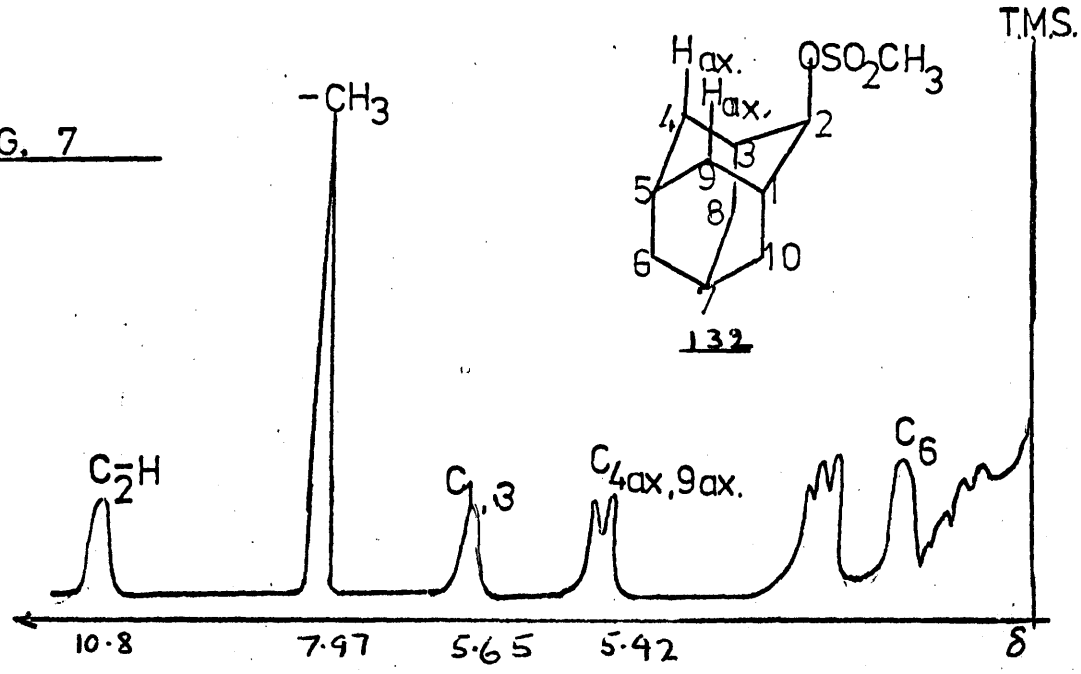


TABLE 7

Integration normalised for CH_3SO_3- = 3H

Entry	CH_3SO_3-	C_1C_3-H	$C_{4,9ax.}$-H	C_2-H	
a	3·00	1·99	2·08		
b	"	1·96	2·08		} d_0
c *	"	2·02	2·12		
d *	"	2·02	2·12		
e *	"			0·86	
f *	"	1·77	1·45		
g *	"	1·91	1·57		} d_1
h *	"	1·85	1·58		
i *	"			0·92	

*average of two recordings

The position of the deuterium was determined by n.m.r. Thus, the do-sulphonate 132 (20 mg.) was taken up in $CDCl_3$ with 80 mg. of europium tris-(1,1,1,2,2,3,3,- heptafluoro - 7,7 - dimethyl -4,6 - octane - dione (hereafter referred to as Eu $(f.o.d.)_3$). The n.m.r. spectrum of the mixture showed the peaks shown and assigned in figure 7. Assignments were checked by double irradiation. The appearance of side bands from $Eu(f.o.d)_3$ in the upper region of the spectrum made accurate integration of this portion unreliable and integration was confined to the lower end of the spectrum. Twenty five runs across the region from $\delta 8$ - $\delta 5.2$ were made using a Varian C.A.T. (no.C-1024) in conjunction with a Varian HA 100 spectrometer. The integrated intensity each of the peaks (δ 7.97, 5.65,5.42) was drawn out six times. The same process was repeated twice manually over the region δ 12 - δ 5.2.

The whole of the above process was then duplicated using the deuterated methane sulphonate prepared above. The figures obtained when normalised for three protons in the sulphonate methyl group in each case are shown in table 7.

The mean integral for protons at C1 and C3 in the undeuterated sample was 2.00 ± 0.04 while for deuterated material the walue was 1.85 ± 0.08. This indicates little (ca. 0.15D) deuterium at the bridge head and indeed it is possible that this arises from the 10% of second deuterium (d_2) incorporated (See scheme 51).

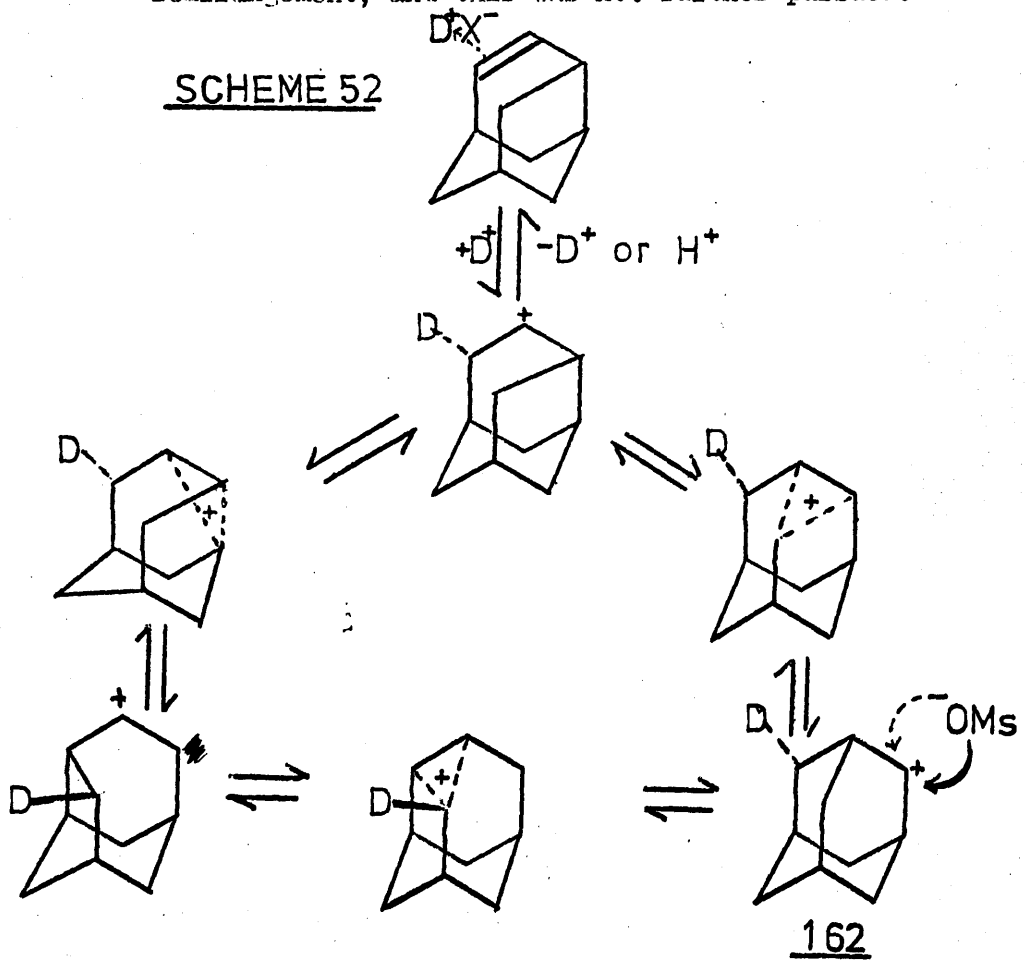
For the C_4 axial and C9 axial protons the mean integrals were; do 2.10 ± 0.02, d, 1.53 ± 0.08. Thus around half (0.47D) of the deuterium was in these positions. This result supports the suggested[67] nature of the cationic species associated with the 2-adamantyl cation 162 provided only the cations/

/cations shown in scheme 52 are involved and that protonation of protoadamantene 127 occurs mainly from the exo - side, the results obtained are those expected through scheme 52.

Protonation of protoadamantene 127 from the endo-side (Scheme 53) would lead to cation 163 and hence loss of deuterium from the C4 and C9 axial positions of the mesylate formed.

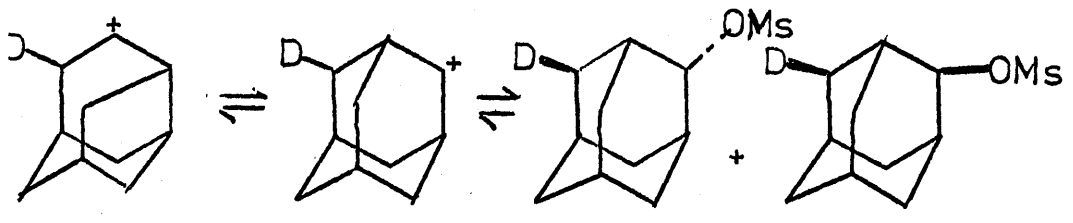
The deuterated mesylate was therefore unsuitable for the study of the deuterium isotope affect during pyrolytic rearrangement, and this was not further pursued.

SCHEME 52



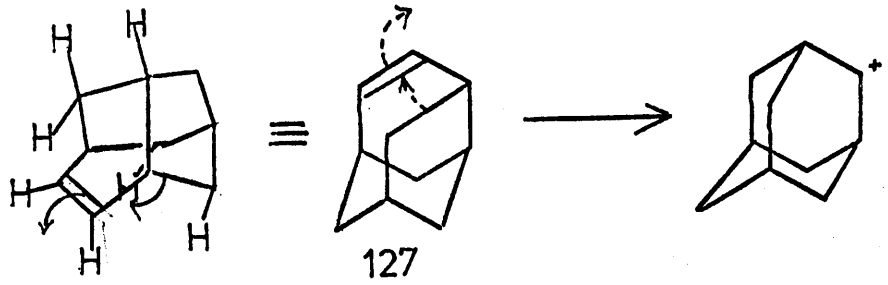
162

SCHEME 53

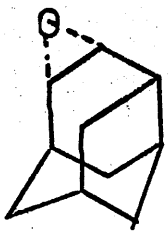


1:1

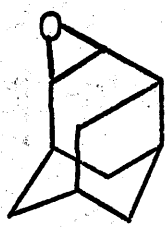
SCH. 54



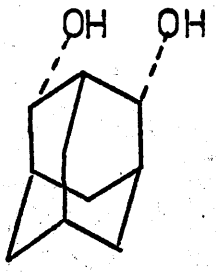
127



163



164



165

SECTION II 2

SOME REACTIONS OF PROTOADAMANTENE.

INTRODUCTION.

Protoadamantene 127 with its rigid, largely unstrained skeleton should make an interesting model for reactions involving addition to a double bond. It differs from the widely used[90] norbornene mainly in that the ends of the double bond are not identical, having greatly differing 1,3 - non-bonded interactions and capability for rearrangement. In protoadamantene the development of carbonium ion character should only be accompanied by rearrangement and anchimeric assistance when such development is in the 4-exo- sense (scheme 54).

Accordingly, the olefin was subjected to epoxidation, hydroboration and oxymercuration with the results detailed below.

In the course of this work all four 4 - and 5 - protoadamantols were isolated and their suspected configuration confirmed by their europium shifted n.m.r. spectra (section II 6). However, since such a determination is somewhat involved, it was preferable to use initially a simpler method based on protoadamantene epoxides and the products of their hydride reduction. This is described below.

RESULTS

(a) Epoxide formation and hydride reduction.

Treatment of protoadamantene 127 with m-chloroperbenzoic acid/sodium carbonate[92] in methylene chloride gave two epoxides (6/1, g.l.c) of which only the minor (endo-) epoxide 164 m.p. 212 - 214°C, could be isolated.

The major epoxide 163 decomposed both an attempted t.l.c. separation and fractional crystallisation to furnish a more polar substance which could be conveniently obtained by chromatographing the epoxide mixture over Grade II acid alumina. The product so obtained showed on n.m.r. ($CDCl_3$) four low field protons (δ 3.86)

and twelve up-field (δ 2.5 - 1.2) and in $D_2O/CDCl_3$ two low field (δ 3.89) and twelve up-field. Infra-red (5×10^{-3}M soln. in CCl_4) showed very strong hydrogen bonding (3616 and 3530 cm^{-1} i.e. $\Delta\nu$ = 86 cm^{-1}). The structure assigned was therefore that of 2 ax, 4 ax, - adamantanediol 165 m.p. 341 - 344 (lit. 305 - 310°C [91,93,94]) Subsequent to our investigation, a report of formation and hydrolysis of the epoxide mixture by Schleyer and co-workers [94] appeared in the literature.

These latter workers, though failing to isolate either epoxide, assigned configurations exo - to the major and endo- to the minor epoxide on the basis of ease of hydrolysis. One can, more rigorously, assign configuration on the basis of n.m.r. spectra.

The n.m.r. spectrum of epoxide mixture shows a clean 1 H quartet at δ 1.1 with splittings of 4 and 12 Hz. Such peaks appearing in 2,2,1 - bicycloheptane - exo - epoxides are thought [95] to arise from anisotropic shielding of one of the protons at C_7 by the oxirane ring. Though there has been some doubt as to whether it was the 7 syn - or 7 anti - proton in the above, it would seem that the requirement for the effect is that the proton should lie close to the perpendicular through the centre of the oxirane ring. Consideration of Prentiss-Hall models of exo- (163) and endo-(164) - protoadamantene-epoxide shows that the effect is only to be expected in the exo - case (163) and the observed splittings are only consistent with the signal expected from the C_7-proton anti - to the oxirane ring, where the dihedral angle (80 - 90°) with the C_8-proton would result in only two significant couplings of the observed magnitude.

The oxirane protons of the minor epoxide appear as quartets (J_{4-5} = 4, J_{3-4} = 7 and J_{5-6} = 6 Hz) while those of the major (in the mixture) are triplets ($J_{4-5} = J_{3-4} = J_{5-6}$ = 4 Hz.). This is consistent with the considerably smaller dihedral $C_3 - C_4$

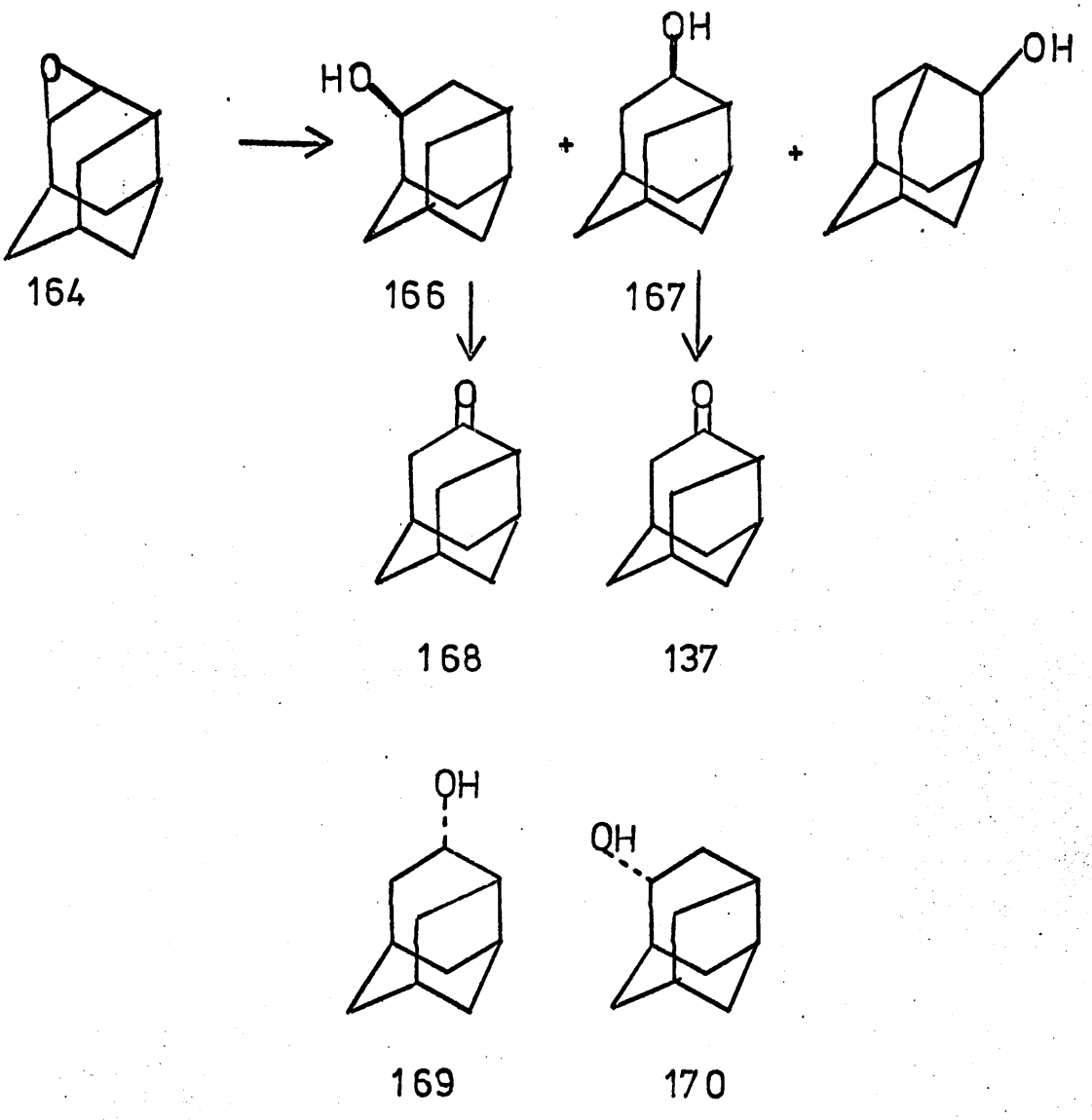
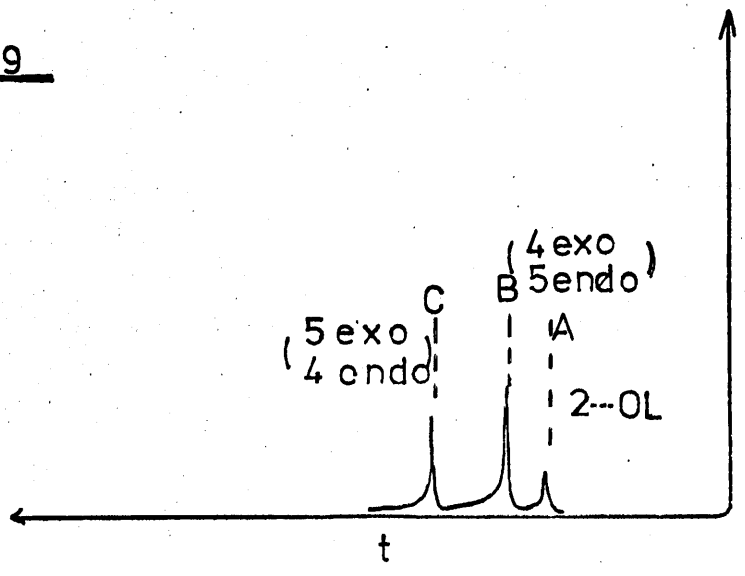

O
HO
OH
OH
164
166
167
O
O
168
137
OH
OH
169
170

FIG. 9


C
B
A
(4 exo
5 endo)
(5 exo
4 endo)
2--OL
t

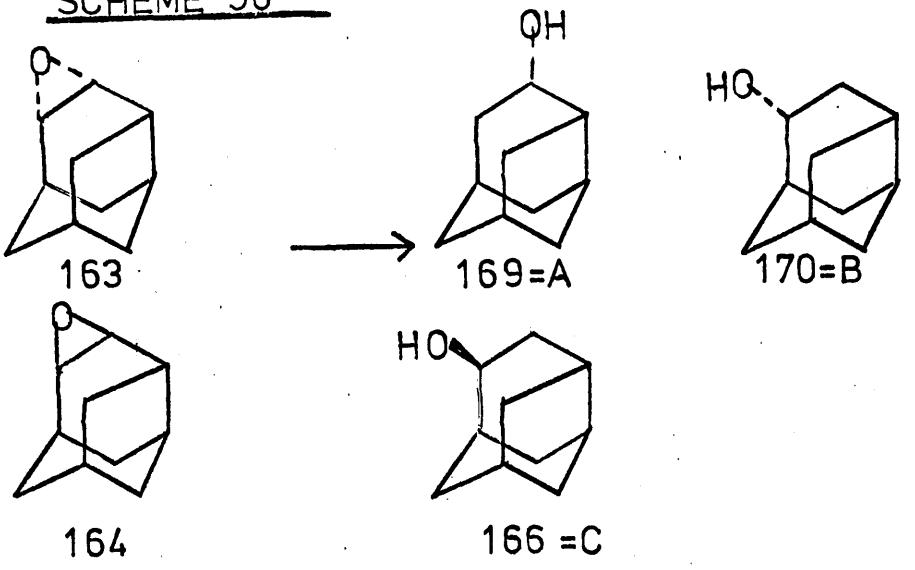
and C_5 - C_6 angles in the minor endo - epoxide model.

Reduction of the minor epoxide 164 (Li Al H_4) afforded the 5 - endo - alcohol 166 m.p. 258 - 260° (95%), 4-endo-alcohol 167 (3%) and 2-adamantanol (2%) as judged by g.l.c. Note, the major alcohol produced from this endo - epoxide must be endo - and its oxidation (Jones) gave the 5-ketone isolated by oxidation of the products of hydroboration of protoadamantene described below (p.43) not the 4-ketone prepared independently by the method of Gill[69].

At this point we are in a position to partially resolve the g.l.c. problem associated with these alcohols, namely that the mixtures of all four 4 - and 5 - protoadamantanols showed only two peaks on all (ten) columns used. The best seperation was obtained on a 50 m. capillary carbowax 1540 column where traces of the form shown in fig. 9 were obtained. Peak A, of shortest retention, was found to correspond to 2-adamantanol observed in small amounts in most runs. Reduction of endo-epoxide gave 5-endo-protoadamantanol 166 at peak B as the major product and 4-endo-protoadamantanol 167 at peak C as the minor. Reduction of 4-proto-adamantanone gave peaks at B and C but, since the 4-endo-alcohol 167 has already been assigned to peak C, 4-exo-protoadamantanol 169 must correspond to peak B. The determination of retention of 5-exo-protoadamantanol 170 required the hydride reduction of protoadamantan-5-one described below (p.44) which showed the major product, the 5 endo-alcohol 166, at peak B and a minor, presumably the 5 exo - 170 at peak C. Thus the relative retention of each alcohol as shown in fig. 9 was obtained.

It is then possible to analyse the results of reduction of the epoxide mixture and to determine the reduction course for the major unisolable exo-epoxide 163.

SCHEME 56



163 → 169=A 170=B

164 166 =C

If the three alcohols are produced in the ratio A : B : C as shown

then $\frac{A}{B+C} = 2$ (i.e. g.l.c. ratio of C-4 ; C-5 ketones on oxidation)

$\frac{A+C}{B} = \frac{80}{17}$ (i.e. ratio of two alcohol peaks on g.l.c.)

Then $A = 2B + 2C$ --------- (1)

and $17A + 17C = 80B$ --------- (2)

(1) × 17

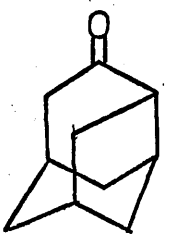
$17A = 34B + 34C$ ------(3)

(2) - (3) $51\,C = 46\,B$

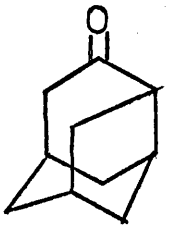
Let $B = 1$ $C = 0.9$

Subst. in (1) $A = 3.8$

Isomer	4-exo	5-exo	5-endo
Ratio	3.8	1	0.9
%	67	17	16



137



168

Reduction ($LiAlH_4$) of epoxide mixture gave (g.l.c.) 2-adamantanol (3%), 4 exo - 169 and/or 5 endo - (166)-protoadamantanol (80%) and 4-endo (167) and/or 5 exo - (170)-protoadamantanol (17%). Oxidation of total reduction product gave (g.l.c.) adamantanone (3%), protoadamantan - 5 - one 168 (32%) and protoadamantan-4-one 137 (65%)

Approximating that no adamantanone (3% in fact) and no 4-endo-alcohol 167 (minor 3% product of minor 14% epoxide in mixture) are produced, the method in scheme 56 shows that exo-epoxide 163 reduced to give 4-exo-alcohol 169 and 5-exo-alcohol 170 in the ratio 3.8/1.

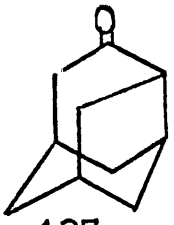
Use of $LiAlH_4$ - $AlCl_3$ mixtures gave similar results.

Hydroboration[96] of protoadamantene 127 under standard conditions (p. 82) gave a mixture of all four protoadamantan - 4 and 5 - ols. As discussed above (p. 42) direct analysis of the mixture by g.l.c. (or t.l.c) was impossible. Preliminary work[62] had indicated the presence of four peaks on g.l.c. Two of these were later shown to correspond to ketones arising by air oxidation of the alcohol mixture.

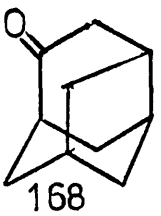
Oxidation ($RuO_2/NaIO_4$) of the total hydroboration product afforded two ketones separable by continuous development preparative t.l.c., protoadamantan-4-one[69,77,78] 137 m.p. 212-214° C (56.5%) and protoadamantan-5-one[100] 168 m.p. 222 - 225°C (40.5%). Small amounts (2-3%) of adamantanone were also present. The protoadamantan-5-one 168 was reduced by the Cagliotti method to a mixture of protoadamantene and protoadamantane (2/1) supporting its skeletal integrity. The europium shifted n.m.r. spectra of these ketones are reported seperately below (p 57).

Preparative t.l.c. of the hydro-boration mixture yielded three isolable bands of material.

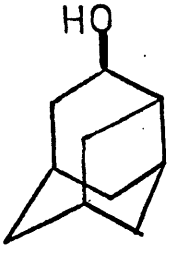
SCHEME 57



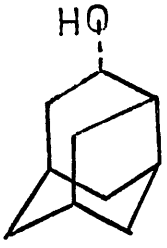
137



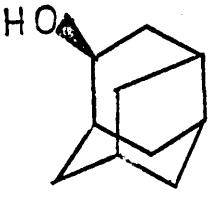
168



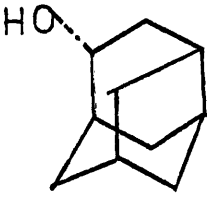
167 = A



169 = B



166 = C



170 = D

If the alcohols are produced in the amounts A, B, C, and D as shown

then (1) $\frac{A+B}{C+D} = 1{\cdot}4$ (i.e. ratio by g.l.c. of C-4 : C-5 ketone on oxidation of total hydroboration product)

(2) $\frac{A+D}{B+C} = 0.67$ (i.e. ratio of two alcohol peaks on g.l.c. of total hydroboration product)

(3) $\frac{A}{D} = 0.71$ (i.e. g.l.c. ratio of C-4 : C-5 ketone on oxidation of material of GREATEST polarity isolated by t.l.c.)

Let A = 1 then D = 1.41

Substitute in (1) and (2)

$\frac{1+B}{C+1.41} = 1.4$ and $\frac{1+1.41}{B+C} = 0.67$

or $B - 1.4C = 0.97$ ---(4) and $B + C = 3.58$ -------(5)

(5) - (4) $2.4\,C = 2.61$

$C = 1.09$

subs. in(5) $B = 2.49$

A : B : C : D is 1 : 2.5 : 1.1 : 1.4

The least polar band corresponded on t.l.c. and g.l.c. to the major product of hydride reduction of (a) the C - 5 ketone 168 and (b) endo-protoadamantene-epoxide 164. Reoxidation gave only the 5 - ketone 168. This material was therefore protoadamantan - 5 endo-ol 166 m.p. 258 - 260°.

The middle t.l.c. band on its comparison with the known[69,78,99] 4-exo-alcohol 169 and its oxidation products comparison with the known[69,77,78,99] 4-ketone, proved to be protoadamantan-4 exo-ol 169.

The most polar band showed only one peak on g.l.c. but oxidation (RuO_2 - $NaIO_4$) gave 4-ketone 137 (58%) and 5-ketone 168 (42%) as judged by g.l.c. This band therefore contained protoadamantan-4 endo-ol 167 and protoadamantan-5 exo-ol 170.

If we assume (a) t.l.c. does not lead to rearrangement and (b) oxidation of total hydroboration product and of material of greatest polarity, isolated by t.l.c. gives ketone ratios truly reflecting the alcohol ratios (n.b. no alcohol remains), we may derive the product ratios for the hydroboration reaction as shown in scheme 57. Hydroboration of protoadamantene yields 4 endo-, 4 exo-, 5 endo- and 5 exo- alcohols approximately in the ratio 1 / 2.5 / 1.1 / 1.4.

The 5-exo-alcohol 170 could not be obtained pure from the hydroboration mixture since it is inseparable from the 4-endo-alcohol. Likewise reduction of the 5-ketone 137 gave only 2-3% of the 5-exo-alcohol and separation was complicated by the presence of 2-3% adamantan-2-ol.

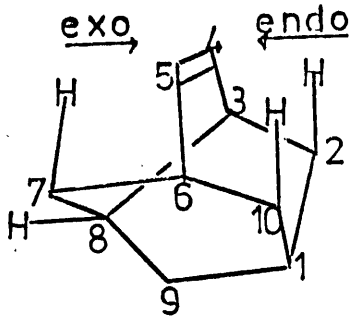
Attempts to obtain the alcohol 170 by equilibration of the 5-endo epimer failed under a variety of conditions (p.85).

Use of $LiAlH_4$ / $AlCl_3$ in the presence of excess acetone or fluorenone, or use of aluminium iso-propoxide and acetone gave the 5-ketone implying that the difficulty was not in abstraction of hydride from the exo- face but in its supply to the endo-face, to give exo-alcohol.

The 5-exo alcohol 170 was obtained after completion of this work, by Mr. Kong Luk of this laboratory, in 70% yield by reduction of 5-ketone 168 with lithium in ammonia.

Oxymercuration[101] of protoadamantene in the usual manner (p.87) gave 4-exo-alcohol 169 ($\lesssim$ 95%), 5-endo (166) , 5-exo-(170)- and 4-endo alcohols ($\gtrsim$ 3%) and adamantan-2-ol (2%). Oxidation gave 4-ketone 137 (94%), 5-ketone 168 (3%) and adamantanone (3%). Amounts were determined by g.l.c. Analogous results obtained by McKervey[102] and Schleyer[103] were brought to our attention subsequent to our completion of this work.

FIG. 10



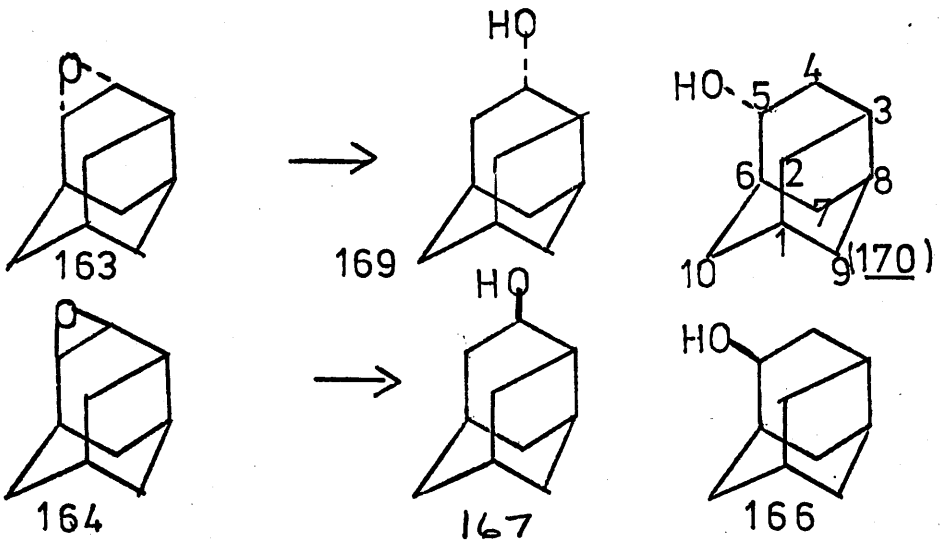


FIG. 11

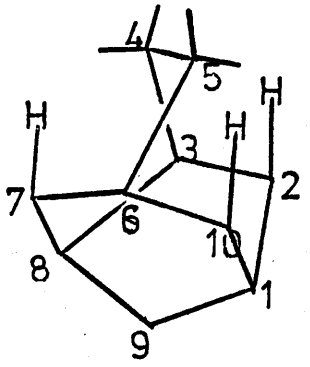
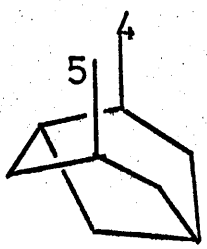


FIG. 12

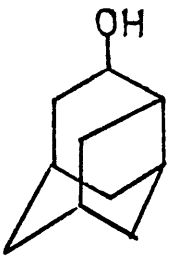


II 2 cont. DISCUSSION

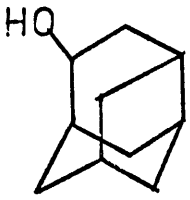
The use of Prentiss Hall scale molecular models shows that consideration of both the saturated and unsaturated protoadamantyl skeleton should be dominated by the 1,3 - nonbonded interactions (see fig.10 and 11) on the exo-face with the hydrogen at C7 and on the endo-face with those at C10 and C2. In the rigid olefin (fig.10) the magnitude of the interaction with the π bond is in the order endo 4 $>$ endo 5 $\gg$ exo 5 $\gg$ exo 4.

The smaller steric interaction on the exo-face is presumably the reason for the formation of the exo-epoxide in excess over the endo - epoxide (6/1). The very similar nature of the 1,3 - interactions in the epoxides is reflected in the product ratios for their steric approach controlled [104] hydride reductions. Thus reduction of exo-epoxide 163 gives 4 exo - 169 and 5 - exo - 170 alcohols in the ratio C. 4/1, while the endo-epoxide gives 95% 5-endo-alcohol 166 since hydride approach in the 4 exo-sense is much less hindered than in the 5 exo-sense.

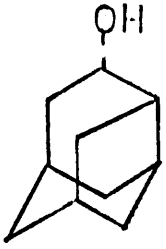
The more flexible saturated system fig. 11 has the added problem of conformation. Completion of the model up to the stage (fig.12) where the C4-C5 bond is omitted shows that, with the C3-C4 and C5-C6 bonds parallel, the distance C4 - C5 is less than the scaled bond length and the model can only be made in the twist conformation shown in fig.11. This conformation andthe angle of twist (C.30°) are discussed in relation to the europium shifted spectra of the alcohols reported below (Section II6. p.63)
Based on this conformation the 1,3 - interactions with syn-hydrogens at C7, C2 and C10 should be in the order 5 endo - $>$ 4 exo - $>$ 5 exo - $\approx$ 4 endo.



167



166



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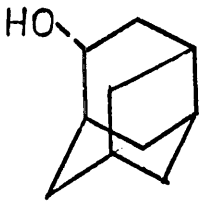
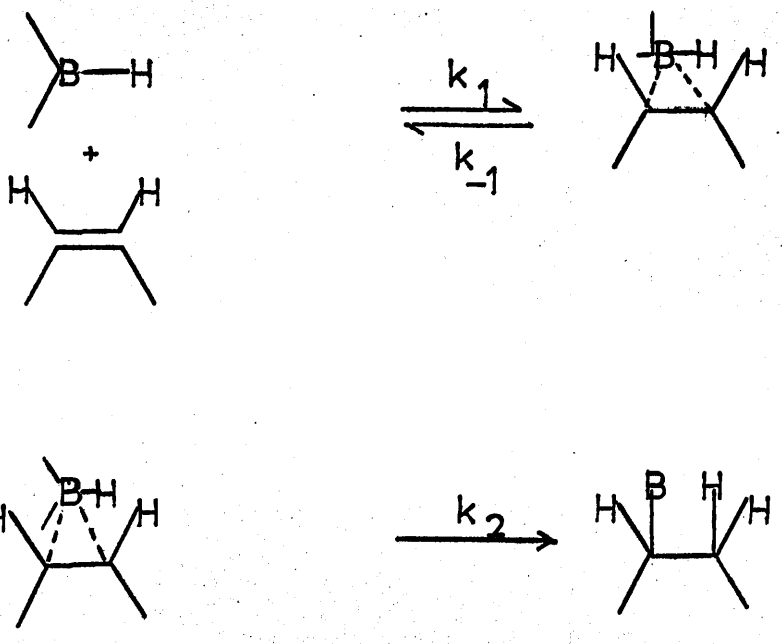


170

SCH. 59



The above shows agreement with the adsorbtion of the corresponding alcohols on silica thus 5 endo-alcohol 166 appears least polar, 4 exo - 169 next least, while 4 endo- 167 and 5 exo - 170 - alcohols are inseparable and most polar.

Consideration of europium shifted n.mr spectra (Section II6 p.ωδ) gives the same order as above for the magnitude of the 1,3 - interactions.

The results of hydroboration of protoadamantene. (the proto-adamantanols - 4 endo - 167 ; 5 endo - 166 ; 4 exo - 169 and 5 exo - 170 formed in the ratio 1/ 1.1 / 2.5 / 1.4) tend to confirm the suspected nature of the mechanism. The most recent view [105] is that reaction proceeds through formation of a B - $\overline{\pi}$ complex in a rapid equilibrium step (scheme 59) followed by slower collapse of complex to borane. If the equilibrium (k_1, k_{-1}) is much faster than the final collapse (k_2) then, applying the steady state approximation for complex i.e.

$$\frac{d[\text{complex}]}{dt} = 0$$

then

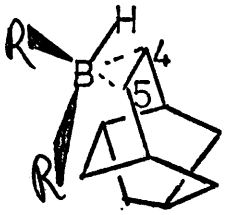
$$k \text{ observed} = \frac{k_2 k_1}{k_{-1} + k_2}$$

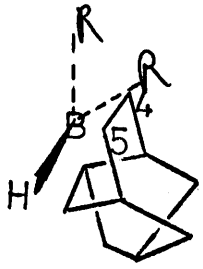
If equilibration is much faster than collapse ($k_{-1} \gg k_2$)

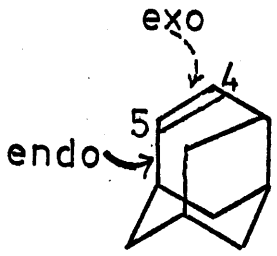
$$\text{then } k_{obs.} \approx k_2 \frac{k_1}{k_{-1}}$$

$$\approx k_2 K$$

FIG 14

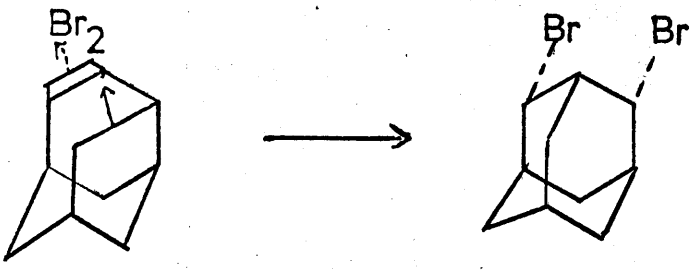






127

SCH. 60



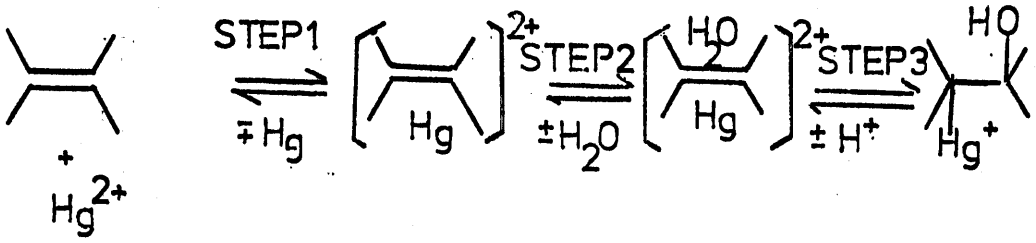
Thus boron (and hence oxygen since the oxidation of boranes appears to occur with exclusive retention of configuration[106]) should appear preferentially on the face of the molecule showing least hinderance since such a B - π complex should be favoured at the equilibrium stage. This effect would appear to be minor where BH_3 (ie excess B_2H_6) is concerned. Though the exo- face of protoadamantene 127 is significantly less hindered than the endo- , the corresponding exo - alcohols (166 and 167) and endo - alcohols (169 and 170) are formed in the ratio of only 2/1. (n.b. a lower selectivity than epoxide formation; exo-/endo = 6/1, p.40)

Steric effects on direction of hydrogen transfer (fig.14) would also appear to be small. Thus, using excess diborane, 4 exo-alcohol 169 is formed in only slight excess (2.4/1.4) over 5 exo - alcohol 170. This might be expected where the boron substitution (R in fig.14) is not of great steric size.

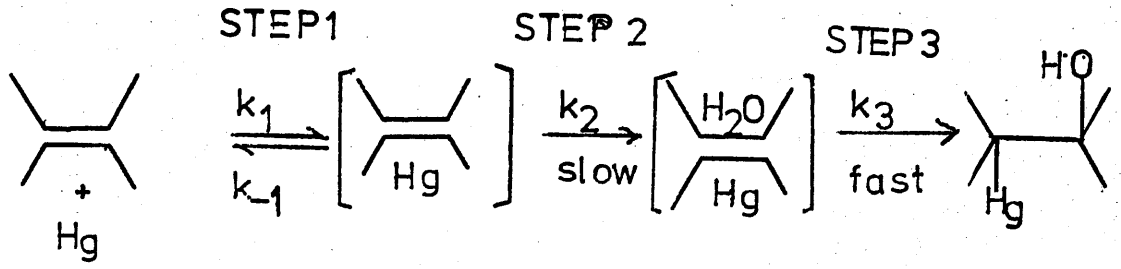
There would appear to be little or no carbonium ion nature in the boron - π complex since negligible ($\gtrsim$ 2%) rearrangement to the adamantane skeleton was observed. It should be noted that bromination of protoadamantene[94] leads almost totally to rearranged product. (scheme 60).

The results obtained on reduction of protoadamantan - 5 - one (95% endo - / 2% exo - alcohol) and the observed failure of the 5 - ketone to accept hydride on the endo - face on attempted equilibration of 5 endo - alcohol, confirm the magnitude of the non-bonded interaction between the 5 endo - and 10 syn - positions in the protoadamantyl skeleton.

SCHEME 61



SCH. 62



Oxymercuration - Discussion

The solvo-mercuration of olefins, though much studied[96,107-115], remains poorly understood.

Winstein and co-workers[111] established that in the presence of acid a series of equilibria (scheme 61) are set up, namely;

(a) formation/dissociation of olefin - mercury complex (step 1)

(b) solvation/desolvation of complex (step 2) and

(c) deprotonation/protonation of solvated complex (step 3).

Thus, since all steps are equilibria, solvomercuration in acid media should give thermodynamically favoured products as is observed[114].

More recently Kreevoy and co-workers[112,113] have established that acid-catalysed de-oxymercuration takes place through

(a) rapid protonation/deprotonation of organo-mercurial

(b) slower desolvation and (c) rapid breakdown of mercury-olefin complex.

If one accepts Kreevoy's hypothesis that acid-catalysised desolvo-mercuration is the microscopic reverse of solvomercuration and assumes that absence of acid does not change the nature of the reaction but only the rate of steps involving H^+, then one can derive a scheme (scheme 62) for the more common acid-free solvo-mercuration.

The formation of olefin - mercury complex (step 1) - remains a rapid equilibrium. Deprotonation/protonation (step 3) becomes a fast irreversible reaction and since step 2 is the slowest step and its product, the solvated complex, is being removed by step 3 as fast as it is formed, step 2 becomes a relatively slow irreversible reaction.

Thus the kinetics take the form:=

$$\text{Rate} = k_2 [\text{Hg - complex}]$$

and applying the steady state approximation

$$\text{ie} \quad \frac{d[\text{Hg - complex}]}{dt} = 0$$

$$\text{then } k_1 [\text{olefin}] \times [\text{Hg}] = k_{-1} [\text{Hg - complex}] + k_2 \times [\text{Hg - complex}]$$

$$\text{Rate} = \frac{k_2 k_1 [\text{olefin}] \times [\text{Hg}]}{k_{-1} + k_2}$$

$$\text{or} \quad k_{\text{observed}} = \frac{k_2 k_1}{k_{-1} + k_2}$$

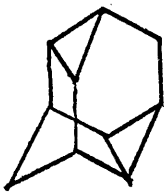
If, for the purpose of simplification, we assume $k_1 \gg k_2$

$$\text{then} \quad k_{\text{obs.}} = k_2 \times \frac{k_1}{k_{-1}}$$

Thus two factors should influence the steric course of the reaction (a) comparative thermodynamic stability of complex on either face of the olefin (if $\frac{k_1}{k_{-1}}$ = K then K exo relative to K endo) and (b) ease of solvent attack on mercury complex (k_2)

If one considers only the alcohol stereochemistry the preferred side of attack of the mercury is relatively unimportant since solvent attack on the same side (as in 2,2,1 - bicycloheptenes[107-110]) or on the opposite side (as in cyclohexenes[114]) seems equally likely.

The above explains the results of oxymercuration of protoadamantene (> 95% 4 exo-alcohol formed) in that solvent approach in the 4 exo-sense is favoured owing to the minimal 1,3 - interactions in that direction and complements the work of Whitham andChamberlain[114] on oxymercuration of substituded cyclohexenes where product stereochemistry appears to be dictated by ease of solvent approach. The result (< 3% rearrangement to adamantane skeleton see p. 48 scheme 60) agrees with the negligible extent of carbonium ion development andhence rearrangement observed in the case of 2,2,1 - bicycloheptenes [107 - 110]



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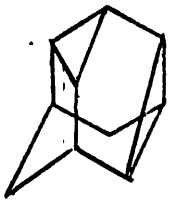

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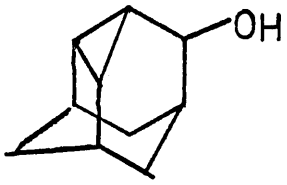
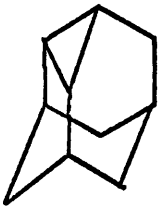


177

SCHEME 64



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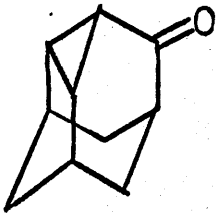

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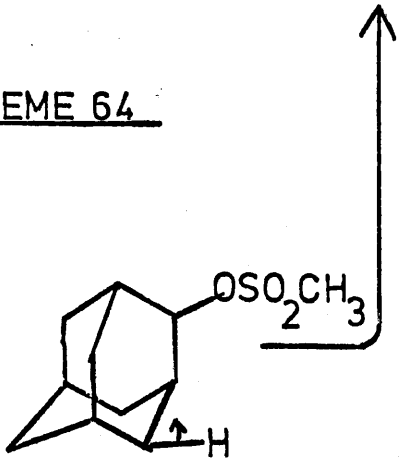
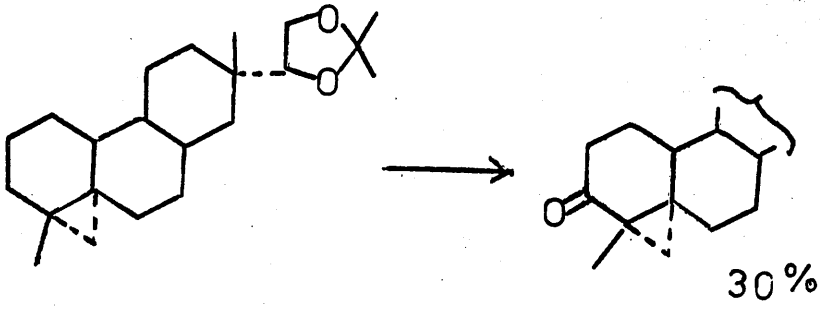
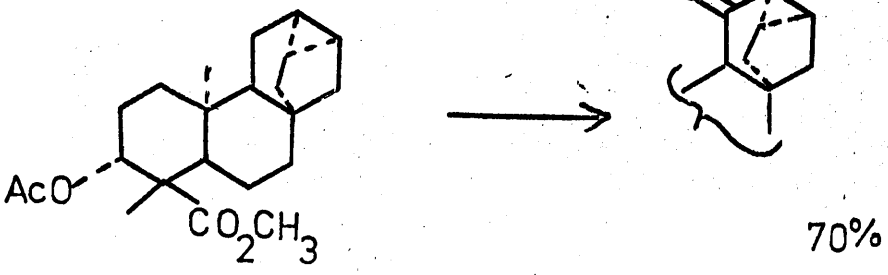


SCH. 65



SCH. 66



(III-3) 2,4 - DEHYDROADAMANTANE DERIVATIVES

We were interested in the possibility of introduning a second cyclopropyl ring into the adamantane nucleus to obtain compounds of the type 175 or 176*[116]. Various routes were considered but one, the pyrolysis of the methylsulphonate of the known 8, 9 - dehydroadamantan - 2 - ol 177[117], (scheme 64) seemed attractive.

Study of the reported[117] synthesis of 177 showed it to be a formidable task involving nine steps and with overall yield of < 3%.

At this time the fortuitous uncovering of an example of α - cyclopropyl oxidation occurring during ozonolysis (scheme 65) carried out[118] previously in this laboratory and the reference to the similar result obtained by Ourrison[119] on ozonolysis of the trachlobane derivative 178 (scheme 66) turned our attention to this possible route. The formation of a β - cyclopropyl oxidation product [redacted] on ozonolysis of the derivative of cycloartenol [redacted] has also been observed.[120]

Dehydroadamantane 126 was treated with ozone in methylene chloride / pyridine (5:1) for 8 hours at -30°C. Chromatography (t.l.c.) showed, in addition to starting material, three other spots two of which stained with dinitrophenylhydrazine. The lesser of these was found on isolation (t.l.c.) to correspond to 2-adamantanone. The major on isolation (t.l.c.) showed i.r. absorbtions at 3038 cm^{-1} and 1703 cm^{-1} and was considered to be 8,9 - dehydroadamantan - 2 - one 181 (reported[117] 3040 cm^{-1} 1705 cm^{-1}). This material was not obtained pure; g.l.c. analysis showed two minor impurities of 1% and 8%. The appearance of minor i.r. absorbtions in the region around 3430 cm^{-1} suggested that one of the impurities might be the corresponding alcohol 177.

*A report[116] of the formation of the dicyclopropyl compound 176 by thermolysis of the ditosylhydrazone of adamantane - 2,6 - dione appeared subsequent to our completion of this work.

The unreacted hydrocarbon from the first ozonolysis was separated by chromatography (column, alumina grade III) and re-ozonised. The combined product on reduction[117] with sodium borohydride gave after t.l.c. separation 8,9-dehydro-adamantan-2-ol 177 (40% from hydrocarbon) m.p. 207 - 209° ([117] 210 - 212°). (Spectroscopic data of the isolated material are given with those previously reported[117] in the relevent experimental section).

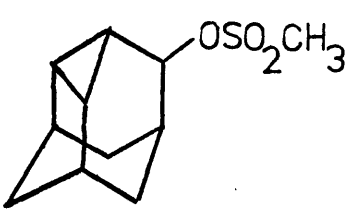
Attempts to prepare the methane sulphonate 182 by normal methods failed as did attempts using alkyl lithium reagents[121] to prepare the alkoxide in ether with its subsequent treatment with methylsulphonyl chloride. Failure was probably due to the instability of the methane sulphonate. Rate studies[117] have suggested that the rate enhancement for solvolysis of 8,9 - dehydro - 2 - adamantyl tosylate compared with 2-adamantyl tosylate should be around 4×10^8.

Pyrolysis was carried out on the known 3,5 - dinitrobenzoate 183 m.p. 119 - 120° ([117] 121 - 122°) by injection of the ester in ether into the pyrolysis tube system described above for the 2-adamantyl ester pyrolyses (p.25). Temperature and pressure used were 550°C and 0.1 mmHg respectively.

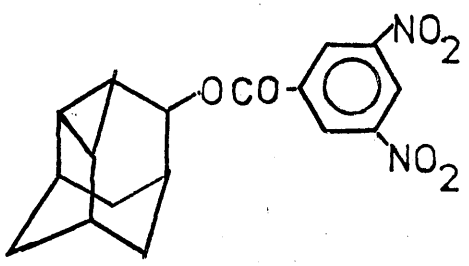
Analysis of the product (t.l.c.) showed absence of starting material but (g.l.c./t.l.c.) showed a large number of hydrocarbon products of retention similar to adamantane.

It would seem that pyrolytic elimination had occurred but that the product(s) had not survived the reaction conditions.

Insufficient time was available for further investigation of the reaction. Work is still proceeding on this problem in this laboratory.



182



183

SCHEME 67

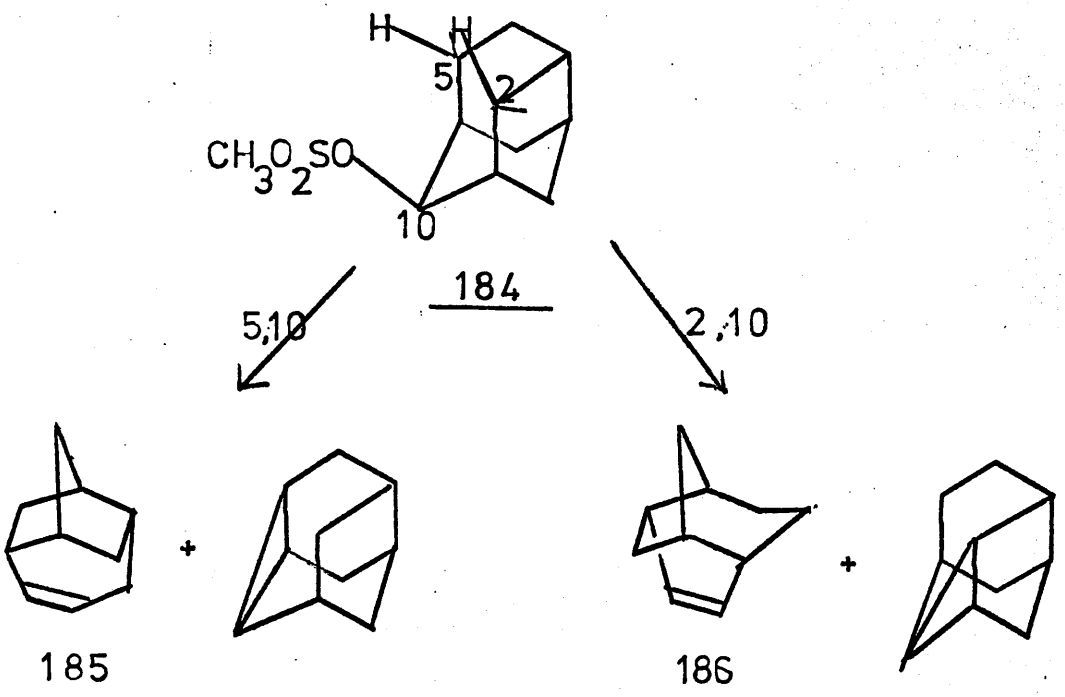
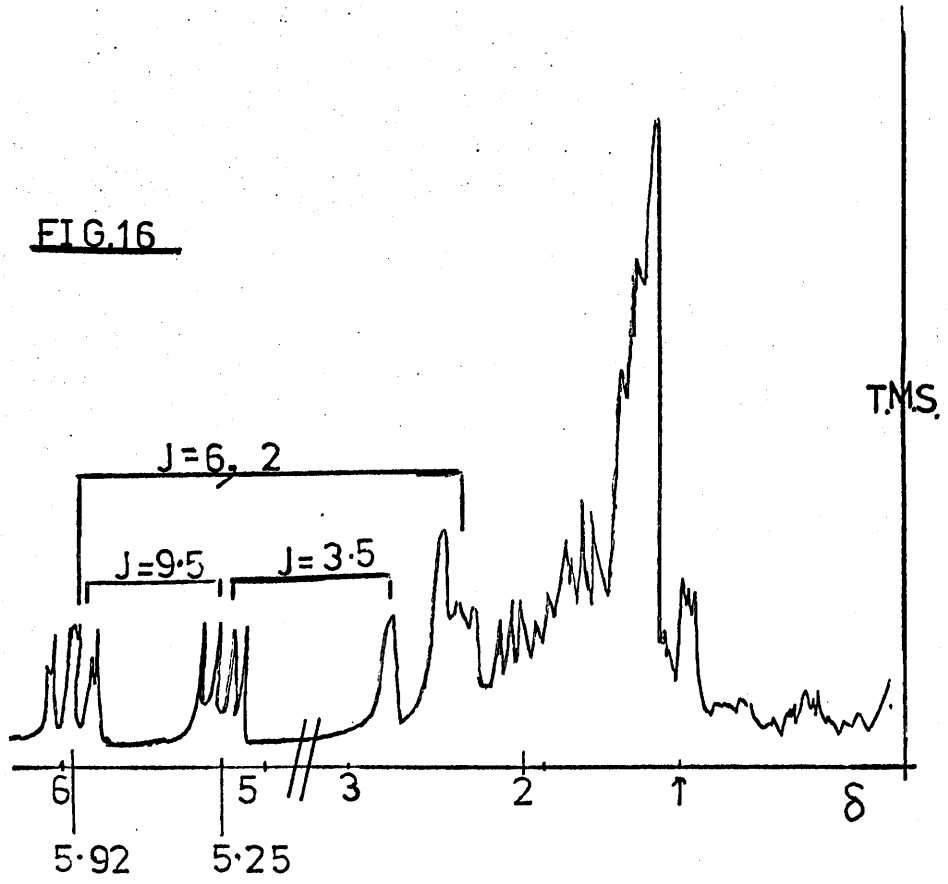


FIG.16



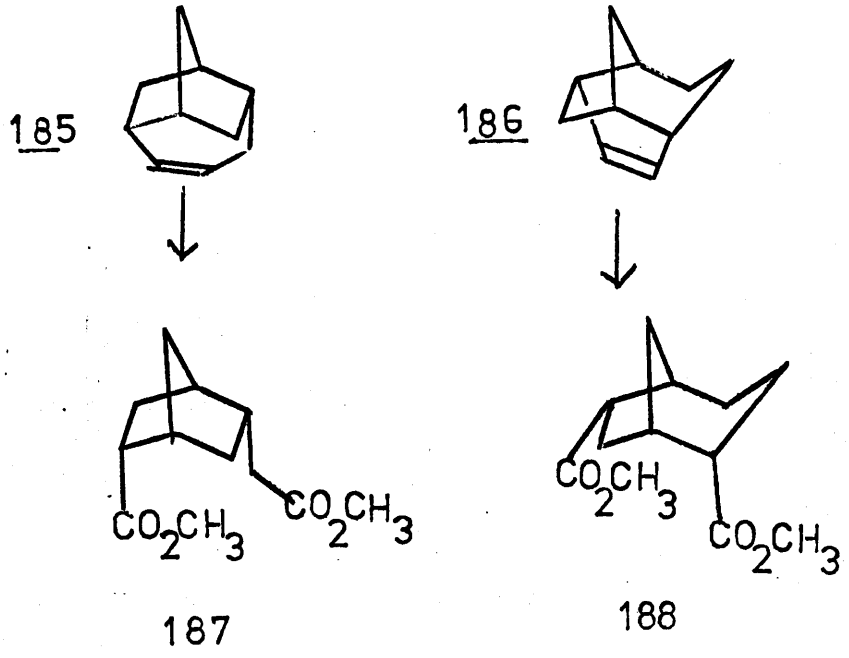
II 4. PYROLYSIS OF 10-PROTOADAMANTYL METHANE SULPHONATE

A sample of 10-protoadamantyl - methanesulphonate[122] 184 was made available to us by Professor C.A. Cupas of Case Western Reserve University, Ohio. Solvolysis of 184 having failed to yield meaningful results, it was hoped that pyrolysis might prove more fruitfull. With the 1,3 - elimination route (scheme 67) in mind, the model is interesting in that the skeleton does not provide the exact anti-periplanar relationship of removable hydrogen, bond capable of migration and ester S-O bond, shown in the 2-adamantyl case. In addition (see scheme 67) four novel products might be obtainable.

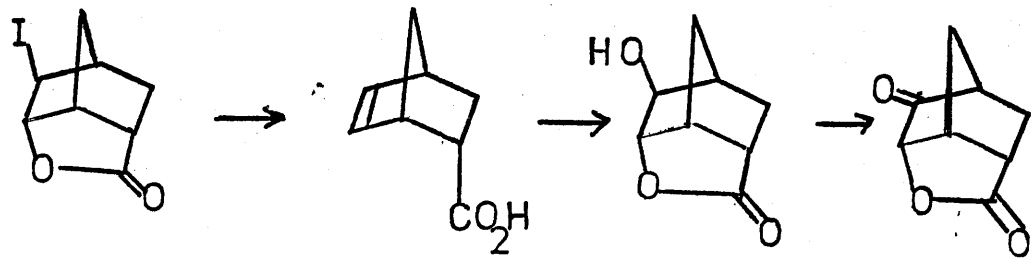
Preliminary small scale pyrolyses (c.10 mg.), carried out at 450 - 500°C and 0.3 - 0.1 mm Hg. by injection of mesylate 184 in ether into the pyrolysis tube system as described above (p.25 for 2-adamantyl-p-toluene-sulphonate, indicated the formation of at least one major product in addition to adamantane.

Pyrolysis of the mesylate 184 at 540 - 560°C and 0.06 mm Hg, in a tube coated at its exit with sodium carbonate in the manner described above (p. 27) for pyrolysis of 2-adamantyl mesylate, gave, after separation over 15% silver nitrate/alumina, adamantane (35%) and another white crystalline hydrocarbon (11%). Chromatography (g.l.c.) had indicated that the new material was formed in about the same amount as adamantane but losses occurred in handling owing to its extreme volatility.

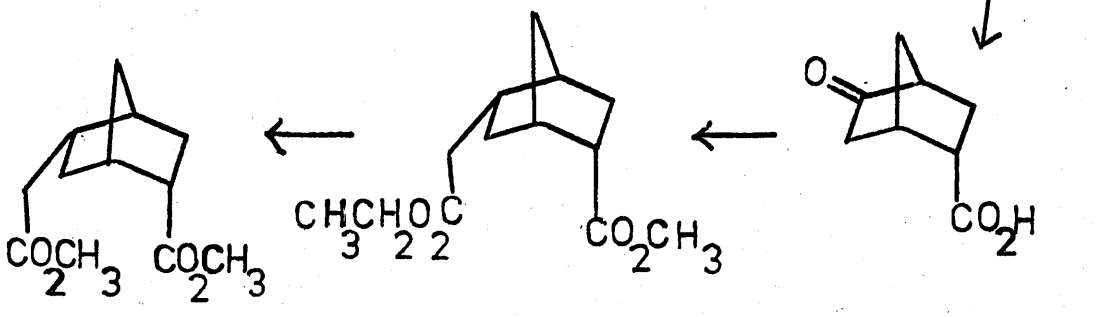
The new material (melting above 200°C) had i.r. absorbtions at 3020 and 702 cm^{-1}, the n.m.r. specrum shown (fig.16) and molecular weight (mass spectrometry) of 134. The data, though indicating that the material was olefinic, is consistent with either of the expected olefins (185 or 186).



187 188



191 192 193 194



187 196 195

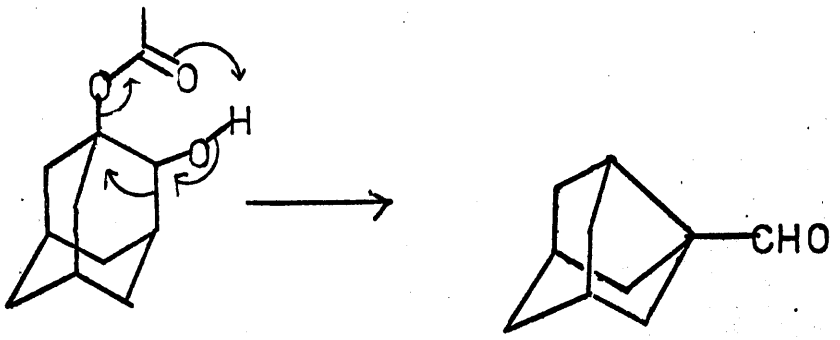
To establish the structure of the olefin it was necessary to compare its methylated oxidative cleavage product (187 or 188) with independently synthesised material.

Endo - 4 - carboxy - bicycle - 2,2,1 - heptane 192 was isolated from a commercial (Koch Light Ltd.) mixture of endo and exo material by formation[124] isolation and reduction [125] of the iodalactone [126] 191. The hydroxylactone 193 was prepared by treatment of 192 with performic acid as described by Henbest [127] and oxidised [128] (RuO_4) to the ketolactone 194. Barium/ammonia reduction gave the keto-acid[126] 195 which on methylation (CH_2N_2), treatment with triethylphosphono-ethyl-acetate/sodium hydride [129] and hydrogenation over platinum gave the diester 196 which was further hydrolised and re-esterified giving the dimethylester* 197 : i.r. 1739, 1435 cm^{-1}: n.m.r. δ 3.64 (3H,s), 3.62 (3H, s) 2.75 (1H, m), 2.48 (2H, m), 2.34 - 1.22 (9H, m) : mass spec. M^+ 226.120 $C_{12}H_{18}O_4$ requires 226.120.

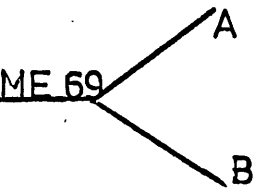
Mr. Luk Kong [131] has continued work on identification of the olefin produced. He has found that osmium tetroxide treatment of the olefin and methylation of the diacid formed gives a product which does not correspond (g.l.c.; i.r.; n.m.r.) to the dimethyl ester 187. Spectoscopic date [131] suggests the dimethyl ester 188. Work on verification of the structure of the olefin is continuing in these laboratories.

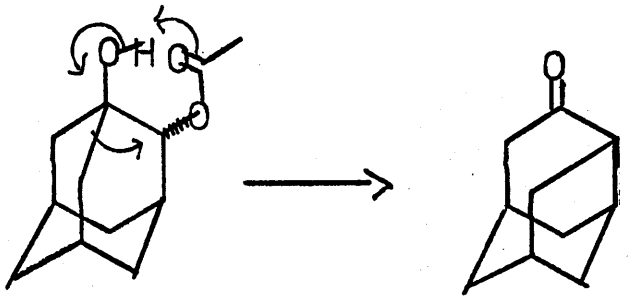
We are at present at a loss to explain the formation of so much (> 50%) adamantane during the above pyrolysis.

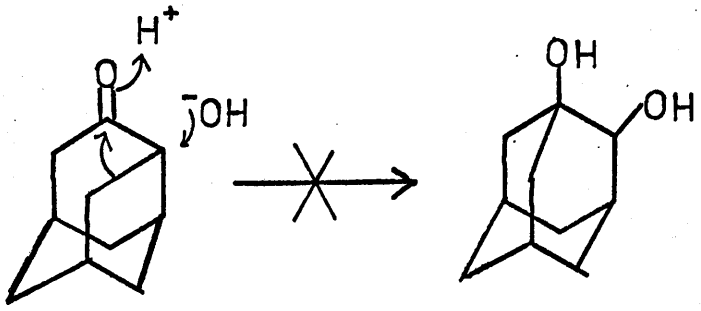
* This work was carried out in collaboration with Mr. Luk Kong in these laboratories.



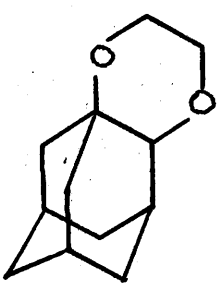
SCHEME 69







137 200



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II.5 MISCELLANEOUS ADAMANTANOID REACTIONS.

At one point 1,3 - eliminations of the type shown in schemes 69A and 69B were considered. These have precedent in the work of Leffingwell and Shackelford[58] on α-hydroxyacetates discussed in the introduction above (p. 19).

The routes available[67] to the starting adamantane-1,2-diol 200 are arduous and time consuming and so some attempts were made to find simpler ones.

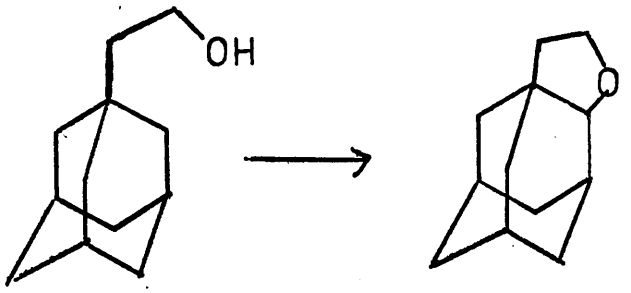
It was thought that reverse pinacol reaction of protoadamantan-4-one 137 might yield the diol 200. Several methods were attempted but all failed.

Refluxing ketone 137 in glacial acetic acid overnight gave no change as did stirring in 50% sulphuric acid at 20° or 50° for periods of up to 14 hr. Similarly an attempt to trap the diol 200 by oxidation where the ketone 137 was stirred at room temperature with Jones Reagent (CrO_3 / 50% H_2SO_4) in acetone for 3 hours gave starting ketone as the only isolable material.

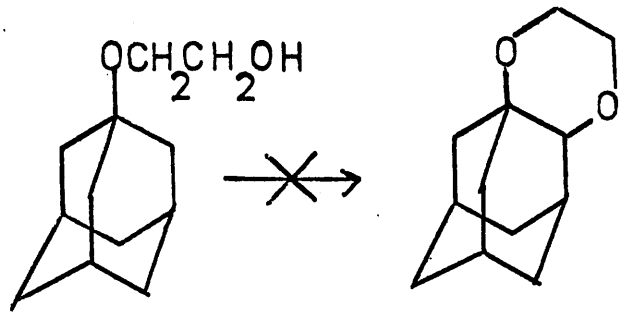
Some rearrangement could be achieved by stirring the ketone 137 with 50% sulphuric acid at around 100°C, however adamantanone was the only new product identified and extensive charring occurred on prolonged treatment.

It was thought possible that a rearranged product such as 205 might be obtainable on attempted ketolisation. The ketone furnished a normal ketal, as judged by n.m.r., which on regeneration in glacial acetic acid gave the starting ketone 137.

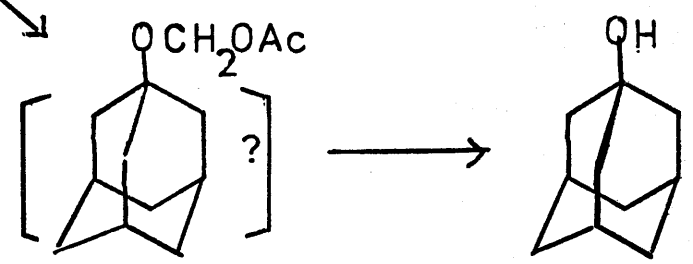
The ethyleneglycol-mono-(1-adamantyl)-ether 204 was prepared in high yield by treatment of 1-bromoadamantane with ethylene glycol in the presence of sodium carbonate. Lunn[77] has reported the closure of the/



202 203

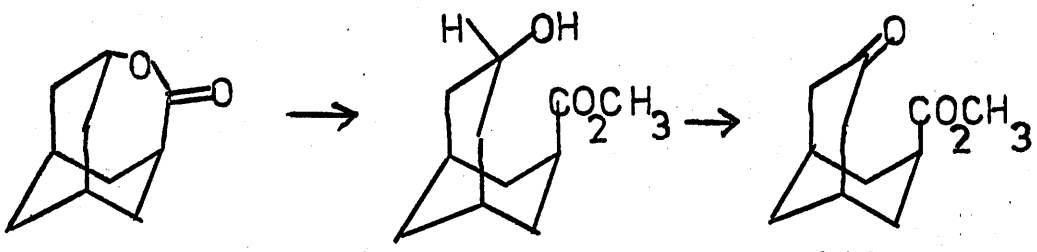


204 205

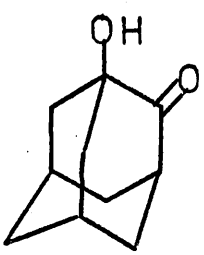


206 135

SCHEME 70



210 212 213



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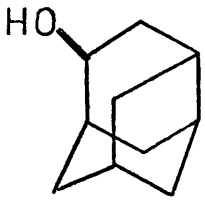
the similar 2-adamantyl-ethanol 202 using lead tetra-acetate, alone or with iodine, to give the tetrahydrofuran 203. The glycol-mono-ether 204 does not close to give the dioxane 205 under similar conditions. Instead, particularly where lead tetra-acetate is used alone in refluxing benzene, an unstable product is formed, the mass spectrum (M^+224), n.m.r. spectrum (δ 5.25, 2H singlet) and i.r. spectrum (ν max. 1735 cm^{-1}) of which suggest structure 206. This material gives 1-adamantanol 135 on attempted chromatography or recrystallisation. Several examples of α- cleavage of alcohols on treatment with lead tetre-acetate appear in the literature.[130]

Since oxahomo-adamantanone 210 (prepared in quantitative yield by m-chloro-perbenzoic acid treatment of adamantanone) was on hand for other work, it was decided to attempt the sequence shown in scheme 70.

Overnight reflux of 210 in methanolic potassium hydroxide followed by acidification and treatment with diazomethane gave an unstable hydroxyester thought to be 212. Oxidation (Jones) gave the ketoester 213 m.p. 85 - 87° (87% from 210). No conditions attempted were successful in achieving acyloin condensation to the keto-alcohol 214. Time was not available for further work on this scheme.



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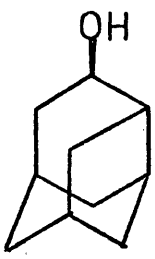
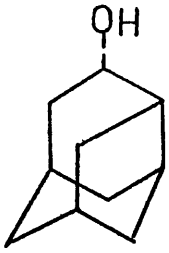


167



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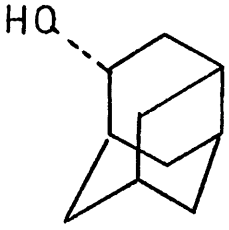

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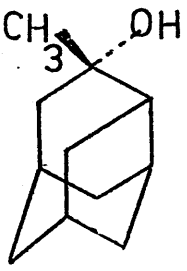

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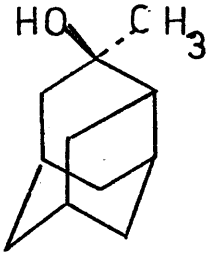

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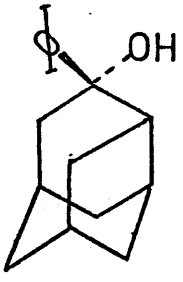

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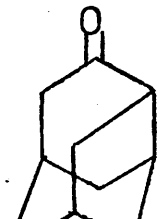
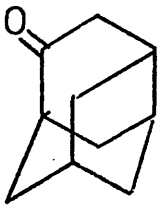
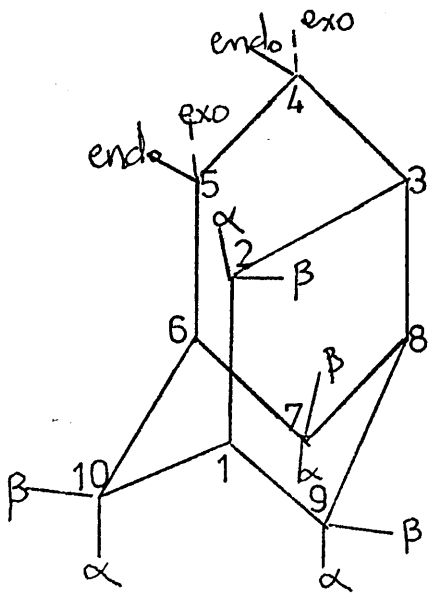


137



168



II.6 EUROPIUM III SHIFTED n.m.r. SPECTRA OF PROTOADAMANTANE DERIVATIVES.

The following chapter deals with the n.m.r. spectra, obtained with the aid of tris-(dipivaloylmethanato)-europium III, of a series of proto-adamantyl alcohols and ketones namely : 4 endo - (167), 4 exo - (169) 5 endo - (166) and 5 exo - protoadamantanol 170 and of 4 endo - methylprotoadamantan - 4 exo - ol 216, 4 exo - methylprotoadamantan - 4 endo - ol 217, 4 endo - phenylprotoadamantan - 4 exo - ol 218, protoadamantan - 4 - one 137 and protoadamantan - 5 - one 168.

A wide variety of techniques have been used [132-133] to assign the spatial distribution of protons on data from lanthanide shifted spectra. Recent theoretical considerations [134] have shown that the induced shift in proton resonance frequency should be given by the equation

$$\frac{\Delta\nu}{\nu_o} = \frac{\beta^2}{6(kT)^2} \times \frac{3\cos^2\theta - 1}{r^3} \times 2A_2^o \langle r^2 \rangle \times g^2(J+1)(2J-1)(2J+3)\langle J \| \alpha \| J \rangle$$

i.e. a factor in T^{-2}, a factor in θ and r, a factor involving crystal field coefficients and a factor in spin states of the lanthanide. This may be simplified if we (a) consider the crystal field term $2A_2^o \langle r^2 \rangle$ the same for all complexes (b) take J factor = 0, which appears [134] to be the case for europium III complexes and (c) use constant temperature.

Thus $$\frac{\Delta\nu}{\nu_o} = A \frac{3\cos^2\theta - 1}{r^3}$$

where r is Eu - H distance and θ is the angle of the Eu - H line with the principal magnetic axis of the complex (this is usually taken as the O - Eu - H angle).

While some examples of computer aided analysis of spectra by varying r and θ of a model to find the best fit of observed and calculated results have been reported [135,136,141], most workers [132,133] have/

have ignored angle effects and used a variety of inverse relationships in distance. Since Eu position cannot reliably be prodicted most workers use O - H distance (R). In the following chapter we will show that while use of O - H distance in place of Eu - H distance is allowable in cases where rotation of Eu complex about the C - O bond is unrestricted, in cases where there is steric constraint on the allowable positions of Eu, the approximation gives misleading results. The reader is referred to discussion of steric effects on europium position in (p.67) 5 - endo - protoadamantanol 166 and the methyl- and phenyl- substituted alcohols 216, 217 and 218.

A recent report[134] has suggested that rigorous evaluation of angular (θ) and distance (r) factors is unwise unless a thorough set of experimental conditions are attempted to evaluate the other factors in the theoretical equation mentioned above. In this study, we have used the reagent to produce a spread spectrum. The peak furthest downfield was assigned to the carbinol proton of the alcohols used and the other peaks assigned on the basis of the couplings revealed by double irradiation. The O - H distance as judged from a model was only used as an aid to peak assignment where (a) the O - Eu - H angle was likely to be small and (b) for any two or more protons were $\frac{\Delta R}{R}$ was large (R being O - H distance). This usually implied protons close to the oxygen function.

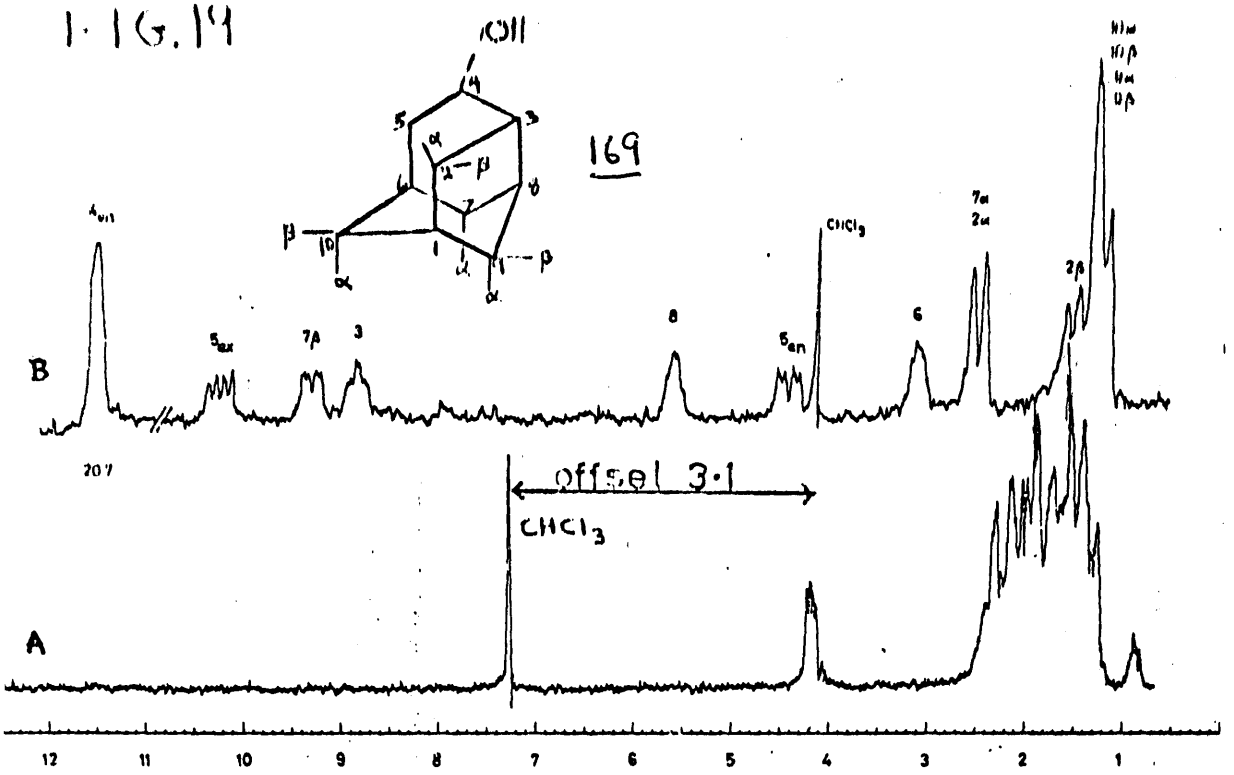
All of the coupling constants observed were consistent, when related through the Karplus relationship, to the angles observed in the model.

NOMENCLATURE

Though all geminal positions may be distinguished as exo -, endo -, syn - or anti - to the 4,3,1 - ring system of proto-adamantane (i.e. 4,3,1,$0^{3,8}$-tricyclodecane), the confusion with the accepted[67] /

usage of "exo" and "endo - protoadamantyl" has led us to use the arbitrary distinctions α and β as shown in the relevant diagrams below.

Fig. 19



Pmr spectra of 4-exo-protoadamantanol ~~(20)~~ 169 [0.4M in $CDCl_3$]. A. Normal spectrum at 100 MHz; B. 100 MHz spectrum of solution used in A with added $Eu(dpm)_3$ (0.26M).

Table 8 Shift- OH distance correlation for4-exo-protoadamantanol

Proton	4en	5ex	7β	3	8	5en	6	7α	2α	2β	10α 9α	9β	10β	1
O H dist. in model	55	65	65	70	85	90	105	105	110	120	135	140	145	145
shift order	1	2	3	4	5	6	7	8		9		10		
max.ΔV = 1														

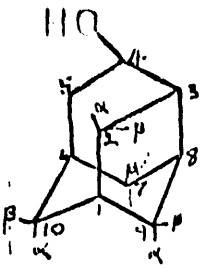
Table 9 Coupling constants for 4-exo-protoadamantanol

protons	J Hz
2α-2β	12.5
2β-3	11
3-4en	3.5
4en-5en	6.5
4en-5ex	< 1

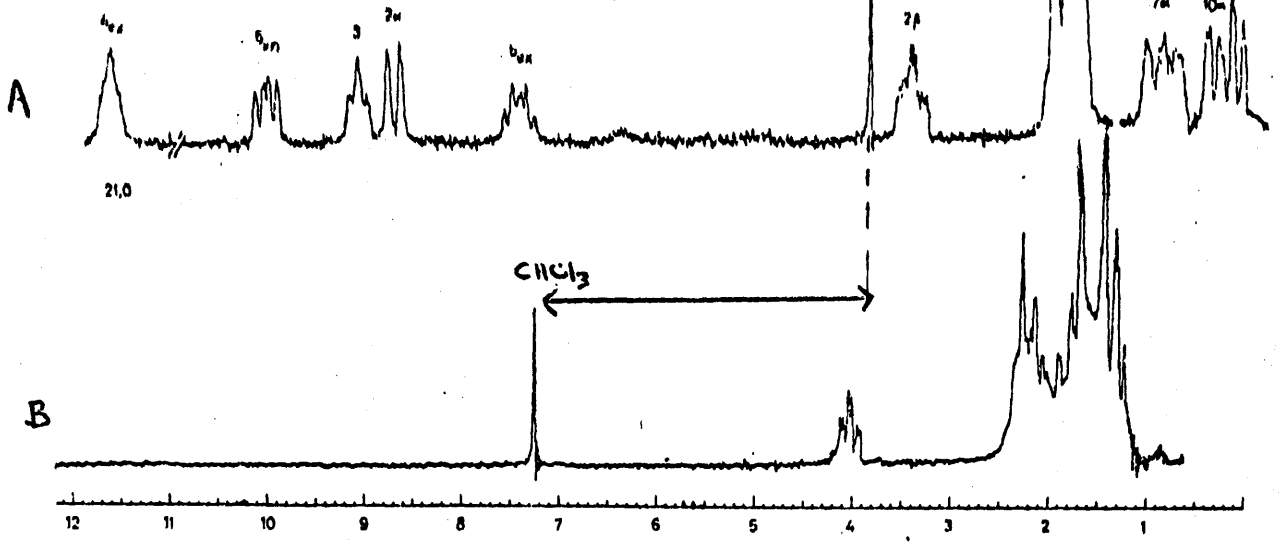
protons	J Hz
5ex-5en	15
5ex-6	8
*6-7β	< 4
7α-7β	12.5
* 7β-8	< 4

* Not mutually distinguishable

FIG. 20



167



Pmr spectra of 4-endo-protoadamantanol ~~(21)~~ 167 [0.4M in $CDCl_3$]. A. Normal spectrum at 100 MHz; B. 100 MHz spectrum of solution used in A with added $Eu(dpm)_3$ (0.26M).

Table 10 Shift-OH dist. correlation for 4-endo-protoadamantanol

Proton	4ex	5en	3	2α	5ex	2β	10β	8	7β	6	1	7α	9β	10α	9α
Rel. OH dist.	55	67	70	72	80	93	120			126	135	142		150	155
Shift order max. $\Delta\gamma = 1$	1	2	3	4	5	6	7					8		9	10

Table 11 Coupling constants for 4-endo-protoadamantanol

Protons	J Hz
1-2α	< 1
2α-2β	13
2α-3	3
2β-3	8.5
2α-9α	3
3-4ex	3.5
3-8	8.5
4ex-5ex	8

Protons	J Hz
4ex-5en	8.5
5ex5en	14
5ex-6	8
5en-10α	≤ 2
9α-9β	10
10α-10β	13.5
3-5ex	≤ 2
5ex-10α	≤ 2

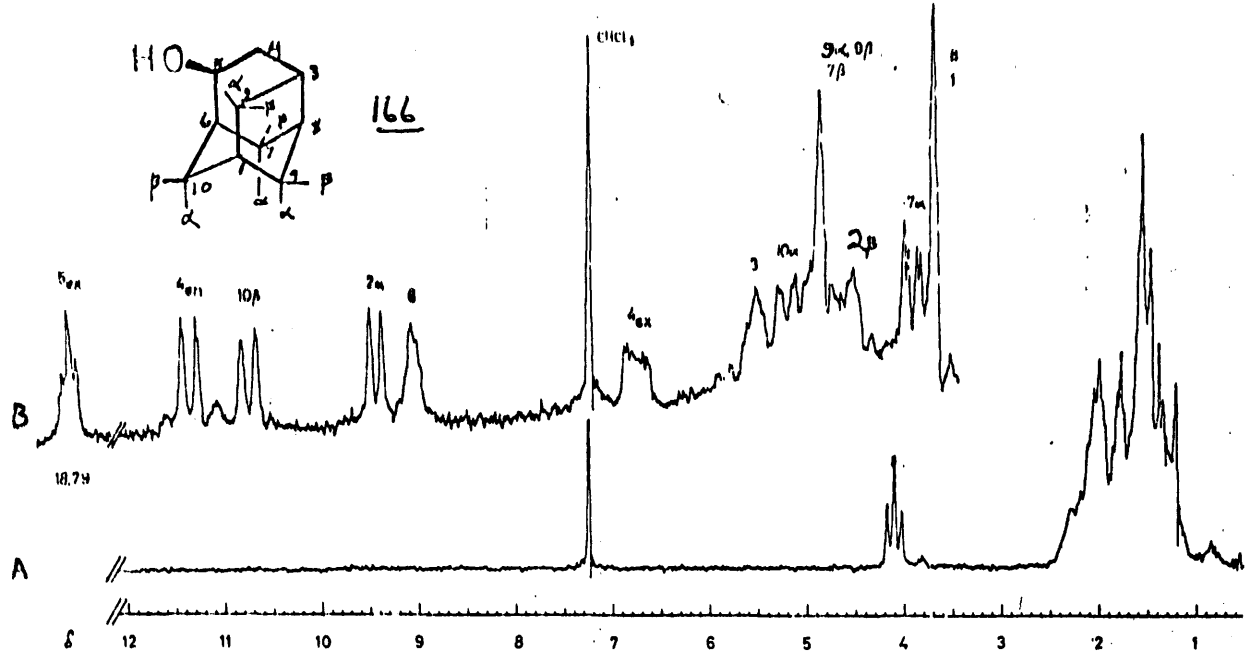


Figure 21 Pmr spectra of 5-endo-protoadamantanol ~~(24)~~ 166 [0.4M in $CDCl_3$]. A. Normal spectrum at 100 MHz; B. 100 MHz spectrum of solution used in A with added $Eu(dpm)_3$ (0.20M).

TABLE 12 Shift-OH dist. correlation for 5-endo-protoadamantanol 166

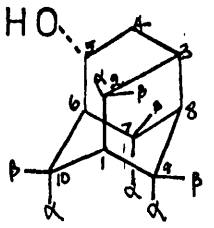
Proton	5ex	4en	10β	2α	6	4ex	1	3	10α
Rel. OH dist. C_4-C_5 bridge twist 30°	55	63	67	70	80	88	105	110	105
C_4-C_5 bridge twist 45°	55	70	60	59	75				
Shift order	1	2	3	4	5	6	X	7	8

Table 13 Coupling constants for 5-endo-protoadamantanol

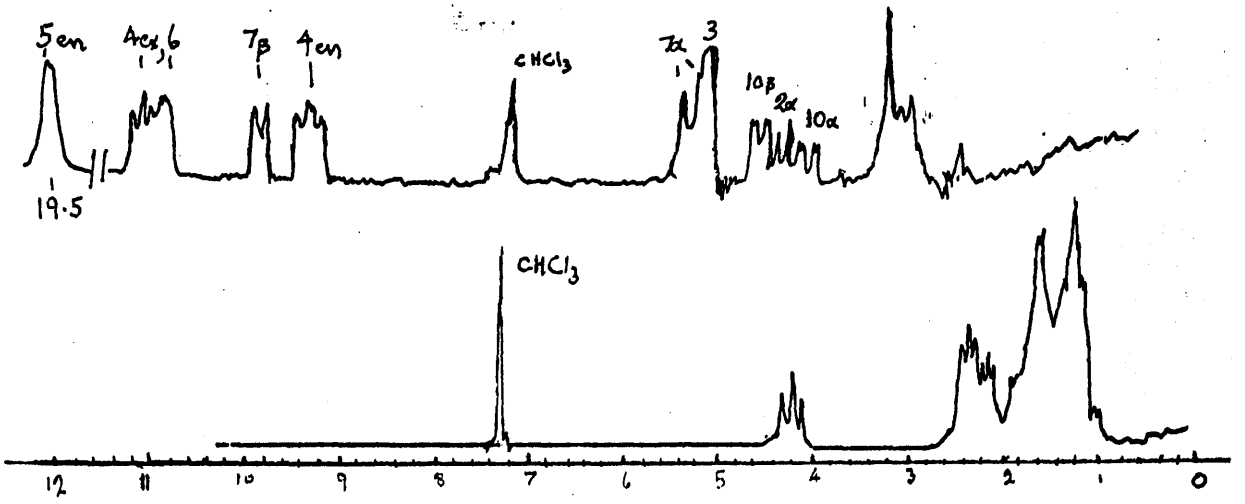
Protons	J Hz
2α-2β	12
2α3	< 2
3-4en	3
3-4ex	3
4ex-4en	16
4ex-5ex	8.5

Protons	J HZ.
4en-5ex	< 1
5ex-6	8
6-7α	4
6-10α	3.5
6-10β	2-3
7α-7β	13
10α-10β	14.5

FIG. 22



170



170
~~166~~ 0·4 M, Eu(d.p.m.)$_3$ 0·2 M in $CDCl_3$

Table 14 Shift - OH dist. correlation for 5-exo-protoadamantanol 170

Pr oton	5en	4ex	6	7β	4en	7α	10β	2α	3	10α	8
Rel. OH dist.	55	65	70	75	80	105	105	110	120	122	130
Shift order	1	2	3	4	5	6	8	9	7	10	

Table 15 Coupling constants for 5-exo-protoadamantanol 170

Protons	J Hz
2α-2β	12
2α-3	≤ 2
4ex-4en	13.5
4ex-5en	7.5
5en-6	≤ 2
6-10α	3.5
7α 7β	12
10α-10β	14

II6 cont. - RESULTS.

The Eu-shifted p.m.r. spectra of 4 exo-protoadamantanol 169 and 4 endo-protoamanantanol 167 appear in figures 19 and 20. Tables (8 and 9) and (10 and 11) give shift order vs. O - H distance (in arbitrary units) correlation and coupling constants observed for each of the alcohols 169 and 167.

The Eu-shifted p.m.r. spectrum of 5 endo - protoadamantanol 166 is shown in fig. 21. The shift/O - H distance correlation (table 12) is interesting in that, with the C4 - C5 bridge twisted at 30° the first five downfield peaks appear in the expected order ($\Delta\nu \propto R$) while when the bridge is twisted to 45° the peak order bears no relationship to O - H distance. This supports the data on vicinal coupling constants compiled below (p. 63) which suggests a C. 30° twist angle for the C4-C5 bridge.

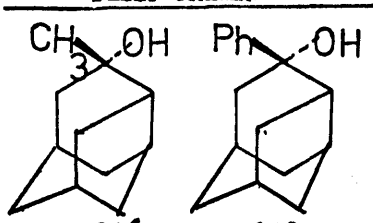
Table 13 lists coupling constants derived for this alcohol.

The Eu-shifted p.m.r. spectrum of 5 exo-protoadamantanol 170 is shown in fig. 22. The seven peaks at lowest field can be assigned unequivocally using double irradiation but assignments H - 10 β , H - 2 α and H - 10 α depend on comparison of peak shape and coupling constants observed with those observed for the same protons in the spectra of the other alcohols. (see figs. 19-22, tables 9,11,13,15).

Table 15 lists coupling constants observed. Table 14 lists O - H distance in the model with shift order observed. The apparent anomalous position of H3 resonance is probably a result of the normal downfield shift of methine relative to methylene hydrogen.

TABLE 15 B

PEAK ORDER

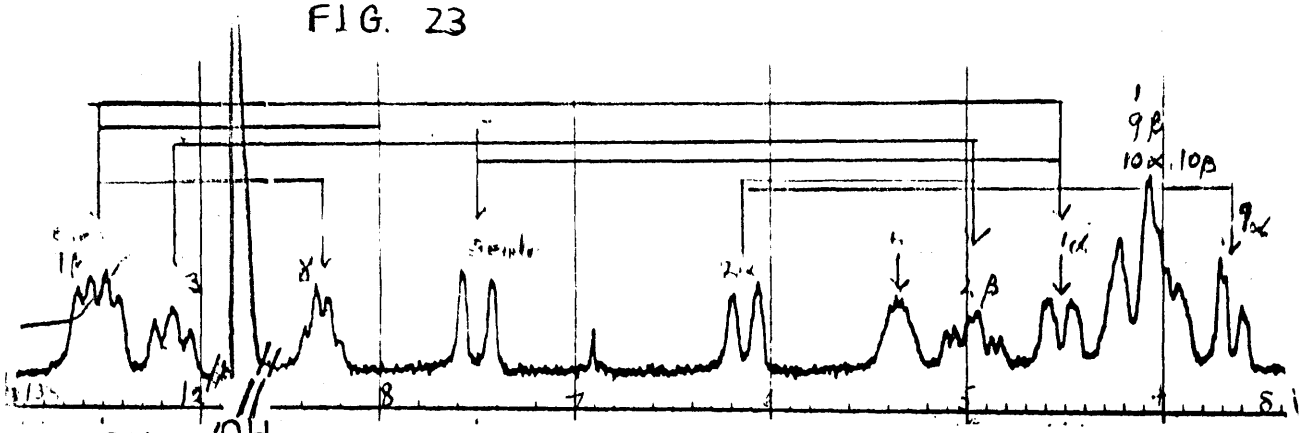


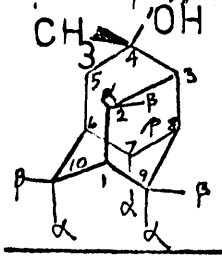
Proton	OH dist.	216	218
5ex	65	1	2'
7β	65		1
3	70	2	2'
8	85	3	3
5en	90	4	
6	105	6	
7α	105	8	
2α	110	5	
2β	120	7	
10α	135	9	
9α	135	10	
9β	140	9	
10β	145	9	
1	145	9	

TABLE 16

Proton	5en	3	2α	5ex	2β	10β	8	7β	6	1	7α	9β	10α	9α
Rel. OH dist	67	70	72	80	93	120	120	120	126	135	142	145	150	155
PEAK ORDER max $\sqrt{}$=1	1	3	2	4	6	7	5	8	7	8	8	8	8	9

FIG. 23

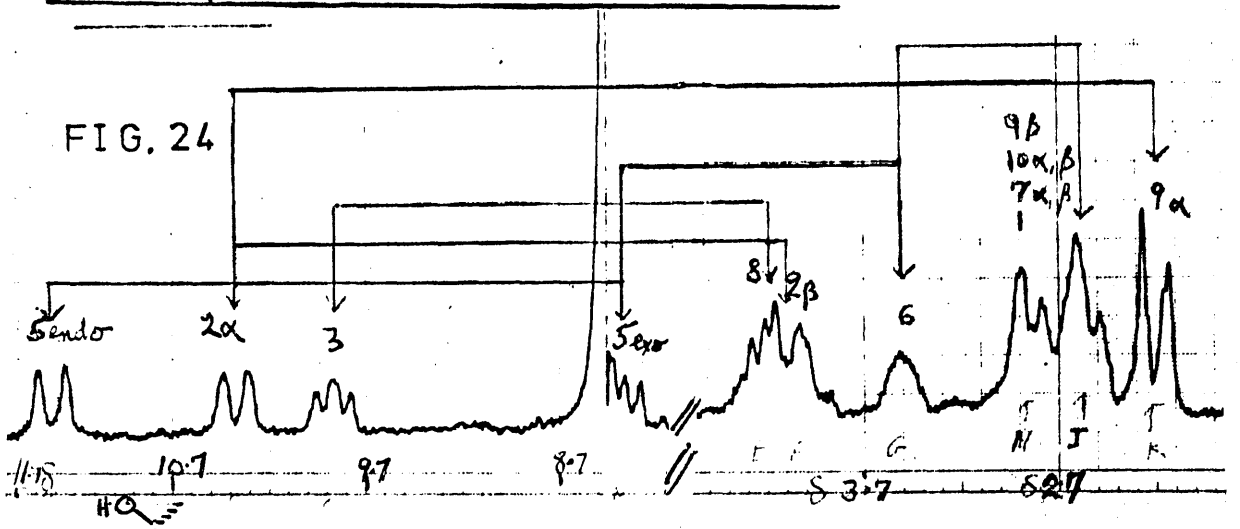




: Eu(dpm) -mole ratio 0·5

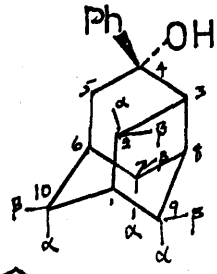
216

FIG. 24

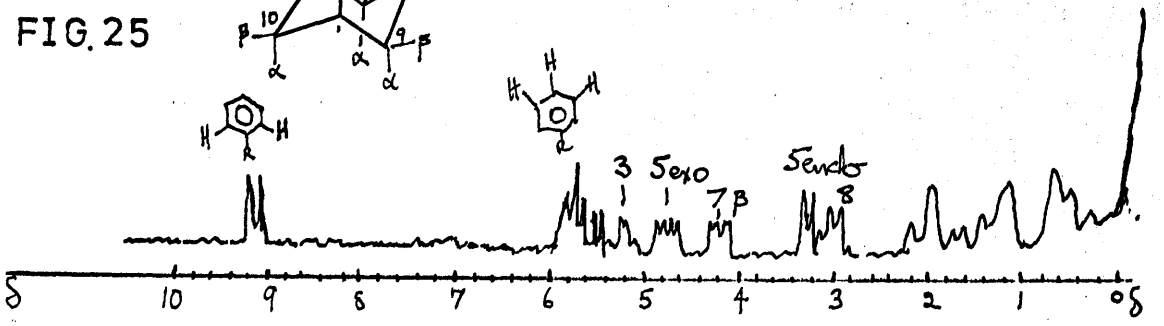


217

FIG. 25



218



The $Eu(d.p.m)_3$ shifted spectra of 4 endo-methylprotoadamantan - 4 exo - ol 216, 4 exo - methylprotoadamantan - 4 endo - ol 217 and 4 endo - phenylprotoadamantan - 4 exo - ol 218 are shown in figures 23, 24 and 25 respectively.

It should be noted that the stated configurations, though suspected on the grounds of solvolytic reactions, are based on the spectra appearing here (see p.62). The spectra were obtained and the peaks assigned by us in the manner described for the unsubstituted alcohols.

The methyl-alcohols 216 and 217 were supplied by Professor Schleyer, who, with co-workers at the University of Princeton, had prepared them by action of methyl-grignard on 4 - protoadamantanone. The phenyl-alcohol 218 was prepared by Dr. D Lenoir of the Organic Chemistry Institute of the University of Bonn by the action of phenyl-lithium on 4 - protoadamantanone. We thank Professor Schleyer and Dr. Lenoir for the opportunity of collaboration in this work.

Table 15B shows the correlation of induced shift with O - H distance for protons in the substituted exo-alcohols 216 and 218. The O - H distance values are in mm as shown in a scale Prentiss Hall model using a 30° twist angle for the C4 - C5 bridge.

It might be expected that endo-substitution might effect the C4 - C5 bridge conformation (fig.26) through increased 1,3 - interactions, however the observed coupling constants for 216 (J 5 exo - 6 = 8 and J 5 endo - 6 = 2 Hz.) suggest, when related to dihedral angle through the Karplus relationship, that the bridge twist remains at around 30°.

Table 16 shows peak order/O - H distance correlation for the endo - alcohol 217.

II.6 - DISCUSSION.

A. Configuration

It should be possible to determine the configuration of any protoadamantyl derivative capable of giving a lanthanide shifted spectrum from the data described above.

The configurations of the 4 - alcohols have been assigned on chemical evidence by others [67,69,71,78] and, along with the 5 - alcohols, by us on the basis of reduction of the corresponding epoxides 163 and 164 (p. 42). The above spectra confirm these assignments. The configurations of the 4-substituted alcohols 216, 217 and 218 however, were not established prior to this investigation and a simplified justification of the assignments should illustrate the method.

The protons referred to below can be distinguished by double irradiation and the peak shapes and coupling constants so derived can be related to those observed in other spectra and to those expected from the model.

The alcohol 216 can be seen (fig.23) to be 4-positional since both C5-protons (couplings with C6 - H make these identifiable) can be seen, while C4 protons are absent. The alcohol function can be seen to be exo - since the greatest downfield shift is shown by the 5 exo - and 7 β protons.

The alcohol 217, at the 4-position since both C5 - protons appear, is endo since the protons showing greatest downfield shift are those at C5 (endo) and C2 (α). In addition the C10 (β) - proton shows considerable downfield shift.

FIG. 28

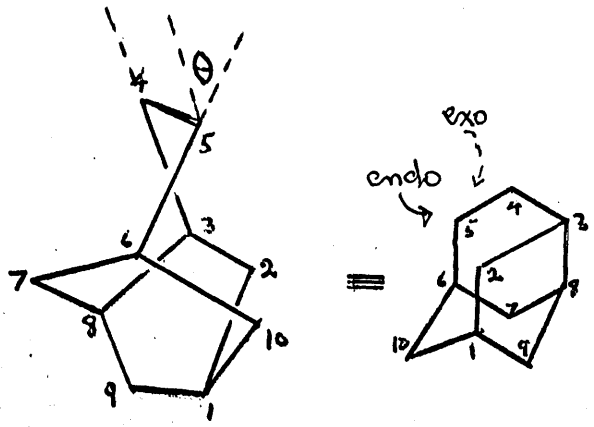
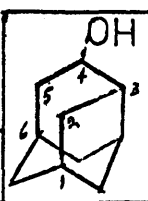
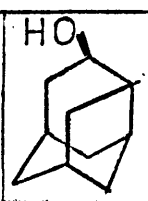
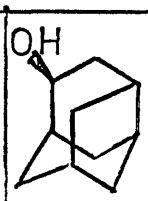
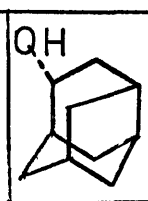


TABLE 17

	θ°obs.							
	A	B	C	———	$J_{obs.}$ Hz ———		———	θ calc.
3 -4en	60	50	75	3.5 *		3		55-60
3 - 4ex	65	72	45		3·5 *	3		55-60
4en-5 en	30	42	0	6·5 6·5*			6,6·5*	35-42
4en-5 ex	92	77	120	<2, <1 *		< 1		80-100
4ex-5 en	145	155	120		8·5, 8 *		7·5, 8*	140-156
4ex-5 ex	28	40	0		8, 8 *	8·5, 8 *		24-35
5en-6	90	100	62	< 2	< 2		< 2	80-100
5ex-6	32	20	55	8	8	8, 8 *		26-35

* unshifted spectra

A C_4-C_5 Bridge angle of 30°

B " " " " 40°

C " " " " 0°

The phenyl-substituted alcohol 218, 4-positional for the reasons above, is exo-, the protons showing greatest downfield shift being those at C7(β) and C5(exo -).

B. Conformation.

As can be seen from a model (see fig. 28), there exists in protoadamantane only one area of conformational mobility, the C4 - C5 bridge. As the twist angle (θ in fig.28) is altered all eight dihedral angles between protons at C6, C5, C4 and C3 alter.

Table 17 lists dihedral angles shown on a model as twist angle is altered from 0° through 30° to 40° and correlates these with the angles predicted by application of the Karplus relationship to the observed coupling constants for the unsubstituted protoadamantanols. The fit appears quite good for a twist angle of 30° as was suggested from the shift/O - H distance correlation for the 5-endo alcohol 166 (see p.60 , table 12). A similar conclusion has been reached by Schleyer and co-workers based on n.m.r. spectra of 4 exo (169) and 4 endo (167) alcohols and of protoadamantane - 4,5 - diols.[103]

There would appear (table 17) to be little variation in coupling constant values for shifted and unshifted spectra. Thus, complex formation would appear to have little steric effect in this case.

It is important that only average values are considered. Coupling constants for many of the protons show slight variation from one compound to another but this is within the range of substituent orientation effects [123, 137].

C Long Range Coupling

Though the observation of such coupling was made more difficult by the peak broadening which accompanies lanthanide induced shift, coupling was observed between the protons (see fig. 29) H_3 - H_5 exo, H_3 - H_5 endo, H_5 endo - $H_{10\alpha}$, H_5 exo - $H_{10\alpha}$ and $H_{2\alpha}$ - $H_{9\alpha}$ principally in the spectra of alcohols 167, 216 and 217. In all except the last, coupling was not accurately determinable (all < 2Hz.) In the case of the "W" coupling $H_{2\alpha}$ - $H_{9\alpha}$ the constant observed (in 167, 216 and 217) was 3Hz.

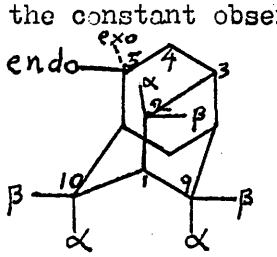


fig. 29

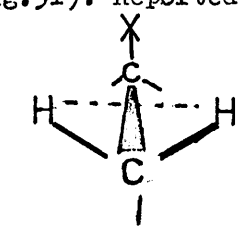
D Geminal Coupling

Theory of geminal coupling has been established for some time [137] and some advances have been made in relating theory to observed data.[123,137] The correlation is sketchy since observation of geminal coupling has been limited to methylene groups adjacent to anisotropy inducing or strongly electronegative functional groups both of which are likely to affect the sign and/or magnitude of the coupling observed. Using lanthanide shift reagents it is possible to observe methylene groups remote from functional groups.

(i) β -Electronegative Substituent Effects:-[123,137]

It has been suggested that β - electronegative substituents should cause algebraic increase in geminal coupling if the substituent is perpendicular to the H - H axis (fig.30) and algebraic decrease if parallel (fig.31). Reported data[123] on this is, however, scarce.

30



31

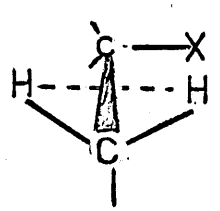
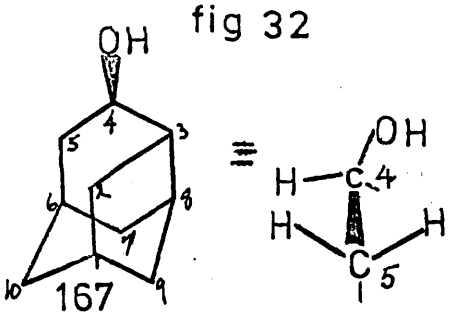
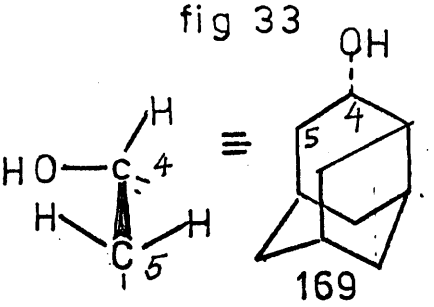


fig 32



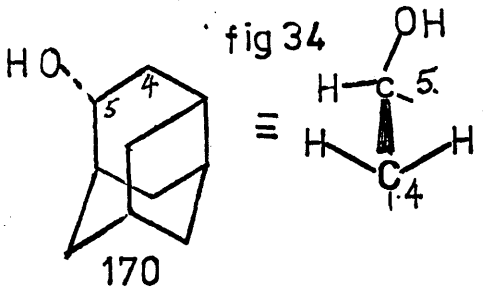
167

fig 33



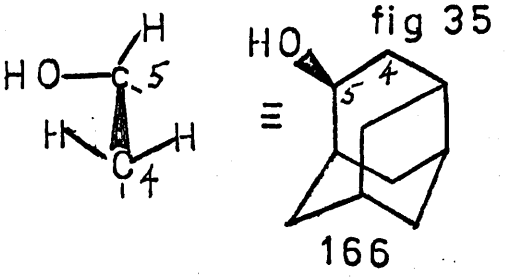
169

fig 34



170

fig 35



166

TABLE 18 Av. values J_{gem} for alcohols 166,167,169,170.

Protons at C :-	2	4	5	7	9	10
J_{gem} av.	12·4	14·8	14·5	12·5	10	14

TABLE *(19

Bond angle distortion order (increasing Θ)	Average J_{gem} obs.	$\nu_{max.}$ (cm^{-1}) for corr. ketone
9	10	1748, 1740 [140]
2	12·4	1743 [140]
7	12·5	—
10	14	1712, 1694 [122]
5	14·5	1727 [100]
4	14·8	1723, 1714 [70] 1729, 1719 [78]

In the case of 4 exo - (169) and 4 endo - (167) protoadamantanols (see fig. 32 and 33), the former, if the geminal coupling constants are negative as expected,[122,137] should have the larger coupling constant. This is observed (J(C5) in 4 exo (169) = 15 Hz. ; J(C5) in 4 endo - (167) = 14 Hz.)

A similar argument (see fig. 34 and 35) suggest that the C4 geminal coupling constant for 5 endo - alcohol 166 (J(obs.) = 14 Hz.) should be more negative than that for 5 exo-alcohol 170 (J(obs.) = 13.5 Hz.)

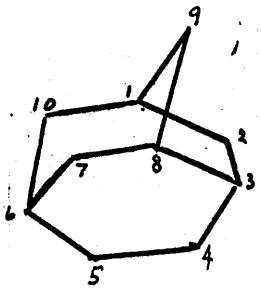
(ii) Carbon - Carbon Bond Angle

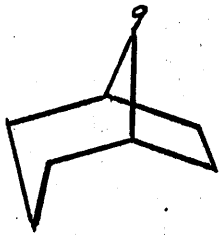
Theory and observation[123,137] show that in general a decrease in geminal H-C-H angle produces an increase in magnitude of observed geminal coupling while increase of H-C-H angle causes the opposite effect. Hence, observed coupling can give an indication of H-C-H angle and, since this angle is inversely related to internal carbon - carbon bond angle, can give information on the latter.

Correlation curves of angle against J have been produced but these are often useless since they rely on data from protons adjacent to functional groups which can greatly effect the coupling observed.[123] For example oxirane couplings are often included though they, unlike the general case, are positive and β -electronegative group orientation is seldom taken into account.

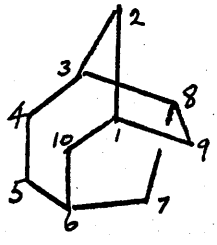
Table 18 lists the average values of the geminal coupling constants derived from the four unsubstituted protoadamantanols. Table 19 correlates these couplings with angle distortion observed in flexible scale models (Prentiss Hall) and with the infra red absorbtion wave number for the corresponding ketones where known. Table 19 is best consulted in conjunction with figures 36 - 39 which show the centres under discussion more clearly.

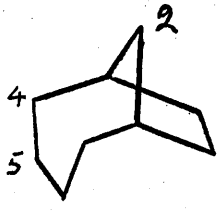
36


9
10
1
2
7
8
3
6
4
5

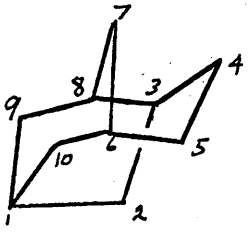

9

37


2
3
8
4
10
1
9
5
7
6


2
4
5

38


7
8
3
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9
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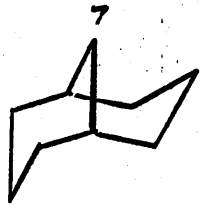
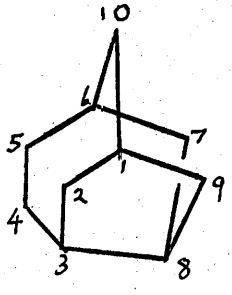
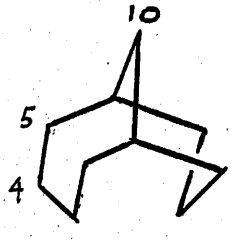
6
5
1
2


7

39


10
6
5
7
1
2
9
4
3
8


10
5
4

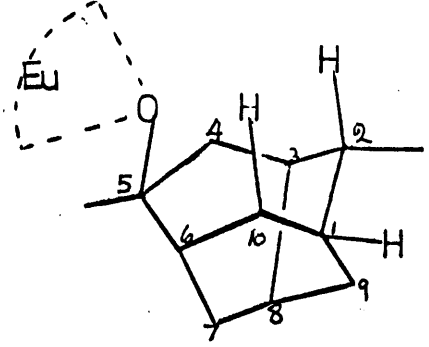
For positions 9, 2, 7 and 10, where the methylene is between two methine positions and remote from the alcohol function the correlation is good and increase in magnitude of J accompanies increasing carbon-carbon angle.

For positions 4 and 5 both on the same two carbon bridge and adjacent to the alcohol function the situation is not so clear. Considering hydroxyl orientation for both epimeric pairs of alcohols, there is a net O-H parallel to H-H-axis effect which will result in an average coupling constant more negative than that dictated by strain alone, however this would appear to a small effect (see p. 64 , 65)

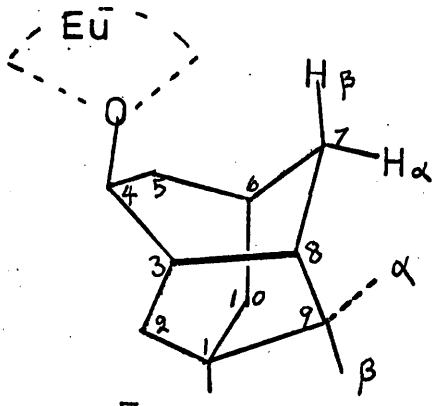
One cannot correlate the angle strain and i.r. date on corresponding ketones (see table 19) from the single carbon bridge series (C9, C2, C7 and C10) with that from the two carbon bridge examples (C4,C5), since one cannot assess the effect on the inserted carbonyl of the adjacent methylene, in the latter two cases. The carbonyl i.r. data and the coupling constant data (table 19) do agree in that the C4 angle appears to be larger than the C5 angle in the protoadamantyl skeleton.

It would seem that observation of geminal coupling with the aid of lanthanide shift reagents could be useful in investigation of angle strain. The strength of the method is that it relates directly to unsubstituted, Sp^3 hybridised carbon atoms. It also avoids the problem, encountered using infra-red absorbtion data from ketones, of multiple peaks (see table 19). Its weakness is that the effect is small and may be swamped by other factors effecting coupling.

fig 40



41



42

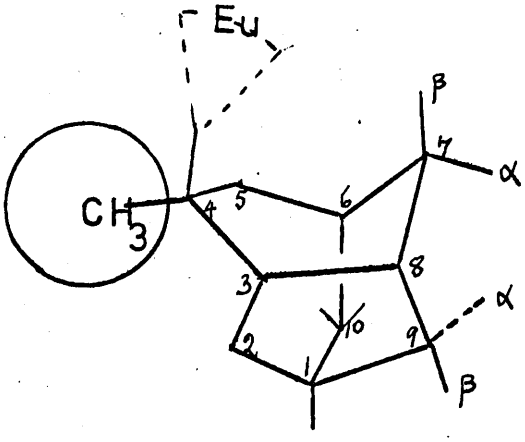
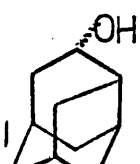
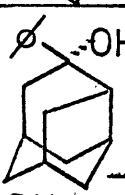


TABLE 20

PROTON	4 en	5 ex	7 β	3	8	5 en	6	7 α	2 α	2 β	10 α	9 α	9 β	10 β	1
REL. O-H DIST.	55	65		70	85	90	105		110	120	135			145	
SHIFT ORD. $\lvert\Delta\nu_{max}\rvert$ 	1	2	3	4	5	6	7	8		9	10				
	X	2′	1	2′	3										
	X	1		2	3	4	6	8	5	7	9′	10	9		

Steric Effects on Europium Position

Throughout the spectra discussed above there occurs scattered evidence that the use of O-H distance to predict relative n.m.r. shift is not satisfactory.

In the case of 5 endo-protoadamantanol 166 (see table 12, p.60), though the six protons at lowest field have shift order consistent with O-H distance order, this latter order suggests that the proton at C1 should appear downfield of those at C10 (α) and C3. It does not, indeed its resonance position, from double irradiation experiment, appears to be in the peak at highest field. This is presumable because the extreme 1,3 - interactions (see fig.40)will result in exclusion of europium complex from the endo - face of the molecule thus increasing Eu - H_1 distance.

For 4 exo - protoadamantanol 169, n.m.r. shift order correlates well with O-H distance order (table 20) but this is not the case with the 4-methyl-(216) or 4-phenyl-(218) substituted alcohols (table 20). In the 4-methyl-alcohol 216 protons at positions 7α , 1, 9 β , 10 α and 10 β (fig. 41 and 42) show very little change in chemical shift on addition of europium complex while that at position 9α shows a small upfield shift. In both 216 and 218 the proton - 7 β appears at relatively low field.

The above may be explained with reference to figures 41 and 42 showing how steric effects of the methyl (or phenyl) should cause the average position of the europium to be much closer to the proton at 7 β (causing downfield shift) but increase the O-Eu-H angle (θ) for protons at 7α , 1, 9α , 9 β , 10α and 10 β to about 50°

Memo p. 57 $$\frac{\Delta V}{V_o} = A \frac{3\cos^2\theta - 1}{r^3}$$

i.e. effect $\longrightarrow$ 0 as $\theta \longrightarrow$ 54°

In the case of 4 exo-methyl-protoadamantan - 4 endo - ol 217, shift order again correlates poorly with O-H distance order.

As can be seen from the spectra of the substituted alcohols (p. 61) there is an overall lessening of europium shift effect with substitution. Such a diminution in hindered alcohols has recently been reported by Demarco and co-workers.[141] It is not clear whether this is totally due to increased O-Eu bondlength or whether, as we think may be possible at least partly, to restricted rotation about the oxygen causing Eu-O time average distance to tend to Eu-O bond length (see fig. 43,44).

fig. 43. free rotation

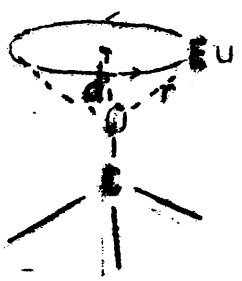
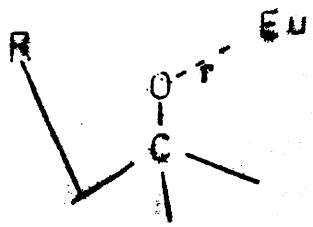


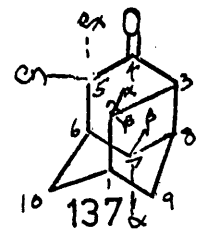
fig. 44 restricted rotation



$$d = r \sin 30^\circ$$

$$r = 2d$$

fig 45



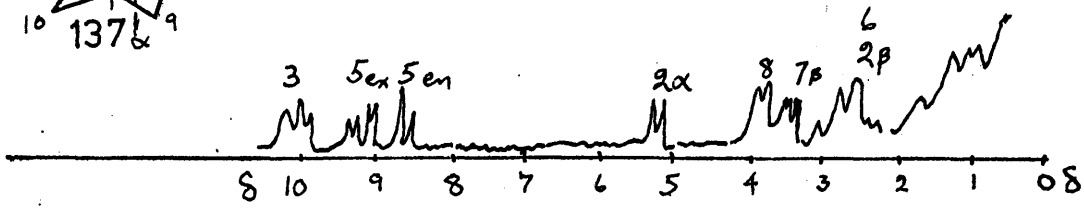
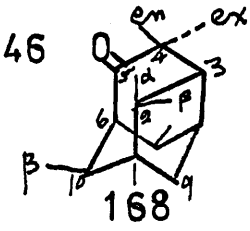


fig 46



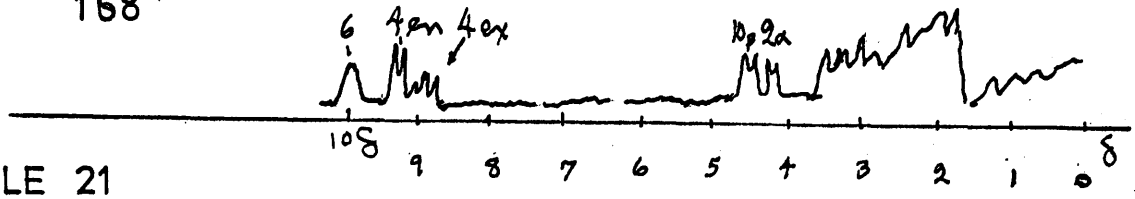
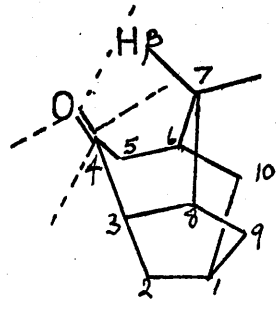
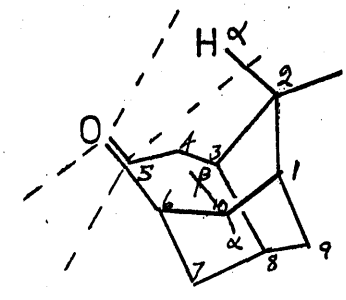


TABLE 21

PROTON	3	5 exo	5en.	7β	2α	8	6	4 en	4 ex	2α	10 β
REL. O-H DIST. 5-ONE							74	74	83.5	87	87
REL. O-H DIST. 4-ONE	72	74	85	88	98	114					
SHIFT ORDER 5-ONE							1	2	3	5	4
SHIFT ORDER 4-ONE	1	2	3	6	4	5					



47



48

II.6 cont. Ketones

The p.m.r. spectra, obtained with the aid of tris(dipivaloyl-methanato)-europium III, of protoadamantan - 4one 137 and protoadamantan-5-one 168 are shown in figures 45 and 46. Though the ratio of shift reagent to substrate was higher than that obtainable for the corresponding alcohols, the induced shifts are no larger. This presumably reflects the less efficient complexing of lanthanide with carbonyl oxygen lone pairs.

Peaks at lowest field were initially assumed as those arising from protons adjacent to the ketone function. Further differentiation was made by use of double irradiation. All peak shapes were compared, where possible, with shapes revealed in the spectra of the alcohols above. The shape of the peak from the proton at C3 in 4-protoadamantanone has already been described by Lunn.[77]

The shift order is generally that predicted by O-H distance order as measured on models (see table 21) however the 7 β -proton in 4-protoadamantanone and to a lesser extent the 2 α -proton in 5-protoadamantanone show at relatively upfield positions. This may be a result of their being in the shielding cone of the carbonyl in each case (see fig. 47 and 48).

A warning should be made on the use of shift reagents with ketones. The n.m.r. spectrum obtained using $<$ 0.5 mole ratio of reagent to ketone 168 showed at lowest field a broad singlet (1H) and a sharp singlet (2H). Increasing the mole ratio of reagent caused downfield shift and broadening of these peaks and only at mole ratios of 0.6 - 0.75 (the maximum obtainable) was the form shown in figure 46 obtained.

PART II EXPERIMENTAL

The following instruments were used: i.r., Perkin-Elmer 225 and 257; n.m.r., Varian T 60 and H A 100; mass spectrometry, A.E.I. MS9; g.l.c., Perkin-Elmer F11; g.c.m.s., LKB 9000A. Solvents for spectroscopy: i.r., CCl_4; n.m.r., $CDCl_3$ with internal tetramethylsilane. Merck Kieselgel G was used for t.l.c. and Woelm alumina, deactivated to the appropriate Brockmann grade, for column chromatography. All melting points recorded are uncorrected.

Adamantane 133 and Adamantanone were purchased from Ralph N. Emanuel Ltd.

2-Adamantanol 128, prepared by lithium aluminium hydride reduction of 2-adamantanone in the usual[72] manner had m.p. 295-298°C (lit.[72] 296 - 299°)

2-Adamantylacetate 129

2-Adamantanol (207 mg) with sodium acetate (0.3g) in acetic anhydride (10ml) was refluxed for 12 hr. Preparative t.l.c. gave 197mg (75%) of a colourless oil, homogeneous by t.l.c. and g.l.c. (1% Ap-L and 5% Q F 1); i.r.; 1730 cm^{-1}; n.m.r., δ 4.92,(mult.,1H), 2.2 - 1.4,(m., 17H) , 2.08 (singlet).

Reduction of the acetate using excess lithium aluminium hydride in refluxing ether for 4 hours gave a quantitative yield of 2-adamantanol m.p. 295 - 297°C.

2-Adamantyl-S-methyl-xanthate 130

2-Adamantanol (0.61g, 4.02 m. mole) was added in hot dry benzene (10 ml) to a suspension of sodium hydride (0.12g, 5m. mole) in 2 ml of the same solvent. The mixture was stirred at reflux under a static/

static nitrogen atmosphere for 6 hr. Carbon disulphide (5 ml.) was added to the cooled, gelatinous mass and the resulting red mixture stirred at 50°C for 4 hr. The addition of methyl iodide (6ml) caused rapid discharge of the red colour but reflux (40 - 50°C) and stirring were maintained for 14 hr. The cooled mixture was filtered through celite, the flask and celite washed with benzene, and the total filtrate evaporated to dryness yielding 0.885 g (91%) of yellow crystalline material m.p. 104 - 108°C. A sample recrystallised from ether/methanol (1/2) gave white needles m.p. 108 - 109.5°C.

	Found	C 59.3%	H 7.3%
$C_{12}H_{18}OS_2$	Requires	C 59.5%	H 7.5%

n.m.r. : δ 5.7, mult., 1H ; δ 2.6, s, 3H; δ 2.4 - 1.6, m, 14H

i.r. : ν_{max} 1222, 1212, 1050, 959, 918 cm^{-1}

2-Adamantyl-p-toluene sulphonate 131 was prepared in the usual[74] manner by treatment of 2-adamantanol (2.03g, 13.4m.mole) with p-toluenesulphonyl chloride (3.4g 17.5 m.mole) in pyridine at room temperature for 3 days, which gave (from methanol) white plates (3.4g, 88%) melting 79 - 82°C. Recrystallisation gave material mp. 82-83°C (lit[74] 82.7-83.7).

2-Adamantylmethanesulphonate 132.

2-Adamantanol (6g, 0.04 mole) was treated with methanesulphonyl chloride (5.73g, 0.05 mole) in pyridine (20ml) for 3 days at room temperature. The mixture was poured into ice-water (150 ml.). The solid, filtered off and recrystallised twice from methanol, gave 8.3g (90%) of white plates m.p. 67 - 68°C.

	Found	C 57.3%	H 7.7%
$C_{11}H_{18}O_3S$	Requires	C 57.4%	H 7.9%

n.m.r. : δ 4.76, mult., 1H ; δ 2.92, s, 3H ; δ 2.3 - 1.3, m, 14H

1-Bromo-adamantane 134

A modification of the method of Stetter[76] was used. Adamantane (10g) was refluxed with excess bromine (15 ml) for 5 hours. The resulting mixture, taken up in ether, was treated sequentially with aq. sodium bisulphite, aq. sodium bicarbonate and brine giving, after drying ($MgSO_4$) and evaporation, 18.6g (85%) of pale yellow crystals melting 112-115°C. A sample recrystallised from methanol melted at 118 - 120°C (lit.[76] 119.5 - 120°C).

1-Adamantanol 135 was prepared in 65% yield by treatment of 1-bromo-adamantane 134 with hydrochloric acid in D.M.F. according to the method of Geluk and Schlatmann[72]. M.p. found was 284 - 286°C (lit[72] 283-285°)

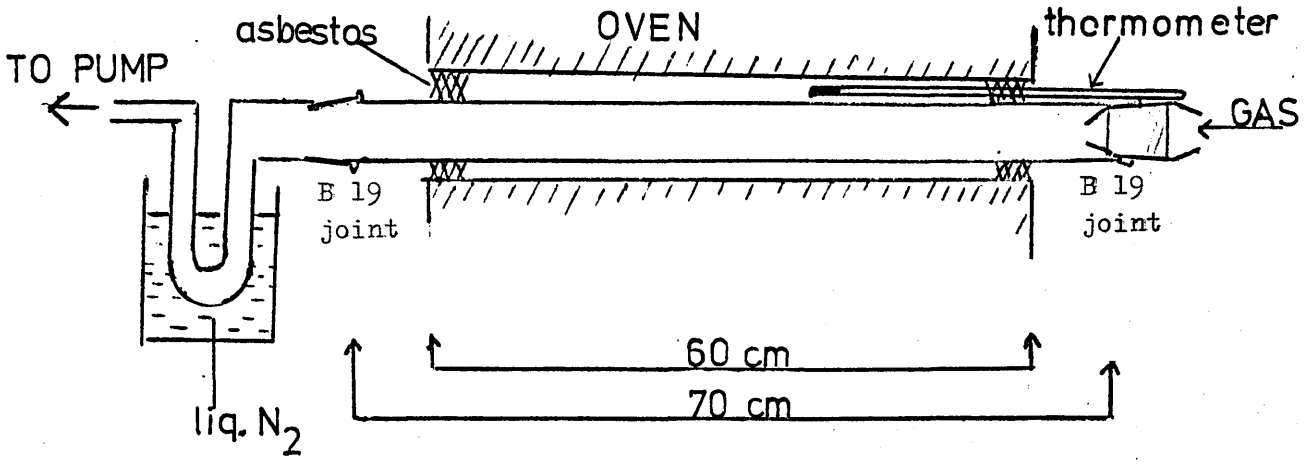
4-Protoadamantanone 137

A modification of the methods of Black and Gill[69] and Lunn[77] was used. Adamantan-1-ol (11g), lead tetra-acetate (36g) and iodine (21g) were stirred in dry benzene at 60° for 2 hours. The mixture, cooled, filtered, washed with aq. sodium bisulphite, water and aq. sodium bicarbonate gave, after drying (Na_2SO_4) and evaporation, a semi-crystalline mass, which on t.l.c. analysis showed substantial amounts of starting alcohol. The above treatment, repeated on the crude material using half quantities of reagents, gave 19g (90%) of crude endo-3-iodomethyl - (3,3,1) - bicyclononan-7-one

(i.r. (CCl_4) 1708 cm^{-1} ; n.m.r. δ 2.95,(2H, d, J = 6.3 Hz); 1.40 - 2.60,(11H, mult.); 0.9,(2H, t.)[69,77])

The crude iodoketone was stirred in pyridine (25 ml) at 55°C for 4 hr., cooled and poured into ice-water. The resulting oil, in ether, was washed with dil. HCl, and water and dried ($MgSO_4$). Removal of solvent gave a brown resin (9g) which, on chromatography (300 g Grade III alumina), gave a white crystalline material (4.9g, 45% yield overall) which melted at 205 - 209°C. Sublimation gave material/

DIAG. 49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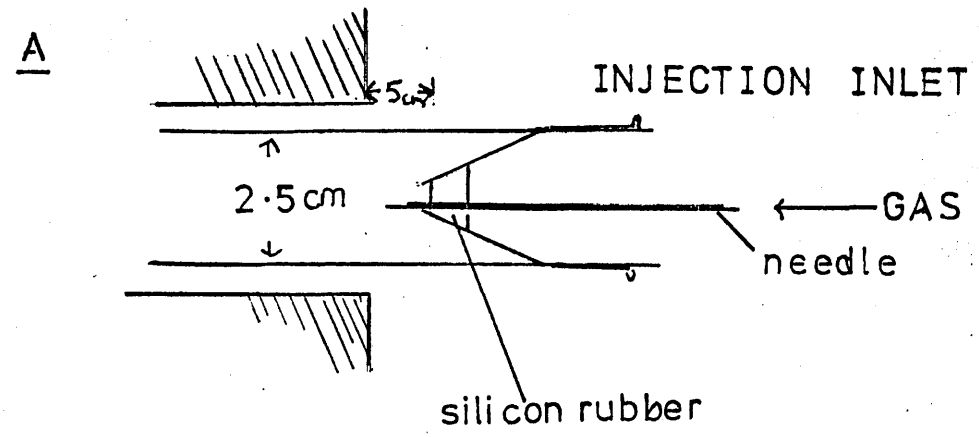
OVEN
thermometer
TO PUMP
GAS
B 19
joint
B 19
joint
60 cm
70 cm
liq. N_2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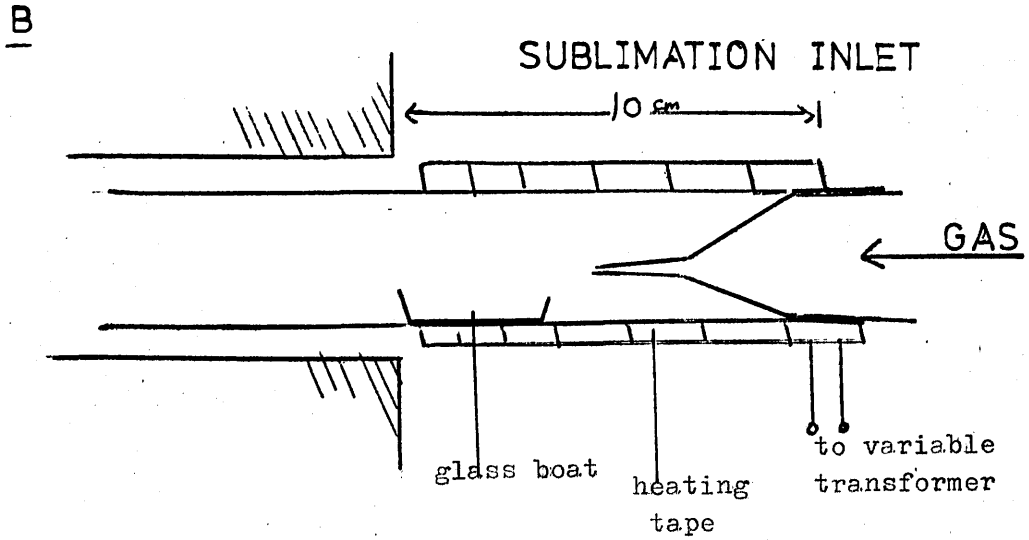
2·5 cm
GAS
needle
silicon rubber


B
SUBLIMATION INLET
10 cm
GAS
glass boat
heating
tape
to variable
transformer

material m.p. 210 - 212°C (lit[69] 212 - 214°), i.r. (CCl_4) 1725, 1715 cm^{-1} (1724, 1713[69])

Protoadamantene 137 from protoadamantanols[69]

Protoadamantan-4-one was treated with lithium aluminium hydride to give a mixture of protoadamantanols (2/1 endo to exo-).[69,78]

The crude alcohol mixture (100 mg) was treated in refluxing benzene (10 ml) under nitrogen with sodium hydride (40 mg) for 5 hours. Carbon disulphide (1ml) was added through a septum and the red solution stirred at 30°C for 3 hours. Methyl iodide (2ml) was then added and stirring continued for 14 hours. The cooled mixture was filtered through celite and evaporated to dryness giving 300 mg of yellow crystalline material.

The crude xanthate in ether (1ml) was injected in 0.2 ml portions into the pyrolysis system described below (see diag. 49A below) maintained at 500°C and under a helium flow at 0.5 mm Hg. The pyrolysate collected at -196°C was chromatographed in pentane through a column of Grade III alumina (2g.). The first fraction (10 ml) was retained and used for g.c.m.s. analysis (1% ApL, 80°) showing a major peak (90%) Retention Index 1100, M^+ 134 and a minor (10%) R.I. 1108, M^+ 136 (corresponds to adamantane).

Pyrolysis of 2-adamantyl esters

The apparatus used (shown in diagram 49) consisted of an electrically heated silica tube (70 X 2.5 cm) with provision for either injection (method A see diag. 49A) or sublimation (method B see diag. 49B). The heated part of the tube (60 cm) was lightly packed with glass wool for most runs. Injection was from a glass syringe through a 6 inch needle directly into the glass wool in the hot zone. Pyrolyses were carried out in a slow stream of He gas at 0.5 - 0.05 mm. Hg. and at temperatures from 460° to 560°. The initial stage of work up was the same in all cases unless otherwise stated below. The tube exit was heated to drive/

drive over any product condensed there. The u-tube was disconnected, fitted with drying tubes (SiO_2), brought to room temperature and washed out with isopentane (c. 10 ml). This solution was passed through a plug (c. 3g) of grade I basic alumina and concentrated by removal of solvent at atmospheric pressure. This material, and a subsequent ether wash of the trap treated in the same way, were analysed by t.l.c. and g.l.c.

Pyrolysis of 2-Adamantylacetate 129

The acetate 129 (100 mg) injected into the pyrolysis tube as an ethereal soln. (50%) at 380°C and 0.5 mm. Hg survived unchanged as determined by g.l.c. and t.l.c. (> 90% recovery). Repeated attempts at 500° and 560°C showed no change.

Pyrolysis of 2-Adamantylxanthate 130

The xanthate 130 (150 mg) was injected in 0.1 ml portions as an ethereal solution (C.10%) into the tube at 500°C and 0.5 mm.Hg. The product, after initial work up as usual, showed on t.l.c. (5% ethyl acetate/petrol) a minor spot Rf. 0.8, a major spot Rf0.4 (corresponds to xanthate 130) and a major spot Rf.0.25 and on g.l.c. (1% Ap-L programmed 80°/10 min; 80 - 180° at 8°/ min) protoadamantene (2%, t_R 5.8 min), adamantane (5%, t_R 6.4 min), 2, 4-dehydroadamantane (2%, t_R 7.2 min) 2-adamantyl xanthate (48% 23.6 min) and a fifth product (43%, t_R 27.4 min).

The above pyrolysis repeated at 550°C and 0.5 mm Hg gave the same peaks in the respective ratios 3%, 1%, 3%, 48% and 45%. The fifth component, separated by preparative t.l.c. (25% ethylacetate/petrol), was a clear oil, M^+ 242, ν_{max} 1649 and 870 cm^{-1}, typical of thiolo-carbonate[80].

Pyrolysis of 2-Adamantyl-p-toluene sulphonate 131

A Portions of sulphonate 131 (20 mg) in ether (0.2 ml) were injected at a variety of temperatures and pressures. The extent of sulphonate/

sulphonate conversion was judged approximately by t.l.c. and the composition of the hydrocarbon fraction analysed by g.l.c. (2m., 1% Ap - L, 80°). Retention indices and molecular ions (M^+ by g.c.m.s.) of authentic (subsequently isolated and characterised) hydrocarbons were protoadamantene (1100, M^+ 134), adamantane (1108, M^+ 136) and 2, 4 - dehydroadamantane (1126 M^+ 134). These were detected in the pyrolysis product in varying amounts (see table 6 p.28). A fourth peak ret. index 1085, M^+ 134 appearing (< 2%) in most runs was not identified. The mass spectra of all hydrocarbons of M^+134 were indistinguishable.

B The sulphonate 131 (100 mg) was placed in a silica boat in the pyrolysis system set up for sublimation (diag. 49B) and the tube pressure and temperature were stabilised at 550° and 0.5 mm Hg. The inlet was then heated by means of heating tape supplied through a variable transformer. Conditions were used which on prior investigation had achieved a maximum temperature of 150° over 15 min. After 30 min. the pressure was brought to atmospheric and the pyrolysate treated in the usual way. Though material from the trap showed (t.l.c.) absence of tosylate, an ether wash of of the pyrolysis tube gave 10 mg. of tosylate. The above process was repeated at 520°C. The composition of the hydrocarbon fractions are recorded on table 6 (p.28).

C The tosylate 131 (30 mg) was placed in a silica boat at the inlet of the pyrolysis tube as set up for injection (diag.49A) at 540°C and 0.5 mm Hg. The tube was then pushed into the furnace till only the inlet holding the septum projected. Material passed rapidly through the tube and was collected and worked up as before. Analysis by g.l.c. (1% Ap - L) showed adamantane as the major (80%) volatile product and t.l.c. showed that conversion was low (c. 30%).

Pyrolysis of 2-Adamantylmethanesulphonate 132

(i) Mesylate 132 (150 mg) was pyrolised using apparatus as in diagram 49B at 520°C and 0.3 mm Hg. Sample introduction by sublimation was carried out as described above for the tosylate 131. Collection and work up as before gave 35 mg (40% of theory) of a hydrocarbon mixture showing the product ratios listed in table 6 (p.28).

(ii) The standard apparatus (diag. 49B) was used however the exit end of the tube and the glass wool within were coated with sodium carbonate. This was applied as a slurry, water being removed by rotating the packed tube in a bunsen flame and leaving the tube in the furnace at 520° for at least 3 hours before use. The mesylate 132 (1.04 g) was then sublimed into the tube and pyrolised at 520° and 0.3 mm Hg in the manner described above for mesylate 132 and tosylate 131. After 20 min. the material collected in the usual manner was passed through an alumina plug (10g, grade III) being eluted with isopentane (50 ml). Removal of solvent through a vigreux column at 45 - 50°C gave white crystalline material (0.55 g, 91% of theory) consisting of (g.l.c.) protoadamantene (40%), 2,4 - dehydro-adamantane (59%) and adamantane (1%).

The above process was repeated on a 2.2 g scale at 550°C and 0.05 mm Hg. In this case sublimation was made more rapid. Prior investigation showed conditions used gave maximum inlet temperature of 220° in 15 min. Higher yield (95%) and lower adamantane contamination ($<$ 10%) were achieved (see table 6 p. 28.)

Glass wool packing

Four pyrolysis runs were made on mesylate 132 using sublimation sample introduction as above in the tube coated at its exit end with sodium carbonate but without glass wool packing. Temperatures and pressures used were in the range 510 - 530°C and 0.5 - 0.3 mm Hg.

Sample sizes were 20 mg, 100 mg, 250 mg and 730 mg approximately. Protoadamantene and 2,4 - dehydroadamantane were produced in similar amounts in each case (40% and 60% ± 5%). Conversion (as judged by t.l.c.) was quantitative for the smallest sample but was progressively lower for the remainder.

Isolation and Characterisation of Protoadamantene 127 and 2,4 - Dehydro-adamantane 126.

The hydrocarbon mixture (1.28g) from pyrolysis was chromatographed on 15% silver nitrate/alumina (50g). The first fraction (100 ml isopentane) gave, on removal of solvent through a vigreux column at 50°C and 760 mm Hg, 2,4 - dehydroadamantane 126 (730 mg, 57%) as a white crystalline solid m.p. 196 - 199° (after sublimation mp. 198 - 202, reported[68] 202.5 - 203.5°C). Combined g.l.c./mass spectroscopy showed; adamantane (1.5% retention index 1108, M^+ 136 and dehydroadamantane (98.5%) r.i. 1126, M^+ 134.

i.r. (CCl_4) 2030 w, 2960 s, 2935, 2855, 1422, 1032 cm^{-1}

n.m.r. (100 MHz, CCl_4) series of multiplets δ 2.5 - 0.8.

The second fraction (100 ml ether) gave, on solvent removal as before, protoadamantene 127 (475 mg. 37%) as white crystals m.p. 179 - 180 (after sublimation 180 - 182°, reported[69] 183 - 185°). Combined g.l.c./m.s showed unknown peak (< 0.5%) retention index 1085, M^+ 134 and protoadamantene (> 99.5%) r.i. 1100, M^+ 134.

i.r. (CCl_4) 3035 m, 2948 s, 2928 s, 2952 s, 1635 w 1452 m, 693 s cm^{-1}

n.m.r. (100 MHz, CCl_4) δ 6.13, (2H, m); 2.8 - 1.2, (12H, m).

O-Deuterio-methanesulphonic acid

Methanesulphonyl chloride (11.4g, 0.1 mole) and D_2O (3g, 0.15 mole) were stirred at 100° under a flow of dry nitrogen for 12 hours, during which time HCl was given off. Excess water and HCl were distilled out at 70° and 0.5 mm Hg and the residue azeotroped (twice) with dry benzene. A drop of residue then showed no precipitate when added to silver nitrate in aqueous acetone. A neat sample showed n.m.r. absorbtions at δ 11.15, s, integrates as 1H, and δ 3.28, s, integrates as 39H, similarly a sample of CH_3SO_3H (ex. B.D.H. Ltd) showed δ 11.07, (s, 1.1 H) and δ 3.17, (s, 3H). Both peak positions varied when water was added.

To 3.23g (33 m mole) of the acid prepared as above was added 153mg (3.3 mole) of anhydrous ethanol. Integrations of n.m.r. signals from methyl triplet (δ 1.4) and singlet (δ 3.2) were in the ratio 1/10. This should be the case only if the acid was pure. (> 90%).

Treatment of protoadamantene 127 with O-deuterio-methanesulphonic acid.

Protoadamantene (80 mg) was suspended in the acid (5 ml), prepared as above, and stirred at room temperature. The mixture became homogeneous after 45 min and was stirred for a further $3\frac{1}{2}$ hours. Water (10 ml) was added, the mixture extracted with ether and the ether washed with water, aq. sodium bicarbonate and brine before drying (Na_2SO_4). Removal of solvent and recrystallisation from petrol gave material (120 mg, 78%) which had m.p. 64 - 66°C. When mixed with authentic 2-adamantyl mesylate 132 the m.p. was 65 - 66°C.

Mass spectrometry showed a parent ion (M^+231) too weak for accurate deuterium analysis which was achieved from the $C_{10}H_{14}D^+$ peak ($\frac{m}{e}$ 135) showing d_0 14.3%, d_1 75.5% and d_2 10.1%

$\frac{m}{e}$	134	135	136
undeuterated material	45	14.5	6.2%
deuterated material	8.5	47.5	22.5%

The n.m.r. spectrum obtained with the aid of $Eu(f.o.d.)_3$ is discussed in the foregoing text (p.38).

4 - Oxahomoadamantan - 5 - one 210

To adamantanone (6g) in $CHCl_3$ (100 ml) was added, with stirring, over 20 min, m-chloroperbenzoic acid (7.75g). After 4h the white solid was filtered off. The filtrate, washed (aq. Na_2SO_3, aq.$NaHCO_3$ and aq.NaCl), dried and evaporated, yielded 210 (6.6g, 99%) m.p. 287-295°. Recrystallisation (ether-petrol) gave m.p. 299-301° (lit[91] 287-295°), i.r. 1737 cm^{-1}.

4a - Hydroxy-adamantan-2-one 156[89,91]

The lactone 210 (5g) was stirred in 50% sulphuric acid (25 ml) at 90° for 24 h. Removal of aliquots showed, by g.l.c. on 5% QF1 at 130°, that lactone was slowly converted to another material (a ketol by i.r. 3360, 1710 cm^{-1} in nujol) which in turn was converted to 156. Product ratios showed no further change after 24 h. Ether extraction of the diluted (100 ml water) mixture and washing and drying as usual, gave, on evaporation of solvent, semi-crystalline solid (4.8 g) which on three crystallisations from ethyl acetate gave 156 (1.8 g, 36%) m.p. 322-324° (lit[91] 316-320°)

Attempted Cagliotti[88] Reduction of Ketol 156

The ketol (39 mg) in methanol (5 ml) was treated with p-toluene-sulphonyl hydrazine (48 mg) at reflux for 5 h. Partial removal of solvent and ice cooling gave no solid. T.l.c. revealed only starting ketol (40% ethyl acetate-petrol).

The above was repeated at reflux for 8 h. and again for 14 h. in methanol containing 2 drops conc. H.Cl. with similar results.

The last attempt was repeated. Reflux was continued for 48 h. and the whole product, after methanol removal, taken up in ether. Washing (aq bicarbonate and brine), drying, and solvent removal gave an oil (25 mg) which was treated with excess lithium aluminium hydride in refluxing dioxan for 14 h. The major product, on preparative t.l.c. and i.r. and n.m.r. comparison, appeared to be 2a, 4a-adamantanediol 165. T.l.c. showed only a trace of 2-adamantanol.

II2 EXPERIMENTAL

Epoxidation[92] of Protoadamantene 127.

Protoadamantene (350 mg, 2.6 m mole), m- chloroperbenzoic acid (600 mg, 3.5 m mole), and sodium carbonate (280 mg, 2.6 m mole) in methylene dichloride (15 ml) were stirred for 16 h. at 20°C. Washing with aq. sodium sulphite, hydrogen carbonate, and brine, and solvent removal from the dried organic layer, gave a crystalline product (316 mg, 81%, calculated as epoxides) consisting of two major components in the ratio 1/6 by g.l.c. (1% Ap - L, 110°C).

Preparative t.l.c. (ethylacetate - light petrol, 1:19), using continuous horizontal development and Sudan Yellow as tracking dye, effected separation of the minor component, 4,5 endo-epoxyprotoadamantane 164 (30 mg), m.p. 212-214°C (after sublimation), ν max. 3005, 2975, 1114, 1038, 932, 883, 862, and 843 cm^{-1}, n.m.r. δ 3.34 and 3.12 (2 quart, 1 H each), 2.7 - 1.1 (12 H,m) (Found; C, 79.77; H, 9.2. $C_{10}H_{14}O$ requires C, 79.95 ; H, 9.39%).

The major exo-epoxide decomposed on attempted isolation by t.l.c. or by fractional crystallisation.

The n.m.r. spectrum of the mixture of epoxides showed in addition to signals from the minor epoxide, the following multiplets assignable to the major epoxide.

: δ 3.06 and 2.82 (2t, 1H each); 1.1(1H, quart., J 12 and 4 Hz) and 2.7 - 1.3 (11 H; m).

2a, 4a - Adamantanediol 165.

The epoxide mixture described above (120 mg) in ether (0.5 ml) was adsorbed on grade II acidic alumina (10g). Light petroleum eluted the minor epoxide (12 mg), followed by mixtures eluted with light petroleum-ether (50:1). Methanol-ether (1:9) eluted 2a, 4a-adamantanediol (80 mg, 59%), m.p. 341-344° (corrected) (recrystallised from petrol-ethylacetate).(lit[93] 305-310°, lit[142] 312-326°) $\nu_{max.}$ (5 X 10^{-3} M) 3616, 3530, 2912, 2868, 2854, 1233, 1100, 1077, 1056, 1007, 970, and 922 cm^{-1}

n.m.r.($CDCl_3$ - D_2O) δ3.89 (2H m) and 2.5 - 1.2 (12H, m)

Lithium Aluminium Hydride Reduction of endo - 4,5 - Epoxyadamantane 164.

The epoxide (20 mg) was refluxed with excess lithium aluminium hydride in ether overnight. Work up as usual gave crystalline material (16 mg), identical by t.l.c. with the similar reduction product of protoadamantan-5-one described below. G.l.c. showed in addition to 5 endo-protoadamantanol (95%), peaks for 2-adamantanol (3%) and 4 endo-protoadamantanol (2%). The Jones oxidation product showed on g.l.c. 5-protoadamantanone (95%), 2-adamantanone (3%) and 4-protoadamantanone (2%).

Lithium Aluminium Hydride Reduction of Protoadamantene-epoxide Mixture.

The epoxide mixture (25 mg) was reduced as for the endo-epoxide above. G.l.c. analysis of the product, and of the mixture of ketones obtained from it by Jones oxidation, allowed an estimate of the alcohols formed in the reduction. This is discussed above (p.43).

Two 10 mg portions of epoxide mixture were treated in refluxing ether for 6 hours with (a) $LiAlH_4$ (5mg), $AlCl_3$ (9 mg) (mole ratio 2:1) and (b) $LiAlH_4$ (5 mg), $AlCl_3$ (18 mg) (mole ratio 1:1). G.l.c. analysis after the usual work up showed peaks for 2-adamantanol, 4 exo- and/or 5 endo-protoadamantanol and 4 endo - and/or 5 exo-protoadamantanol in the ratios 7 : 90 : 3 and 10 : 85 : 5 respectively.

Hydroboration[96] of Protoadamantene 127

Into protoadamantene (268 mg, 2 m mole) in tetrahydrofuram (5 ml) stirred magnetically under nitrogen in a two neck flask equipped with reflux condenser and rubber septum, was injected an excess of diborane in THF (2 ml of 1 M soln. "Alpha Inorganics") at 0°C. The mixture was stirred at 0° for 1h and 23° for 5h. An alkaline solution of hydrogen peroxide (1 ml 30% H_2O_2 + 1 ml 10% NaOH) was added dropwise followed by stirring at 30 - 40°C for 15 min and at 20-23°C for 1 h. Potassium carbonate (1g) was added, the suspension stirred for 5 min and the aqueous layer separated and extracted with ether. The combined organic layers were washed with brine and dried (Na_2SO_4). Removal of solvent gave an oil (400 mg) which on preparative t.l.c. gave a crystalline mixture (250 mg, 82% calculated as protoadamantanols).

Analysis by g.l.c. on QF 1, SE 30, Ap-L, butanediol succinate, dinonyl phthalate, bis-(2-ethylhexyl) sebacate - sebacic acid, polyethylene glycol adipate, Bentone 34 and Carbowax (3m.) showed only two peaks. On standing in air a sample developed additional peaks later shown to correspond to 4- and 5-protoadamantanone. A(50 X 0.0005)m Carbowax 1540 column at 135°C showed three peaks apparently corresponding to 2-adamantanol (t_R11 min, 3%), 4 exo-protoadamantanol (t_R12 min 58%) and 4 endo-protoadamantanol (r_R 13.6 min, 39%). Preparative t.l.c. of a sample (10 mg,) using ethylacetate-petrol, 1:4) furnished three bands of material (Rf. 0.35, 0.43, 0.48). Each band was separately oxidised as follows: the material (1-3 mg) was dissolved in acetone (0.2 ml) in a sample tube and 2 drops of 2N Jones Reagent added. The tube was capped and shaken for 2 min. Ether (0.4 ml) and water (0.4 ml) were added, the tube shaken, and the aqueous layer removed with a pipette. Anhydrous potassium carbonate (c.100 mg) was added, the tube shaken, and portions of the supernatant removed for g.l.c.

The top band (Rf.0.48) corresponded on t.l.c. to the alcohol produced by reduction of the minor epoxide 164 (see above) and of 5-protoadamantanone 168 (see below). On g.l.c. it corresponded to 4 exo-alcohol 169 but oxidation gave 5-protoadamantanone 168 (isolated as below) (ie 5 - endo alcohol.)

The mid spot (Rf. 0.43) corresponded on t.l.c. and g.l.c. to 4 exo alcohol 169 and gave 4-ketone 137 on oxidation (ie 4-exo-alcohol).

The bottom spot (Rf.0.35) corresponded to 4 endo-alcohol 167 on t.l.c. and g.l.c. but gave on oxidation 4 - and 5 - protoadamantanone in the ratio 71 : 100 (ie 4 endo + 5 exo - alcohol).

The ratio of alcohols produced in the reaction is discussed above (p.42,43).

Oxidation[97,128] of the Hydroboration Product

The mixed alcohols (200 mg) were dissolved in CCl_4 (10 ml) and ruthenium dioxide (20mg, Johnson-Matthey Ltd.) added. Aq. sodium periodate (10%) was run in dropwise with stirring until a permanent yellow colour persisted. On adding MeOH(0.5 ml) after 15 min the clear mixture became black. The product, obtained by solvent extraction as usual, consisted of a crystalline mixture (200 mg, 92%) of 2-adamantanone (3%, retention index 1325), 5-protoadamantanone 168 (40.5%, 1338) and 4-protoadamantanone 137 (56.5%, 1364) (by g.l.c. on 4 m. capillary, 2% SE 30, 150°C).

The major ketones were separated by horizontal-continuous development - preparative t.l.c. using Sudan Yellow as a tracking dye. Protoadamantan-5-one 168 (80 mg) thus obtained had after sublimation (110°, 14 mm Hg) m.p. 222 - 225° (lit[100] 226-227°); ν_{max} 1727 cm^{-1} (Found C, 79.85; H, 9.4 ; $C_{10}H_{14}O$ required C, 79.95; H 9.4%). Protoadamantan-4-one (100 mg) m.p. 210-212° (lit.[69] 212-214°) was identical (n.m.r. and i.r.) with authentic material.

Caglioti[88] Reduction of 5-Protoadamantanone 168

The ketone 168 (12 mg, 0.08 m mole) and toluene-p-sulphonyl hydrazine (17 mg, 0.091 m mole) were refluxed for 12 h in methanol (5 ml) containing HCl (1 drop, conc.) The product, obtained from the dried ($MgSO_4$) ether solution, was reduced with excess lithium aluminium hydride in refluxing dry dioxan for 3 h., according to Djerassi[88]. The hydrocarbon product was separated by filtration/

filtration through Grade II neutral alumina (2g) in light petrol. G.l.c. analysis (2m 1% Ap-L, 80° and 50 m (x0.5 mm) Carbowax 1540, 65°) showed that the product consisted of protoadamantene (32%) and protoadamantane (68%), compared with a sample prepared by hydrogenation of protoadamantene in ether over 10% palladium-charcoal m.p. 208- 210 (lit[100] 210-212°).

Lithium Aluminium Hydride Reduction of 5-Protoadamantanone 168

The ketone (50 mg) was reduced with an excess of hydride in refluxing ether for 3 h. The product (48 mg) afforded, on preparative t.l.c. and sublimation, 5-endo-protoadamantanol 166 (35 mg) as white needles m.p. 258-260°, ν_{max} 3600 cm^{-1} (Found C78.85; H, 10.55 $C_{10}H_{16}O$ requires C, 78.9; H 10.6%)

G.l.c. (50 m. Carbowax 1540, 135°C), of the crude reduction product, showed a major peak (95%) of 5 endo-protoadamantanol 166, inseparable from the 4 exo-alcohol and a minor peak (5%) of 5 exo-protoadamantanol 170, inseparable from the 4 endo alcohol 167. Re-oxidation of a sample of crude product showed (g.l.c. 4m. capillary, 2% SE 30, 150°) 5-protoadamantanone 168 (> 98%).

Attempted equilibration of 5 endo-Protoadamantanol 166

(a) The alcohol (20 mg, 0.13 m mole) in isopropanol (5 ml, redistilled from calcium hydride) was treated with aluminium isopropoxide[143] (20 mg) and acetone (2ml) at reflux for 48 h. The mixture was poured into dil. HCl and extracted with ether, the ether being washed with water, aq. sodium hydrogen carbonate and brine before drying (Na_2SO_4). G.l.c. (50 m X 0.5 mm Carbowax 1540, 135°C) showed (A) 5-protoadamantanone (t_R 7.6 min, 85%), (B) 4-protoadamantanone (t_R 9 min, 2%), (C) 5-endo alcohol (t_R 9.8 min, 13%) and (D) 5 exo-alcohol (t_R 11 min, 1%)

(b) The above process repeated, but without using acetone, showed by g.l.c. : A 65% , B 2% , C 32% , D 1%

(c) Lithium aluminium hydride (76 mg, 2 m mole) and aluminium chloride (1.07 g, 8 m mole)[144] were mixed in ether (60 ml, redistilled from $LiAlH_4$) in a flame dried flask under a flow of dry N_2 . The alcohol (20 mg, 0.13 m mole) in ether (5 ml) was treated with 1 ml (0.13 m mole, H^-) of the above solution and the mixture refluxed for 2 h. Acetone (1 ml) was added and reflux continued for 1 hr. G.l.c. after work-up as before showed A 75% , B . 2%, C 2%, D 1%

(d) A variety of conditions were used using differing ratios of $LiAlH_4$ to $AlCl_3$, in ether, THF and dioxan, and in the presence of acetone fluorenone, or in the absence of ketone. The best method used (ie that which showed highest conversion to 5 exo-protoadamantanol) is described below.

In a dry flask equipped with magnetic stirrer, reflux condenser and rubber septum, was placed aluminium chloride (7 mg 0.05 mmole). The system was flushed with nitrogen and the N_2 atmosphere maintained using a balloon. Lithium aluminium hydride (0.016 m mole) was then injected as 1.6 ml of 0.01 M solution in ether. After stirring for 30 min, the alcohol (10 mg., 0.065 m mole) was added in dry dioxan (6 ml) and the mixture heated at 110° for 1 h. Fluorenone (1 mg in 1 ml dioxan) was added and reflux continued. The ratio of components determined by g.l.c. was A, 25; B, 2; C, 60 ; D 13% (after 24 h.) and A, 58 B, 2 C, 15 D, 25% (after 3 days). After 4 days a number of unidentified peaks began to appear in increasing amounts.

Hydroxymercuration of Protoadamantene 127

Mercuric acetate (160 mg) was dissolved in water (2ml) and tetrahydrofuran (2 ml) added. Protoadamantene (77 mg) in THF (2 ml) was added and the mixture stirred at 18-20°C for 4 hours. The mercurial was reduced by addition of a mixture of sodium hydroxide (1 ml, 3 M) and sodium borohydride (1ml, 0.5 M in 3 M NaOH). Brine was added, the THF layer extracted, and the aqueous layer re-extracted with ether. Solvent removal from the dried (Na_2SO_4) combined organic layers gave an oil (80 mg). T.l.c. showed one spot corresponding to 4 exo-protoadamantanol. G.l.c. (50 m. X 0.5 mm Carbowax 1540, 135°C) showed 4 exo - and/or 5 endo - protoadamantanol (t_R 12 min, 95%), 2-adamantanol (t_R11 min,c, 2%) and 4 endo - and/or 5 exo - protoadamantanol (t_R13.6 min, c. 2%). An oxidised (Jones) sample showed on g.l.c. (4m. cap. 2% SE30, 150°) three peaks; 2-adamantanone (t_R9.3 min, 2%), 4-protoadamantanone (t_R 10.2 min, 95%) and 5-protoadamantanone (t_R11 min, 3%). The total oxidation product was identical by ir with authentic 4-ketone.

Experimental II. 3

8,9 - Dehydroadamantan-2-one 181

Ozone[118,119] was bubbled through a solution of 2,4 - dehydroadamantane (500 mg) and pyridine (2ml) in methylene chloride (10 ml) at -28°C for 8 h. T.l.c. (ethylacetate - petrol, 15 : 100) showed in addition to starting material a minor spot (Rf.0.5) corresponding to 2-adamantanone and two major spots (Rf. around 0.35) the upper of which stained with 2,4 - dinitrophenylhydrazine. The hydrocarbon fraction was separated by chromatography on Grade III alumina (10g) being eluted with isopentane. I.r. comparison showed this to be identical with starting material. The remainder of the material was eluted with ether and a portion (50 mg) subjected to t.l.c. The band showing a positive D.N.P. test was isolated giving 20 mg of crystalline material; i.r. ($CHCl_3$) 3038, 2940, 2862, 1703, 1340, 1050, 935, 886 (lit.[117] gives for the ketone 181, 3040, 2940, 2864, 1705, 1343, 1053, 939, 880 cm^{-1}).

8,9-Dehydroadamantan-2-ol 177

The unreacted hydrocarbon from the above reaction was recycled as before. The product of this and the previous run were combined (490 mg) and treated with excess sodium borohydride in methanol, according to Baldwin and Fogelsong,[117] yielding on preparative t.l.c. and sublimation, a crystalline material (250 mg, 44% from hydrocarbon) mp. 207 - 209°C (lit.[117] 210.5 - 212.5°); i.r. ($CHCl_3$) 3618,3430, 3035, 3010, 2940, 2960 cm^{-1}.

G.l.c. (2m, 5% QF1, 100°) showed two peaks of 2% (t_R 1.6 min) and 98% (t_R 2.2 min).

8,9 - Dehydroadamantyl - 3,5 - dinitro - benzoate 183.

Dehydroadamantanol (100 mg) was treated with 3, 5-dinitrobenzoyl chloride (210 mg) in pyridine, according to Baldwin and Fogelson[117], yielding the 3, 5 - dinitrobenzoate 183 (146 mg, 71%) m.p. 119 - 120° (lit[117] 121.5 - 122.5°), n.m.r. δ 9.2 (3H, s); 5.56 (1H, m) ; 2.5 - 1.2 (12H, m).

Attempted formation of 8,9-Dehydroadamantyl-2-methane-sulphonate 182.

(A) To methanesulphonyl chloride (230 mg, 2 m mole) in pyridine (5 ml) was added with stirring 8,9-dehydroadamantan-2-ol (200 mg, 1.3 m mole). The solution, yellow at first, rapidly became bright pink, fading slowly to brown on stirring for 3 days at 0°C. Ether (25 ml) was added and the solution washed with dil. HCl, aq. sodium hydrogencarbonate and brine before drying (Na_2SO_4). Solvent removal gave a yellow oil (500 mg). T.l.c. showed six spots, the major corresponding to starting alcohol. N.m.r. showed a large number of singlet peaks around δ 3 where the s-methyl signal might be expected.

(ii)[121] A two necked 10 ml flask fitted with magnetic stirrer and rubber septum was flushed with N_2 and the N_2 atmosphere maintained by use of a balloon. 8,9-Dehydroadamantanol (240 mg, 1.6 m mole in 1.5 ml ether)was injected, the solution cooled to 0°C, and treated with butyl lithium (1 ml, 1.8 M soln.) at 0°C for 30 min with stirring. Redistilled methane sulphonyl chloride (183 mg, 1.6 m mole) was then added in ether (2 ml) and the mixture stirred at room temperature for 3 h. After filtration and removal of solvent - 15°C, 20 mm Hg), crystallisation from petrol was attempted without success. Removal of solvent gave an oil which showed on n.m.r. multiple peaks in the region δ 2.8 - 4 p.p.m.

Treatment of 8,9-Dehydroadamantane 126 with Methane sulphonic Acid

Dehydroadamantane (10 mg) was stirred at 20-22°C with methane sulphonic acid (1 ml). The solution became homogeneous after 7 min. Stirring was continued for 1 h. The mixture was diluted with 10 ml ether and washed with water, aq. sodium hydrogen carbonate (twice) and brine. Drying ($MgSO_4$) and solvent removal gave an oil (14 mg) which on recrystallisation from petrol yielded 2-adamantyl methanesulphonate (8 mg, 47%) m.p. 66-67°C (mixed with authentic material m.p. 66-67°).

Attempted Pyrolysis of 8,9-Dehydro-2-adamantyl 3,5-Dinitrobenzoate

The dinitrobenzoate (80 mg) in ether (0.3 ml) was injected into the pyrolysis system described in detail above for 2-adamantyl ester pyrolysis in two equal portions one at 550°C and 0.1 mm Hg and one at 490°C and 0.2 mm Hg. T.l.c. of the product, treated in the usual manner, showed the absence of dinitrobenzoate and the presence of non polar material. G.l.c. (1% Ap-L, 80°) showed adamantane (c. 20%) and five peaks of similar retention.

Experimental II.4

Pyrolysis of 10-Protoadamantyl Methanesulphonate 184.

The sulphonate, m.p. 79-81°C, was supplied by Professor C. Cupas, having been made by standard methods from the corresponding alcohol derived from the known 10-protoadamantanone.[122]

Pyrolysis (20 mg in 0.1 ml ether) by injection of sample in the manner described in detail above for 2-adamantyl tosylate (p.74) at 500°C and 0.5 mm Hg gave complete conversion of mesylate as judged by t.l.c. Analysis by g.l.c. (1% Ap-L, 80°) showed a major unknown (35%, t_R 5.4 min), adamantane (60%, t_R 6.6 min) and a series of minor peaks (5% together, t_R 6, 7.8, 8.4 and 9.2 min). Three further attempts at 480°, 520° and 550° showed almost identical results.

Pyrolysis by sublimation of sample (200 mg), in the manner described for 2-adamantyl mesylate (p.76), in a tube coated at its exit end with sodium carbonate, at 550° and 0.06 mm Hg, gave, after the usual work-up, crystalline material (80 mg, 67% based on M.W.134). G.l.c. (1% Ap-L, 80°) showed the unknown (40%), adamantane (58%) and the minor peaks described above (c.2%). Chromatography over 15% silver nitrate-alumina (5g) gave, on elution with isopentane (50 ml), adamantane (95% by g.l.c., i.r. and n.m.r. identical with authentic material). Elution with ether (70 ml) gave a white crystalline hydrocarbon (13 mg, 11% from mesylate, $>$ 98% one peak by g.l.c.) subliming at 122-126°C, 760 mm Hg; i.r. 3012, 705 cm^{-1}; n.m.r. (CF_3Cl) δ 5.95 (1H, m) ; 5.25 (1H, quart) ; 2.9 - 1.2 (12H, m). A sealed tube m.p. was not satisfactorily achieved owing to lack of sufficient material however m.p. was above 200°C. Molecular weight (by mass spectrometry) was 134).

Purification of Bicyclo-2,2,1-heptene-5-carboxilic Acid.

The crude acid (10g, ex. Aldrich) dissolved in aq. sodium hydrogencarbonate (200 ml, 0.5 M) was added to a solution of iodine (37g) and KI (72g) in water (150 ml) and allowed to stand overnight in the dark. The resulting precipitate was washed with water, shaken with chloroform and aq. sodium thiosulphate, and the layers separated. The aqueous layer was re-extracted with chloroform and the combined organic layers washed (aq. $NaHCO_3$) and dried (Na_2SO_4). Solvent removal and recrystallisation from petrol-ethylacetate gave the iodolactone 191 (12.1g, 66%) m.p. 55-57°C (lit[125] 55-58°)

The iodolactone 191 (12g), in glacial acetic acid (30 ml), was treated, at 15°C, with zinc dust (8.6g) over 10 min. Further acetic acid was added (10 ml) and the mixture stirred at 15°C, with zinc dust (8.6 g) over 10 min. Further acetic acid was added (10 ml) and the mixture stirred at 15°C for 3.5 h and 20°C for 2 h. The solid was filtered and washed with acetic acid. The filtrate was diluted with water (200 ml) and extracted twice with ether. After drying and ether removal, the organic residue was distilled, (134°C, 16 mm Hg) and recrystallised from pentane, furnishing bicyclo-2,2,1-heptene-endo 2-carboxylic acid 192 (5g) m.p. 45-46°C (lit[125] 44 - 45.5°)

Hydroxylactone 193[127]

To the acid 192 (5g), in 98% formic acid, was added, over 5 min and at 45°, hydrogen peroxide (10 ml, 30%). The mixture was stirred at 50° for 1h, steam distilled till no more formic acid came over and saturated with sodium carbonate. Continuous extraction with ethylacetate and solvent removal gave 193 (4.8g) m.p. 157 - 158° (from ether) (lit[127] 160°);
i.r. 3612, 1770, 1054, 1012, 890 cm^{-1}.

Ketolactone 194[128]

A suspension of ruthenium dioxide (0.3g) in CCl_4 (130 ml) was added to hydroxylactone 193 (4.6g) and sodium periodate (15g) in water (130 ml) and stirred for 48 hours. Isopropanol was added dropwise till the yellow colour was discharged. The aqueous layer was separated, filtered through celite and extracted continuously giving, after solvent removal, an oil (3.8g) shown (g.l.c., 1% O V 17) to consist of 193 and 194 in the ratio 1 : 4. Chromatography over silica (400 g) gave, on elution with 1% CH_3OH/chloroform, 194 (3g) m.p. 200 - 203°C (lit[128] 202 - 203°); i.r. 1755 cm^{-1}

Experimental II.5.

Attempted Rearrangement of Protoadamantan-4-one 137.

The ketone 137 (20 mg) was dissolved in glacial acetic acid (5 ml) and stirred at room temp. Samples (0.5 ml) were removed after 1, 3, 5 and 15 h, diluted with aq. bicarbonate and extracted with ether. The dried ether layers were concentrated and subjected to t.l.c. and g.l.c. (4m, 2% SE30, 150°), showing only the starting ketone 137.

Ketone 137 (10 mg) was suspended in 50% sulphuric acid and stirred at 20° for 14 h. Analysis, (t.l.c. and g.l.c.) as before, showed no change.

The above repeated at 50°C gave material which showed streaking on t.l.c. G.l.c. showed only starting ketone (> 95%).

A repeat run at 100°C gave material showing considerable streaking on t.l.c. G.l.c. (as before) showed adamantanone (10%) and protoadamantan-4-one (70%). Minor unidentified peaks were also observed. After 14 hours the sulphuric acid mixture was dark brown in colour.

The ketone (20 mg) was dissolved in a solution of chromium trioxide (0.5g) in acetic acid (5 ml) and stirred for 6 h. at room temperature. Ether (15 ml) was added and the mixture washed with water, aq. bicarbonate and brine. Removal of solvent, from the dried ($MgSO_4$) ether layer, gave an oil (15 mg) which, apart from material on the base line, showed, on t.l.c. (10% ethyl acetate-petrol), only starting ketone 137.

The ketone (35 mg) was treated, in benzene, with p-toluene-sulphonic acid (20 mg) and ethylene glycol (5 ml) at reflux for 14 h in a "Dean and Stark" system. Water was uptaken by silica gel. Work up as usual gave a clear oil (42 mg) homogeneous by t.l.c. and g.l.c. (5% QF1, 2% SE.30); n.m.r. δ 3.8 (4H, m) ; 2.5 - 1.0 (14H, m).

Treatment of the above oil (40 mg) with methanol - HCl (10 ml + 2 ml, 8 M) for 12 h, addition of ether and ether extraction and washing as usual, gave ketone 137 (27 mg) on comparison by t.l.c., g.l.c. and i.r.

Ethylene glycol-mono-(1-adamantyl)-ether 204

was prepared by treatment of 1-bromoadamantane 134 (315 mg) with sodium carbonate (2g) in dioxan-ethyleneglycol (10 ml) 4:1 at reflux for 15h. The cooled, filtered solution was washed with water and brine, dried (Na_2SO_4) and evaporated yielding material (280 mg, 98%) m.p. 31 - 33°. Preparative t.l.c. and sublimation (80°, 0.1 mm Hg) gave material m.p. 34 - 35° ; i.r. 3595, 2905, 2845, 1448, 1350, 1300 cm^{-1} ; n.m.r. ($CDCl_3$ - D_2O) δ 3.53 (4H, m) ; 2.13 (3H, m) ; 1.9 - 1.5 (12H, m). (Found C 73.3, H 10.3 $C_{12}H_{20}O_2$ requires C 73.4, H 10.3%).

Treatment of 204 with Lead Tetra-acetate.

A. The glycol-mono-ether 204 (150 mg) was treated with lead tetra-acetate (346 mg) in refluxing benzene for 16 hr. The mixture, filtered, washed with bicarbonate, and dried ($MgSO_4$), showed, on t.l.c., two spots. The minor spot (Rf 0.3), on separation, was identical (t.l.c., g.l.c., i.r., n.m.r.) with authentic 1-adamantanol. The major spot (Rf 0.65), on attempted isolation, by t.l.c. or crystallisation, decomposed to give 1-adamantanol. The material showed, in addition to peaks ascribed to 1-adamantanol, i.r. 2910, 2850, 1738, 1363, 1353, 1258, 1222, 1158, 1005, 932 cm^{-1}; n.m.r. δ 5.25 (2H, s) ; 2.15 (3H, m); 1.96 (3H, s) : 1.8-1.5 (12H, m) ; mass spec. M^+ 224.

B. Treatment of 204 (50 mg) with iodine (63 mg) and $Pb(OAc)_4$ (111 mg) in benzene at 20° gave material, after work up as before, showing (t.l.c.) 204, adamantanol and nine other components.

Methyl (bicyclo - 3,3,1 - nonan - 3 - one - 3 endo - carboxylate)213

4-Oxahomoadamantan - 5 - one (see p. 79) 210 was treated with 10% methanolic - KOH overnight at reflux. The neutralised (H_2SO_4) solution was extracted with ether, washed and dried (Na_2SO_4). T.l.c. showed streaking and lactone 210. The ether solution was treated with excess diazomethane yielding, after the usual work up, an oil (430 mg) homogeneous by t.l.c. and g.l.c. (> 98% on 1% Ap-L, 130°) ; i.r. (liq.film) 3350, 1730 cm^{-1}; n.m.r. δ 4.05 (1H, m) ; 3.6 (3H, s) ; 2.8 (1H, s, exchanges in D_2O) 2.4 - 1 (13H, m). The material decomposed on standing to form lactone 210 as judged by t.l.c. and g.l.c.

The above material was oxidised (Jones), without further purification, yielding after the usual work-up, a crystalline solid. Preparative t.l.c. gave material (213) (400 mg, 67% from lactone 210) m.p. 85 - 87°; i.r. 1737, 1710, 1205, 1170 cm^{-1}, n.m.r. δ 3.62 (3H, s) ; 2.48 - 1.0 (13H, m). Analysis could not be obtained as the material was thermally unstable (on standing for 10 days at room temperature the m.p. was $> 290^{\circ}$). Mass spectrometry showed M^{+} 196.

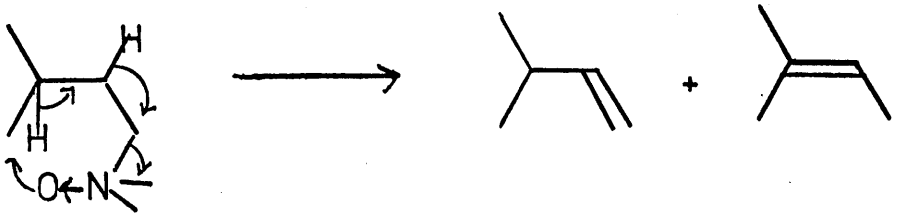
Attempted Acyloin Condensation of Keto-ester 213.

To a dry flask, fitted with "dricold" condenser, dropping funnel and magnetic stirrer, under an atmosphere of N_2 was added ammonia (20 ml) and sodium (115 mg). Keto-ester 213 (290 mg in 20 ml ether) was added over 30 min and stirred for 1 h. Methanol (0.5 ml) was added and the solvent distilled off. The residue, in ether, was washed and dried yielding a semi crystalline material (205 mg). T.l.c. (ethylacetate - petrol, 15 : 85) showed ten components. The desired product was not isolated.

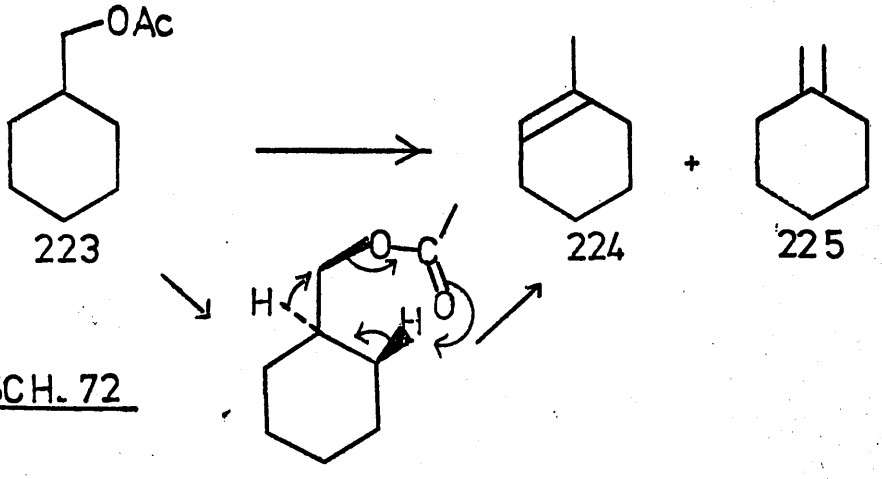
PART III

CYCLOHEXYLCARBINYL and DECALYL SERIES

SCHEME 71

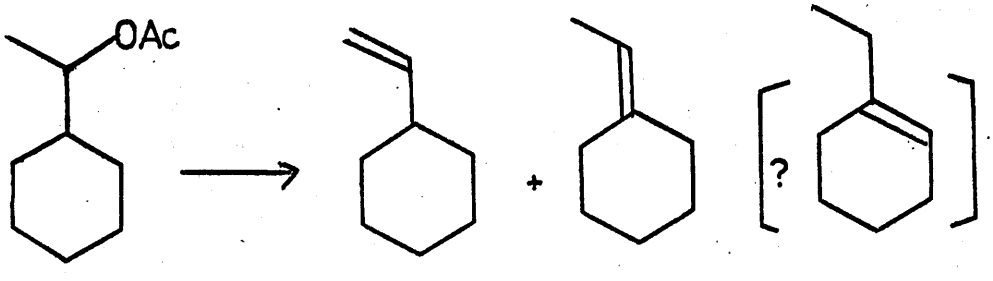


220 221 222



223 224 225

SCH. 72

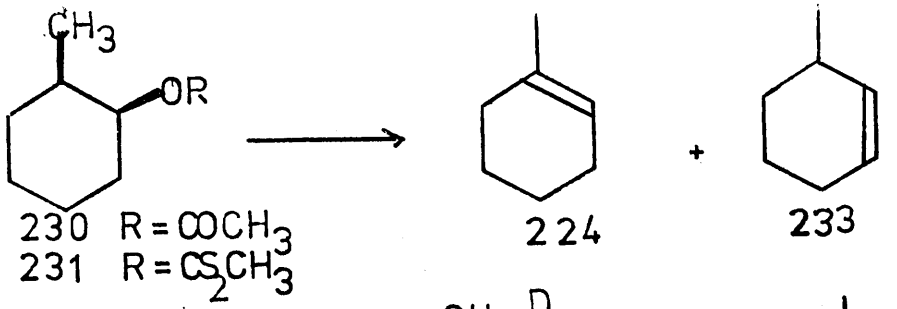


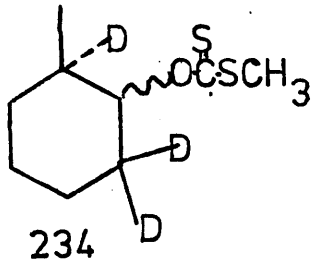
226 227 228 229

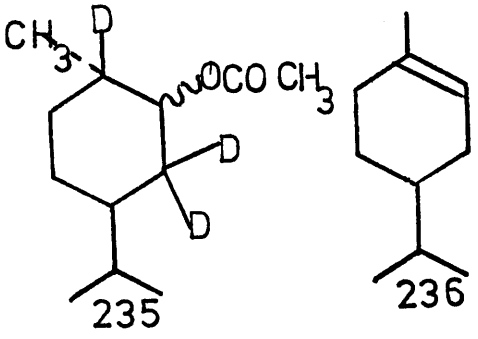
It had been hoped that the 1, 3 - elimination mechanism discussed above for the pyrolysis of adamantyl esters might explain the observation of two other reported phenomena occurring during ester pyrolysis namely (a) the production, in some cases[1,2,17,146,147], of minor amounts of olefin isomers with the double bond β, γ - to the deporting ester function and (b) apparent anti 1, 2 - eliminations[1,11,27,28,29].

(a) Cope[168], on pyrolysis of isoamylamine N-oxide 220, obtained, in addition to the expected product 221, significant amounts of 2-methylbut-2-ene 222 which he suggested might have arisen by α, γ-elimination with shift of the β-hydrogen. (scheme 71)

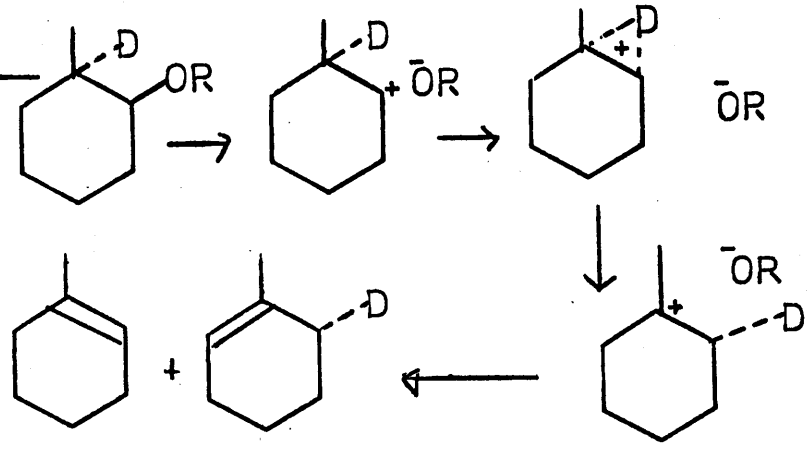
While earlier reports[145,147,148] had indicated some disagreement over the specificity of ester pyrolysis it became generally accepted[1] that elimination occurred to give α, β -elimination products only. However, Eglinton and Rodger[17,146] on pyrolising cyclohexylcarbinyl acetate 223, obtained 1-methylcyclohexene 224 (6 - 7%) in addition to the expected methylenecyclohexane 225. These workers[17,146] had used more sophisticated analytical methods, including g.l.c. on silver nitrate columns, than had been available to earlier workers and had found that the amount of anomalous product did not vary much over a range of pyrolysis conditions. It was decided therefore to try to duplicate this work and ascertain whether the anomalous product might arise through a 1,3 - mechanism such as is shown in scheme 72. In addition it was decided to attempt pyrolysis of methylcyclohexylcarbinyl acetate 226 for, though pyrolysis of this ester has been reported[149] as giving rise to only the expected products 227 and 228, the analytical method used, fractional distillation followed by infra red spectroscopy, would not have detected minor amounts of 1-ethylcyclohexene 229 which might be produced through a 1, 3 - elimination such as in scheme 72.

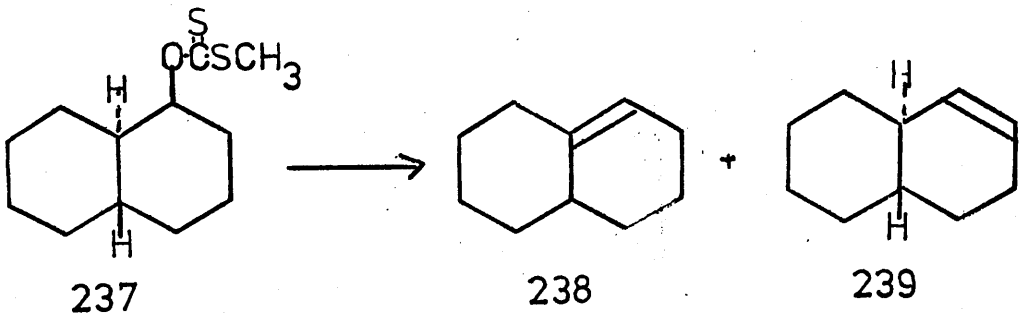

CH3
OR
230 R = COCH3
231 R = CS2CH3
224
233


D
S
OCSCH3
D
D
234

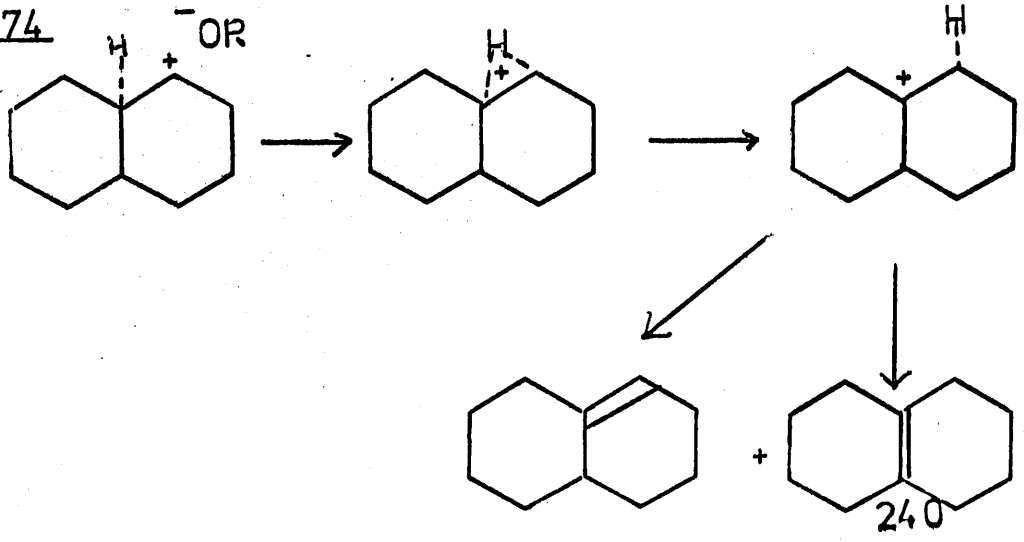

CH3
D
OCO CH3
D
D
235
236

SCH 73


D
OR
D
OR
D
OR
OR
D
D


S
OCSCH3
H
H
237
238
H
H
239

SCH. 74


H
OR
H
H
240

(b) Many instances are recorded[1,2,11,27,28,29] of ester pyrolysis occurring with apparent anti-elimination. A typical example is that reported by Djerassi and Briggs[11] where pyrolysis of cis-2-methylcyclohexyl acetate 230 or - xanthate 231 led to formation of 1 - methylcyclohexene 224 in addition to the expected 3 - methylcyclohexene 233.

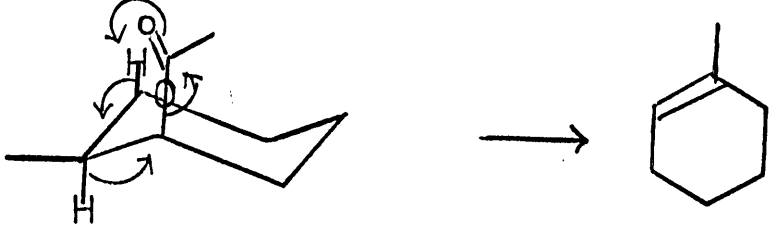
In this case[11], when the methine hydrogen was replaced by deuterium, the 1-methylclohexene 224 produced showed between 40 - 80% retention of deuterium. A similar result is described by the same authors[11] on pyrolysis of a mixture of 2,6,6 - trideuterio-2-methylcyclohexyl - S - methyl xanthates 234 where the 1-methylcyclohexene 224 formed showed a deuterium composition which included 6% d_3 species.

Thomas and Willhalm[150] have reported a similar result on pyrolysis of an epimeric mixture of trideuterated - carvomenthyl-acetates 235 where the minor product menth - 1 - ene 236 contained around 20% d_3.

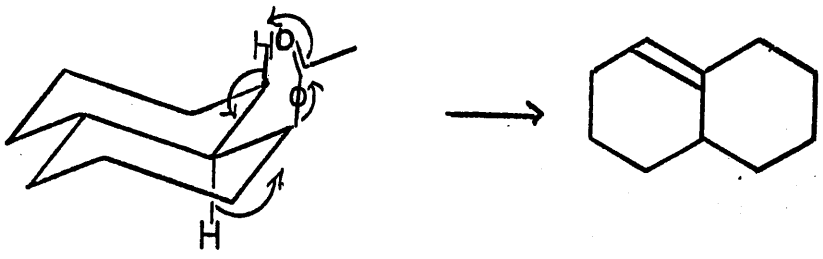
Djerassi and Briggs[11] have suggested an ion pair route (scheme 73) as giving rise to the anomalous product 224 This route however would not appear to explain the results observed by Huckel[28] for trans-1-decalylxanthate 237 where pyrolysis gave 20% of the "anti-elimination" product Δ 1,9 - octalin 238 in addition to the expected product 239 (80%). In this case the ion migration route (scheme 74) would result in carbonium ion formation at the bridge-head and should hence lead to the thermodynamically more stable[151] Δ 9,10 - octalin 240 which is not observed[28].

We considered it possible that the apparent anti-elimination was occurring via 1,3 - elimination with hydrogen shift (scheme 75 and 76) in a manner analogous to the 1,3 - elimination with alkyl shift described for 2-adamantyl esters (scheme 77)(see Part II,1,p.24)

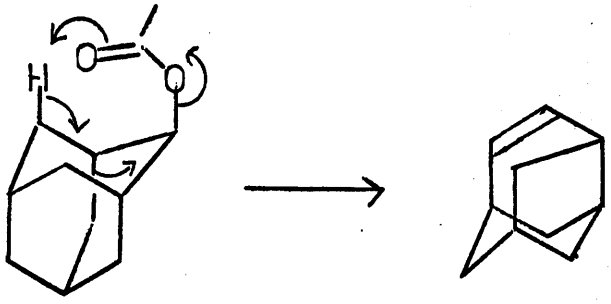
SCH.75

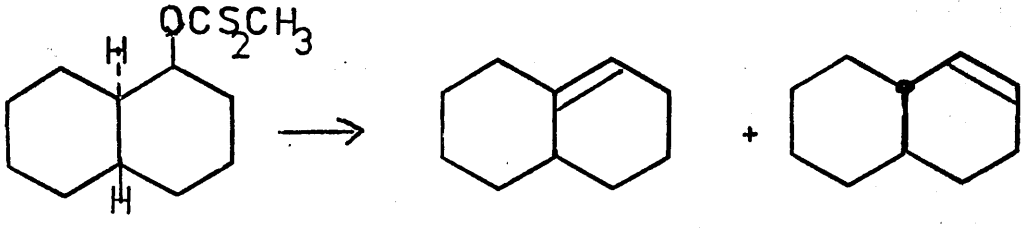


SCH.76

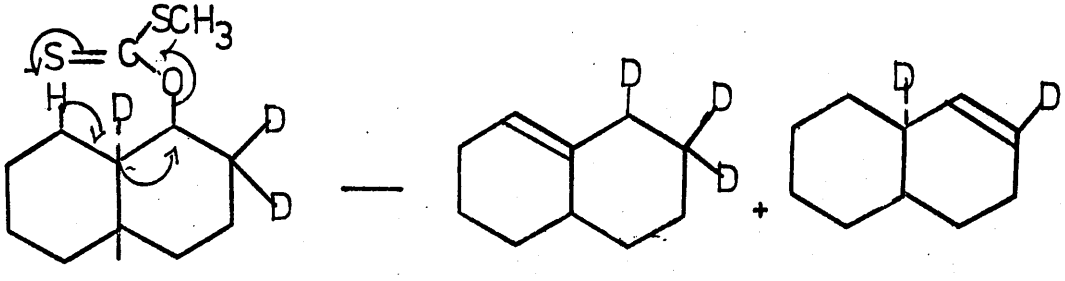


SCH.77





237 238 239



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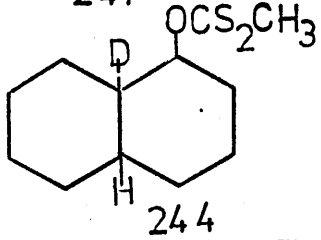

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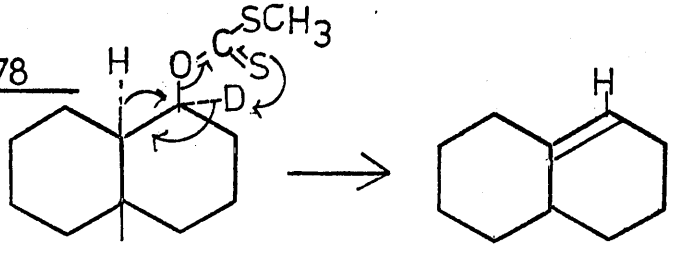
SCH 78



245

and other examples listed in the introduction of this thesis. In the decalyl case (scheme 76) it was considered that steric effects might restrict the approach of the ester function to the axial C10 hydrogen and so preclude the formation of Δ 9,10 - octalin 240.

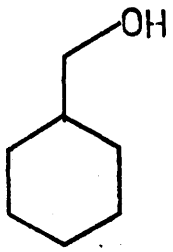
It was decided to attempt to investigate the above hypothesis using the (1c, 9c, 10t)*-1-decalyl system. This system was chosen since the favoured conformation of the fairly rigid ring system should be that in which the cleaved and migrating bonds bear an anti-periplanar relationship to each other which appears to favour the 1,3 elimination mechanism. (see schemes 76 and 77 and discussion of 2-adamantyl ester pyrolysis p.24).

Huckel[28] had pyrolised xanthate 237 (prepared in situ and uncharacterised) and had identified the Δ 1,9 - octalin 238 as its nitroso-chloride adduct. The first requirements therefore were to prepare xanthate 237 of proven configuration and purity, check that pyrolysis did indeed give significant amounts of Δ 1,9 - octalin 238 and show that this olefin (238) did not arise by isomerisation of the expected Δ1,2 - octalin 239. In addition, if the 1,3 - mechanism were to operate the trideuterio-xanthate 241 should give trideuterio - Δ1,9 - octalin 242.

Use of the 9-monodeuterio xanthate 244 would facilitate mass spectrometric and n.m.r. analysis of the pyrolysis product. Some unsuccessful routes to 244 are discussed below.

In addition the 1-monodeuterio xanthate 245 might be required to test the existance of an ∝-elimination[40] mechanism (scheme 78).

* the system of nomenclature, capable of distinguishing all four stereo-isomers of any positionol isomer of decalol, is that suggested by Huckel[38].



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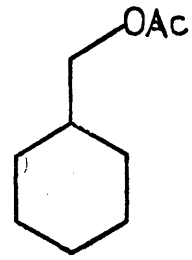

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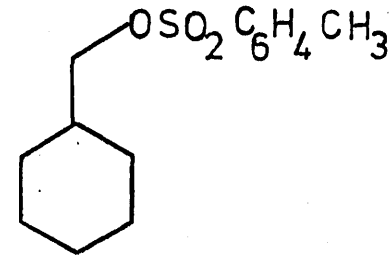

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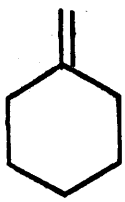

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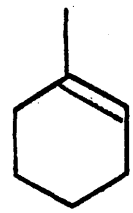

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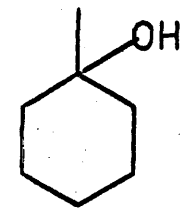

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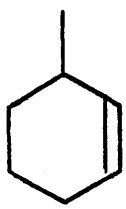

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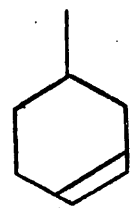

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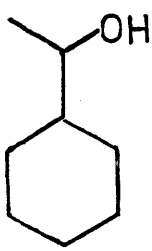

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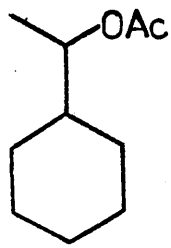

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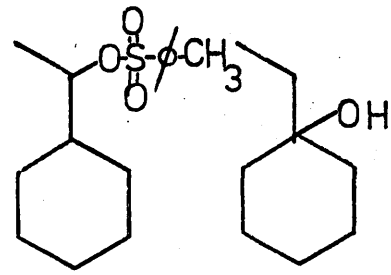

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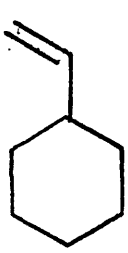

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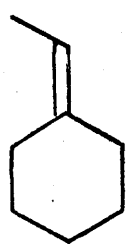

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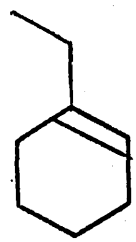

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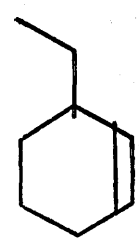

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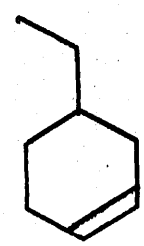


256

RESULTS (A) Cyclohexylcarbinyl and Methylcyclohexylcarbinyl Series.

Cyclohexylcarbinol[152] 246, its acetate[17] 223 and its - p - toluenesulphonate[153] 247 were prepared by adaptations of standard procedures as was methylenecyclohexane[154] 225. 1-Methylcyclohexene 224 , prepared by iodine-catalised dehydration[155] of 1-methylcyclohexanol 248 was found (g.l.c., 15% Ap-L) to contain 5% 225 and 3% of 3-methylcyclohexene 249.

A mixture of methylcyclohexene isomers,(224 , 225, 249 and 250) was obtained by passage of 225 over alumina at 300° [156]. Compounds 224 and 225 were identified in the mixture by g.l.c. comparison[157] with independently prepared samples. Two peaks appeared corresponding to 3-methyl-249 and 4-methylcyclohexene 250, but no unique assignment was made. Skeletal rearrangements in the above equilibration process are reported[156] not to exceed 1 - 5%.

Methylcyclohexylcarbinol[149] 252, its acetate[149] 226 and its p-toluenesulphonate 253 m.p. 25.5-26.5° were prepared by standard methods and characterised as described in the Experimental section as was 1-ethylcyclohexanol 254.

Iodine catalysed dehydration[155,17] of methylcyclohexylcarbinol 252 gave an olefin mixture which on comparison (g.l.c., 30% silver nitrate-triethylene glycol - celite) was shown to contain vinylcyclohexane 227 (5%), ethylidenecyclohexane 228 (15%) and 1-ethylcyclohexene 229 (80%). Similar treatment[17,155] of 1-ethylcyclohexanol (254) gave an olefin mixture consisting mainly (80%) of 1-ethylcyclohexene 229; n.m.r. δ 0.95 (3H, t); 5.4 (1H, m). The second largest component from dehydration of both (252, 254) was identical on g.l.c. as above and was undoubtedly ethylidine-cyclohexane 228.

On passage over alumina at 300°[156], the olefin mixture (227, 228, 229) from dehydration of 252 showed (g.l.c., 30% silver nitrate column) one other peak. This, since no others appear on repeated passage, must represent both 3-ethyl-255 and 4-ethylcyclohexene 256.

The silver nitrate g.l.c. columns used, while being the best available for separation, gave variable relative retentions as previously reported[151] and contaminated g.l.c. detectors used. This restricted their use.

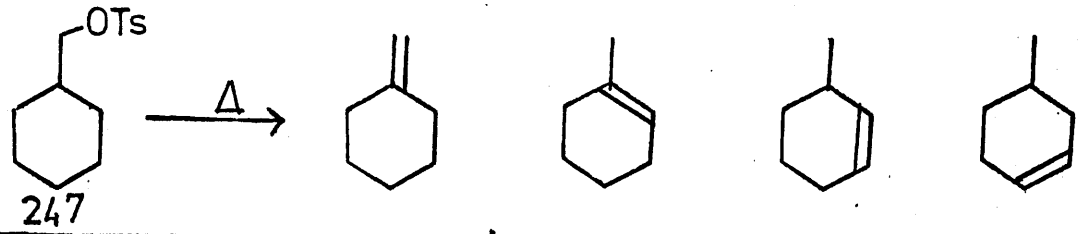
Pyrolyses-Cyclohexylcarbinyl- and Methylcyclohexylcarbinyl Esters.

All pyrolyses were carried out in a silica tube (70 x 1.5 cm), lightly packed with glass wool and heated to around 500° along 60 cm. of its length. A forward flow of nitrogen at 0.5 - 1 mm Hg. was maintained throughout. Collection was by means of a 'U' tube immersed in liquid nitrogen. Details of individual pyrolyses are given in the following experimental section.

Pyrolysis of cyclohexylcarbinyl acetate 223 gave methylenecyclohexane 225 only. While g.l.c. showed a minor (5%) contaminant, this corresponded to cyclohexene and was thought to arise from cyclohexylacetate (2-3%), in the starting material, which had been formed from cyclohexanol (1-2%) impurity in the starting alcohol 246. 1-Methylcyclohexene 224 was not present in amounts $> 0.1\%$, except in samples where the crude pyrolysate had been allowed to stand at room temperature for some time (10 - 15 min. standing gave 3 - 4% of anomolous product 224).

The pyrolysis of cyclohexylcarbinylacetate 223 reported[146] as giving rise to 1-methylcyclohexene 224 was carried out at atmospheric

TABLE 23



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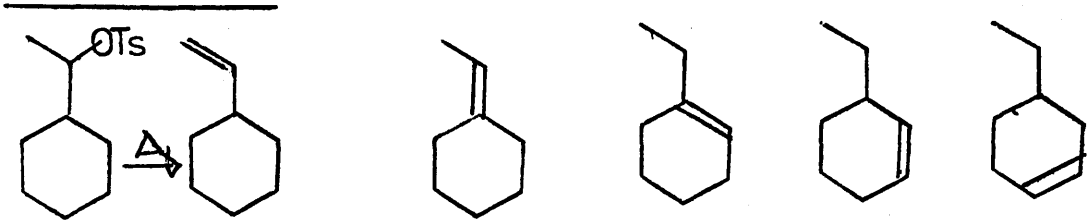
RUN	225 %[1]	224 %	249 + 250 %
1	5	80	15
2	20	70	10
3	15	75	20



RUN	227	228	229	255 + 256
1	0·5	5	75	19·5
2	6	15	70	9

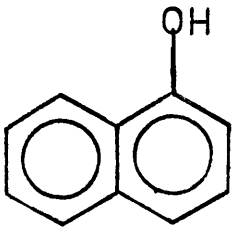
pressure while our method used pressures of 0.5-1 mm.Hg. It seems unlikely that higher pressure promoted on alternative unimolecular pyrolysis mechanism and likely that it caused more olefin-acid contact and hence acid catalysed rearrangement of the initially formed olefin 225.

Pyrolysis of methylcyclohexylcarbinyl acetate 226 gave vinyl-cyclohexane 227 and ethylidene-cyclohexane 228 as the only olefin products (99%).

Pyrolysis of cyclohexylcarbinyl-p-toluene sulphonate 247 led to a mixture of methylenecyclohexane 225, 1-methyl-224, 3-methyl-249 and 4-methyl-cyclohexene 250 in varying amounts (table 23). Methylcyclohexylcarbinyl-p-toluenesulphonate similarly gave mixtures of vinylcyclohexane 227, ethylidenecyclohexane 228, 1-ethylcychohexene 229 and 3 - (255) and/or 4-ethylcyclohexene 256 (the latter two are not mutually distinguishable by g.l.c. conditions used) (table 24).

In view of the large amounts of, and the variable yields of, all possible double-bond isomers in the above pyrolyses, it seems almost certain that extensive acid catalysed isomerisation was occurring. While the amount of isomerisation might have been reduced by coating the exit of the pyrolysis tube with sodium carbonate, as described for the pyrolysis of 2-adamantyl esters above (p.76), it would have been impossible to rule out acid-catalysed-isomerisation even under these conditions.

There is thus no evidence to suggest that α, γ - elimination with β - hydrogen shift is involved in formation of β, γ -isomers on ester pyrolysis in the gas phase. Such products most likely arise by acid catalysed isomerisation of the initially formed α, β -elimination products.



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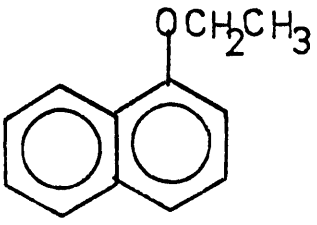

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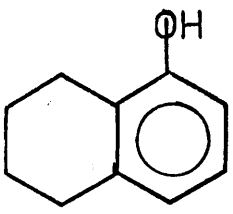

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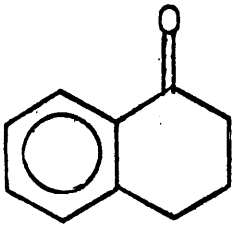

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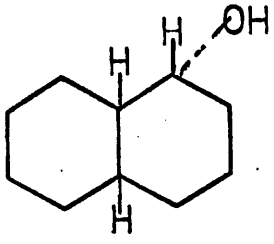

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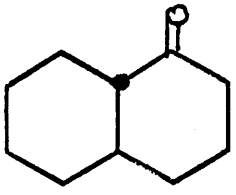

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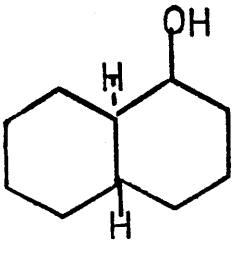

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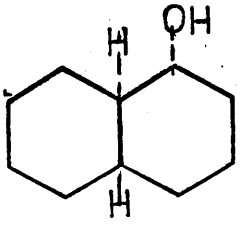

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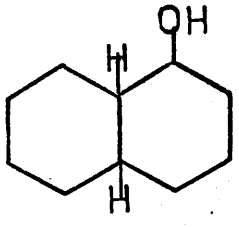

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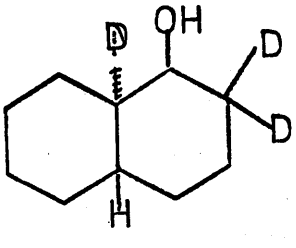

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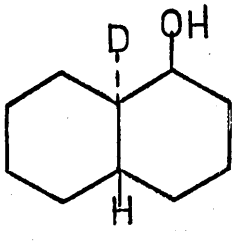


271

RESULTS - Decalyl Series

The aims of this section have been outlined above (p. 99)

Considerable difficulty was experienced in hydrogenating commercially available 1- oxygenated - naphthalene derivatives. The smooth reduction of 1- naphthol 260 at 100 Kg/cm^2 over ruthenium, reported by Cope[158], gave, in our hands, only starting material 260 and what appeared to be 1 - naphthyl-ethyl-ether 261. The similar method reported by Stone[159] using rhodium-carbon, gave only 5,6,7,8-tetrahydro-1-naphthol 262 as did the method of Myres[160] using rhodium alumina catalyst at 3-4 Kg/cm^2. The reduction of tetralone 263 over rhodium alumina at 3-6 Kg/cm^2 was only partly successful as was the atmospheric pressure reduction of 1-naphthol 260 over platinum described by Dauben[161]. One highly successful run using rhodium-alumina at 100 Kg/cm^2 and 50°C gave 97% hydrogenation and a 64% isolated yield of (1c, 9c, 10c)-1-decalol 264 m.p. 90-91°C (lit.[38] 93°), but this could not be repeated.

Another method which we used with some success was the partial hydrogenation of tetralone 263 followed by Jones oxidation to a ketone mixture and separation of the decalone 265 by extraction and decomposition of its bisulphite adduct. Tetralone is apparently incapable of forming such an adduct. The 1-decalone obtained by this method was treated at reflux with sodium methoxide in methanol to obtain t-1-decalone 265 m.p. 31-33° (from pentane)(lit[158] 32°.

(1c, 9c, 10t)-1-Decalol 266 m.p. 47-48 (lit[38] 49°) was obtained in 63% yield by catalytic hydrogenation[162] of t-1-decalone 265 with platinum in acidified (HCl) methanol.

(1t, 9c, 10t)-1-Decalol 267 m.p. 57-59 (lit[38] 63°; [161] 58-59°) was obtained by separation[163] by t.l.c. of the major product of lithium aluminium hydride reduction of t-1-decalone 265 which afforded a 5 : 1 mixture of 267 and 266.

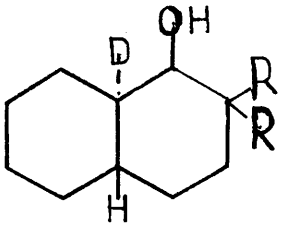
(1t, 9c, 10c)-1-Decalol 268 was not isolated but a fourth peak on g.l.c. (5%,Q.F.1) considered as corresponding to this alcohol was distinguished from peaks corresponding to the three isolated alcohols (264, 266, 267) in the mixture of saturated (i.r. checked) alcohols resulting from hydrogenation of 1-naphthol. This alcohol 268 was identified in a similar manner by Huckel[38] who subsequently prepared it (m.p. 55°C) by oxidation with ozone of cis-decalin.

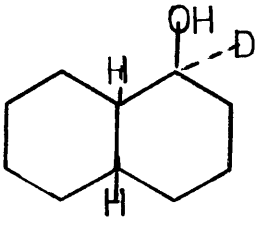
β -Deuterated decalols 270 and 271 were required and, since the normal method of preparation (hydrogenation of t-1-decalone 265 under acidic conditions) was expected to lead to deuterium loss or scrambling, alternative reduction methods were investigated and results followed by g.l.c.

Lithium aluminium hydride reduction of ketone 265 gave only minor amounts (c.20%) of the desired axial alcohol 266, the major product being the equatorial alcohol 267. Separation of the two proved difficult. Chromatography (t.l.c.) gave pure axial -266 only with considerable sacrifice of material while crystallisation of 266 proved impossible in the presence of even minor amounts of its epimer 267.

Use of lithium (tri-t-butoxy) aluminium hydride gave better axial-266/equatorial 267 ratios (70/30) but conversion was rather low ($<$ 50%). Lithium (tri-methoxy) aluminium hydride, prepared in situ, gave better conversion (80%) but poorer ax./eq. ratio (1 / 1).

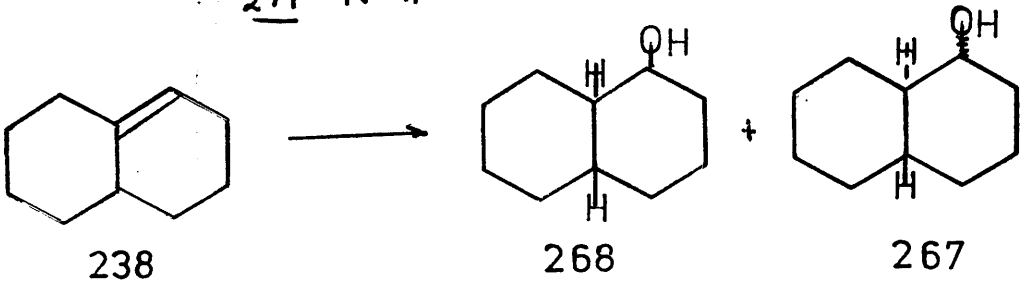
Having regard to the success of Brown[164] in achieving high ax./eq. ratios on reduction of cyclic ketones with dialkyl boranes, the ketone 265 was reduced using dicyclohexyl-borane, prepared in situ, giving axial - 266 and equatorial - 267 alcohols in the ratio 81/19.



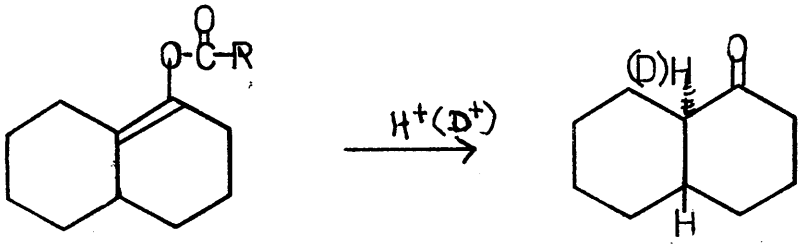


270 R = D
271 R = H

272

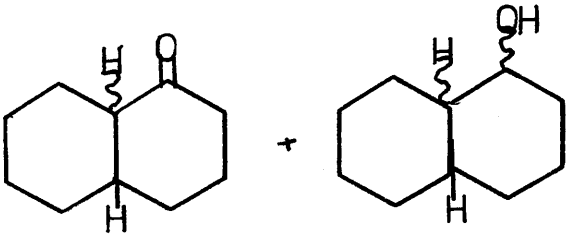


238 268 267



275 $R = CF_3$
276 $R = CH_3$

$LiAlH_4$



O-Deuterio-methanol was prepared by treatment of trimethyl-borate with D_2O and this, with sodium (5%), used to deuterate ketone 265.

Though mass spectrometry indicated 62% d_3 content for the ketone, trideuterio - (1c, 9c, 10t)-1-decalol 270 produced from it by reduction with dicyclohexyl borane had deuterium content 80% d_3, 15% d_2, 3% d_1 and 2% d_0.

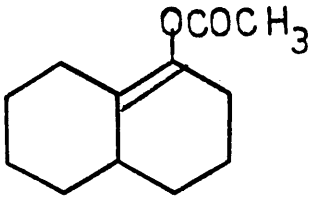
1-Deuterio-(1c, 9c, 10t)-1-decalol 272 (95% d_1, 5% d_0, no low field proton on n.m.r.) was prepared from t-1-decalone by reduction with dicyclohexyl-deuterio-borane.

Attempted routes to 9-Deuterio-(1c, 9c, 10t)-1-decalol 271

Hydroboration of Δ 1, 9 - octalin 238 gave the decalols 267 and 268 (c. 1:1) as judged by g.l.c. (5% QF1). Use of B_2D_6 should give the corresponding deuterated alcohols, but these are inseparable by t.l.c. While it might be possible to oxidise the mixture without deuterium loss, re-reduction would give an intractable mixture of all four isomeric alcohols and ketone separation without deuterium loss is unlikely.

It was hoped to hydrolise enol esters of the type 275 or 276 in deuteronic solvents under conditions which would not give 9 -deuterium loss. It was found however that the enol-trifluoro-acetate 275 hydrolised too readily to be isolated, while the enol-acetate 276 required minimal conditions (e.g. 10h. reflux in methanol over sodium carbonate) likely to cause 9 -deuterium exchange.

Lithium aluminium hydride[165] reduction of enol-acetate 276 gave mixed 1-decalols and 1-decalones (35:45 at 20° and 20:80 at -70°C). At -70° the decalone ratios were 56-trans : 44 -cis as judged by g.l.c. on 2% SE 30 at 90°. Thus, though $LiAlH_4$-D_2O should give deuterated alcohols and ketones, the difficulties would be those discussed above for hydroboration.



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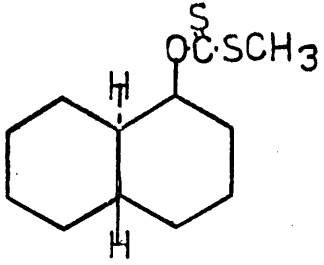

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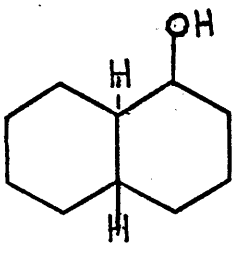

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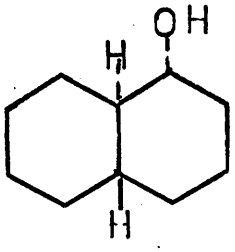


267

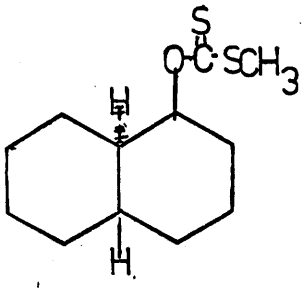
Treatment of enol acetate 275 with methyl lithium in ether followed by D_2O quenching gave a multiplicity of products from which it seemed unlikely that deuterated ketone could be isolated. Routes to deuterio-decalol 271 were abandoned at this stage.

Decalyl xanthate - Formation and Purity

Initial attempts to form (1c, 9c, 10t)-1-decalyl-s-methyl-xanthate 237, by treatment of the alcohol 266 with sodium hydride in refluxing benzene followed by carbon disulphide and methyl iodide, appeared on n.m.r. evidence (double s-methyl, and broad methine peaks) to give rise to epimeric impurity. Use of potassium hydroxide[2] or sodamide[2,28] gave very low yields of xanthate. Nace[2] has reported formation of β-cholestanyl-xanthate in 65% yield in an attempt to form α-cholestanyl-xanthate and, indeed, comments that "such epimerisation .. .. may occur more frequently than is realised and account for some reports of trans-elimination". Thus it was important to find a method of establishing epimeric purity.

Synthetic mixtures of trans-fused-1-decalyl xanthates showed one spot on t.l.c., while the only g.l.c. column not causing decomposition (SE30) gave only one peak.

The analytical method finally used was the reduction of xanthate with lithium aluminium hydride in ether, followed by analysis of the resulting alcohols by g.l.c. on a column (5% QF1) known to separate all four isomeric 1-decalols. The method is not ideal since tests showed that (1t, 9c, 10t)-1-decalol 267 (eq.) could not be detected in admixture with (1c, 9c, 10t)-1-decalol 266(ax.) below a limit of 2-3%, owing to peak tailing. Use of the method showed 5-20% of epimeric impurity in xanthate 273 produced by standard methods.



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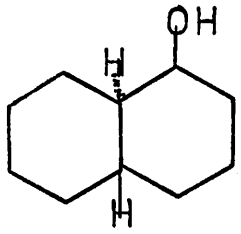

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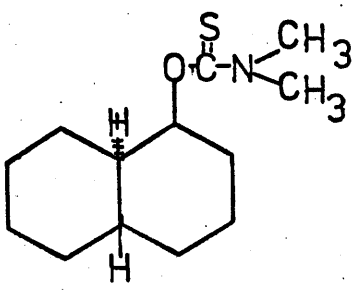


279

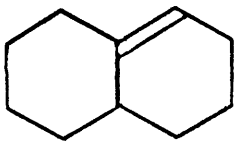
Control experiments showed that axial-1-decalol 266 was epimerised on treatment with sodium hydride in refluxing benzene and epimerisation continued on treatment with carbon disulphide and methyl iodide. Reducing temperature seriously reduced yields. Use of a dry nitrogen atmosphere and of fresh sodium hydride, washed free of its suspending white oil, gave significant improvement. Even better results were obtained when, in addition, lower (25-40°) temperatures were used during the period of reaction of the alkoxide with carbon disulphide and methyl iodide.

The above improvements were used and each batch of xanthate was tested by hydride reduction. Only material shown to produce > 97% of one alcohol was used in critical experiments.

Attempts to avoid epimerisation by use of synthetic methods similar to those reported[166] for trithiocarbonates failed thus:-

Axial-1-decalol 266 in triethylamine or pyridine, on sequential treatment with thiophosgene and methyl thiol, or sodium methylmercaptide, gave only minor amounts of xanthate 237 as judged by t.l.c. The major product (g.l.c.) was a mixture of octalins. Similar results were obtained on treatment of thiophosgene with sodium mercaptide followed by treatment with decalol 266 plus triethylamine.

The preparation and pyrolysis of N-dimethylthiocarbamates has been reported.[167] In the hope that this might avoid epimerisation, we prepared (1c, 9c, 10t)-1-decalyl-N-dimethyl-thiocarbamate 279. The n.m.r. spectrum of 279 showed more than two methyl- and more than one methine peaks indicating that epimerisation had taken place.



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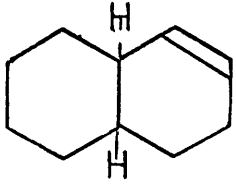

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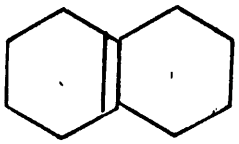

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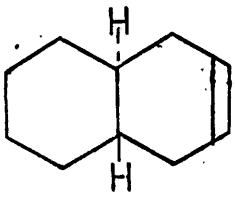

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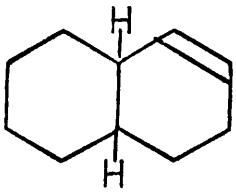

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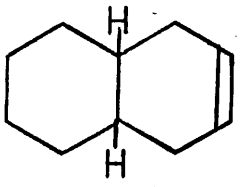

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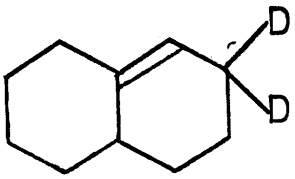
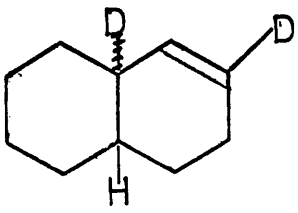


281 B



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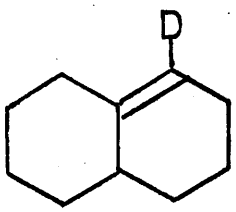

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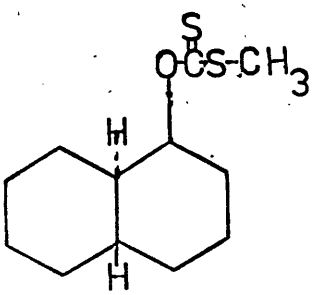

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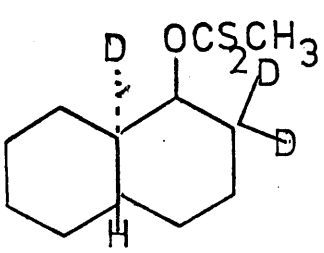

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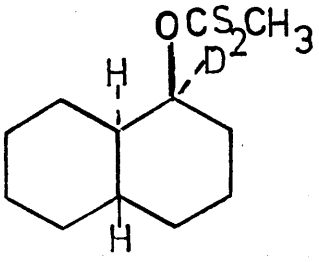

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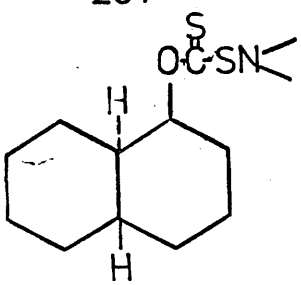

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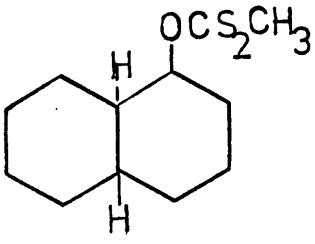

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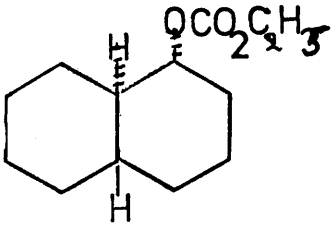

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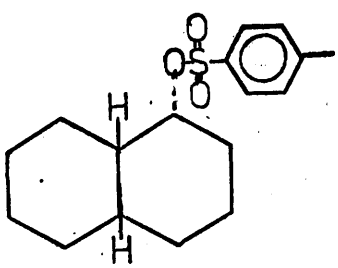

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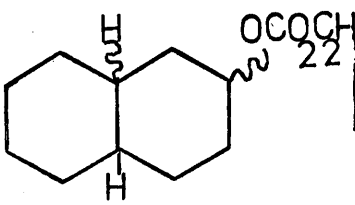

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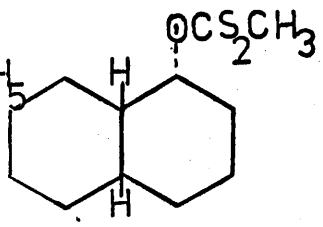

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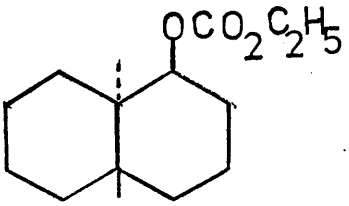
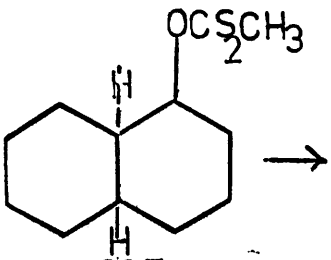


Octalin Standards

Powell and Whiting[151] have described the analysis by g.l.c. of octalin mixtures from pyrolysis of 1- and 2-decalyl methyl-carbonates. We prepared mixtures of octalins as follows : t - Δ1,2 - 239 and Δ 1,9 - octalin 238 by pyrolysis of (1t, 9c, 10t)-1-decalyl ethylcarbonate 281 ; Δ 1,9 - octalin 238 (90%) by sodium ethoxide treatment[38] of (1c, 9c, 10c)-1-decalyl-p-toluene sulphonate 282 ; Δ 9,10 - octalin 240 as major (80%) product of phosphoric acid treatment[151] of isomeric 2-decalols (ex. Koch Light Ltd.) ; t - Δ 2,3 - 284 and t - Δ 1,2 - octalin 239 by pyrolysis[151] of epimeric, mainly trans-fused, 2-decalyl ethylcarbonates 285 ; and cis-fused - Δ 1,2 - octalin 286 as the major (c. 90%) product of pyrolysis of (1c, 9c, 10c)-1-decalyl xanthate 287[28,29]. (This, anomalous pyrolysis, is discussed below).

Using the rational of Powell and Whiting[151] it was possible, from the above olefin mixtures, to identify on g.l.c. (15% Ap-L, 120°) : Δ 9,10 - 240, Δ 1,9 - 238, t - Δ 1,2 - 239 and t - Δ 2,3 - 284 octalins. Difficulty arose over cis - Δ 1,2-octalin 286 which was not separable, in our hands, from Δ 1,9-octalin 238 and over cis - Δ 2,3 - octalin 288 reported[151] as being inseparable from Δ 9,10 - octalin 238 on Ap-L.

The absence of appreciable amounts of cis-fused octalins in the mixture from pyrolysis of xanthate 237 was established as follows: The total pyrolysis product, apparently Δ 1,9 - 238 and t - Δ 1,2 - octalin 239 was separated on a 15% silver nitrate-alumina column. The Δ 1,9 - fraction, which might have contained cis - Δ 1,2 - octalin 286, was treated with excess diborane in T.H.F. followed by Jones oxidation. Analysis by g.l.c.



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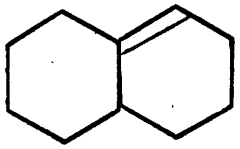

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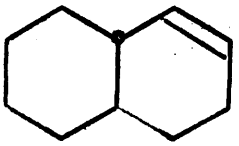

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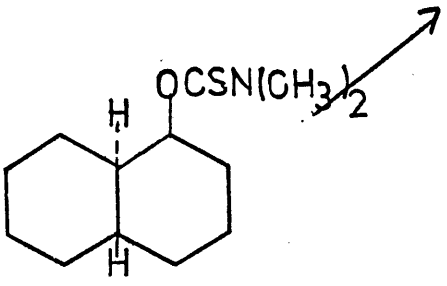

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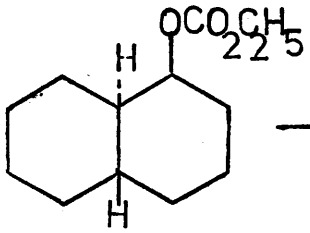

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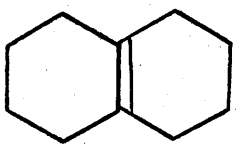


240

+ 238 + 239

showed 1-decalone (> 98%) under g.l.c. conditions (5% QF 1) shown to separate this ketone and cis - and trans-fused 2-decalones obtained by oxidation (Jones) of a commercial (Koch Light) mixture of cis and trans-fused 2-decalols.

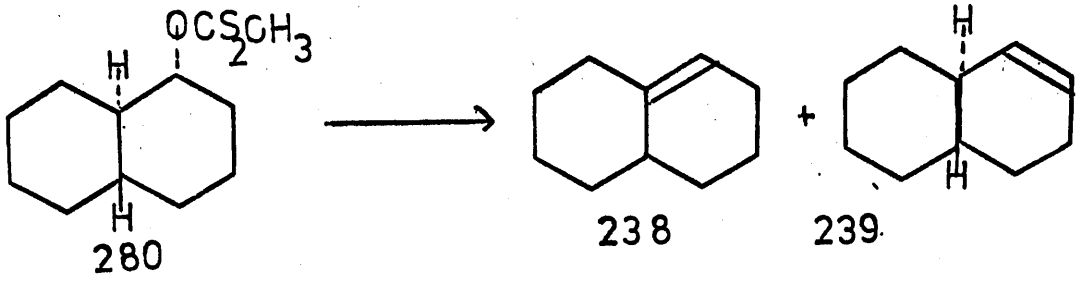
Pyrolysis of Decalyl Esters

The apparatus and general conditions used were those described above (p. 102) for cyclohexylcarbinyl esters. Individual pyrolyses are described in the Experimental Section below. Unless otherwise stated, pyrolysis was carried out by injection of sample in ether into the hot zone of the tube at 500° and 0.2 - 0.5 mm Hg. in a flow of nitrogen.

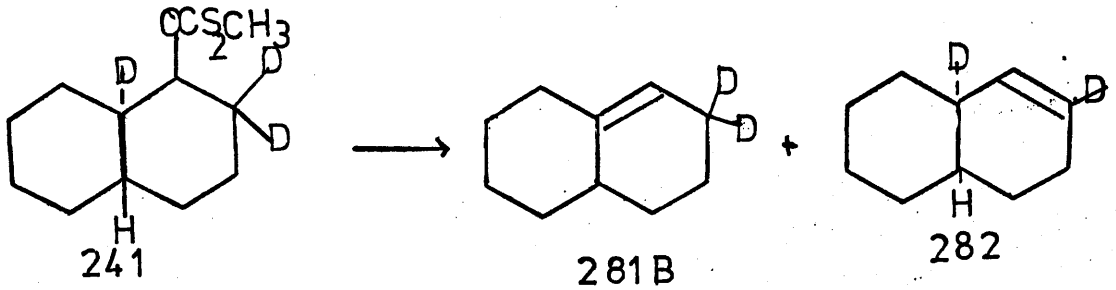
Pyrolysis of (1c, 9c, 10t)-1-decalyl-S-methylxanthate 237 consistently gave, in six pyrolyses, t - Δ 1,2 - octalin 239 (85%) and Δ 1,9 - octalin 238 (15% ± 3%). The corresponding - ethyl-carbonate 290 gave t - Δ 1,2 - octalin 239 (90%), Δ 1,9 - octalin 238 (8%) and Δ 9,10 - octalin (2%) in two pyrolyses. The crude N-dimethylthiocarbamate 279 gave t- Δ 1,2 - octalin 239 (70%) and Δ 1,9 - octalin 238 (30%) in one run. All percentages were determined by g.l.c. on 15% Ap - L at 60 to 100°.

The relatively small amounts of anomalous product 238 and the presence of 240, expected from catalysed rearrangement[151], in the carbonate 290 case, led us to concentrate on the xanthate pyrolysis.

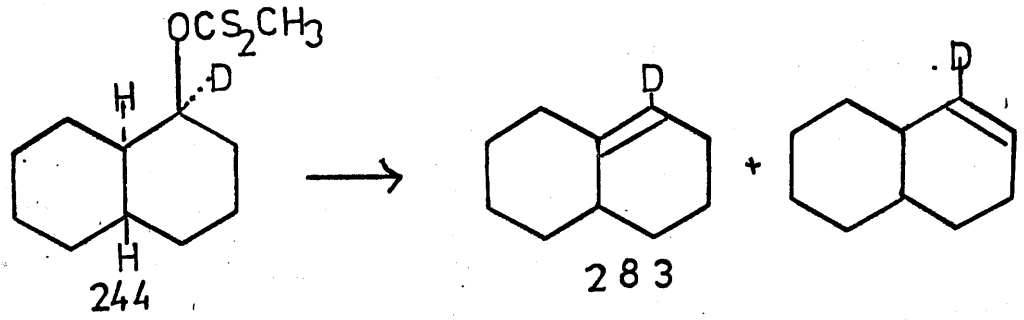
Pyrolysis of (1c, 9c, 10c)-1-decalyl xanthate 287 (m.p. 86-87°, lit[158] 87°) gave cis - Δ1,2 - octalin 286 and, on n.m.r. evidence, Δ1,9 - octalin 238. Integration of signal from Δ 1,9 -



280 → 238 + 239



241 → 281B + 282



244 → 283

olefinic proton against that from Δ 1,2 - octalin protons suggests about 12% of Δ 1,9. A similar result is reported by Huckel[28,29] (Δ 1,9 - 10%, Δ 1,2 - 90%) and Whiting[151] reports a similar apparent anti-elimination on pyrolysis of the corresponding methylcarbonate (Δ 1,9 - 25%, Δ 1,2 - 75%). This pyrolysis was not further studied because g.l.c. separation of the two olefins produced was not achieved.

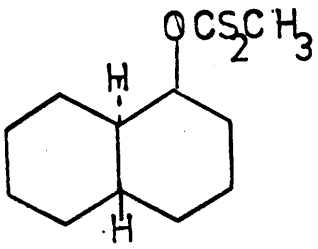
Pyrolysis of (1t, 9c, 10t)-1-decalyl xanthate 280 gave in our hands Δ 1,9-octalin 238 (60%) and t - Δ 1,2-octalin 239 (40%).

Pyrolysis of 2,2,9 - trideuterio - (1c, 9c, 10t)-1-decalyl-xanthate 241 ($d_3$68, $d_2$16, $d_1$10 and d_o6%) gave (g.c.m.s.) Δ 1,9 - octalin 281$_B$(20% ; $d_3$2, $d_2$54, $d_1$34 and d_o9%) and t - Δ 1,2 - octalin 282 (80% ; $d_3$0, $d_2$65, $d_1$25 and d_o 15%). On n.m.r., unlabelled Δ 1,9 - octalin 238 shows a broad singlet at 5.35 ppm while the labeled 281 has a sharp singlet (5.35). The material 282 has asharp singlet at 5.48 p.p.m. A secondpyrolysis gave 281 20% and 282 80% with mass spectra almost identical to those above.

While the above results already rule out α -elimination[40], 1-deuterio-(1c,9c,10t)-1-decalyl xanthate 244 ($d_1$82%) was pyrolised giving Δ1,9 - octalin (18%, 73% d_1) and t - 1,2 - octalin (82%, 80% d_1).

The apparently significant deuterium loss on formation of Δ1,9 - octalin from 244 can be partly explained thus : Equatorial xanthate which should have d_1 content of zero may account for up to 5% of total xanthate ($d_1$82%). This will give Δ1,9 - and Δ1,2 - octalin in the ratio 60 : 40 and so around 3/20 of Δ 1,9 - octalin will have d_1 = 0 while the remainder has d_1 = 82 (approx), giving a net deuterium content of around 70%.

The Δ 1,9 - octalin, supposedly 283 was separated by chromatography (15% silver nitrate-alumina) and hydroborated in T.H.F. Oxidation and mass spectrometry, after the usual work up, showed decalone (M^+ 152). Accurate deuterium content could not be established, owing to contamination of sample, but was less than 10%, indicating that the olefin had the expected structure 283.



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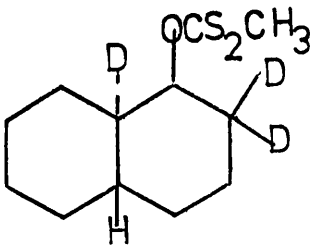

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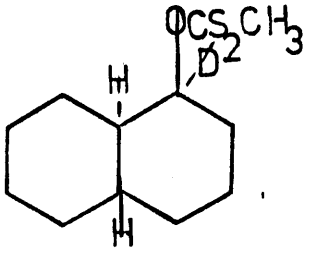

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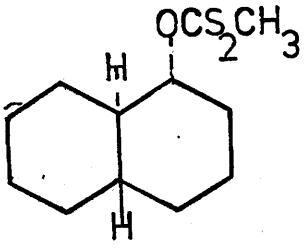

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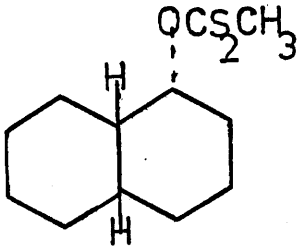

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DISCUSSION

Possible Mechanisms of Apparent Anti-Elimination

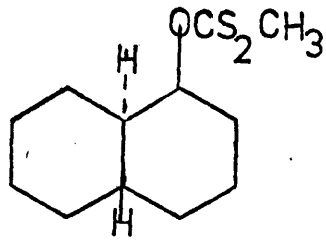
From the results above on pyrolysis of trideuterio-xanthate 241 and 1-deuterio-xanthate 244, it is obvious that neither 1,3 - elimination with 2 - H shift (p.99-100), which would require the formation of d_3 - octalin from 241, nor α -elimination (p. 99-100) which would require d_0 - Δ 1,9 - octalin formation from 244, can explain the apparent anti-elimination in (1c, 9c, 10t)-1-decalyl esters. Let us then consider alternative explanations.

Nace[2] has suggested that many apparent anti-eliminations may arise through epimeric impurity in starting ester (see p.107).

Since the epimer, (1t, 9c, 10t)-1-decalyl xanthate 280 gave Δ 1,9 - octalin and t - Δ 1,2 - octalin in the ratio 3-2, to account for 15% of Δ 1,9 - octalin in pyrolysis of the (1c, 9c, 10t) - xanthate 237 on the basis of epimeric impurity one would require 25% of such impurity. Analysis by the hydride reduction procedure showed that the limit of epimeric impurity was 5%.

In the case of (1c, 9c, 10c) - xanthate 287 the sharp (86-87°C) melting point alone indicates a high degree of purity.

Since epimerisation might occur under pre-pyrolysis conditions, the (1c, 9c, 10t) - xanthate 237 was pyrolised (a) at lower (300 - 350°C) temperatures and higher nitrogen flow rates and (b) in an evacuated sealed tube at 180-210°C for 20 min. Both of these methods resulted in about 50% recovery of xanthate. The olefins were once again in the ratio 5 - 6/1 and the recovered xanthate appeared identical by n.m.r., i.r., and hydride reduction (g.l.c.) with starting material. Repeated partial pyrolysis of recovered



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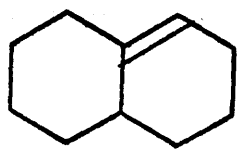

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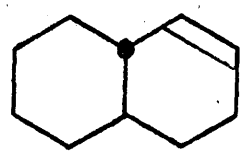

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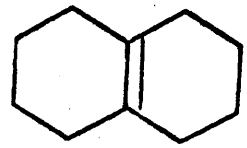

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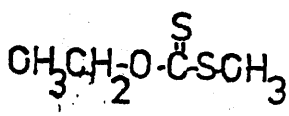

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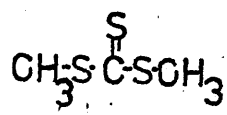

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xanthate gave identical results.

Thus it seems unlikely that xanthate isomerisation is responsible for the anomalous product. The possibility that xanthate 237 isomerises to a material which then pyrolises much faster than the original, and is hence not detected, cannot entirely be ruled out.

A second source of apparently anomalous pyrolysis products appears (on examining the literature) to lie in incorrect characterisation of olefin products. The g.l.c. scheme (p.109) for detecting the octalins, however, seems foolproof and well tried[151] and the isolated products have the expected i.r. and n.m.r. characteristics.

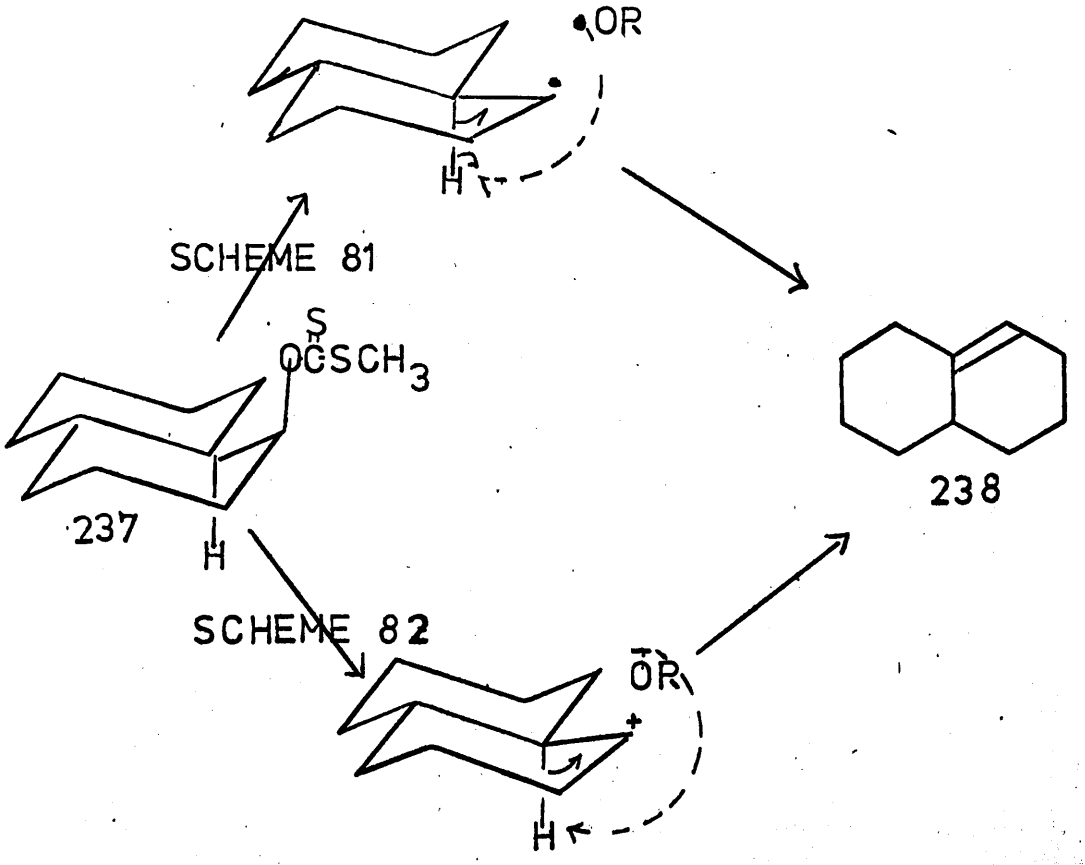
A third serious possibility is that the anomalous Δ 1,9 - product arises by isomerisation of the normal Δ 1,2 - product. Pure t - Δ 1,2 - isomer 239, separated by $AgNO_3$/alumina chromatography, was passed through the pyrolysis system under pyrolysis conditions (a) alone and (b) in the presence of a large excess of ethyl-S-methyl xanthate 284 and dimethyl-trithiocarbonate[11] 285. In no case was isomerisation detected ($\not>$ 0.5%) in one run. Three runs of olefin alone gave 2-3% of Δ 1,9 - olefin, but Δ 9,10 - olefin, not present in the original pyrolysis, also appeared in increasing (2-5%) amounts. Thus, isomerisation of major product, t-Δ 1,2 - octalin does not account for the anomalous Δ 1,9 - olefin.

A fourth possibility is that authentic △ 1,9 - olefin might arise from authentic (1c, 9c, 10t) - xanthate 237 through surface catalysed processes. McColl[8] in his review of halide pyrolyses covers such processes in detail and Djerassi[11] reporting on 2-methylcyclohexyl-ester pyrolyses also refers to the possibility in xanthate pyrolyses.

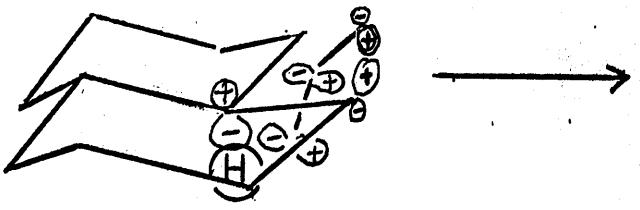
Such a course seems unlikely in the case of (1c, 9c, 10t) - xanthate 237 when one considers the very similar results obtained by Huckel[28], who distilled the product olefins (238 20%, 239 80%) slowly from molten xanthate at atmospheric pressure and 205-210°C and those obtained in this work employing vapour phase pyrolysis at 500° and 0.5 mm Hg. reaction occurring in 0.5 - 3 sec. Similarly, changes in temperature from 300° to 550°, in pressure from 0.06 to 1 mm Hg and in scale (5 - 1, 140 mg) in the same system, have little effect on product ratios as does the conduct of pyrolyses on either fresh or repeatedly used tubes and packings. The sealed tube pyrolysis at 180 - 210° also gave very similar results.

Since the normal pathway leading to t - △ 1,2 - olefin is open to (1c, 9c, 10t) - xanthate 237, involvement of hetrogeneous processes in the formation of △ 1,9 - olefin should lead to large variation[8,11,53] in product ratios with changes in pressure, surface to volume ratio and the age and condition of pyrolysis tubes. This, however, is not observed.

Some authors[4,5,6,8,11] have considered pyrolytic elimination to occur through a non concerted path where the first step is homolytic or hetrolytic cleavage of the c-o bond of the ester.



SCHEME 83



Such routes might account for the anomalous product (Δ 1,9-octalin 238) in this case (see schemes 81 and 82). We have argued against such routes in the Introduction of this thesis (p.2, 22). The main argument is on grounds of activation energy which must not exceed that of normal pyrolysis (30 - 40 Kcal/mole) by more than about 5 Kcal if the anomalous product is to be observed in the presence of normal product. It is difficult to see how, if the ester radical (scheme 81) or ester cation (scheme 82), is to move round to the opposite face of the molecule to abstract the 9-hydrogen, the energy can be less than the bond dissociation energy (86 Kcal/mole for homolytic[16], and 220 Kcal/mole for hetrolytic[16] fission).

The final mechanism for anti-elimination to be considered here is that it is a (a,s,a) concerted elimination[3] (see Introduction p. 8) as shown in scheme 83. From a model it can be seen that the thiocarbonyl group in (1c, 9c, 10t) xanthate 237 (and (1c, 9c, 10c) -xanthate 287) can approach the anti-9-hydrogen fairly closely and, though the geometry is not optimal for overlap, it can be improved by distortion of the σ -bond framework. So little is known of transition state energetics of concerted reactions that it is impossible to say what effect poor overlap or σ -bond distortion would have on activation energy.

SUMMARY

None of the above suggestions readily explains the observed anti-eliminations occurring on pyrolysis of decalyl esters though the last (concerted (a,s,a) - elimination) is preferred by this author. A more rigorous examination of this and other suggestions

is required, particularly a thorough refutation of the involvement of surface catalysed radical chain processes, perhaps by detailed kinetic investigation. Such work would have required a great deal of experimental effort and time. It was therefore regretfully decided to abandon this investigation and concentrate on the experimentally more accessible problems in the field of adamantanoid chemistry described in the foregoing sections of this thesis.

III EXPERIMENTAL

General experimental conditions used were as described for Experimental II (p.70).

Cyclohexylcarbinol[152] 246

Cyclohexyl magnesium chloride, prepared from chlorocyclohexane (14.5g) and magnesium (3.3g), was treated with excess formaldehyde yielding, after distillation (75-77°C, 13 mm Hg) cyclohexylcarbinol (8.2g, 59%) b.p. 90° at 18 mm Hg (lit[152] 88 - 93° at 18 mm Hg), t.l.c. homogeneous. G.c.m.s. shows major component (98%) M^+ 114 and minor component (2%) corresponding to cyclohexanol M^+ 100; n.m.r. δ 3.42 (2H, d J = 6); 2 - 0.8 (12H, m) ; i.r. (liq. film) 3420, 1030, 1040 cm^{-1}.

Methylcyclohexylcarbinol 252[17,149]

Acetophenone (60g) in 50 ml ethanol containing 5 ml 10% acetic acid was hydrogenated at 95 - 100°C and 100 Kg./cm^2 for two hours in the presence of ruthenium (as 0.5g RuO_2 - Johnson Matthey Ltd). The liquid reaction mixture and autoclave washings ($CHCl_3$) were distilled at reduced pressure. After solvent and a small fraction (b.pt. 185-187°, 760 mm. Hg.) had boiled off, the remainder of the mixture (61.5 g, 96%) came over as an oil (b.p. 189-192°)
homogeneous by t.l.c. and g.l.c. (1% SE30, 1% Ap-L, 5% QF1); i.r. (liq.film) 3383 cm^{-1} no aromatic or carbonyl peaks.

Cyclohexylcarbinyl acetate 223[17]

Cyclohexylcarbinol (5g) was treated with acetic anhydride (15 ml) in the presence of sodium acetate (3g) at 100° for 2 hours. The total mixture was put onto a column of grade II alumina (200 g) and eluted with benzene. The first 200 ml of eluant was distilled at reduced pressure leaving a clear oil.

g.c.m.s. : major component (97%) M^+ 156 base peak $^m/_c$ 96

minor component (2-3%) M^+ 142 base $^m/_c$ 82

i.r. : 1735, 1240, 1038 cm^{-1}

Methylcyclohexylcarbinol acetate 226[17,149]

The alcohol 252 (20g) was treated with acetic anhydride (45 ml) and sodium acetate (4g) for 2 hours at 100°C with stirring. The mixture was distilled yielding 21g (79%) of a clear oil (b.pt. 203 - 204°C / 760 mm. Hg.)

t.l.c. (benzene) : one spot Rf 0.5

g.l.c. (1% Ap - L 90°) : One peak

n.m.r. : δ 4.7,(1H, M) 2.0,(3H, s); 1.15,(3H, d J = 6)

i.r. : 1732, 1242 cm^{-1}

Cyclohexylcarbinyl-p-toluenesulphonate 247

To the alcohol 246 (5g. 0.044 mole) in dry pyridine (20 ml) at 0°C was added, with stirring, p-toluenesulphonyl chloride (10g, 0.053 mole)

(10g, 0.053 mole). The resulting yellow solution was stirred for 15 min and set aside at 4°C for 2 days. The contents of the flask were then poured onto a mixture of ice (20g) and conc. hydrochloric acid (15 ml) and the flask well washed out with water. On stirring for 15 min, the resulting solid was collected by filtration, washed with ice-water, redissolved in ether and sequentially washed with dilute hydrochloric acid, sodium bicarbonate solution and brine. Drying over sodium sulphate and evacuating to dryness gave an oil (0.3g) which on recrystallisation (petrol at -70°C) gave colourless plates (7.2g) m.p. 30.5 - 31.5°C (lit[153] 31 - 31.5°); n.m.r. : δ 7.5, (4H, quartet); 3.8(2H, d); 2.43(3H,s) 2.0 (11H, m).

Methylcyclohexylcarbinyl-p-toluenesulphonate 253

The method used was the same as that described above for cyclohexylcarbinol. The alcohol 252 (4.6g, 0.036 mole), in pyridine (20 ml), treated with p-toluenesulphonyl chloride (7.6 g 0.042 mole) for 2 days gave, after recrystallisation, needles (7.1g, 70%) m.p. 25.5 - 26.5°; n.m.r. δ 7.45 (4H,q); 4.42 (1H, m) ; 2.42 (3H,s) ; 2.3 - 0.8 (14 H, m) includes doublet (J = 6) at 1.2. (Found C, 63.7; H, 7.96 requires C, 63.8; H 7.85%)

1 - Methylcyclohexanol 248[17,155]

To 5g. (0.21 g. atom) magnesium turnings in 10 ml ether in a flamed dry, 100 ml, three-necked flask fitted with dropping funnel, magnetic stirrer and reflux condenser with drying tube, was added a crystal of iodine and 10 ml of a solution of 21.3g (0.15 mole) methyl iodide in 30 ml ether. The flask was heated till reaction started and the remainder of the methyl iodide

solution added dropwise so as to maintain steady reflux. Reflux and stirring were continued for 1 hour, heating the flask as required.

Cyclohexanone (9.8g, 0.1 mole) in ether (20 ml) was then added dropwise over 20 min and the mixture stirred for 2 hours.

After hydrolysis in ice (20g) and sulphuric acid (50 ml,5M), the product was extracted into ether, washed with aqueous sodium bicarbonate, dried over sodium sulphate and evacuated to dryness, yielding a clear oil (9.5g) b.pt. 152-155 (lit[155,17] 155°) ; i.r. : (liq. film) 3450 cm^{-1}, carbonyl absorbtion absent.

1-Ethylcyclohexanol 254

The method used was the same as that described for 1-methylcyclohexanol above. Ethyl bromide (25g, 0.23 mole) was treated with magnesium (8g, 0.28 g. atom) and the resulting Grignard treated with cyclohexanone (17.6 g, 0.18 mole). Hydrolysis on ice/sulphuric acid yielded after extraction and drying a clear oil (14g, 60%) homogeneous by t.l.c. and g.l.c. (1% SE30, ApL); i.r. 3460 cm^{-1} carbonyl absorbtion absent.

1-Methylcyclohexene[155,157] 224

To 1-methylcyclohexanol (2g, 0.0175 mole), in a 5 ml flask with a Vigreux column and collection condenser, was added iodine (2.5g, 0.01 mole) and the flask placed in an oil bath at 190°C. Fractions, collected over the range 70-89°C, were found to separate into a colourless aqueous layer and a red organic layer. Comparison (t.l.c.) of the organic layers showed them to be identical. The combined fractions, in pentane, were washed with aq. sodium bisulphite then brine and dried over sodium sulphate. Removal of solvent at reduced pressure gave 0.7g of a colourless mobile liquid b.pt. 108-110°(lit[17,157] 110°);

g.l.c. (15% AP-L, 120°) - One peak (> 90%); i.r. 3020, 800 cm^{-1}; n.m.r. δ 5.4 (1H,m), 1.65 broad singlet.

1-Ethylcyclohexene 229[155]

The method used was the same as that described above for 1-methylcyclohexene 224. 1-Ethylcyclohexanol (2g, 0.016 mole) was treated with iodine (2g 0.008 mole) at 190-200°C. Fractions boiling at 75-110°C were collected. These gave, on purification as above, 1.0 g of a mobile liquid : i.r. 3015.920 cm^{-1}; n.m.r. δ 5.4(1H, m) ; 2.2-1.3 (10Hm); 0.95 (3H, t, J = 6); g.l.c. (30% silvernitrate in triethylene glycol - celite) . 80% one peak

Ethylidene cyclohexane 228 and vinylcyclohexene 227

Methylcyclohexylcarbinol (1g, 0.0078 mole) with iodine (1.27 g, 0.005 mole) was heated at 130°. Fractions boiling at 82-96°C were collected yielding, on treatment as before, 0.4 g of a volatile oil. N.m.r. shows methyl triplet (see 1-ethylcyclohexene above) and a methyl doublet (δ 1.15). Absorbtions in region δ 5 - 4 are complex. G.l.c. (30% $AgNO_3$/triethylene glycol 25°C), shows three peaks (a) 80%, t_R 9.4 min (b) 15%, t_R 14 min and (c) 5% t_R 26 min. The peak (a) corresponds to 1-ethylcyclohexene 229 (b) corresponds to the minor product of methylcyclohexylcarbinyl acetate pyrolysis (presumably ethylidenecyclohexane) and (c) to the major product of the same pyrolysis (presumably vinylcyclohexane). The peak order is that expected[157] on the basis of interaction of Ag^+ with the olefins.

Methylenecyclohexane[154] 225

The preparative method used was that described in detail by Corey[154] whereby cyclohexanone (10.8g, 0.11 mole) was treated with triphenylphosphine-methylene-ylid prepared in situ by treatment of methyl-triphenylphosphonium bromide (35.7g,0.10 mole)

with sodium hydride (0.1 mole) in dimethylsulphoxide. The yield was 4.8g (50%) of methylenecyclohexane b.pt. 34-36°/5 mm Hg (lit[154] 42°/ 7 mm Hg); g.l.c. (15% AP-L) One peak; i.r. 3015, 900, 865 cm^{-1}; n.m.r. δ 6.6,(2H, sharp s).

Methylcyclohexene isomerisation[156]

Methylenecyclohexane (100 mg) was injected in a stream of nitrogen into a silica tube (70 X 1.5 cm) filled with granular alumina and heated to 300°C. The tube effluent on condensation in an acetone/solid CO_2 trap yielded 93 mg. of an olefin mixture consisting of (g.l.c. comparison on 15% AP-L) methylenecyclohexane (45%), 1-methylcyclohexene (35%) and two other peaks (15% and 10%).

Ethylcyclohexene isomerisation[156]

Use of the method described above for methylcyclohexane isomerisation when applied to the product of dehydration of methylcyclohexylcarbinol (100 mg)(see p.122) gave material which on g.l.c. (30% $AgNO_3$/triethylene glycol/celite) showed the presence of vinylcyclohexane (2%), ethylidenecyclohexane (35%), 1-ethylcyclohexene (40%) and one other peak (c 20%). Repassage of material through the furnace as before showed no further peaks.

Pyrolysis of cyclohexylcarbinyl acetate 223

(Apparatus as in diag. 49B, p.73,but with a tube 70 x 1.5 cm)

The acetate 223 (0.5g, 0.003 mole) was distilled over a period of 30 min through a silica tube (70 X 1.5 cm) lightly packed with glass wool and electrically heated along 60 cm of its length at 500°C ($\pm$ 10°C). A forward flow of nitrogen at 0.5 mm Hg was maintained throughout. The product, collected

in a liquid nitrogen cooled 'U' tube, was taken up in isopentane, washed with aq. sodium bicarbonate and dried over sodium sulphate. The solvent was distilled off through a vigreux column at atmospheric pressure leaving 0.19g (61% of theory) of clear oil. Use of i.r. showed absence of carbonyl absorbtions. n.m.r. : δ 4.6 sharp singlet integrates for 2H. g.l.c. (15% Ap - L 100°) Two peaks were observed the major (95%) corresponded on cross injection to methylene cyclohexane and the minor (5%) to cyclohexene (see p.119). No 1-methylcyclohexene was observed ($<$ 0.1%) its expected retention being checked by cross injection of authentic material. Use of a 30% $AgNO_3$/triethylene glycol g.l.c. column showed only two peaks as above.

Pyrolysis of methylcyclohexylcarbinyl acetate 226

The apparatus method of pyrolysis and treatment of product were identical to that described above for cyclohexylcarbinol acetate 223, 0.5 g of ester yielding 0.25g of product. Examination of product (g.l.c.) showed c.20% unchanged ester. The olefinic material was seperated by chromatography on 10g of Grade II alumina being eluted with 50 ml of isopentane. Removal of solvent as described above gave 0.12g (37% of theory) of a clear oil; n.m.r. δ 6.1 - 4.8 multi-line system; g.l.c. (30% $AgNO_3$/triethylene glycol/celite) shows two peaks (a) t_R 14 min. (35%) corresponding to ethylidenecyclohexane and (b) t_R 26 min (65%) corresponding to vinylcylohexane. 1-Ethylcyclohexene (t_R 9.4 min) was absent ($<$ 1%).

Pyrolysis of cyclohexylcarbinyl-p-toluenesulphonate 247

The apparatus , method of pyrolysis and initial treatment of product were those described above for pyrolysis of the acetates (223, 226). The sulphonate (3g) gave a brown oil (2.0 g) which gave, on distillation (98-103°, 760 mm Hg), an oil (0.67g, 62%); g.l.c. : (15% Ap-L 100°) showed four major and one minor (< 5%) peak. The major peaks corresponded to those obtained by isomerisation of methylene-cyclohexane (see p. 123).

The above pyrolysis and product treatment was repeated twice with similar results the combined olefin ratios are discussed above (see p.103)

Pyrolysis of methylcyclohexylcarbinyl-p-toluenesulphonate

The apparatus, method of pyrolysis and initial treatment of product were the same as those described above for the pyrolysis of the acetates 223, 226.

The sulphonate (0.8g) gave a brown oil (0.4g) which on t.l.c. showed the presence of unchanged sulphonate and more polar material. Column chromatography on 10g Grade III alumina gave, on elution with isopentane (50 ml), 0.2g of a clear oil. G.l.c. (30% Ag NO_3-celite) showed four major peaks which corresponded in retention with those obtained on isomerisation of ethylcyclohexene isomers (see p. 123).

EXPTL. III CONT. - DECALYL SERIES

Hydrogenation of 1-Naphthol 260

(a) 1-Naphthol (10g, vaccuum distilled and recrystallised from ethanol, m.p. 96-97°) in ethanol (200 ml) was hydrogenated at 100 Kg /cm^2 and 50° for 6h. in an autoclave (which had been thoroughly washed with distilled water and ethanol), over Rh-alumina (1g, 5%). Distillation of the filtered mixture gave mixed decalols (9.7g) b.p. 120-125° (13 mm Hg) (lit[161] 119-127, 13 mm Hg). Recrystallisation from benzene (three crops) yielded (1c, 9c, 10c)-1-decalol (6.9g, 64%) m.p. 91-92° (lit[28] 93°) i.r. 3620, 1450, 1060, 1032, 942 cm^{-1}; n.m.r. ($CDCl_3$ - D_2O) δ 3.7 (1H m) : 2.2 - 1.2 (16H m).

(b) Attempted hydrogenation of 260 (10g) over ruthenium dioxide (0.5g) at 100 Kg/cm^2 and 20°C in ethanol gave as judged by t.l.c. and g.l.c. (5% QF1, 100°) unchanged 260 (> 90%). Preparative t.l.c. of a sample gave a minor product apparently 1-naphthyl-ethyl-ether; i.r. 3055, 1600, 1582, 1465, 1392, 1272, 1242; n.m.r. δ 8.4-6.6 (7H, m) ; 4.2 (2H, q J = 6.2) ; 1.5 (3H, t J = 6.2).

(c) Hydrogenation[159] of 260 (10g) in ethanol (150 ml) at 110 Kg/cm^2 and 20° for 5h. over Rh-carbon (1g, 5%) gave (t.l.c.) one product (30%) in addition to starting material. Preparative t.l.c. of a sample yielded 5, 6, 7, 8 - tetra hydro-1-naphthol m.p. 66-67° (from ethylacetate-petrol) (lit[169] 68°); i.r. 3602, 3020, 1575, 700, 660 cm^{-1}; n.m.r. δ 7.4-6.4 (3H, m) ; 4.6 (1H, s exchanges in D_2O); 2.65 (4H,m); 1.8 (4H, m).

(d) Hydrogenation of 260 (5g) in ethanol (50 ml) at 3 - 4 Kg/cm^2 and 20°, over Rh-alumina (1g,5%) gave, after 12h, 5,6,7,8, - tetra-hydro-1-naphthol (5g, 98%).

(e) Hydrogenation of 260 (5g) in acetic acid (20 ml) at room temperature and pressure over platinum (0.1g, Adams) gave (t.l.c.) three products which appeared (i.r.) to be a mixture of saturated alcohols (3620 cm^{-1}), unsaturated alcohols (3602, 1575 cm^{-1}) and acetates (1730 cm^{-1}).

t-1-Decalone 265

1-Tetralone (12g) in ethanol (50 ml) was hydrogenated over rhodium-alumina (2g, 5%) at 20°C and 6 Kg/cm^2 for 12h. The crude product on filtration and solvent removal was oxidised (Jones). Reaction and work-up in the usual manner gave an oil (11.5g) which on g.l.c. (5% QF1, 110°) showed two peaks (25%, t_R 2.6 min 1-tetralone and 75%, t_R 4.2 min 1-decalone). The oil was stirred with saturated aq. sodium bisulphite for 4h. and left at 0° overnight. The mixture was filtered, the solid washed with ether, and the filtrate retreated with bisulphite (5g.). The combined solid was dissolved in saturated aq. sodium carbonate (100 ml) which was then extracted (twice) with ether. Evaporation of the washed and dried ether layers gave an oil (5.9g). G.l.c. showed : (5% QF1, 110°) one peak (t_R 4.2 min) ; (2% SE 30, 100°) two peaks (4/1, t_R 3.8, 4.1 min).

The oil was refluxed with 5% sodium in methanol for 1h, extracted into ether, washed, dried and evaporated. Recrystallisation from pentane at -10°C gave 265 as plates (4.6g) m.p. 31-33° (lit.[158] 33°); i.r. 1712 cm^{-1}; mass spec. M^+ 152.

265 - M.p. 31-33° was also obtained by Jones oxidation and base treatment as above of mixed 1-decalols resulting from hydrogenation of 1-naphthol 260 (above).

(1c, 9c, 10t)-1-Decalol 266 and (1t, 9c, 10t)-1-Decalol 267

t-1-Decalone 265 (2.95g) in methanol (50 ml) containing one drop conc. HCl was hydrogenated[162] at room temperature and pressure over platinum (0.4g, Adams) for 3h. G.l.c. (5% QF1, 60°) showed a major (80%, t_R 5.6 min, 266) and a minor (20%, t_R 6.6 min 267) peak. Crystallisation (ethyl acetate-petrol) gave (1c, 9c, 10t)-1-decalol (1.85g, 63%) m.p. 47-48° (lit[28] 49°).

Preparative t.l.c. of the mother liquors yielded two bands (a) (less polar) 266 as above (0.41g, 14%) m.p. 46 - 48° and (b) (1t, 9c, 10t)-1-decalol 267 (0.5g, 17%) m.p. 57-59° (lit[28] 63°, lit[161] 58-59.5°).

The alcohol mixture 266 and 267 was also obtained, by reduction with alumino-hydrides of t-1-decalone 265 (50 mg portions) yields and product ratios were determined by g.l.c. (5%QF1, 60°).

Lithium aluminium hydride in ether at reflux for 3h. gave, as reported by Moritami[162], the decalols (c.100%) 266 and 267 in the ratio 1 : 4.

Lithium tri(t-butoxy) - aluminium hydride[170] in refluxing THF overnight gave (60% yield) 266 and 267 in ratio 7 : 3.

Lithium tri(methoxy) - aluminium hydride[170] was prepared in situ using 1 ml of c. 1M. lithium aluminium hydride in ether and 1 ml of c. 3 M dry methanol in ether. This in refluxing ether overnight gave (c. 80% yield) of 266 and 267 in ratio 1:1.

Use of dicyclohexyl borane (see p. 129) gave (75 - 90% yield on three attempts) 266 and 267 in ratio 4:1.

O - Deuterio - methanol

Trimethyl borate (104g) was refluxed overnight with deuterium oxide (68g) in a flamed dry flask fitted with magnetic stirrer, reflux condenser and balloon seal. Distillation (with stirring at 60 - 80°) gave the alcohol. N.m.r. of methanol showed δ 4.78 (integrates 1 unit); 3.35 (3 units). The deuterated alcohol showed δ 4.75 (1 unit), 3.35 (64.5 units) consistent with $>$ 95% deuterium content.

2,2,9 - Trideuterio-t-1-Decalone

t-1-Decalone (980 mg) was heated at reflux for 1h. with 5% sodium / deuterio - methanol (10 ml). The solvent was removed and the residue azeotroped with dry benzene. The process was repeated. The residue in dry ether (10 ml) was washed with two 2 ml portions of D_2O and the ether layer filtered through a plug of freshly roasted magnesium sulphate. Removal of solvent gave an oil (960 mg) which by mass spectrometry had d_3 content of 62% (alcohols subsequently produced from this had higher d_3). N.m.r. (benzene) showed δ 1.8-0.8 (m). t-1-Decalone 265 showed δ 2.3 - 2 (3H, m); 1.8 - 0.8 (13H, m).

2,2,9 - Trideuterio - (1t, 9c, 10t) - 1 - Decalol 270

To a solution of sodium borohydride (380 mg, 10 m mole) in diglyme (20 ml), stirred at 0° under nitrogen in a flask fitted with dry-ice/acetone reflux condenser, was added, through a septum, cyclohexene (1.97g, 24 m mole) and, over 15 min, boron trifluoride etherate (1.7g, 12 m mole). The solution was stirred at 0° for 2 h.

Trideuterio ketone 265 (912 mg, 6 m mole) in diglyme (5 ml) was added and the mixture stirred at 0° for 2h and room temperature

overnight. Hydrogen peroxide (5ml, 3M, NaOH and 5 ml 30% H_2O_2) was added dropwise with stirring and stirring continued at 40-50° for 30 min and room temperature for 1h. The reaction mixture was diluted with ether (100 ml) and washed with water (twice) and brine before drying over magnesium sulphate. Removal of solvent and preparative t.l.c. gave the alcohol 270 m.p. 46-48° (500 mg, 54%); n.m.r. δ 3.72 (sharp singlet, 1H). Mass spectrometry showed, on correction for M + 1 and M + 2 from the spectrum of undeuterated material, d_3 80%, d_2 15%, d_1 3%, d_o 2%.

1-Deuterio-(1c,9c,10t)-1-Decalol 272

t-1-Decalone (304 mg) was reduced with a two-fold excess of dicyclohexyl deuterio-borane prepared in situ from sodium borodeuteride (125 mg), cyclohexene (656 mg) and boron trifluoride etherate (568 mg), in the manner described above for trideuterio-1-decalone, yielding alcohol 272 m.p. 46-48° (190 mg, 62%). N.m.r. showed absence of carbinol proton. Mass spectrometry, using the usual corrections from spectrum of unlabeled material 266, showed d_1 95%, d_o 5%.

Attempted Routes to 9-deuterio-1-decalol 271

(a) Hydroboration of $\Delta^{1,9}$ - octalin 238 (10 mg) in tetrahydrofuran using 1 ml of 1M diborane solution (Alpha Inorganics) and work up in the usual manner gave (95% yield by g.l.c., 5% QF1 at 60°) decalols 267 and 268 in the ratio 3:2. Other decalols accounted for 5% of product.

(b) Enol-trifluoroacetate 275 was prepared by reflux in ether for 8h of t-1-decalone (152 mg), trifluoroacetic anhydride (630 mg) and trifluoro-acetic acid (10 mg). Removal of volatiles left a clear oil (272 mg, V max. 1785, 1678 cm^{-1}).

The oil, stirred in water - THF 1:3) for 10 min gave on extraction into ether, washing and drying, an oil (ν max 1710 cm^{-1}).

The preparation was repeated and attempts made to purify the trifluoro acetate by micro-distillation. This and preparative t.l.c. led to substantial ketone (ν max 1710 cm^{-1}) contamination.

(c) Enol-acetate 276 was prepared according to House[171], b.p. 65-70° (0.3 mm Hg) (lit[171] 68-79° at 6 mm); i.r. 1750, 1695 cm^{-1}; n.m.r. δ 1.92(3H,s) (lit.[171] 1750, 1695 cm^{-1}; 1.93 (3H,s))

The mildest conditions found to hydrolise the enol-acetate (to 50% by t.l.c.) were reflux in methanol over sodium carbonate for 14 h.

Treatment[171] of the enol acetate (120 mg) in ether (15 ml) with methyl lithium (1ml, 1M in ether, Alpha Inorganics) gave at least six products as judged by t.l.c.

Enol-acetate (120 mg) in ether (10 ml) was treated with excess lithium aluminium hydride (1 ml of 1M solution in ether) in a modification of the method of Dauben[165]. After stirring for 10 min at 20°, the usual work up gave (as judged by g.l.c. on 5% QF1 at 60° on comparison with authentic materials) enol-acet ate 276 (10%), mixed 1-decalones (45%) and decalols 264 (10%), 266 (12%), 267 (21%) and 268 (2%).

Reaction on the same scale for 20 min at -70° gave, as before, enol acetate 10%, 1-decalones (82%) and mixed 1-decalols (8%). The decalone portion was shown (2% SE 30, 110°) to consist of trans (56%) and cis (44%) compounds.

(1c, 9c, 10t)-1-Decalyl-S-Methyl Xanthate 237

The most successful method, used to produce xanthate for pyrolysis experiments, is described first. Initial attempts are described later.

To a flamed, 25 ml, two necked flask fitted with rubber septum, magnetic stirrer, reflux condenser and balloon seal, was added sodium hydride (240 mg, 10 m mole) and dry benzene (5 ml). (The hydride had previously been suspended in dry petrol and filtered through sintered glass under nitrogen). The system was flushed with dry nitrogen and the nitrogen atmosphere maintained. The alcohol 266 m.p. 48° (860 mg, 5.6 m mole), in benzene (5 ml), was injected and the mixture stirred at reflux for 12 h. On cooling, carbon disulphide (2 ml) was added and the orange mixture stirred at 50° for 14h. Methyl iodide (3ml) was then added and stirring continued at 40-50° for 48h. The cooled mixture was filtered through celite being washed with benzene. On solvent removal, preparative t.l.c. gave a yellow oil (890 mg, 65%). With care a portion of xanthate could be extracted, free of the bright yellow contaminant, as a colourless oil. This, though crystallising from methanol at -10°, melted below 5°C; i.r. 2925, 2928, 1450, 1250, 1223, 1131, 1063, 1052, 1036, 980, 965, 916 cm^{-1}; n.m.r. δ 5.74(1H, m); 2.54 (3H, s); 2.3-0.8 (16H, m); mass spec. M^+ 244, base peak $\frac{m}{e}$ 136.

Reduction of a sample (20 mg) with excess lithium aluminium hydride in refluxing ether for 5h. showed on g.l.c. (5% QF1, 60°), after the usual work-up, decalol 266 (98%) and decalol 267 (2%).

Micro-distillation yielded bright yellow dimethyltrithiocarbonate[11] 285 (30 mg) b.p. 70-80°, 0.5 mm Hg; M^+ 138; n.m.r. δ 2.76 (s).

Preliminary Experiments on Formation of Xanthate 237

Xanthate preparation, along the lines described above, was attampted using 1.5 fold, 3 fold and 5 fold excess of sodium hydride in air. Yields of xanthate by preparative t.l.c. were 15%, 35% and 29% respectively. The n.m.r. spectrum of each batch showed impurity in the region of the Cl-proton (δ 5.74) and a minor extra methyl peak (δ 2.53). Hydride reduction of a sample showed decalols 286 (85%) and 287 (15%).

Refluxing a sample (20 mg) in 5% methanolic potassium hydroxide or in 2% methanolic - HCl for 8 h. gave larger (> 20%) yields (by g.l .c., 5% QF1) of 287.

The alcohol 266 mp. 48° (50 mg) was treated with sodium hydride (100 mg) in refluxing benzene for 48 h, water added and the organic layer extracted washed and dried. Analysis by g.l.c. (5% QF1) showed decalols 266 (75%) and 267 (20%) and 1-decalone 265 (5%).

The above treatment of alcohol 266 under nitrogen using sodium hydride in oil showed 266 (90%), 267 (9%) and 265 (c. 1%).

The process repeated using fresh, oil-free sodium hydride under nitrogen showed 266 (> 96%).

Attempted Alternative Preparations of Xanthate 237

1-Decalol 266 m.p. 48° (20 mg) in triethylamine (1 ml) was added to a stirred solution of thiophosgene (23 mg) in benzene (5 ml) at 5° and stirred at 5-10° for 14 h. Methyl thiol (100 mg) was added and stirring continued for 20 hours at 0-10°C. Ether (10 ml) was added and the solution washed with dil HCl, aq. bicarbonate and water and dried. T.l.c. showed a minor spot corresponding to xanthate and a major non polar spot. G.l.c. (15% Ap-L, 130°) showed the non polar material (eluted from 5g of grade III alumina in pentane) to consist of t-Δ 1,2- octalin (50%), Δ 1,9 - octalin (35%) and minor unidentified peaks on comparison with authentic samples.

The above, repeated using pyridine as base, showed (t.l.c.) xanthate as a minor and hydrocarbons as major products. Similarly, a repeat run using triethylamine as before but with sodium mercaptide (100 mg) in place of methyl thiol gave (t.l.c.) largely hydrocarbon.

Sodium methylmercaptide (70 mg) was added, with stirring, to thiophosgene (115 mg) in ether (15 ml) and stirred at room temperature for 14 h. Decalol 266 (154 mg) was added in ether (10 ml) containing triethylamine (1 ml) and stirring continued overnight. T.l.c. showed starting alcohol 266 and non-polar material but no xanthate.

(1c, 9c, 10t)-1-Decalyl-thiocarbamate 279

Decalol 266 m.p. 48° (155 mg) in pyridine (5 ml) was added to N-dimethylthiocarbamyl chloride (250 mg) in pyridine (5 ml) and stirred at 0° for 3h, 20° for 4h and 40° overnight. The extent of reaction being followed by t.l.c. Extraction with ether, washing with dilute HCl, aq. bicarbonate and brine, drying and solvent removal, gave a brown oil (160 mg). Preparative t.l.c. (ethylacetate-petrol 15:85) gave (Rf 0.5) starting alcohol and (Rf 0.75) the thiocarbamate 279 (crystallisation was not achieved) n.m.r. δ 5.55 (1H,m); 3.43 (3H,s); 3.18 (3H,s); 2.4 - 0.6 (16H,m). The presence of minor peaks around 5.4 and 3.3 p.p.m suggest that this compound is stereoisomerically impure.

Pyrolysis of 279 (50 mg in 0.5 ml ether) at 500° and 0.5 mm Hg, as described below for pyrolysis by injection of xanthates, gave by g.l.c. comparison Δ1,9 - octalin (30%) and t-Δ 1,2-octalin (70%).

(1t, 9c, 10t)-1-Decalyl-S-methyl xanthate 280

By the method described for synthesis of xanthate 237 above (p.132), 1-decalol 267 m.p. 59° (910 mg) treated under nitrogen in refluxing benzene (15 ml) with sodium hydride (240 mg) (12 h), carbon disulphide (2 ml, for 5h) and methyl iodide (3 ml, for 14h) gave, on work-up as before xanthate 280 as a yellow oil (1122 mg, 78%) i.r. 2925, 2828, 1230, 1132, 1065, 1060, 1054, 980, 970, 928 cm^{-1}; n.m.r. δ 5.34 (1H, m); 2.54 (3H,s); 2.3 - 0.6 (16H,m); mass spec. M^+ 244, base $\frac{m}{e}$ 136.

(1c, 9c, 10c)-1-Decalyl -S-methyl xanthate 287

By the method described for xanthate 237 (p.132), 1-decalol 264 m.p. 92° (705 mg) treated under nitrogen with sodium hydride (216 mg) in refluxing benzene for 12h, carbon disulphide (2 ml for 5h.) and methyl iodide (3 ml for 14h) gave, on work-up as before, crude xanthate 297 as a yellow solid. Recrystallisation from methanol gave needles (905g, 81%) m.p. 86-87° (lit[158] 86.6-87.2); n.m.r. δ 5.61 (1H,s); 2.55 (3H,s); 2.3-1.0 (16H,m).

2,2,9 - Trideuterio-Xanthate 241

By the method described for xanthate 237 (p. 132), trideuterio alcohol 270 (1250 mg) treated with sodium hydride (300 mg), carbon disulphide (3 ml) and methyl iodide (5ml) gave, on work up and preparative t.l.c. as before, the xanthate 241 (1450 mg, 67%) as a pale yellow oil. Hydride reduction of a sample as before showed (g.l.c.) decalols 266 (97%) and 267 (c. 3%). N.m.r. showed a spectrum as for xanthate 273 but proton (5.74) appears as a sharp singlet. Mass spectrometry, applying the usual corrections from unlabelled material showed d_3 68%, d_2 16% d_1 10%, d_o 6%.

1-Deuterio Xanthate 244

By the method described for xanthate 237 (p.132), treatment of deuterio alcohol 272 (138 mg) with sodium hydride (46 mg), carbon disulphide (1 ml) and methyl iodide (1 ml), gave, on work up and preparative t.l.c. as before, xanthate 244 (111 mg, 52%); n.m.r. as for 237 but showing no proton at δ 5.74. Mass spectrometry, applying the usual corrections, showed d_1 80% and d_o 20%.

(1c, 9c, 10c) - 1 - Decalyl p-Toluenesulphonate 282 prepared in the usual manner, as described by Huckel[38], in 84% yield had m.p. 92-94° (lit.[38] 96°)

(1t, 9c, 10t) - 1 - Decalyl Ethylcarbonate 281

The method of preparation of carbonates is a modification of that reported by O'Connor and Nace[21]. Ethyl chloroformate (327 mg) was added dropwise with stirring to dry pyridine (3 ml), 1-decalol 267 m.p. 59° (153 mg) in 2 ml of the same solvent added, and stirring continued at room temperature for 24 h. The mixture, diluted with ether (20 ml), was washed with dilute HCl, aq. bicarbonate and brine. Removal of solvent from the dried ($MgSO_4$) ether layer and preparative t.l.c. gave a clear oil (130 mg, 60%) homogeneous by t.l.c. and g.l.c. (5% QF1, 2% SE30, 1% OV 17); i.r. 2980, 1745, 1264 cm^{-1}; n.m.r. δ 4.6 - 4.0 (3H, contains singlet and quartet J = 6.2); 2.2 - 1.8 (19H, m, contains triplet δ 1.3).

2-Decalyl Ethylcarbonate Mixture 285

2-Decalol (200 mg, Koch Light Ltd, mainly trans fused epimeric mixture) was treated with ethyl chloroformate (500 mg) in pyridine in the manner described above for ethylcarbonate 281.

Work-up and preparative t.l.c. as before gave an oil (250 mg) i.r. 1745 cm^{-1}; n.m.r. δ 5 - 2.9 (3H, m. includes q. J = 6.3); 2.3 - 0.8 (19H, m, includes t. J = 6.3).

(1c, 9c, 10t) - 1 - Decalyl Ethylcarbonate 290

1-Decalol 266 m.p. 48° (250 mg) was treated with ethyl chloroformate (500 mg) in pyridine in the manner described above for ethylcarbonate 281. Work-up and preparative t.l.c. as before gave 290 (100 mg, 29%) i.r. 1745 cm^{-1}, n.m.r. δ 4.8 (1H, m); 4.18 (2H,q); 1.9 - 0.9 (19 H, m, includes t, 1.3).

Micro distillation gave an analytical sample (Found C, 69.06; H, 10.06 $C_{13}H_{22}O_3$ requires C, 68.99; H, 9.8%)

$\Delta^{1,9}$ - Octalin 238[38]

(1c, 9c, 10t) - 1 - Decalyl - p-toluene - sulphonate 282 was stirred at 50° for 24 h with a solution of sodium (77 mg) in ethanol (13 ml). The solution, diluted with isopentane (10 ml), was washed with water, dilute HCl, aq. bicarbonate and brine before drying over sodium sulphate. Removal of solvent at 50°, followed by micro-distillation, gave $\Delta^{1,9}$ - octalin (240 mg, 55%) : i.r. (liq. film) 3005, 1655, 812, 804 cm^{-1}; n.m.r. δ 5.36 (1H, s), 2.6 - 0.6 (20 H, m, note impurity by g.l.c.); g.l.c. (15% Ap-L, 130°) $\Delta^{1,9}$ - octalin 238 (80%, t_R 19.2 min) and $\Delta^{9,10}$ - octalin 240 (15%, t_R 22 min)

$\Delta^{9,10}$ - Octalin 240

Mixed 2-decalols (Koch Light Ltd.) (2g) were refluxed in orthophosphoric acid (15 ml) at 150° for 4h. The olefin was distilled out (120 - 180°), diluted with isopentane and washed with water. Removal of solvent gave an oil (500 mg); g.l.c. (15% Ap - L, 130°) showed 240 (70%, t_R 22 min) and $\Delta^{1,9}$ octalin 238 (c. 20% t_R 19.2 min) minor amounts of other octalins were also present.

Decalyl Ester Pyrolyses

All pyrolyses were carried out by injection of sample, neat or in solution, through a 6 inch steel needle into the hot zone of a silica tube (70 X 1.5 cm), lightly packed with glass wool, maintained along 60 cm of its length at around 500°C and under a slow flow of nitrogen at a pressure around 0.3 - 0.6 mm Hg. (see diag.49A,p.73)

Collection was by means of a "U" tube immersed in liquid nitrogen. The time taken from injection to observation of aerosol at the exit was 0.5 - 5 sec. Pyrolysis conditions were maintained for 10 min and the system flushed with nitrogen. The disconnected U-tube was washed out with pentane (5 - 10 ml) and this solution passed through a plug (2 - 5g) of alumina before t.l.c. and g.l.c. analysis.

(1t, 9c, 10t) - 1 - Decalyl xanthate 280 (200 mg) in ether (0.3 ml) was pyrolised at 500° and 0.5 mm Hg. G.l.c. showed as follows: (2% SE 30, 130°) minor xanthate peak (5%, t_R 7.2 min) and a major (95%) peak of shorter retention; (15% Ap-L, 130°) t- $\Delta^{1,2}$- octalin 239 (41%), $\Delta^{1,9}$ octalin 238 (59%).

(1t, 9c, 10t)- 1 - Decalyl Ethylcarbonate 281 (120 mg) in methanol (0.2 ml) was pyrolised at 500° and 0.5 mm Hg. G.l.c. (5% QF1, 120°) showed starting carbonate (15%) and a peak (85%) of shorter retention; (15% Ap-L, 130°) showed $\Delta^{1,9}$ - octalin (54%), t - $\Delta^{1,2}$ - octalin (45%) and $\Delta^{9,10}$ - octalin (1%)

Mixed 2-Decalyl carbonates (285) (100 mg) in methanol (0.1 ml) were pyrolised at 500° and 0.5 mm Hg. G.l.c. (15% Ap-L, 130°) showed two major peaks, the t - $\Delta^{1,2}$ - octalin 239 and t - $\Delta^{2,3}$ - octalin 284 in the ratio 1:1.

(1c, 9c, 10c) - 1 - Decalyl Xanthate 287 (250 mg) in ether (0.3 ml) was pyrolised at 500° and 0.5 mm Hg. T.l.c. showed absence of xanthate while g.l.c. (15% Ap - L, 130°) showed only one peak (t_R 15.4 min) apparently cis - $\Delta^{1,2}$ - octalin. N.m.r. showed δ 5.54 (2H, m), 2.4 - 1 (16.4 H, m) on four integrations.

The significance of the integration observed and the appearance of a peak (C. 0.12 H) at 5.38 p.p.m. are discussed in terms of $\Delta^{1,9}$ - octalin impurity in the foregoing text.

(1c, 9c, 10t) - 1 - Decalyl Ethylcarbonate 290 (100 mg) in methanol (0.2 ml) was pyrolised at 500°C and 0.3 mm Hg. G.l.c. (5% QF 1, 120°) showed conversion of C. 70%; (15% Ap - L, 130°) showed t - $\Delta^{1,2}$ - 239 (90%), $\Delta^{1,9}$ - 238 (8%) and $\Delta^{9,10}$ - octalin 240 (2%).

Pyrolysis of (1c, 9c, 10t) - 1 - Decalyl xanthate 237

Pyrolysis of crude 237 (50 - 120 mg in C. 0.2 ml ether) by the method described above gave t - $\Delta^{1,2}$ - octalin and $\Delta^{1,9}$ - octalin in ratios ranging from 87 : 13 to 72 : 28.

When samples, which on reduction ($LiAlH_4$) and analysis of the decalols so produced showed > 97% stereochemical purity, were used, the variation in product ratio was reduced. Three attempts on each of two batches of xanthate gave $\Delta^{1,9}$/t - $\Delta^{1,2}$ octalins in the ratio 15 $\pm$ 3 : 85 $\pm$ 3 on pyrolysis at temperatures between 440 and 520° and pressures between 0.2 and 0.6 mm Hg.

In one attempt of the above pyrolysis (on 750 mg of xanthate 237) the product, on work up as usual, was isolated by removal of solvent isopentane giving a volatile oil (C. 350 mg, C. 83%). This was chromatographed over 18% silver nitrate - alumina (20g). Elution with isopentane gave what appeared to be $\Delta^{1,9}$ - octalin. Elution was continued till all $\Delta^{1,2}$ - octalin was eluted and the column flushed with ether. No other hydrocarbons were detected

by g.l.c. in any fractions.

Solvent removal through a Vigreux column from combined $\Delta^{1,9}$ octalin fractions gave a clear oil (c. 10 mg) which was treated with 1 ml of 1 M solution of diborane in tetrahydrofuran. Reaction at room temperature for 2h and work up in the usual manner gave an oil (12 mg) which was oxidised (Jones) in acetone and the product extracted into ether.

G.l.c. (5% QF 1 and 2% SE 30) showed t-1-decalone (> 95%) by comparison with authentic material which in turn could be identified as distinct from the two ketones arising from Jones oxidation of commercial (Koch Light) 2-decalol. These latter ketones were not present in the hydroboration - oxidation product.

Partial Pyrolysis of Xanthate 237 was achieved by pyrolysis (150 mg in 0.2 ml ether) at 460° and 0.2 mm Hg in the normal manner but with increased nitrogen flow. Contact time was in the order of 1 - 2 sec. T.l.c. showed c. 50% conversion. G.l.c. (15% Ap - L) showed $\Delta^{1,9}$ - octalin and t - $\Delta^{1,2}$ - octalin in the ratio 20 : 80.

The unreacted xanthate, separated by t.l.c. showed i.r. and n.m.r. spectra identical to those of starting xanthate. Repeat pyrolysis of recovered xanthate gave the same olefins in almost the same ratio (16 : 84).

Xanthate recovered from the second pyrolysis (showing i.r. and n.m.r. spectra as before) was repyrolised giving the same olefins in the same (16 : 84) ratio.

Partial pyrolysis was also carried out by placing 210 mg of material 237 in a sealed evacuated glass tube and heating it in an oven at 180 - 210° for 20 min. T.l.c. showed c. 50%

conversion while g.l.c. showed $\Delta^{1,9}$ - octalin and t - $\Delta^{1,2}$ - octalin in the ratio 18 : 82. The xanthate recovered by t.l.c. was identical by i.r. and n.m.r. with starting material.

Pyrolysis of 2, 2, 9 - Trideuterio - (1c, 9c, 10t) - 1- decalyl xanthate 244

Pyrolysis (of 1.14 g) was carried out in the usual manner by injection of three neat portions over a period of 15 min. into the tube at 500°C and 0.5 mm Hg.

Passage of the total product in isopentane (100 ml) through an alumina column (5g, Grade III) and removal of solvent gave an oil (500 mg, 77%).

A portion (5 mg) on g.c.m.s. showed t - $\Delta^{1,2}$ - octalin (80%, $d_3$0, $d_2$65, d_1 25 and d_o 10%) and $\Delta^{1,9}$ - octalin (20%, $d_3$2, $d_2$54, $d_1$34 and d_o 9%)

The bulk of the pyrolysate chromatographed over 15% silver nitrate - alumina, as described above for the corresponding undeuterated material, gave $\Delta^{1,9}$ octalin (25 mg) : n.m.r. δ 5.35 (1H, sharp singlet); 2.4 - 0.8 (13H, m) and t - $\Delta^{1,2}$ - octalin (210 mg) : n.m.r. δ 5.48 (1H,s); 2.4 - 0.7 (13H, m).

A second pyrolysis (110 mg in 0.1 ml ether) gave the same products in the same ratio ($\pm$ 2%) and with the same deuterium content ($\pm$ 2%).

Pyrolysis 1 - Deuterio - (1c, 9c, 10t) - 1 - Decalyl xanthate 244

The xanthate (111 mg) in ether (0.3 ml) was pyrolised at 490° and 0.3 mm Hg. in the normal manner. G.c.m.s. showed $\Delta^{1,9}$ -octalin (18%, 73% d_1 and 27% d_o) and t - $\Delta^{1,2}$ - octalin (82%, 80% d_1 and 20% d_o).

A portion of $\Delta^{1,9}$ - octalin was separated on silver nitrate - alumina, treated with 1 ml of 1 M diborane solution and oxidised as described above (p. 140) for the corresponding undeuterated material. Mass spectrometry failed to give accurate deuterium analysis owing to contamination of sample with material of higher molecular weight however peak at $^{m}/_{e}$ 153 was $<$ 10% of 152 peak (1-decalone M^{+} 152).

Ethyl-S-methyl Xanthate 284

Ethanol (1 ml) was stirred for 1h with sodium hydride (500 mg) in benzene (10 ml), carbon disulphide (2 ml) added, and stirring continued for 2 h. Methyl iodide (3 ml) was added to the red mixture and stirring continued overnight. Filtration through celite and solvent removal gave a clear oil (2g) : n.m.r. δ 4.65 (2H, q), 2.58 (3H, s), 1.42 (3H,t).

Attempted Rearrangement of t - $\Delta^{1,2}$ - octalin 239

(a) Octalin 239 (50 mg) prepared and separated as described above (p. 139) was injected (in 0.1 ml ether) into the pyrolysis system at 500° and 0.5 mm Hg. G.l.c. (15% Ap-L) of the collected material showed only 239 (> 99%).

The process was repeated on recovered olefin 239. After three such passages, g.l.c. (15% Ap-L, 130°) showed t - $\Delta^{1,2}$ - octalin (92%), $\Delta^{1,9}$ - octalin (3%) and $\Delta^{9,10}$ - octalin (5%).

(b) The above process was repeated using t - $\Delta^{1,2}$ - octalin (20 mg), dimethyl trithio-carbonate (20 mg) and ethyl-s-methyl-xanthate (20 mg.) The collected material (after one passage) showed (g.l.c. on 15% Ap-L) t- $\Delta^{1,2}$ - octalin as the only olefin (> 99%).

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