STUDIES OF THE FRAGMENTATION OF ORGANIC COMPOUNDS INDUCED BY ELECTRON IMPACT

A thesis presented by

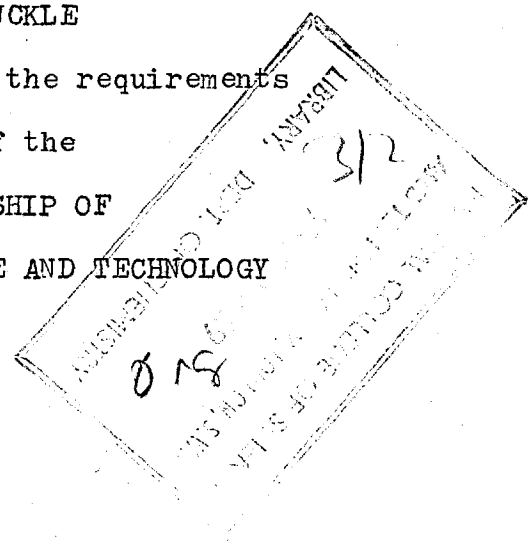
DEREK RICHARD BUCKLE

in partial fulfilment of the requirements

for the award of the

DIPLOMA OF MEMBERSHIP OF

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY



Linstead Laboratory,
Imperial College of Science and Technology,
London, S.W.7.

July 1969.

Abstract

The existing information concerning the preferential elimination of ortho-substituents in certain aromatic systems is reviewed and correlations with structural features made.

The mass spectra of over twenty 1-aryl anthraquinones are discussed and the general fragmentation pathway elucidated by deuterium labelling, mass measurement, and metastable ion analysis. A particular reference is made to the ortho-effect the principles of which are described in the review.

Model compounds for the terminal diaryl polyene carotenoids have been prepared and their fragmentation discussed with emphasis to the cyclisation modes within the polyene chain and between the chain and the aryl rings.

An improved synthesis of the natural product dunnione is presented and the mass spectra of its specifically deuteriated analogues have been used to interpret the fragmentation of the mould metabolite atrovenetin. A unique rearrangement of β-naphthol-3,3-dimethylallyl ether is discussed and evidence in support of a four-membered ring intermediate given.

Finally the anomalous loss of C_3H_4O from 1,2-dihydro santonin and of C_5H_8O from anhydrodimedones is considered and model compounds are used to determine the necessary structural features for this fragmentation.

To my wife.

" Read not to contradict and confute, nor to
believe and take for granted, nor to find
talk and discourse, but to weigh and consider."

Francis Bacon

(essays "Of Studies")

Acknoledgements.

To Dr.E.S.Waight I would like to express my sincere gratitude for his friendly guidance and encouragement, both of which will be long remembered.

I am indebted also to Professor D.H.R.Barton for the invaluable opportunity of working in the organic chemistry research laboratories at Imperial College, and to the Science Research Council for financial support over the last three years.

To my colleagues, Drs. D.J.Blythin, D.G.B.Boocock, R.Lawrence and T.C.Smale and Messrs. J.Bilton, D.R.Clarke and J.D.Spence, I owe thanks for their friendship and often helpful discussions.

The technical assistance of Messrs. R.Carter, E.Pepper and J.C.Watson who supervise the laboratory facilities has been of immence value, and their friendship greatly appreciated. My thanks are also conveyed to Mrs.A.I.Boston for A-60 n.m.r. spectra; Mr. P.Jenkins for HA-100 n.m.r. spectra, and to the Microanalytical Laboratory staff for their prompt and accurate service. I would also like to express my appreciation to Messrs. P.Boshoff and J.Bilton for the maintainance of the mass spectrometer.

Finally thanks are due to my wife and parents whose help and encouragement have been limitless.

Contents.

Abstract	Page	2
Acknowledgements		5
Introduction		8
A Review of the Ortho-Effect in Mass Spectrometry		14
Part 1 - 1-Aryl Anthraquinones.		40-77
1 , 1 Discussion of Experimental Work		41
1 , 2 Discussion of Mass Spectra		53
Part 2 - Terminal Diaryl Polyenes.		78-104
2 , 1 Discussion of Experimental Work		79
2 , 2 Discussion of Mass Spectra		86
Part 3 - Atrovenetin and its Model Compounds.		105-132
3 , 1 Discussion of Experimental Work		106
3 , 2 Discussion of Mass Spectra		122
Part 4 - Cyclohexenone Derivatives.		133-164
4 , 1 Discussion of Experimental Work		134
4 , 2 Discussion of Mass Spectra		142
Part 5 - Experimental Section.		165-258
5 , 1 1-Aryl Anthraquinones		167
5 , 2 Terminal Diaryl Polyenes		189

5 , 3 Atrovenetin Models 209

5 , 4 Cyclohexenone Derivatives 228

5 , 5 Mass Spectra 245

References. 259

Introduction

The invention of the mass spectrograph by Aston[1] in 1919 saw the birth of the modern mass spectrometer and the science of mass spectrometry, but even so it was not until some 15 years ago that the full potential of this now powerful tool was recognised and given the experimental impetus it undoubtedly deserves. The requirement of milligram quantities, indeed for direct insertion only microgram amounts, makes this technique invaluable for naturalproducts, some of which are only isolable in minute quantities. The concept of mass spectral mechanisms can be used both post factum and predictively at the present time with a considerable degree of success, but the paucity of reference data imposes a limit on the extent to which prediction may be used.

No discussion of the instrument (an AEI MS 9 spectrometer) will be given as this information is readily obtainable from the numerous texts now available. However, a few of the basic principles will be given on account of their importance in any mass spectral work. The three most important equations governing ion formation are shown below, the first generating negative ions will be discussed no further as these ions are relatively unimportant in the mass spectra of organic compounds.

$$M + e^- \longrightarrow M^- \qquad \text{(i)}$$

$$M + e^- \longrightarrow M^+ + 2e^- \qquad \text{(ii)}$$

$$M + e^- \longrightarrow M^{n+} + (n+1)e^- \qquad \text{(iii)}$$

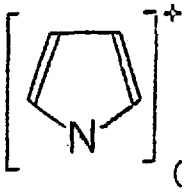
Equation (iii) controls the formation of multiply charged ions, but it is only in the spectra of aromatic compounds that these are of sufficient stability to be of importance. This leaves equation (ii) as defining the process by which the majority of the ions are formed.

The concept of charge localisation offers a ready explanation for the wide occurrence of α-cleavage as a primary fragmentation process in so many substances possessing heteroatoms (e.g. amines, ethers and thioethers), but considerable controversy exists over this, some authors preferring charge delocalisation. However, the technique of assigning the charge to a particular atom has proved to be of extreme value in the rationalisation of ion decomposition mechanisms. In the mechanisms described later localisation of the charge will be assumed and a single barbed arrow ⌒→ infers a single electron shift and a double barbed arrow ⇀ represents a two electron shift.

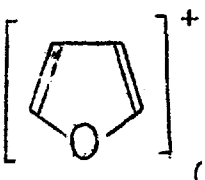
Before proceeding to the main body of this thesis mention should be made of the doubt relating to the use of arrows to represent fragmentation modes since these cannot be a true interpretation of the electronic processes which are taking place.

The loss of carbon monoxide from α-pyridone and α-pyrone has been extensively studied and the cyclic structures (A) and (B) are invariably quoted as the structures of the $[C_4H_4N]^+$ and $[C_4H_4O]^+$ ions which result. Energy considerations

however,[2] would appear to prefer acyclic forms for both.



(A).



(B).

Similarly it has been suggested[3] by comparison of benzene and its open chain isomers that the former proceeds through ionized 1,3-hexadiene-5-yne (C).

$$[CH_2 = CH - CH = CH - C \equiv CH]^{+\cdot}$$

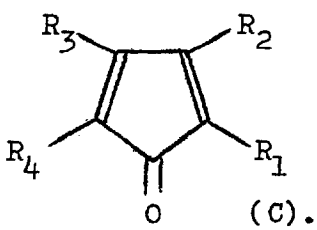
(C).

Further, an elegant approach has recently been used to demonstrate that doubly-charged benzene also has an open chain structure.[4] For the reaction $C_6H_6^{++} \longrightarrow CH_3^{+} + C_5H_3^{+}$ the energy released was calculated as 2.8 ev., an energy which is only consistent with an open chain structure for the parent doubly-charged benzene ion.

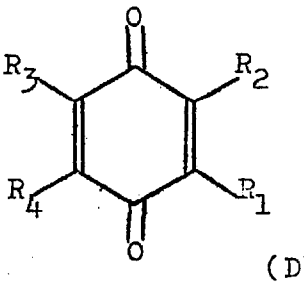
This work casts some doubt on the convention of representing ions formed from cyclic molecules by cyclic structures. In order to verify whether or not an ion were cyclic would necessitate individual energy studies but at present there is a dearth of information on this subject. As the true structure of the daughter ions is known with certainty in relatively few instances, and likewise for the parent ions, it is reasonable to suggest that the mechanism taking place

cannot be postulated with certainty.

These points are further impressed by consideration of the recent work of Bursey and Elwood[5] on sustituted tetracyclones and p-benzoquinones shown by (C) and (D) respectively.

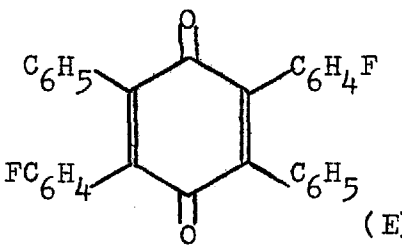


(C).

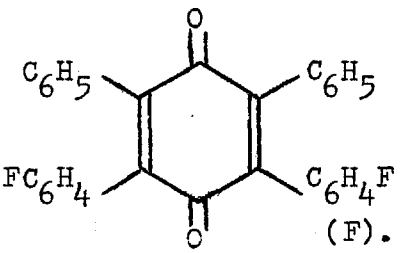


(D).

It was observed that 2,5-bis-(p-fluorophenyl)-3,6-diphenyl benzoquinone (E) and its isomer (F) lost two molecules of carbon monoxide to form an ion which could then fragment to charged disubstituted acetylene species.



(E).

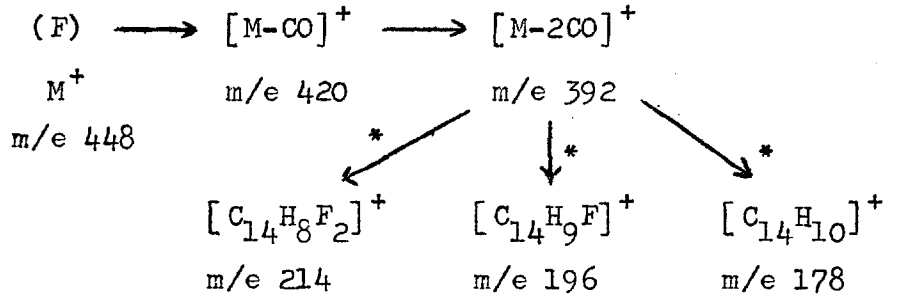


(F).

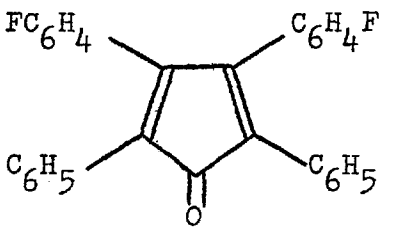
Using integrated metastable ion intensities for the formation of the three acetylenic fragments from compound (F) it was shown that the cyclic structure for the $[C_4R_4]^{+\bullet}$ ion formed by stepwise loss of carbon monoxide from (F) was not solely of the square type (see scheme 1). Furthermore, since the ratios of the metastable ion intensities were not appreciably different from those of the cyclopentadienones (G) and (H), 1 : 3.1 : 0.89 and 1 : 3.2 : 0.93 respectively,

the structure of the $[C_4R_4]^{+\cdot}$ ion formed from the benzoquinone was probably identical to that from the cyclopentadienones.

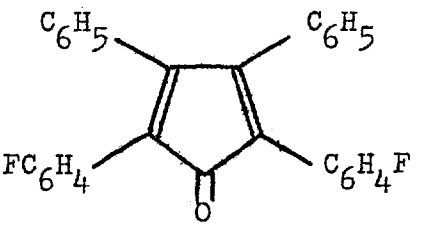
Scheme 1.



metastable ratio 1 : 3.3 : 0.87

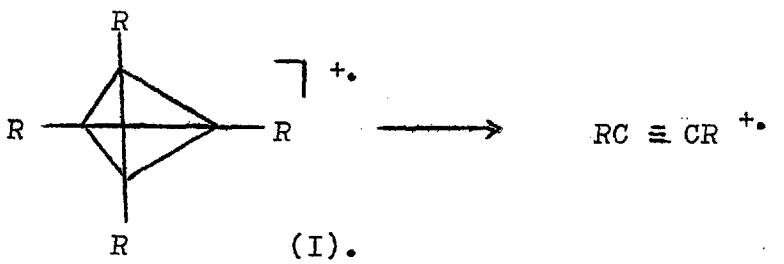


(G).



(H).

The isomer (E) also gave a qualitatively similar spectrum with metastable ions showing that not only a cyclic but even a tetrahedral structure is involved since the simpler monocyclic structure, square or rectangular, could not produce three daughter ions. It was therefore suggested that the structure of the $[C_4R_4]^{+\cdot}$ ion might be represented in part by (I).



(I).

The possibility of other forms also was not excluded on account of the voltage dependence of the ions which indicated a complex route for formation. Consequently it would appear that the classical cyclobutadiene ion postulated by Beynon for anthraquinones[6] could not account for the observed fragmentation. This does not, however, nullify the existence of this type of ion.

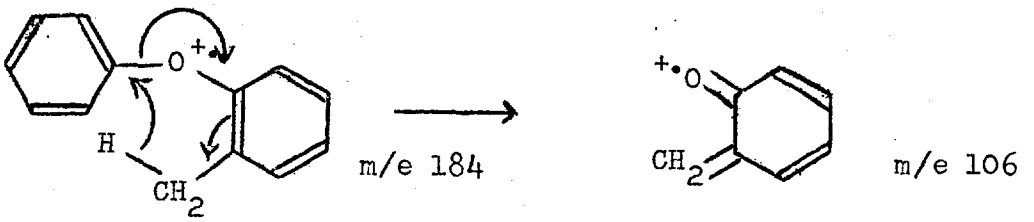
Because of the difficulty of realising the fruits of the above ideas it is intended to retain cyclic structures for ions in the conventional manner but discretion should be exercised in their interpretation. The important point, however, is the existence of an ion at a given mass and this is indisputable.

Review of the Ortho-Effect in Mass Spectrometry

1. Preamble.

When the mass spectra of positional isomers of substituted aromatic rings are compared obvious differences between the spectra of the ortho-isomer and those of the meta- and para-isomers are sometimes observed. Prevalence of these differences constitutes an ortho-effect, the outcome of which is essentially the preferential loss of the ortho- over the the meta- or para-substituent. Because the para-isomer gives a spectrum identical in many cases with that of the meta-isomer this effect clearly cannot be electronic, but must owe its presence purely to the position of the sustituent relative to the side-chain causing the effect. This review will be a discussion of this effect, its energetics and the evidence for its occurrence.

At the outset a distinction must be drawn between this effect and that in which the ortho grouping influences side-chain fragmentation. For example, in diaryl ethers the presence of an ortho methyl group[7] completely alters the decomposition mode and gives an ion at m/e 106 which is absent in both the meta and the para compounds. Moreover, the latter isomers give peaks with similar intensities and have almost identical spectra.

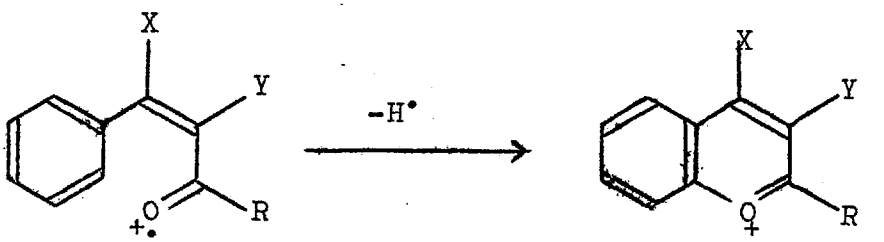


This rearrangement fragmentation is widespread in mass spectrometry but is outside the scope of this review and will not be considered further.

2. Formation of six-membered ring systems.

(a). Acyclic side-chain derivatives.

The prerequisit for cyclisation with concomitant elision of the ortho substituent is that a more stable ion may be formed, a condition which is adequately satisfied when the aromatic character of the ion is increased. It is for this reason that a potentially aromatic system must be in evidence before the ortho-effect is observed. To clarify this statement a simplified general formula (1)[8] is given below:



(1). (2).

This formula encompasses numerous different classes of compound containing only C, H, and O in the side-chain but other types are to be discussed later. Table 1 lists the M^+ and $[M-1]^+$ values expressed as a percentage of the strongest ion from which it may be seen that considerable losses of H• from the aromatic ring are observed in all of these compounds.

The driving force for the formation of ion (2), which is

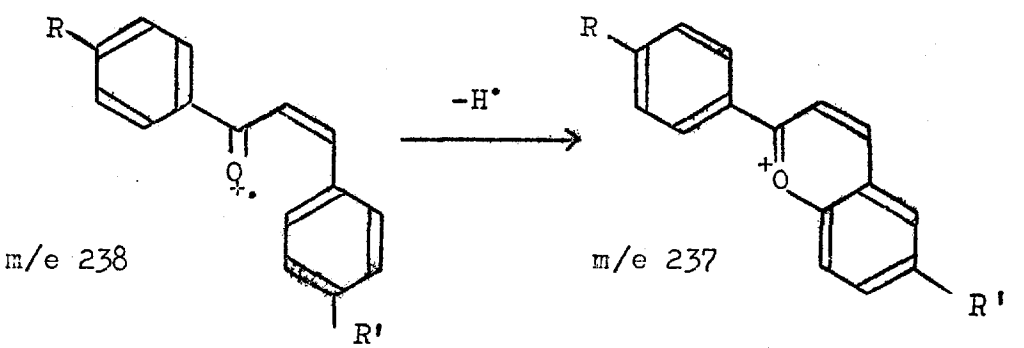
essentially an intramolecular attack of electrophilic oxygen, is generation of the aromatic benzopyrilium ion[8]. Although not restricted to six-membered ring formation (vide infra) the ortho-effect is most conspicuous when this can be achieved.

Table 1.

Relative loss of H° from (1). for X = Y = H

R	M^+	$[M-1]^+$
$-CH_3$	45%	27%
-OH	100%	62%
$-OCH_3$	50%	17%
-Ph	92%	100%
$-CH:CH.CH_2Ph$	55%	60%

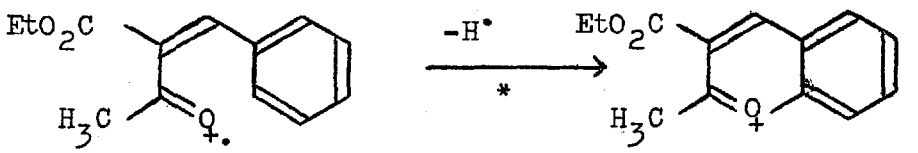
In the mass spectrum of the methoxyl substituted benzalacetophenones (3a) and (3b)[9] similar losses of H° from the molecular ion were found but no structures were proposed. The results indicate that these ions are very similar and that stabilisation via the conjugative effect of the methoxyl group occurs to approximately the same extent in both.



(3).a. R=OMe, R'=H (78%)
b. R=H, R'=OMe (100%)

a. R=OMe, R'=H (46%).
b. R=H, R'=OMe (42%).

The aryl β-keto ester (4) has a metastable ion corresponding to 3.3% of the base peak, for the loss of H• from the molecular ion[10] which is indicative of a very favourable process of very low activation energy.



(4). m/e 218 (100%) m/e 217 (80%).

Although little work has been done on the energetics of the ortho-effect information on this can be gleaned from several papers. For example, competitive reactions have been observed in the alkyl esters of cinnamic acid[11] in which the magnitude of the $[M-1]^+$ peak diminishes rapidly as the size of the alkyl group increases (Table 2).

Table 2

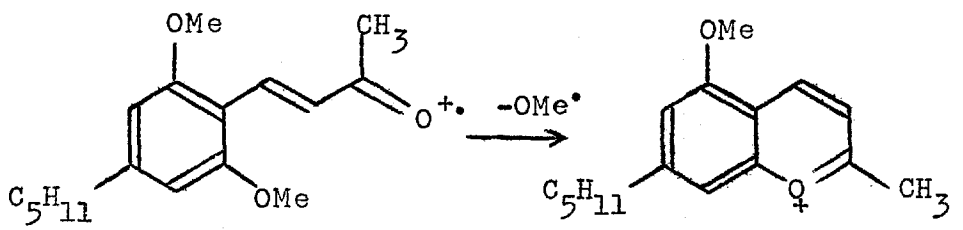
Relative intensities of H• loss from alkyl cinnamates.

Ester	M^+	$[M-1]^+$
Methyl	50.8%	16%
Ethyl	28.8%	2.7%
isopropyl	26.9%	nil

The base peak at m/e 131 in all of these derivatives is due to elimination of the alkoxy fragment which becomes more

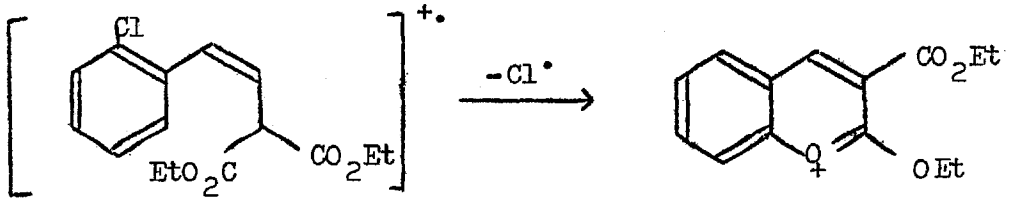
facile as stabilisation of the removed radical increases. These results clearly emphasise the need to consider other alternative fragmentation modes when investigating the ortho-effect, especially if these are low activation energy and consequently facile transitions.

So far only the expulsion of an hydrogen atom has been discussed but this is by no means the only radical which can be lost in the formation of an oxonium ion. The natural product β-olivetyl-1-vinylmethyl ketone[12](5) has been shown to lose methoxyl to form the most abundant ion for which the benzopyrilium structure (6) has been suggested.



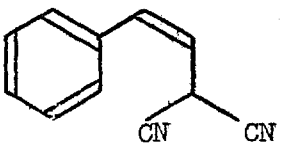
(5). (6).

In the above example only methoxyl can be lost from the ortho-positions since both are identically substituted. In the mass spectra of αβ-unsaturated esters[13] with o, m, and p chloro substituents the m and p isomers showed little loss of Cl• or of H• and had almost identical spectra whereas the o-isomer (7) had no M^+ but a prominent $[M-Cl]^+$ ion (60%).



(7).

The preferential loss of Cl$^{\bullet}$ over H$^{\bullet}$ emphasises the ortho-effect in this case and cyclisation to the oxonium ion is strongly indicated. The equivalent unsubstituted dicyanide[13]



shows little $[M-1]^+$ (ca. 8%), presumably because the resulting cyclic ion is non-aromatic in the newly formed ring.

Work on substituent effects in benzylidene acetones with o-, m- and p- methoxyl groups[14] gives a clear indication of the ortho-effect and from Table 3 the facile loss of methoxyl from this position is demonstrated.

Table 3

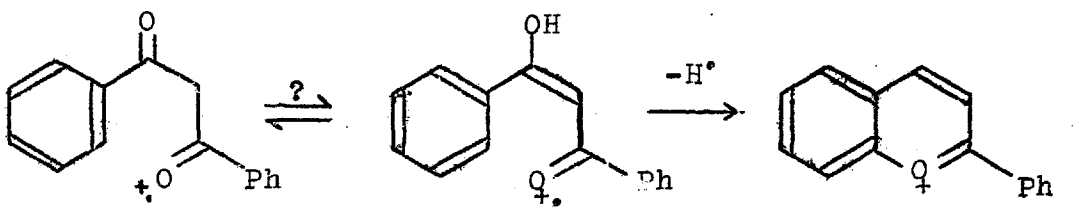
Relative loss of H$^{\bullet}$ and OMe$^{\bullet}$ from o-, m- and p- methoxyl substituted benzylidene acetones.

Substituent		M^+	$[M-1]^+$	$[M-OMe]^+$
o-OMe	%RA	20.4	4.0	100
	% Σ	5.1	1.0	25.2
m-OMe	%RA	100	50	62.5
	% Σ	13.2	6.7	8.3
p-OMe	%RA	57.5	12.5	6.7
	% Σ	18.4	4.0	2.1

In the p-methoxyl case the base peak is at $[M-15]^+$ due to cleavage of the ether linkage and it is this which explains

the difference between the m- and p- values. Here then is an example where competing fragmentations can influence the results to a considerable and recognisable extent.

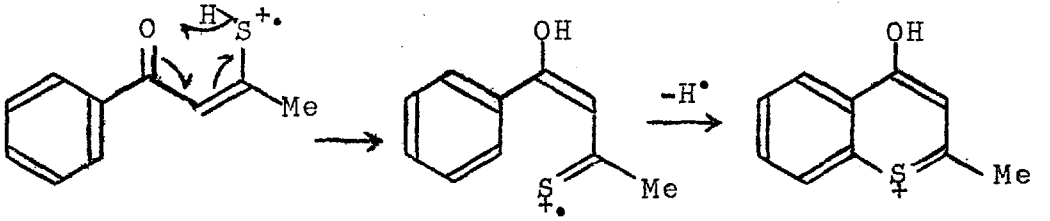
One should now consider examples of those compounds exhibiting the ortho-effect but which do not fill the requirements of (1) for X = Y = H. The ability of β-diketones to enolise to a conjugated system is well known even though the ability to do this in the mass spectrometer is subject to considerable doubt[14a]. However, the mass spectra of aryl β-diketones have been studied[15] and these compounds have been shown to form oxonium ions in the expected manner. It is assumed that only the molecular ion of the enolic form, which is the most abundant form in the unionised molecule, is able to undergo this cyclisation.



M^+ 70% $[M-1]^+$ 60%

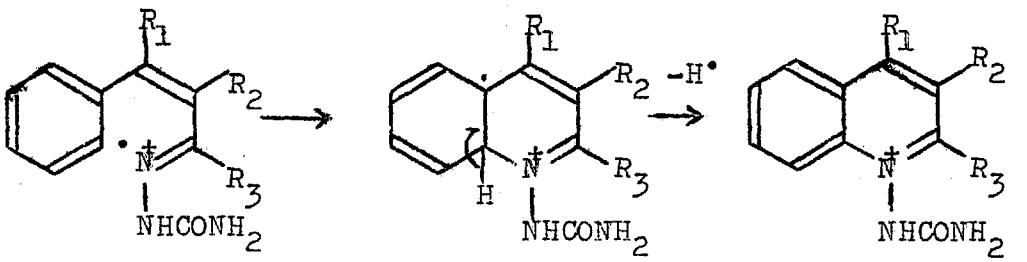
Since it was observed[5] that aromatic β-diketones and some of their derivatives showed a marked tendency to form $[M-1]^+$ ions, whereas such ions were not present in acetyl acetone, it is evident that the hydrogen atom lost is abstracted from the aromatic ring. Deuterium labelling verified this by showing that hydrogen loss was exclusively from the benzene nucleus and not from the methylenic position. Moreover,

replacement of one phenyl group by methyl reduced the $[M-1]^+$ peak to 34%, the relative intensity of the M^+ remaining about the same. Similar results are obtained from the mass spectra of β-keto thiones[16], the aromatic derivatives readily losing an hydrogen atom. Expectedly the diphenyl compound eliminates $H^\bullet$ to an increased degree.



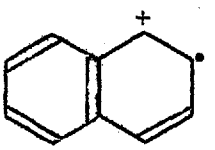
m/e 178 (58%) m/e 177 (100%)

αβ-Unsaturated semicarbazones[17] have been observed to form quinoline type ions when derived from aromatic unsaturated aldehydes, and it is suggested that these ions are formed by attack of the electron deficient nitrogen atom on the ortho-position of the benzene ring followed by rearomatisation by elision of the ortho-substituent at the site attacked. The mechanism which has been postulated is shown below:-



1-Aryl butadienes[14] also exhibit the loss of an ortho-substituent, as do the analogous diaryl polyenes (discussed

later). The former are postulated to fragment with formation of the naphthalene radical ion (8). The relative losses of $H^{\bullet}$/substituent for o- and p- nitrophenyl butadienes, from which the ready loss of NO_2 from the ortho-position is evident are shown in Table 4.



(8).

Table 4

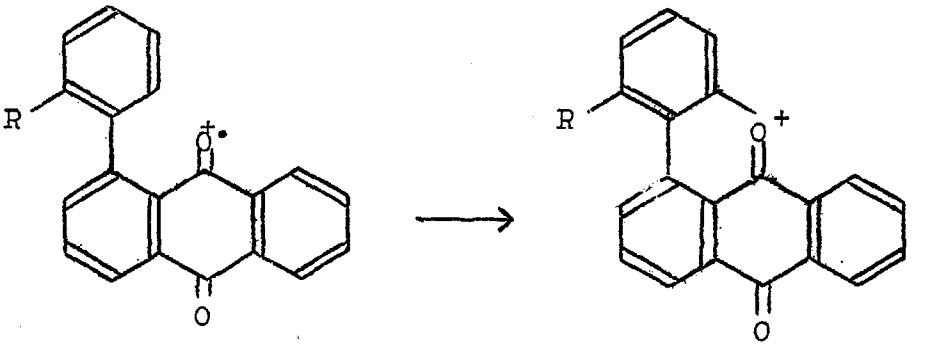
Relative loss of $H^{\bullet}$ and $NO_2^{\bullet}$ from o- and p- nitro phenylbutadienes

Substituent, X	M^+	$[M-1]^+$	$[M-X]^+$
H	91.6%	100%	-
p-NO_2	30.6%	2.7%	30.0%
o-NO_2	52.1%	4.3%	100%

All values are given as a percentage of the strongest ion. The base peak in the p-isomer is due to the $[M-NO_2-1]^+$ ion

(b). Cyclic side-chain derivatives.

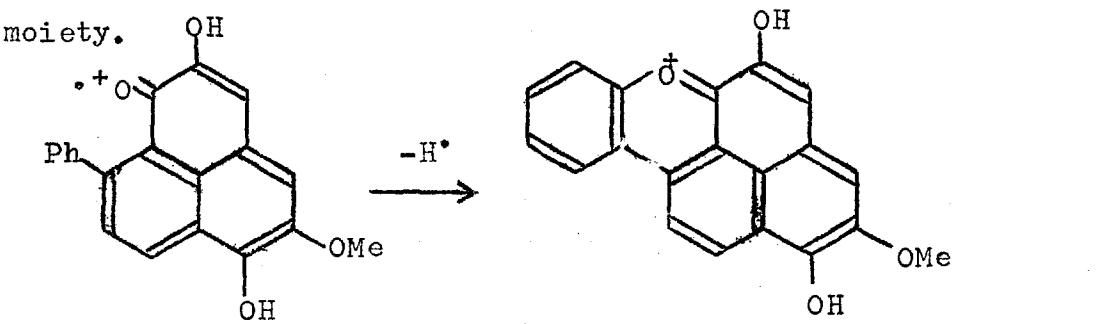
There are very few examples of this type of compound exhibiting the ortho-effect in the literature, one of the best examples being the 1-aryl anthraquinones[18] (9). Here a large variation in intensity of the $[M-1]^+$ ions in the ortho series has been attributed to a rapid increase in the rate of loss



(9). R = H, Me, OMe, NO_2

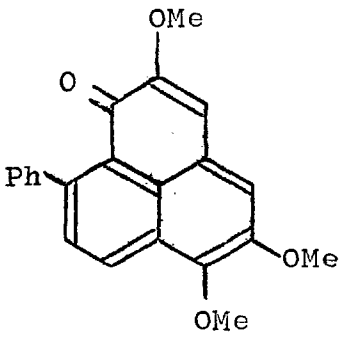
of R in the order R = H < CH_3 < OMe < NO_2 consistent with the displacement of R• by oxygen, while the rate of H• elision is practically independent of the nature of R. The ortho-effect in 1-aryl anthraquinones is discussed more fully, however, in the next section.

Another example of note is haemocorin aglycone (10) which forms the most abundant ion by loss of H• from M^+ [18]. The structure of this ion is suggested to contain the pyrilium moiety.

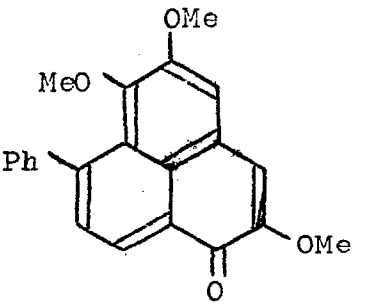


(10) M^+ 67% $[M-1]^+$ 100%

Being a tautomeric system haemocorin aglycone forms two dimethyl ethers, one having an intense $[M-1]^+$ peak (100%) and the second having M^+ (100%) with the $[M-1]^+$ (20%). On the basis of these observations the ortho-effect was used to confirm that the former was compound (a) and the latter (b).[18]



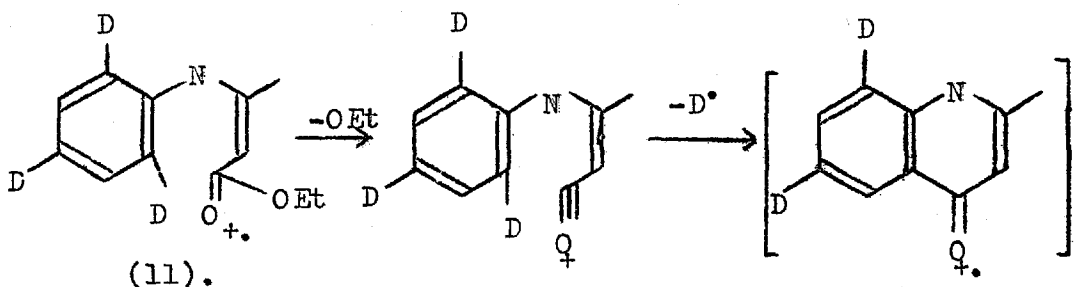
(a).



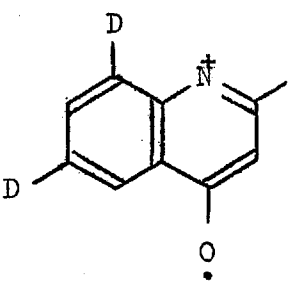
(b).

(c). Ortho-effect in ions other than the molecular ion.

Often it is found that a system which does not exhibit an ortho-effect in its molecular ion might well do so at some further stage in the fragmentation pathway when the conditions are more favourable. Thus in the mass spectra of aromatic enamines[19] (11) it is the $[M-OEt]^+$ ion which shows preferential ortho loss, although no metastable ions are quoted to substantiate this.



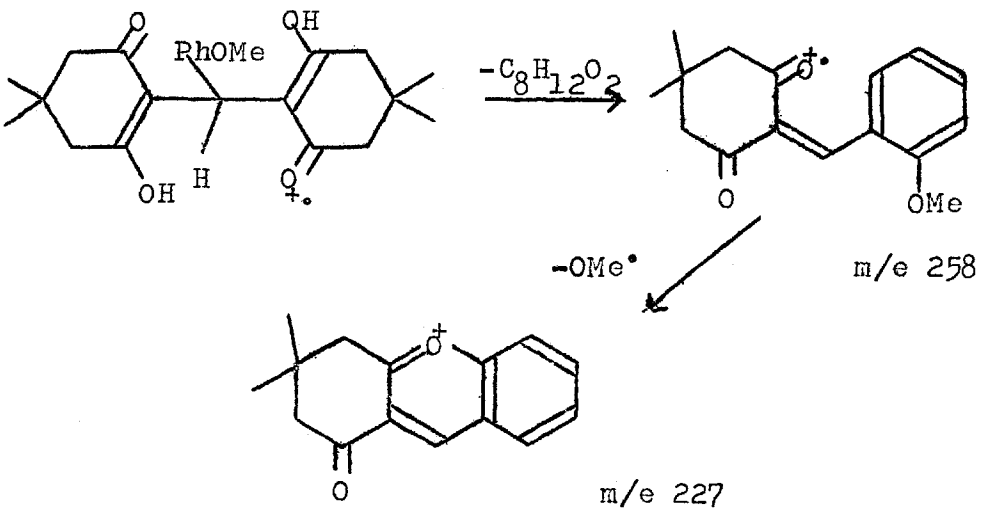
(11).



(12).

Compound (11) loses C_2H_5DO and C_2H_6O from its molecular ion in the ratio 85 : 15 and the loss of D° is rationalised according to the above scheme. In the deuteriated derivative M^+ is ca. 7% and $[M-(OEt+H)]^+$ is 100%. The ortho-effect in this case generates the aromatic quinolinium ion (12) without hydrogen/deuterium scrambling.

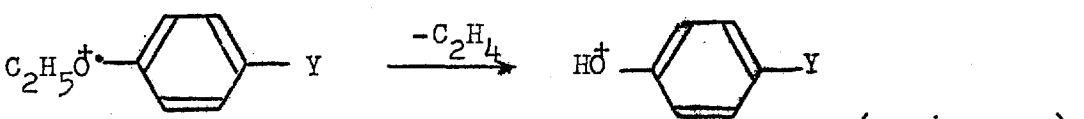
Similarly in the mass spectra of aryl dimedones[20] the base peak corresponds to loss of dimedone from the molecular ion followed by elimination of the ortho-substituent to give an ion at m/e 227. This scheme is rationalised below for the ortho-methoxy derivative.



It is noteworthy that the molecular ions of these aryl dimedones do not show the loss of the substituent or H°, presumably because such a loss does not result in an increase in the aromatic character of the fragment ion.

3. Some Theoretical Considerations.

Extensive deuteriation experiments have been carried out on compounds exhibiting the ortho-effect, the most important of which were on benzalacetophenone[8]. Complete deuteriation of the aromatic ring adjacent to the olefinic double bond demonstrated that 85% of the total hydrogen lost was from the benzene ring of the styryl group and that only 6% came from the other ring. It was also observed that in benzalacetone[8] with deuterium in the o-, m- and p-positions approximately equal amounts of deuterium and hydrogen were lost. In consequence it would appear that some form of rearrangement of the hydrogen atoms in the phenyl ring is taking place. Further investigation of this apparent scrambling has been carried out by Mc.Lafferty et al.[21] who suggest that the similarity of the mass spectra of many m- and p-isomers may be due to randomising isomerisations in the molecular ions and not just to similarities in decomposition rates of different bonds. Thus in compounds of the type:-

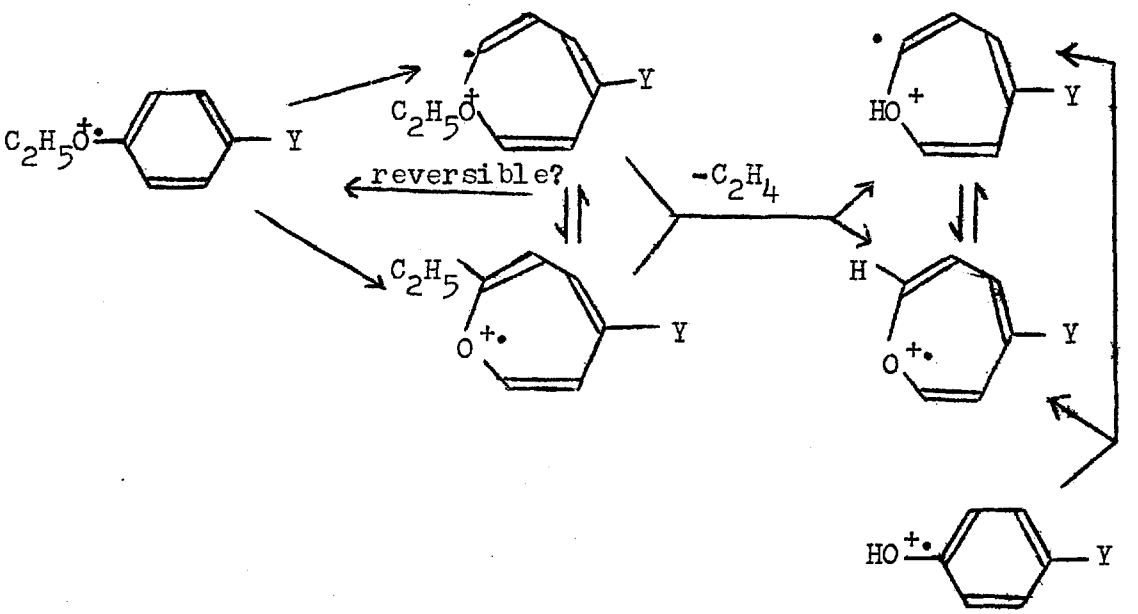


(or isomers)

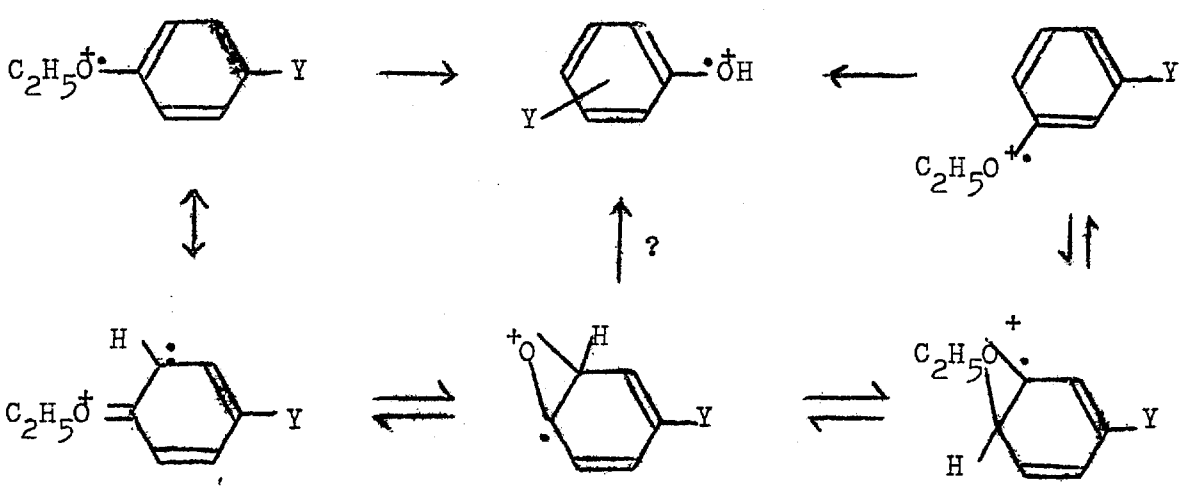
flat topped metastable ions at m/e 46.4 (m/e 94-m/e 66) in phenetol and phenol were of identical width and height. From this it was concluded that the $C_6H_6O^+$ ions were of identical structure. For all but the CH_3, NO_2, CO_2H and CHO derivatives

it was shown that the rate of formation and rate of subsequent decomposition of $[M-C_2H_4]^{+\bullet}$ is independent of ring position (m or p) of that substituent, an observation which was explained on the basis of Schemes 1 and/or 2 below.

Scheme 1



Scheme 2



These mechanisms would certainly explain the results in this example but do not account for the observed effects in other compounds where methyl and nitro groups also appear to be scrambled.

An alternative mechanism has been enunciated by Williams et al.[22] to account for this randomisation. In 2-deuterio pyridine and 2,6-dideuterio pyridine [23] HCN and DCN are lost in the ratio 4 : 1 and 3 : 1 respectively (determined from metastable ion intensities) which is indicative of complete randomisation of the H and D atoms in the molecular ion even at low electron voltages. However, in the case of 2,4,6-[$^{2}H_{3}$] benzonitrile [24] although HCN and DCN are expelled statistically at 70ev. only $[M-DCN]^{+}$ fragments are formed at 13ev. Thus in benzonitrile itself the rate of scrambling is slow compared to loss of HCN when the energy is supplied by 13ev. electrons. Williams[22] gives three alternative explanations for this phenomenon: (i). H-scrambling via the fission and reformation of C-H bonds, occurring without scrambling of the carbon and heteroatoms; (ii). apparent scrambling which actually involves randomisation of the carbon and heteroatoms but does not involve C-H fission; and (iii). A combination of these two. It has been shown that 1,3,5-[$^{14}C_{3}$] mesitylene is isomerised on photolysis to 1,2,4-[$^{14}C_{3}$] trimethyl benzene labelled exclusively in the 1,2,4 positions [25] which is clear evidence that the apparent 1,2 shift of a methyl group is the outcome

of ring carbon interchange. Photochemical isomerisation of this kind has been asserted to occur *via* non-benzenoid intermediates of the prismane (13) and benzvalene(14) type[26] and these compounds have been isolated in certain photochemical reactions.



(13).



(14).

It has been stressed [28] that as internal energies (5-7ev) in the forms of benzene molecular ions undergoing randomisation are comparable to the 4-5ev. available from a mercury resonance lamp, scrambling *via* prismanes and benzvalenes on electron impact is a distinct possibility.

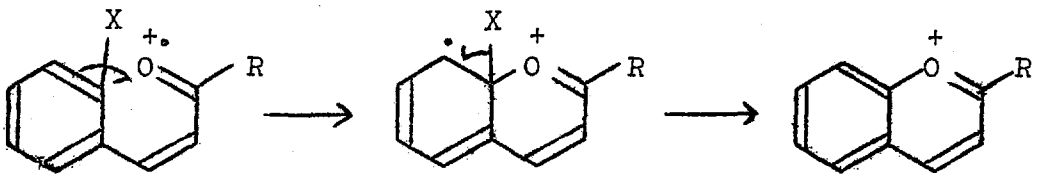
This mode of scrambling adequately explains all the observed results since it is evident that if groups can be isomerised in this fashion then there is a competition between loss of the *ortho*-substituents and loss of other groups which were formerly *meta*- or *Para*. The *ortho*-effect may now be rationalised in the following manner. When the energy of isomerisation is low then one might expect complete scrambling of the *ortho*-, *meta*- and *para*-positions as is indeed the case for benzalacetones,[8] when the substituents are deuterium and hydrogen. That the energy is low is consistent with the small size of the H and D atoms as opposed to other substituents,

and therefore little steric hinderance in the transition states. With larger groups the energy is higher and direct competition between elision of the true ortho-substituent and randomisation results. It is suggested that when a group becomes essentially ortho loss of this fragment occurs in the normal manner, and consequently the factors influencing the extent of the ortho-effect are the bond energies of the C-X bond (where X = substituent) and the size of the substituent and its blocking effect in the transition state. It would therefore be expected that a large group with a low C-X bond energy, e.g. Br, would have an appreciable ortho-effect. The converse is also true as shown by H/D and fluorine substituents. (A further discussion of 1-aryl anthraquinones and this effect will be found in the relavent section below).

One other factor to be considered is the proximity of the ortho-position to the electophilic attacking group. It is without doubt that if the two moieties are very close then the steric interaction might influence the rate of loss of the substituent. The precise effect is dependent on the mechanism taking place and this may be one of two distinct types: (i). It is possible that the C-X bond is broken leaving an aromatic radical site which subsequently attacks the electrophilic heteroatom to give the oxonium species. In this type the transition state is not hindered by the X group and will depend solely on the ease of fission of the C-X

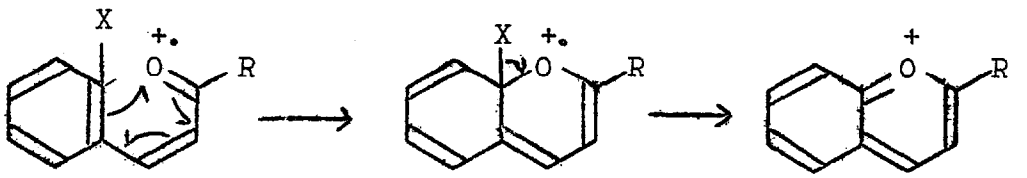
bond and the proximity of the charged and radical centres.

(ii). Electrophilic attack on the intact aromatic nucleus generating a species which is highly dependent on the size of X so that the rate of decomposition of this intermediate will increase with increasing steric bulk and decreasing C-X bond energy. In the former the radical site might be expected to randomise as rapidly as, if not more rapidly than, hydrogen itself and in consequence would result in complete randomisation of the substituents. As this is rarely observed it is generally assumed that the reaction is an intramolecular attack by electrophilic oxygen (or other radical site) on the intact aromatic system to give an intermediate (15) which then loses the X group to regenerate the aromatic benzopyrilium ion:

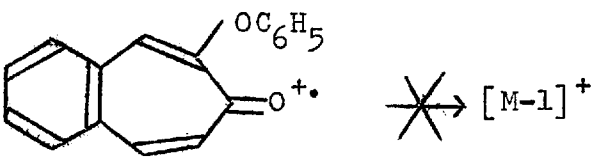


(15).

An alternative view of the above mechanism involves the concerted electron shift in a six-membered transition state illustrated below, followed by regeneration of the aromatic ring by elimination of the ortho-substituent.

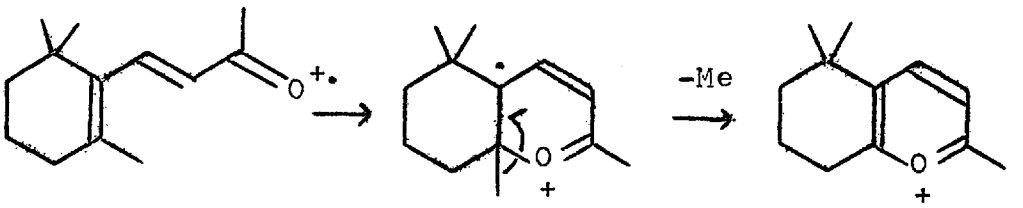


It is suggested that the formation of an aromatic ring is an essential prerequisit for the ortho-effect to proceed and it is this characteristic which dominates all of the known examples. The requirement of aromatic ring formation is adequately demonstrated in benzotropones of the type shown below since these compounds do not exhibit $[M-1]^+$ ions in their mass spectra.[29]

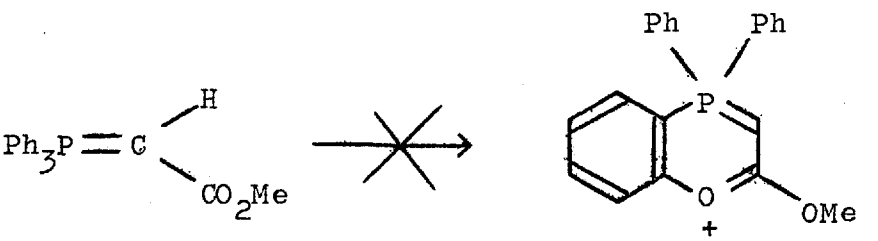


Although there is a need for the newly formed ring to be aromatic in nature there is no need for the molecular ion to be so, this fact thereby allowing the ortho-effect to be extended to cyclohexenes with the necessary structural features. Thus in the mass spectrum of trans-β-ionone [30] selective deuteriation has proved conclusively that 75% of the methyl group lost from the molecular ion had its origin on the ring double bond, a cyclic oxonium ion being postulated for the product. This type of reaction can be further extended to non-cyclic precursors but as these can no longer be considered

to exhibit ortho-effects they will not be discussed.

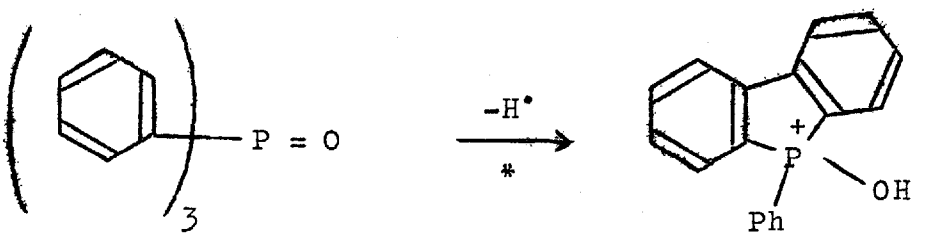


The mass spectra of some alkylidenetriphenyl phosphoranes have been studied and reactions were observed without H/D scrambling in labelled phenyl rings.[31] In the undeuteriated compounds the $[M-1]^+$ ions were often > M^+ ions, but the formation of the cyclic oxonium ion (16) was discounted since the carbonyl function was not necessary for the H• loss.



(16).

The structure of the $[M-1]^+$ ion was formulated as (17) on account of the above evidence and the further decomposition modes of the $[M-1]^+$ ion .

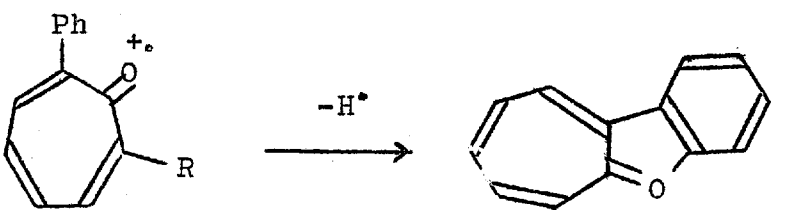


(17).

These results might suggest that the absence of H/D scrambling is indicative of an alternative fragmentation pathway to that of the normal ortho-effect. However, the sole existance of the above example is insufficient to permit generalisation.

4.. Formation of five-membered ring systems.

Unlike the formation of six-membered cyclic ions by the ortho-effect there appears to be no restrictions as to charge distribution in the formation of five-membered rings. Moreover, from the results quoted in the literature it would appear difficult to discern on first sight which compounds might be expected to exhibit this effect and those which might not. The first examples cited were the tropones (18) with R = H, OH, and NH_2, which all showed appreciable $[M-1]^+$ ions whereas the 4 and 5 phenyl tropolones did not. [32]

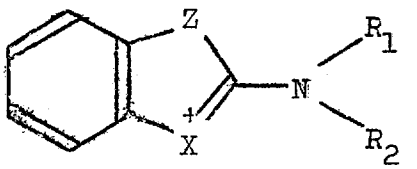


(18). R = H, OH, NH_2 $[M-1]^+$

It was suggested [32] that the cyclic oxonium ion could only be formed in the presence of a suitable substituent on a carbon atom adjacent to that bearing an heteroatom. A similar ion might also be postulated for 2-hydroxy biphenyl which loses an hydrogen atom to a marked extent from its M^+ whereas the 4-hydroxy isomer eliminates H• to a considerably

reduced extent.[32] In both of these cases the aromatic character of the ion is altered and conjugation is maintained through the heteroatom. The fact that a small increase in the conjugation has occurred is taken to be the driving force for the cyclisation.

A more extensive investigation of this effect has been carried out by Maccoll *et al.*[33] on phenyl ureas, thioureas and carbamates. They found that less than 0.5% loss of Cl$^{\bullet}$ from the molecular ion of the *meta*- or *para*-compound occurred although there was about 36% loss from the *ortho*-derivative. There was, however, very little loss of H$^{\circ}$, Me$^{\bullet}$ or OMe$^{\circ}$ from the *ortho*-positions, this being credited to the weakness of the C-Cl bond. The ion (19) was postulated from the results of their work. The formation of a five-membered ring was deduced after a study of *o*-, *m*- and *p*-chloro acetanilides when it was found that *m*- and *p*-derivatives were identical in the mass spectrometer whereas the *o*-isomer was unique in possessing an abundant $[M-Cl]^+$ ion.



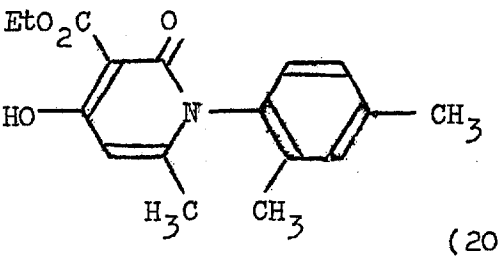
(19).

X = Z = O $R_1 = R_2$ = Me

X = O, Z = NH R_1 = H, R_2 = Ar, or $R_1 = R_2$ = alkyl

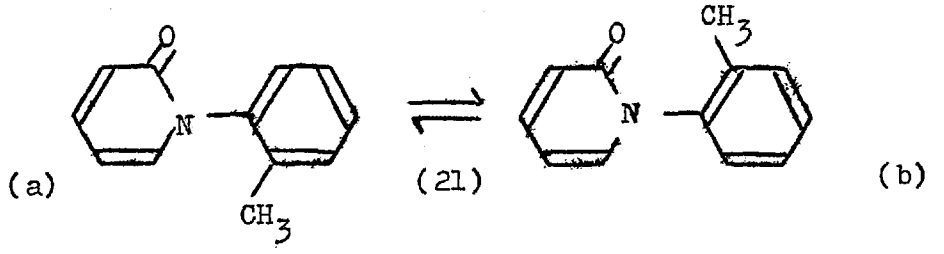
X = S, Z = NH R_1 = H, R_2 = H or Acetyl

From these observations it is infered that the formation of a five-membered ring is less favourable than a six-membered ring possibly due to a proximity effect combined with the low energy difference between parent and daughter ions. Steric effects play a large rôle in these observations as the work of Djerassi et al.[34] and of Lawrence and Waight [35] conclusively show. In the substituted pyridone (20) a large $[M-15]^+$ peak was observed which was considerably more intense than the $[M-1]^+$ peak, the ratios being $M^+ : [M-1]^+ : [M-CH_3]^+ = 1 : 0.06 : 1.42$.[34]



(20).

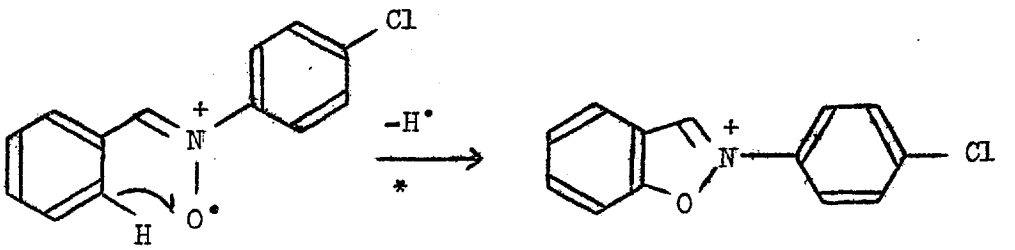
This result is explained on the basis of Me-Me as well as Me-O interaction, the methyl group being of greater steric bulk than the carbonyl group. As the requirement for the ortho-effect is planarity in the final product then one would expect loss of the methyl radical to be preferential to that of an hydrogen atom on steric grounds. Moreover, in 1-[o-tolyl]-2-pyridone (21) elision of H° is more prominant than that of Me°, the ratio being $M^+ : [M-1]^+ : [M-15]^+ = 1 : 1.13 : 0.32$ showing the preference of the conformation (21a) over (21b).[35]



(a) (21) (b)

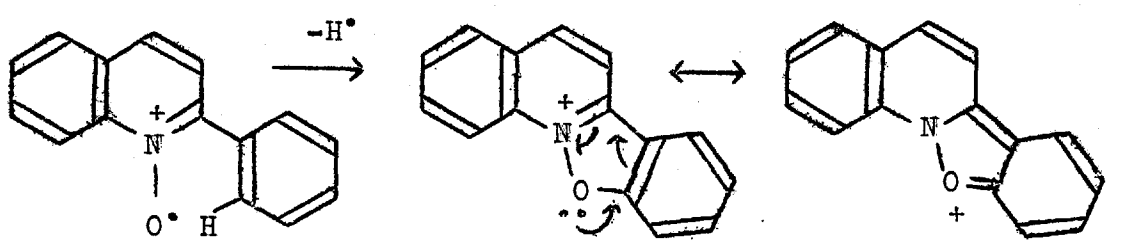
From these two examples we observe that in (20) the intrinsically more likely elimination of a methyl radical is conformationally assisted whereas in (21) it is opposed. This is unambiguous proof of the existance of spatial requirements in the formation of five-membered rings.

Several other examples of five-membered ring formation are known but none of these appear to have been specifically examined for the ortho-effect. Typical amoung these is the mass spectrum of the nitrone (22) which loses an hydrogen radical to give the cyclic ion (23).[36]



(22). m/e 231, 233 (23). m/e 230, 232

This equation is consistent with deuterium labelling and with the reduction of the $[M-1]^+$ ion abundance caused by nitro groups on the ring from which the hydrogen radical is to be lost. Similar to these results are those found for quinoline and isoquinoline N-oxides which form the base peak by elision of H•.[37]

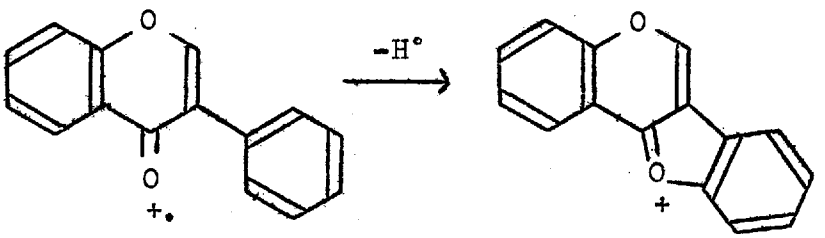


m/e 221 15% (70ev) m/e 220 100% (70ev) etc.

100% (17ev) 42% (17ev)

Compounds of this type without the phenyl ring do not exhibit $[M-1]^+$ peaks, this being the justification for depicting the $H^\bullet$ lost as originating in the aromatic ring.

The diagnostic value of the five-membered ring ortho-effect is adequately demonstrated in the natural flavones where isomer identification is now possible with the aid of mass spectrometry. It was shown that whereas isoflavones exhibit a large $[M-1]^+$ ion (base peak) followed by the loss of carbon monoxide, the normal flavones lose both $H^\bullet$ and CO.[9]



m/e 222 (91%) m/e 221 (100%)

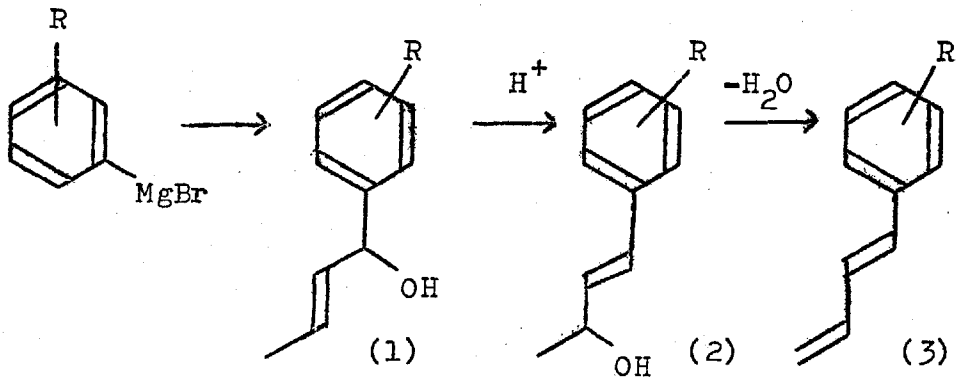
In all of these systems a γ-aromatic cation is generated in analogy with the aromatic character of the six-membered ring type. It might be generalised therefore that aromaticity of the final ion is a necessary requirement for all forms of the ortho-effect regardless of the size of the ring formed, and that the extent of the effect is determined by the nature of the group lost and the strength of the bond binding it to the aromatic nucleus.

Part 1.

1-Aryl Anthraquinones.

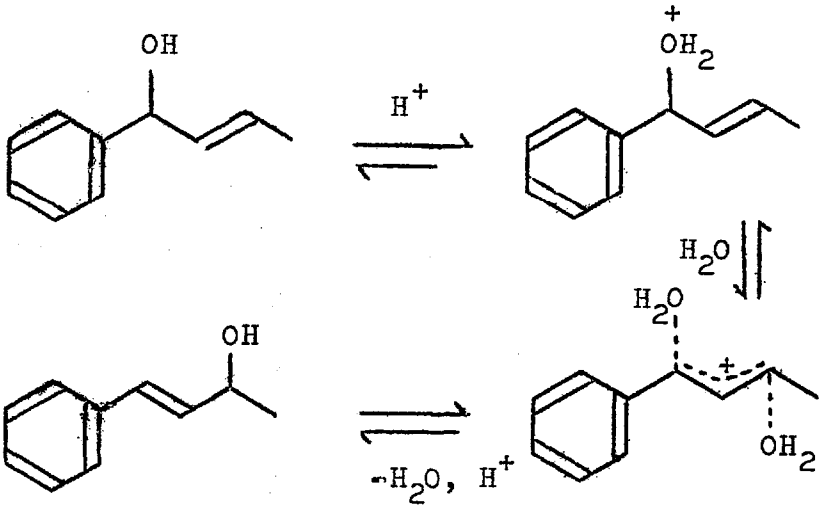
1 , 1 Discussion of Experimental Work.

Several 1-aryl anthraquinones have been prepared together with some deuterium labelled analogues, to assist in the mass spectral interpretation of these compounds. Four of these derivatives have previously been prepared [38] and the procedure given in the literature by these authors was adopted for some of the new compounds. This method proceeds via the 1-aryl butadiene (3), made by condensation of the Grignard reagent of the appropriately substituted bromobenzene with crotonaldehyde at $0^{o}C$, followed by acid rearrangement of the propenyl carbinol (1) generated and dehydration.



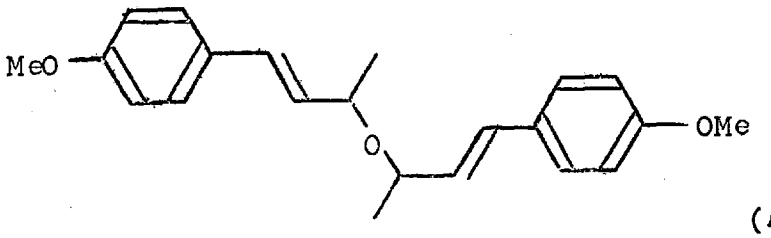
Since the anionotropic rearrangement of allylic alcohols is specifically catalysed by acids [39] the intermediate styryl carbinol (2) need not be isolated, and the aryl butadienes may be conveniently prepared by distillation of of the propenyl carbinols from anhydrous potassium bisulphate whereby rearrangement and dehydration occurs in a single step. Should the styryl carbinol be required, however, dilute acid treatment gives it directly and in quantitative yield

from the allylic alcohol according to the equations below, all of which are equilibria.[39]



This procedure presented little difficulty in all but the anisyl compounds which were extensively polymerised on distillation from potassium bisulphate. In an attempt to obviate this difficulty p-anisyl propenyl carbinol was heated at 60°C over potassium bisulphate for 10 mins. and ether extracted without distillation. As it was thought that the process of distillation was the cause of resinification the above modification should have avoided this. However, from the ethereal extract a white solid was obtained which although having a similar i.r. spectrum to the expected compound differed considerably in melting point. The mass spectrum indicated a molecular weight of 338m.u. and was mass measured as $C_{22}H_{26}O_3$. The elemental analysis was in good agreement with this. Moreover, on the basis of the n.m.r. spectrum the

structure of this novel compound was assigned to the dicinnamyl ether (4).



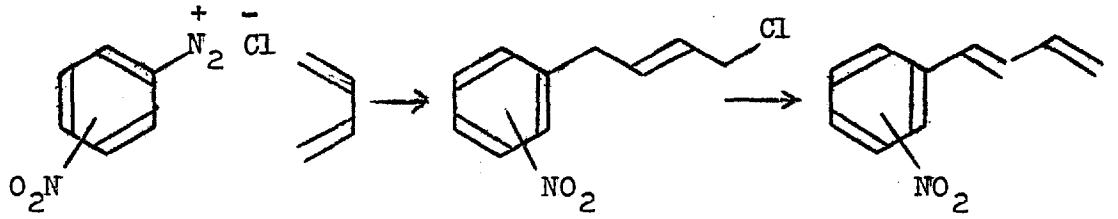
(4).

n.m.r. spectrum: τ = 8.73 (d. J = 6 Hz, 6H) ; τ = 6.19 (s. 6H) ; τ = 4.84 (q. J = 6.0 Hz, 2H) ; τ =4.32-3.35 (m. 6H) τ = 2.91 (1,4-disubstituted aromatic quartet, 8H) m.p. 108 - 110°C. Furthermore, the u.v. spectrum was indicative of the styryl chromophore : λ_{max} 263.5mμ (4.69) λ_{inf} 294.0mμ (3.96) ; λ_{inf} 305mμ (3.76).

This ether is suggested to arise by carbonium ion formation in the styryl isomer followed by nucleophilic oxygen attack from a second styryl molecule, and is presumably irreversible. It is conceivable therefore that this might be the first stage of the polymerisation sequence observed on distillation.

The powerful electron withdrawal properties of the nitro group results in the known disinclination of nitro compounds to form Grignard reagents and on account of this the nitrophenyl butadienes (3, R = NO_2) were necessarily prepared by an alternative route. Electrophilic attack of butadiene on nitrophenyl diazonium compounds under vigorously controlled

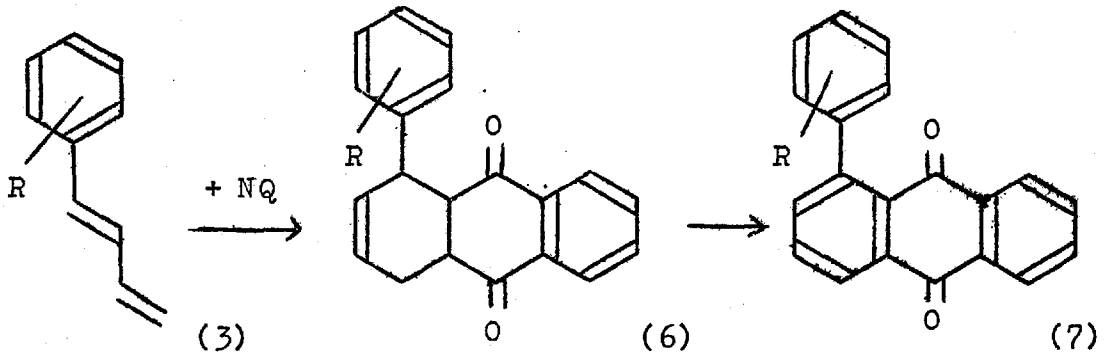
conditions [40] results in the formation of chlorobut-2-enes such as compound (5) which on treatment with methanolic potassium hydroxide dehydrohalogenate to the diene in good yield.



(5)

ortho-Fluorophenyl butadiene was similarly prepared since ortho-bromofluorobenzene is known to produce only polymeric residues as a result of benzyne formation under the conditions of Grignard preparation. [41]

1-Aryl anthraquinones (7) may be prepared from the appropriately substituted aryl butadiene (3) and naphthoquinone by Diels-Alder reaction followed by dehydrogenation of the tetrahydro adduct (6) so formed. [38]



(3) (6) (7)

This reaction was first used by Diels and Alder [42] who prepared 1-phenyl anthraquinone (3, R = H) by the direct

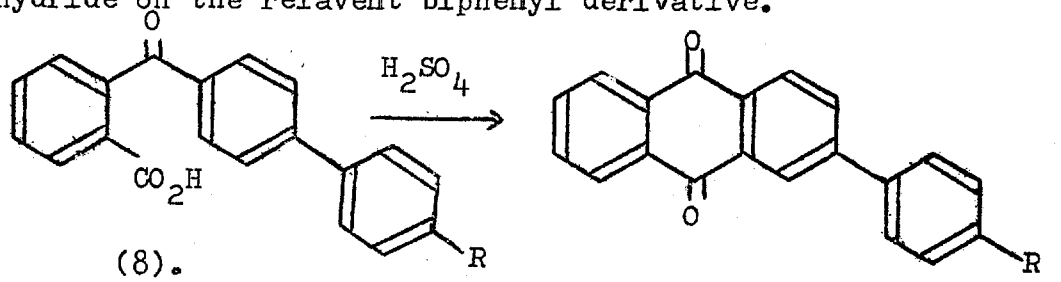
combination of 1-phenylbutadiene and naphtho-1,4-quinone. In this instance the initially formed tetrahydro adduct is air oxidised to the fully aromatic quinone. Adduct formation proceeds well for most butadiene derivatives and is influenced predominantly by the electronic effect of the aryl substituent rather than its steric bulk. In consequence it is found that the rate of adduct formation is retarded by electron-donating substituents (e.g. methoxyl) and accelerated by those which are electron withdrawing (e.g. nitro).[43] This is consistent with the theoretical argument [44] that the order of decreasing activity for 1-nitrophenyl buta-1,3-dienes is :

m-nitro < phenylbutadiene < p-nitro < o-nitro

Depending on the reaction conditions the initially formed tetrahydro adduct may remain as such or be oxidised to the dihydro adduct or even further to the anthraquinone itself. It has been shown that the dihydro adduct still retains the 1,4 protons,[38, 45] an observation which is consistent with the known greater lability of the 11 and 12 protons in this and similar systems. When the diene reaction is carried out in nitrobenzene solution the reaction is invariably accompanied by dehydrogenation of the hydroaromatic product. This dehydrogenation only occurs, however, when the dienophile possesses two carbonyl groups and it has been suggested that proton removal is preceded by enolisation.[46] Loss of the

two remaining hydroaromatic hydrogen atoms then depends on the stability of the intermediary dihydrobenzene nucleus. Usually this dehydrogenates either by hydrogen transfer to an hydrogen acceptor in the mixture or to oxygen in the atmosphere. It has been shown that the formation of aniline accompanies the dehydrogenation in nitrobenzene solution.[46] The difficult removal of nitrobenzene in small scale reactions leads to impure and often intractible products so that its versatility as a solvent for these reactions is considerably reduced. It is for this reason that formation of the tetrahydro product in benzene followed by air oxidation in the presence of alkali was preferred.

Several 2-aryl anthraquinones were also prepared by sulphuric acid dehydration of the appropriate benzoyl benzoic acid (8), itself formed by Friedel Crafts reaction of phthalic anhydride on the relavent biphenyl derivative.[47]



(8). R = H, Br, Cl

Substitution in the para-position of the biphenyl is predictable from the resonance effects of the substituent, R, which distribute electron density at the ortho- and para-positions of the second ring. The absence of any ortho-derivative in the product is a result of the increased steric hindrance in

this form which makes it energetically unfavourable.

Deuteriated Analogues.

Three specifically labelled bromobenzenes were required for conversion to the corresponding anthraquinones, the method of preparation of each being briefly described below.

The lability of aromatic protons in acidic media is now a well characterised phenomenon, and it is also known that attack of the D_3O^+ cation on the benzene ring is governed by the normal rules of aromatic substitution.[48] As a consequence of this [2,4,6,N,N,N-$^2H_6$]-anilinium bromide is readily prepared from aniline hydrobromide on exchange with deuterium oxide, and can be converted by the Sandmeyer reaction with cuprous bromide to [2,4,6-$^2H_3$]-bromobenzene.[49]

Monobromination of [2,4,6-$^2H_6$]-anilinium bromide with a solution of bromine in dioxan gives the p-bromo derivative exclusively and this compound undergoes facile deamination on diazotisation and hypophosphorous acid treatment to give [3,5-$^2H_2$]-bromobenzene.[50]

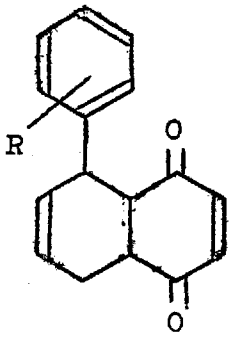
The final deuteriated bromobenzene precursor required was ortho-[$^2H_3$-methyl]-bromobenzene. Ethyl o-bromobenzoate was reduced with lithium aluminium deuteride to o-bromo-[α,α-$^2H_2$] benzyl alcohol and the tosylate of this further reduced with lithium aluminium deuteride to give the required labelled compound with a high degree of specificity and incorporation.

All three bromobenzenes were converted to the anthraquinones

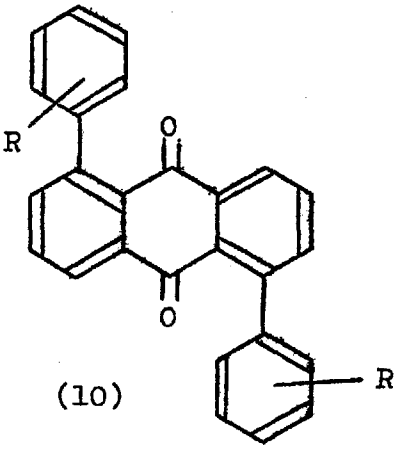
in the predescribed manner.

Miscellaneous Derivatives.

Attempts were made to prepare some 1-aryl naphthaquinone derivatives of type (9) by Diels-Alder reaction of the butadiene and benzoquinone, but only bis-adducts could be isolated from the reaction mixture. This would appear to suggest that the dihydro benzoquinone (9) first formed is a more powerful dienophile than benzoquinone itself.



(9)



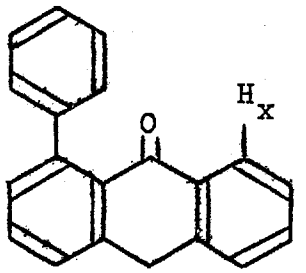
(10)

In view of this observation some form of explanation will be given. It may be realised that in benzoquinone itself cross-conjugation of the two C-C double bonds effectively delocalises the π electron density over the whole molecule, whereas in the mono-adduct the full electron withdrawal effect of the carbonyl groups is acting on a solitary double bond. The electron density of each olefinic bond in benzoquinone is therefore greater than that of the sole double bond in the mono-adduct. In view of the low C-C double bond electron density requirement of dienophiles this argument is consistent

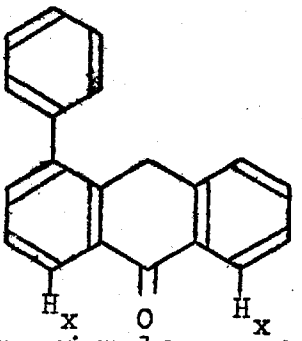
with the greater reactivity of the mono-adduct to further Diels-Alder reaction over that of benzoquinone itself to form the mono-adduct. In consequence the mono-adduct is transformed into the diadduct at a rate faster than that at which it is formed.

Aromatisation of the di-adducts is easily accomplished with hot alcoholic potash, or even by prolonged refluxing in benzene, but as these products were not required a full investigation of this was not carried out.

1-Phenyl anthraquinone was quantitatively reduced both by alkaline dithionite and tin and concentrated hydrochloric acid to the anthrone which was shown by n.m.r. to be a 1 : 1 mixture of the two possible isomers A and B.



A



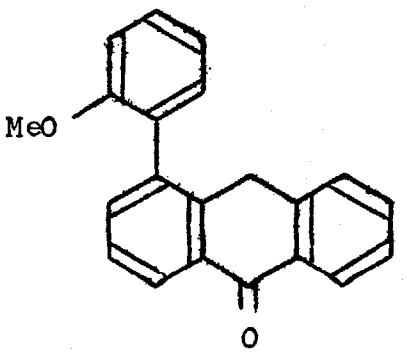
B

In the n.m.r. spectrum the methylene signals appear as two singlets of equal intensity at τ = 5.61 and τ = 5.87 respectively, the latter appearing at higher field on account of the ring current of the 1-aryl substituent- which u.v. spectroscopy shows to adopt a position perpendicular to the anthrone nucleus. Furthermore, the mixture has 1.5 low field aromatic protons (H_x) consistent with a 50% mixture of A and B.

Fractional crystallisation from methanol gave first the least soluble isomer A, m.p. 190 - 191.5°C and from the mother-liquor the more soluble isomer B was isolated by crystallisation from ethyl acetate, m.p. 139°C. Each isomer was characterised by the position of the methylene group in the n.m.r. spectrum and by the number of low-field aromatic protons present. Moreover, the fractional loss of $H^{\bullet}$ from the molecular ions of the two isomers was sufficiently different to distinguish the two. Thus for A, we find :

$$\frac{[M-1]^+}{M^+ + [M-1]^+} = 65\%;$$ and for B this ratio becomes 12%.

A sample of o-anisyl anthrone prepared by Fawcett from the anthraquinone showed an AB quartet for the methylene group in the n.m.r. spectrum centred at τ 5.89 and 6.12 (J_{ab} = 15.5Hz). The presence of two low-field protons in the aromatic region identified this as isomer C. Non-equivalence of the methylenic protons, thus leading to an AB quartet, is to be expected in view of the restricted rotation about the C-C bond joining the anisyl ring to the anthrone nucleus.

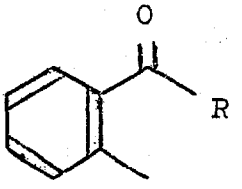


C.

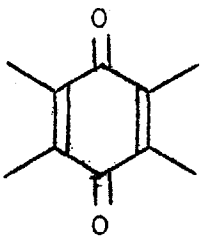
Ultra Violet Spectra Considerations.

The u.v. spectra of 1-aryl anthraquinones closely resemble that of the unsubstituted anthraquinone despite the fact that the aryl substituents are directly attached to the chromophoric system. The absence of spectral interaction in this system has been acredited to steric inhibition of a similar character to that in phenyl anthracenes which opposes the adoption of a uniplanar arrangement of the two chromophoric systems.[43] This behaviour is in contrast with that of amino, methoxy, and nitroanthraquinones which exhibit the expected substituent effects.[51]

The use of Dreiding and Catalan models clearly demonstrates this steric influence, and shows that even in the unsubstituted 1-phenyl anthraquinone restricted rotation about the phenyl ring and the anthraquinone nucleus exists. In anthraquinone itself there are two major chromophores, the benzenoid (11), giving bands at λ_{max} 2500 and 3300 A and the quinonoid (12), giving bands at λ_{max} 2625 and 2725 A [51], and it is these bands which are affected on addition of auxochromes to the quinone nucleus.



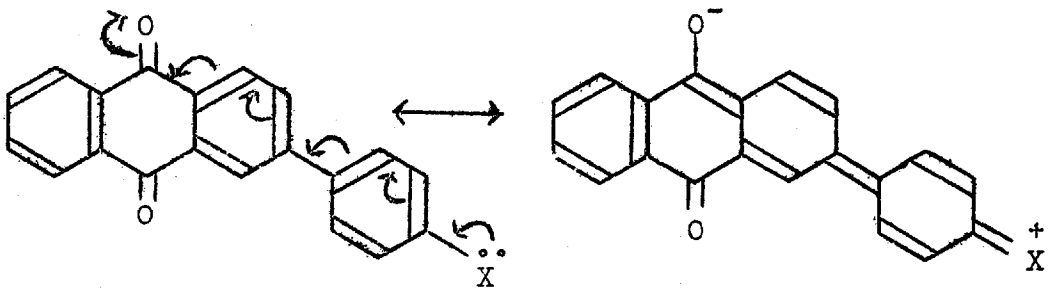
(11).



(12).

Examination of the u.v. spectra of the 1-aryl anthraquinones shows that the observed absorption can be readily diagnosed as a direct summation of the extinction coefficients of the substituted benzene and anthraquinone. This direct addition infers that the two chromophoric systems are unconjugated and that the bond linking the two systems must be essentially single in character in accord with the result cited above.

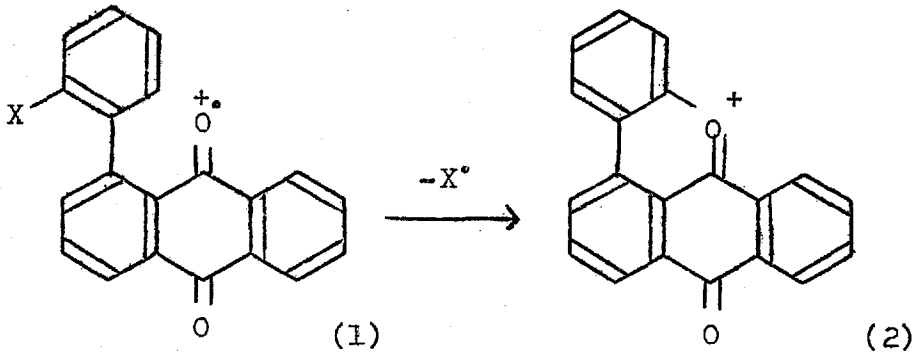
In the 2-aryl anthraquinones, however, the band intensities in the u.v. spectra are considerably different from those of anthraquinone over the 2400 to 3000 A region, a result which indicates partial if not complete overlap of the aryl and anthraquinone π orbitals. The bathochromic shift of the benzenoid 2500 A peak to 2750 A is consistent with the resonance participation shown below:-



From the u.v. spectra it is therefore possible not only to differentiate between 1-and 2- aryl anthraquinones, but also to demonstrate restricted rotation in the former as opposed to free rotation in the latter.

1 , 2 Discussion of Mass Spectra.

The mass spectra of a wide variety of anthraquinones have been reported by Beynon and Williams [52], but apparently none containing aryl substituents. It has been observed in the 1-aryl anthraquinones (1) investigated by Waight [18], however, that the base peak in all the spectra occurs at 283 m.u. corresponding to the ion (2) formed by loss of the X radical from the molecular ion.



(1) (2)

A further investigation of this suggested cyclisation reaction has been carried out with a view to elucidation of the mechanism by which it occurs. It should be noted that the formation of oxonium ions is well authenticated in electron induced fragmentations (see review) and their stability is amply demonstrated in the naturally occurring anthrocyanidines, which exist as benzopyrilium salts.

In the parent compound (1; X = H ; mass spectrum 1) extensive elision of an hydrogen atom from the molecular ion occurs and this constitutes the primary fragmentation of this

derivative. With substituents in the ortho-, meta-, or para-positions of the aryl nucleus preferential loss of the ortho-substituent is observed suggesting a mechanism peculiar to this position. Structures of type (2) are consistent with this observation and will form the basis of the following discussion.

The abundance of the molecular ions of the ortho-substituted compounds show considerable variation, a characteristic which is also evident in the $[M-1]^+$ ions. Appreciably smaller differences exist for the M^+, $[M-1]^+$ and $[M-X]^+$ ions in the meta and para series and for the $[M-X]^+$ ions in the ortho series (see Table 5).[53] On reduction of the electron voltage to 15ev. no change in the relative abundances of the M^+, $[M-1]^+$ and the $[M-X]^+$ resulted from which it was concluded that ortho loss was a low energy requirement fragmentation.

Examination of 1-[2,4,6-$^2H_3$-phenyl] and 1-[3,5-$^2H_2$-phenyl] anthraquinones (Table 6) shows that there is an approximately equal probability of loss of any hydrogen atom in the phenyl group to give the $[M-1]^+$ ion. Complete hydrogen randomisation thus occurs in the phenyl group of the molecular ion prior to fragmentation when hydrogen or deuterium are the only substituents. The results in Table 6 make no allowance for the deuterium isotope effect, which usually lies within the range 0.6 - 1.0 in favour of hydrogen loss, and which occurs

Table V.

INTENSITIES ($\%\Sigma_{60}$) OF IMPORTANT IONS IN THE MASS SPECTRA OF 1-ARYLANTHRAQUINONES (I)

	X	m.p.°	Ion											
			M^+	$[M-1]^+$	$[M-X]^+$	$[M-17]^+$	$[M-X-CO]^{+*}$	$[M-1-CO]^+$	$C_{13}H_{10}^+$	$C_{10}H_8^+$	$C_7H_7^+$	$[M-15]^+$	$[M-30]^+$	$[M-31]^+$
1.	Hydrogen	†	16·9	31·6	$(M-1)^+$	0·36	1·17	$(M-X-CO)^+$	3·79	0·69	—	—	0·28	—
2.	*o*-Methyl	†	6·47	1·48	36·5	6·06	0·47	1·27	1·70	0·44	0·43	$[M-X]^+$	—	—
3.	*m*-Methyl	164–165	8·96	11·30	15·41	0·22	0·27	0·46	1·33	0·36	0·36	$[M-X]^+$	—	—
4.	*p*-Methyl	178·5–179·5	8·55	12·20	3·34	0·34	0·38	0·60	2·02	0·60	0·38	$[M-X]^+$	—	—
5.	2,6-Dimethyl	179–180	16·62	1·06	17·09	3·46	0·89	2·90	0·47	—	—	$[M-X]^+$	—	—
6.	*o*-Ethyl	151·5–152·5	10·12	0·68	44·1**	1·59	0·43	—	1·40	0·29	—	2·08	—	—
7.	*o*-Methoxyl	†	3·01	0·29	36·5	0·13	0·67	1·15	1·64	0·29	0·13	1·09	—	$[M-X]^+$
8.	*m*-Methoxyl	155–156	14·40	13·14	15·41	0·14	0·28	0·59	0·76	0·20	0·22	5·68	—	$[M-X]^+$
9.	*p*-Methoxyl	196	10·40	9·68	8·34	0·43	0·29	0·54	1·09	0·43	0·086	3·84	—	$[M-X]^+$
10.	*o*-Fluoro	215–217	12·75	13·95	15·02	0·75	0·70	1·61	1·18	0·24	0·16	—	—	—
11.	*m*-Fluoro	206	15·75	27·4	2·81	0·56	0·21	1·31	0·37	0·17	0·18	—	—	—
12.	*p*-Fluoro	184	18·61	33·3	2·19	0·93	0·18	12·7	0·30	0·12	0·086	—	—	—
13.	*o*-Chloro	212	0·036‡	0·177‡	43·0	—	0·63	—	2·82	0·68	—	—	—	—
14.	*m*-Chloro	187–189	14·06‡	23·9‡	12·2	0·52‡	0·36	0·88	3·70	0·77	—	—	—	—
15.	*p*-Chloro	189–190	16·35‡	26·5‡	9·36	0·63‡	0·33	0·91	3·20	0·57	—	—	—	—
16.	*o*-Bromo	222–224	0·0078‡	0·0193‡	35·9	—	0·064	—	3·35	0·81	0·40	—	—	—
17.	*m*-Bromo	202–203	9·51‡	13·87‡	14·82	0·25‡	0·31	—	2·79	0·70	0·70	—	—	—
18.	*p*-Bromo	212–213	13·86‡	19·57‡	10·58	0·56‡	0·41	—	3·68	0·87	0·18	—	—	—
19.	*o*-Nitro	†	0·023	0·086	39·6	0·03	1·02	1·74	3·94	0·92	0·026	—	1·74	—
20.	*m*-Nitro	248	5·76	6·76	7·40	0·76	0·44	1·32	2·99	0·67	0·84	—	3·45	3·45
21.	*p*-Nitro	273–273·5	2·27	2·61	3·48	0·97	0·21	1·93	1·37	0·34	0·54	—	8·75	9·80

† Samples prepared by Dr. J. S. Fawcett.
‡ Total intensity for both halogen isotopes.
** Including contribution from $[M-1-CO]^+$.
* $C_{19}H_{11}O^+$

Table 6.

Hydrogen loss from the molecular ion of 1-phenyl anthraquinone.

Deuteriation studies.

	1-[2,4,6-$^2H_3$]-phenyl			1-[3,5-$^2H_2$]-phenyl		
Ionising voltage ev.	12	70	70	12	70	70
m/e	obs*	obs*	calc†	obs*	obs*	calc†
287	65.0	16.6	22.8	0	1.2	0
286	25.9	28.9	25.9	57.0	13.9	20.0
285	9.3	44.1	38.8	36.0	41.5	34.8
284	0	8.9	11.6	7.0	35.6	35.9
283	0	1.5	0.9	0	7.8	9.3
Fraction loss $^2H_1$	-	0.535	0.60	-	0.36	0.40

* Observed relative ion intensities corrected for ^{13}C isotope contributions.

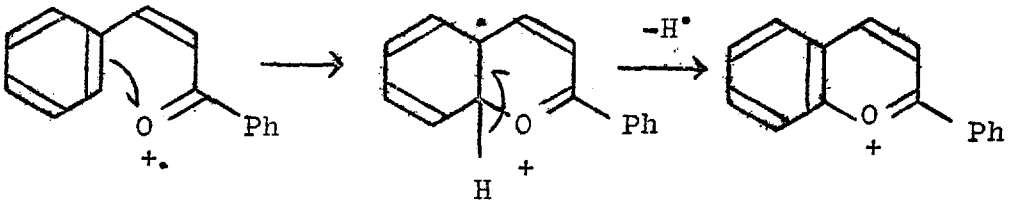
† Calculated intensities assuming :

(a). Complete scrambling of the phenyl hydrogen atoms.

(b). No isotope rate effect in loss of ^2H compared with ^1H.

on account of the increased energy of the C - D bond. The observed 0.535 fraction of $^2H_1$ loss from the trideuteriated compound would attain the theoretical value of 0.600 for an isotope effect of 0.89. This value is in complete agreement with the result obtained from the dideuteriated compound and is well within the empirical range.

Examples of side-chain cyclisation on to an aromatic nucleus are numerous in the literature, the largest group encompassing the cinnamoyl radical.[8] Chalcone is illustrative of this class.

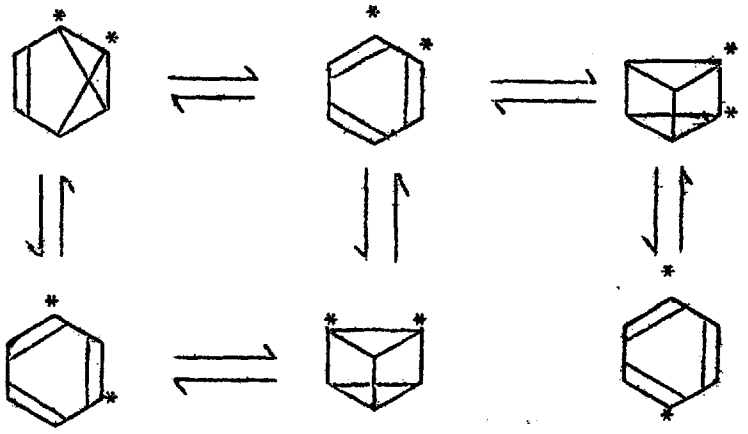


The [2,4,6-$^{2}H_{3}$]-derivative exhibits random loss of deuterium during the cyclisation and it was suggested that scrambling proceded by migration of H or D to the radical site followed by further migration to the newly formed radical site.[8]

A survey of the literature shows that most aromatic compounds exhibit similar randomisation of the aromatic protons . Thus benzene [28] and pyridine [23] have completely randomised hydrogen atoms in their molecular ions over the whole voltage range from their ionisation potentials upwards. Benzonitrile,[24] however, shows complete scrambling only in the region 20 - 70 ev. Below this threshold value the specificity of hydrogen abstraction increases until at 13 ev. it is exclusively ortho to the nitrile entity.

Williams has suggested [23, 24] that randomisation takes place via non-benzenoid intermediates of the prismane and benzvalene type and not by C - H bond cleavage. In support

of this postulate the work of Kaplan et al.[25] on ^{14}C labelled mesitylene may be considered. (see review).



An analogy for this is available from photochemical studies where both prismanes and benzvalenes have been isolated by the photochemical isomerisation of benzene.[28] The two electronically excited species shown below have been suggested to account for these reactions.[26]



From the above it is considered that for randomisation to occur the molecular ion must be in an electronically excited state, a requirement which in benzonitrile necessitates ionisation being accomplished by electrons with energies in excess of 20 ev.

With substituents other than hydrogen or deuterium on

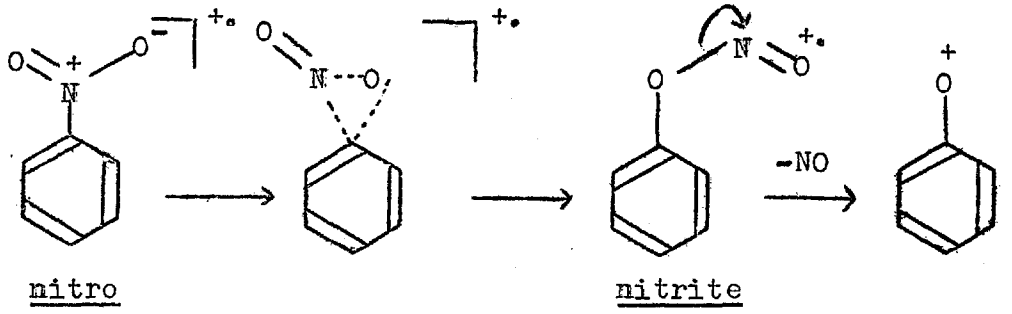
the aryl ring complete randomisation of the substituents is not observed and a distinct difference exists between the ortho-compounds relative to the meta- or para. This difference is illustrated by the ortho- and para-anisyl compounds in mass spectra 3 and 4 respectively. The former isomer shows extensive loss of methoxyl from the molecular ion to form the base peak at m/e 283, the M^+ being only 8% relative abundance of this ion. The para-isomer, however, loses methoxyl to a lesser extent and now has its molecular ion as the base peak. Furthermore, whereas the para-compound has an intense $[M-1]^+$ ion no equivalent ion is present in the spectrum of the ortho-compound. In addition, the increased stability of the parent ion of the para-compound enables fragmentations other than the ortho-effect to give rise to important ions in the mass spectrum. The preferential elimination of the methoxyl radical over the hydrogen atom is clearly seen from a comparison of the unsubstituted phenyl anthraquinone (mass spectrum 1) and the ortho-anisyl derivative (mass spectrum 3). Whereas elision of the hydrogen atom is the most favoured fragmentation mode in the unsubstituted compound a comparable loss in the anisyl analogue is non-existent and gives place to more favourable loss of the methoxyl radical. A similar effect is noticed in other derivatives and will be discussed later.

As substituents are eliminated from other than the ortho-

position it is suggested that incomplete scrambling of the substituent must be occurring in the molecular ion prior to fragmentation, a suggestion for which two alternatives exist:
(a). The first is that the substituent, X, is lost by a process dependent only on the C - X bond strength, and that once lost a hydrogen transfer to the radical site with concomitant oxonium ion formation follows.
(b). Alternatively scrambling of the type postulated for hydrogen and deuterium may be taking place, but to a lesser extent by virtue of increased steric hindrance in the transition states.
No differentiation between these alternatives is possible, but it is probable that the latter is the most accurate representation. It is suggested therefore that attack of electrophilic oxygen ensues exclusively at the ortho-position with subsequent elision of the resident group with the proviso that some scrambling of the positions is inevitable. On account of this, competition exists between elimination of the ortho-substituent and randomisation of the positions, the factors influencing each having been discussed in the review.

Similarity of the meta- and para-positions, resulting in almost identical spectra in a number of examples, may be rationalised on the assumption that although randomisation and ortho loss are simultaneous processes, the high energy

barrier of the former for all substituents other than H/D results in the meta- and para-isomers appearing as a hybrid of the two forms. This loss of positional identity is least evident in the nitro compounds which are capable of fragmentation in their own right. Thus, in the para-nitro anthraquinone (mass spectrum 5) the most abundant ions are formed by loss of nitric oxide from the M^+ and $[M-1]^+$ ions, whereas in the meta-derivative (mass spectrum 6) these ions represent only 50% of the most abundant ion. A plausible mechanism for this elimination invokes the three-membered ring isomerisation to the nitrite proposed by Beynon et al.[54]



nitro nitrite

Examination of the mass spectra of simple aromatic nitro compounds [54] reveals that $[M-NO]^+$ ions are abundant when powerful electron releasing groups are present in the para-position, an effect opposite to that in 1-aryl anthraquinones. The ease of NO loss from the para-compound must then be due to some unknown effect, possibly electronic, which may be of a special type such as occurs in ortho-nitrobenzaldehyde.[55]

The meta- and para-anisyl anthraquinones have very similar mass spectra and both form an important $[M-15]^+$ ion

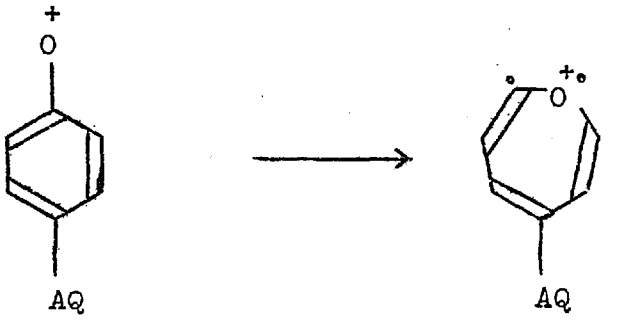
(mass spectrum 4 for p-isomer), which undergoes ring contraction with elimination of carbon monoxide, followed by loss of an hydrogen atom. It does not, however, lose hydrogen directly from the $[M-15]^+$ ion. The scheme is shown below.

$$\underset{\text{m/e 314}}{M^+} \xrightarrow{*} \underset{\text{m/e 299}}{[M-Me]^+} \xrightarrow{*} \underset{\text{m/e 271}}{[M-Me-CO]^+} \xrightarrow{*} \underset{\text{m/e 270}}{[M-Me-CO-H]^+}$$

The <u>para</u>-nitro compound behaves rather differently in that the $[M-NO]^+$ ion loses an hydrogen atom to a considerable extent (mass spectrum 5), followed by loss of carbon monoxide as illustrated below.

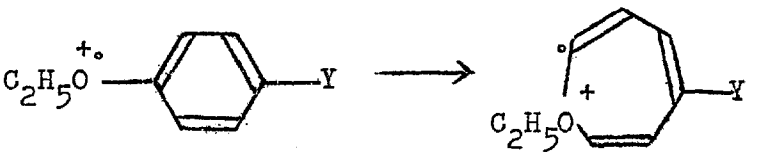
$$\underset{\text{m/e 329}}{M^+} \xrightarrow{*} \underset{\text{m/e 299}}{[M-NO]^+} \xrightarrow{*} \underset{\text{m/e 298}}{[M-NO-H]^+} \xrightarrow{*} \underset{\text{m/e 270}}{[M-NO-H-CO]^+}$$

This difference indicates that the $[M-NO]^+$ and the $[M-Me]^+$ species are formed with considerably different energies and possibly possess different structures. This argument is consistent with the nitro compound being of lower energy by virtue of that expended on rearrangement from the nitro to the nitrite form prior to fission. It is suggested that the ion formed from the methoxy compound by methyl elimination has sufficient energy for rearrangement, possibly to a seven membered ring moiety :-



The ring expanded form has analogy with that postulated by McLafferty for aryl ethers [21] and is presumed incapable of direct hydrogen loss.

e.g.



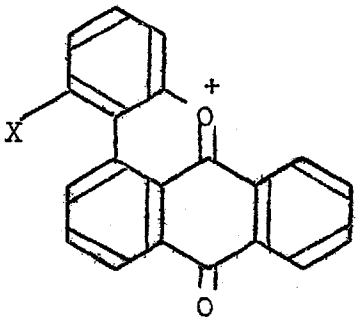
Analysis of the $[M-1]^+$ ion intensities of the ortho-substituted anthraquinones (see Table 5) shows that these ions are formed to highly variable amounts depending on the substituent. These differences are attributed to a rapid increase in the rate of elimination of X in the order :-

$$X = H < F < CH_3 < OCH_3 < Cl < NO_2 < Br$$

consistent with decreasing C - X bond energy and the displacement of X by oxygen to give the ion (2).

A low abundance of the $[M-1]^+$ ions in the ortho- methyl

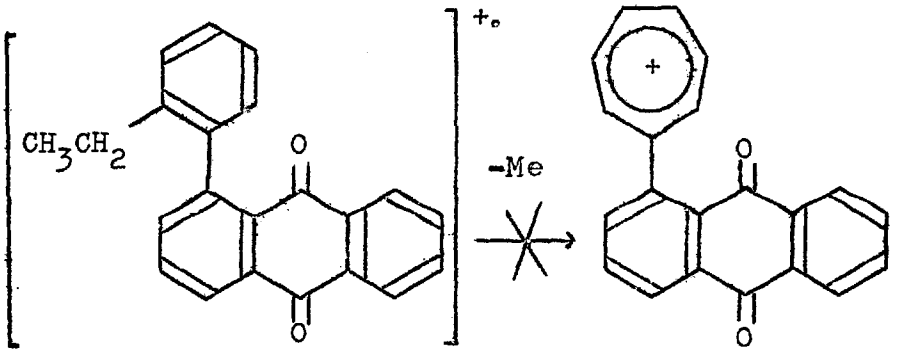
and ortho-methoxy compounds suggests the operation of a steric factor similar to that in biphenyls in which there is overlap between the substituent, X, and the hydrogen atom at C_2 (see compound 3). This could lead to a reduction in the rate of formation of (3) if X were sufficiently large. Support of this is given from the u.v. spectral data from which restricted rotation about the 1-1' bond is evident.



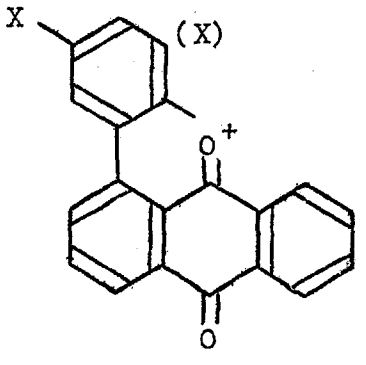
(3)

Furthermore, the molecular ion in 1-(2,6-dimethylphenyl)-anthraquinone is appreciably more intense than in o-tolyl anthraquinone while the $[M-Me]^+$ ion is less intense, a fact which suggests difficulty in attaining coplanarity of centres in ion (3) when X = Me. A further point is that the $[M-1]^+$ ion in the ortho- ethyl and ortho-isopropyl compounds is even weaker than in the ortho-methyl homologue, even though the molecular ion of the ethyl derivative is more abundant than that in the methyl compound. It may also be noted that in 1-o-ethylphenyl anthraquinone the ion at m/e 283 remains the base peak and that loss of methyl from the molecular ion is unimportant. This suggests that ring expansion in the alkyl substituted derivatives to form the tropylium ion is

insignificant.



In all the meta and para compounds other than those containing fluorine the $[M-1]^+$ and $[M-X]^+$ ion intensities are similar, a singularity which is attributed to the known reluctance of nuclear aromatic fluorides to give $[M-F]^+$ ions.[56] The intensities of the $[M-1]^+$ ions in all of the anthraquinones is essentially independent of whether the substituent is meta or para, and this high relative stability is credited to their having the structures below. Table 7 shows the relative intensities of the M^+ ions expressed as a fraction of the $[M-1]^+$ ion from which the close similarity of the meta- and para-isomers is readily discerned.



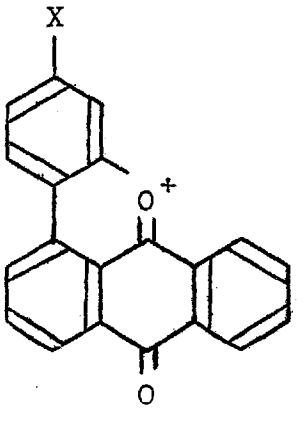
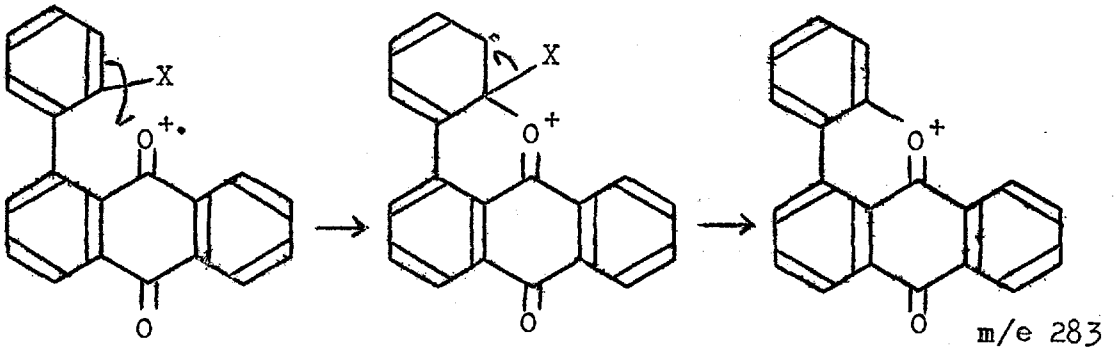


Table 7.

Relative intensities of (M^+/ $[M-1]^+$) for meta- and para-phenyl anthraquinones.

Compound	nitro	methyl	bromo	chloro	fluoro	methoxyl
m	0.842	0.793	0.653	0.592	0.564	1.126
p	0.852	0.704	0.699	0.611	0.562	1.000

A discussion of the mechanisms by which the ortho-effect has been suggested to proceed has been made in the review in the preceding section, it will suffice therefore to recap only that mechanism which best fits the results observed in the aryl anthraquinones. The most plausible mechanism appears to involve attack of electrophilic oxygen at the ortho-position of the aromatic nucleus with subsequent rearomatisation of the ion by expulsion of the resident ortho-substituent. The scheme is illustrated below:

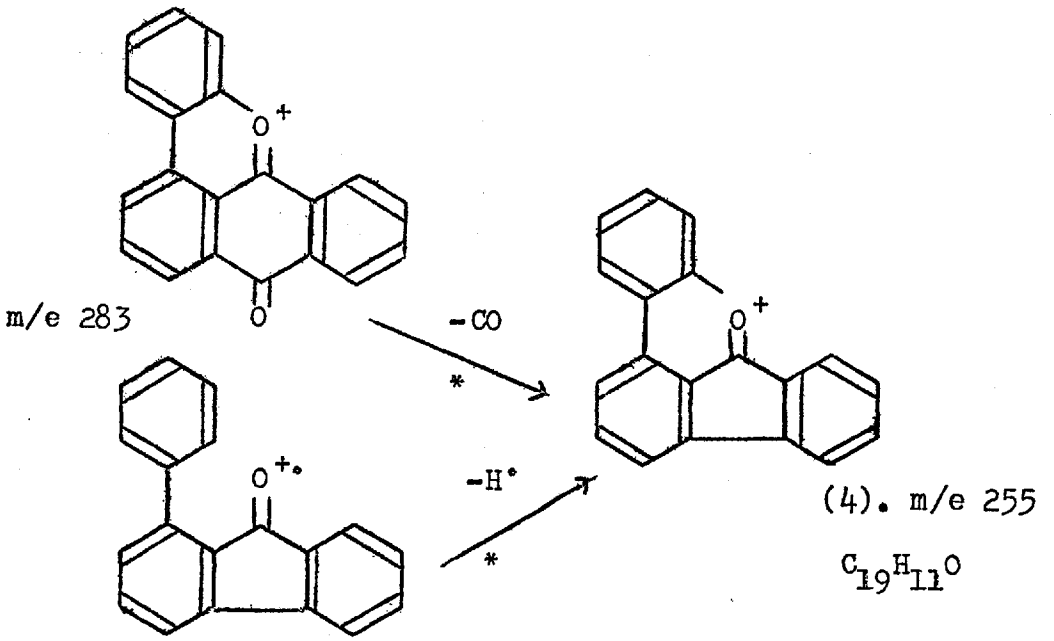


m/e 283

An alternative mechanism involving initial fission of the C - X bond is untenable on the grounds that the resulting

radical site would be expected to randomise with greater ease than H/D atoms even, with the production of identical spectra for all three isomers. It is conceivable, however, that these two mechanisms may be occurring simultaneosly.

Evidently loss of carbon monoxide from the molecular ions of 1-aryl anthraquinones does not occur - even in the hindered 2,6-dimethyl analogue - suggesting that loss of this type is a high energy process relative to the ortho-effect. By analogy with the suggestion that anthraquinone itself fragments through fluorenone and biphenylene type ions [6] by successive eliminations of carbon monoxide, it is postulated that 1-phenyl anthraquinone passes through a 1-phenyl fluorenone intermediate (4). Support of this comes from 1-phenyl fluorenone which exhibits an identical mass spectrum below m/e 255. (mass spectrum 7).

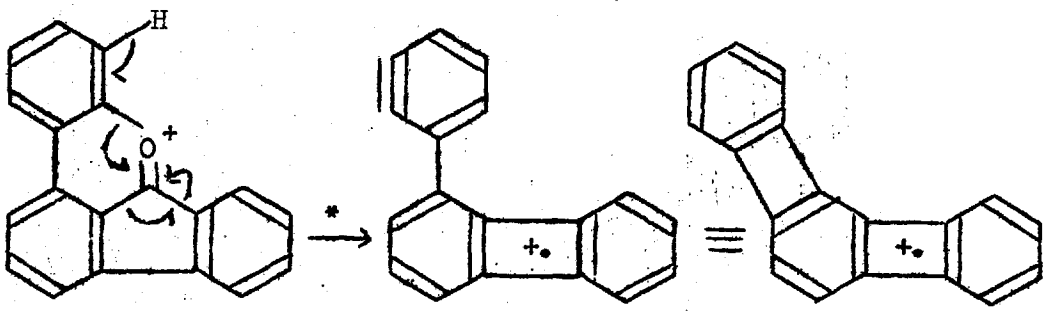


Moreover, it is well-known that if the abundances of metastable ions formed from different precursors relative to the daughter ions are the same then the parent ions are of identical structure. Application of this principle to the transition 255 - 226 m.u. in 1-phenyl fluorenone and 1-phenyl anthraquinone, for which there are metastable ions at m/e 200 gives values of 0.0056 and 0.0050 respectively for the intensity ratio $M^*/(m/e\ 226)$. This excellent agreement demonstrates that an ion of identical nature to that of the $[M-1]^+$ ion of 1-phenyl flurorenone is formed on consecutive elimination of H° and CO from 1-phenyl anthraquinone.

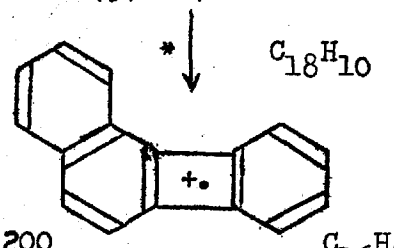
Further, during pyrolysis of 1-phenyl anthraquinone it was possible to isolate 1-phenyl fluorenone in low yield, a result which is suggestive of preferential loss of the C_{10} carbonyl on electron impact. Pyrolytic loss of carbon monoxide from anthraquinone itself has not been observed, and has been disputed on the grounds that initial breaking of an aryl-CO bond leads to unfavourable loss of conjugation.[57] Clearly there is some tendency for this to occur, however, even though energetically disadvantageous. Moreover, Brown and Solley [57] have detected biphenylene from fluorenone pyrolysis.

Additional fragmentation of (4) leads to loss of the elements of HCO (shown by accurate mass measurement) and labelling indicates that the phenyl ring is the origin of the proton. It is suggested that this elimination initially

generates a benzyne type ion which favourably cyclises on to the anthraquinone nucleus forming the stable 1,2-triphenylene ion (5). Support of benzyne ions as intermediate structures is evident from the abundant ion at m/e 76, attributed to benzyne itself.



(4). m/e 255 (5). m/e 226

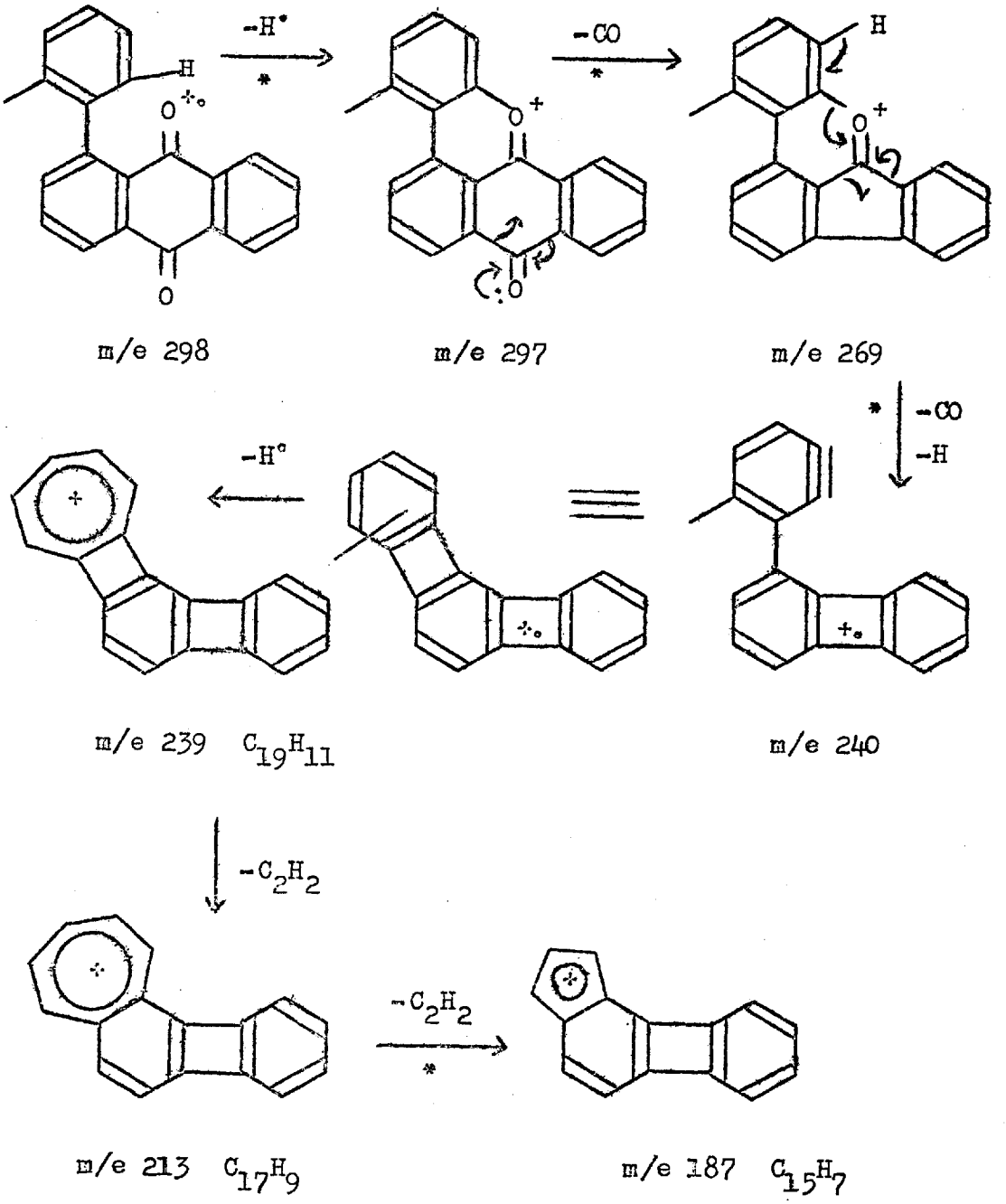


(6) m/e 200 $C_{16}H_8$

Ion (6), formed by the loss of acetylene from (5), is shown by mass measurement to have the formula $C_{16}H_8$ and is thought to have the stable benzobiphenylene structure on account of its reluctance to undergo further decomposition. The above reaction scheme is apparent in all of the 1-aryl anthraquinones prepared and gives rise to transitions well characterised by metastable ions (designated by *).

Besides fragmenting to form the characteristic ions at m/e 283, 255, 226 and 200, the alkyl derivatives also produce abundant ions at m/e 239 ($C_{19}H_{11}$) which are absent in the

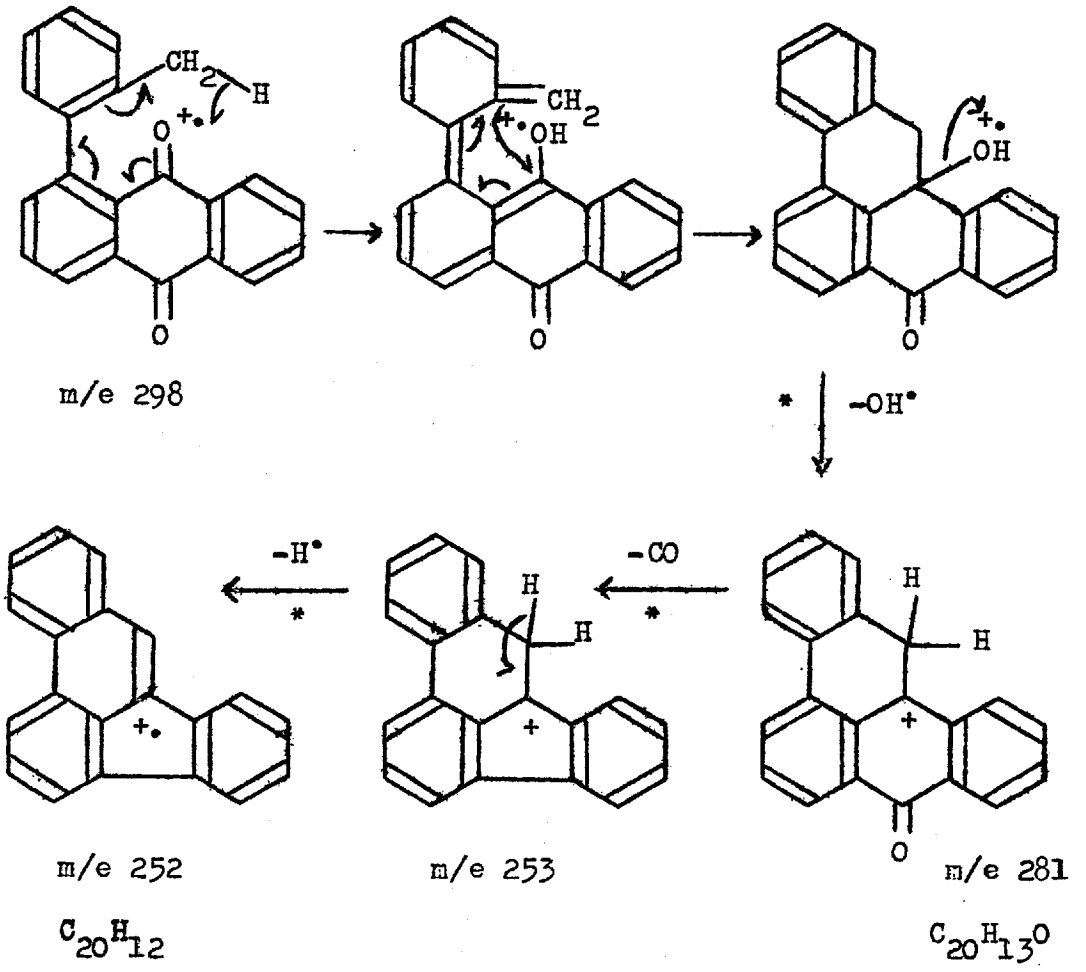
other derivatives. A plausible mechanism for the formation of this ion is given below, the ortho-tolyl compound (mass spectrum 9) being used to illustrate the fragmentation scheme.



This scheme is consistent with deuterium labelling of the methyl group which causes a displacement of the ion at m/e 239 to m/e 241, and with the known inclination of alkyl aromatics to ring expand to tropylium ions.

One other fragmentation worthy of note concerns the considerable loss (ca. 23% relative abundance) of the hydroxyl radical from 1-o-tolyl anthraquinone (mass spectrum 9). Deuteriation of the methyl group causes the elimination of OD° from the molecular ion, and a shift of the ion from m/e 281 to m/e 283. Computation of the ^{13}C isotope contribution of the m/e 283 ion (which also includes the $[M-CD_3]^+$ fragment) to the ion at m/e 284 shows that no loss of OH° occurs from the deuteriated derivative. Furthermore, the absence of hydroxyl elimination from the meta- and para-tolyl compounds demands participation of the C_9 carbonyl. It is proposed that proton migration via a concerted transition state ensues followed by rearomatisation with elision of the hydroxyl radical as shown below. The resulting ion then undergoes consecutive elimination of carbon monoxide and an hydrogen atom to form the stable ion at m/e 252.

A similar sequence is observed in the ortho-ethyl homologue in which the ions at m/e 281 and m/e 253 are shifted 14 m.u. to higher mass. The latter ion is capable of both H° and Me° loss but is found to decompose only with the elision of the methyl radical. This is easily rationalised on the



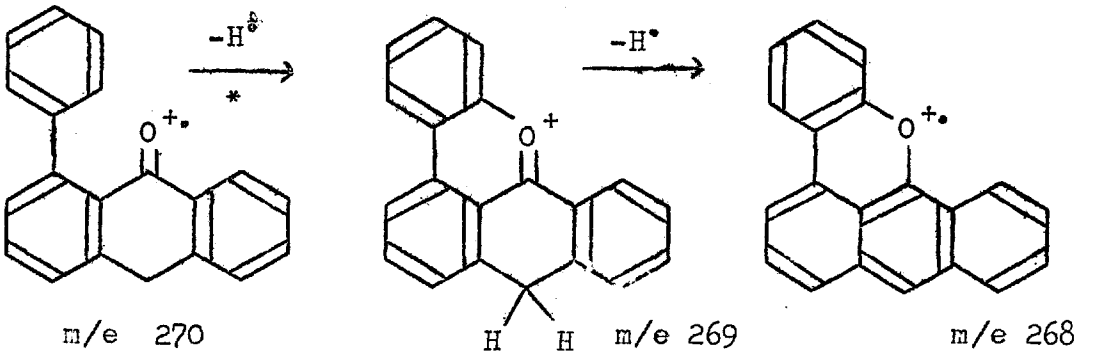
basis of the C - C and C - H bond energies, 59 K cal/mole and 87 K cal/mole respectively, the fragmentation proceeding by elimination of Me; by virtue of the lower energy required, to form the m/e 252 ion. As expected from the above mechanism, the ortho-isopropyl and tertiary butyl homologues displayed a progressive decrease in hydroxyl loss (see Table 8).

Table 8.

Loss of the hydroxyl radical from 1-o-alkylphenyl anthraquinones.

Substituent	$[M-OH]^+$
Me	23%
Et	3.6%
i-Pr	2.9%
t-Bu	0.0%

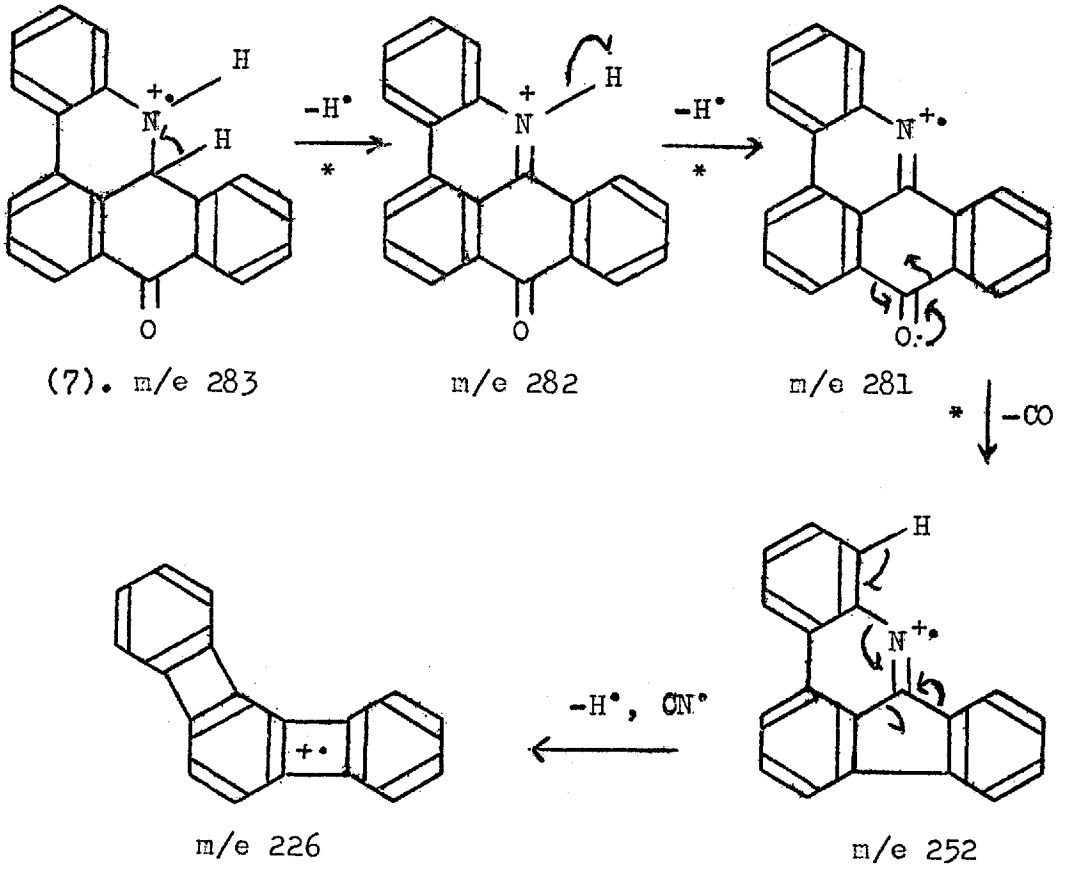
The behaviour of 1-phenyl anthrone (mass spectrum 8) is similar to that of the anthraquinone, the essential difference being the ability to form an abundant $[M-2]^+$ ion by elimination of an hydrogen atom from the benzylic position.



m/e 270 m/e 269 m/e 268

Azanaphthanthrone (7) (mass spectrum 10) forms comparable ions to 1-phenyl anthraquinone and is able to form the stable aromatic species at m/e 226 which is the characteristic hydrocarbon fragment in all these compounds. The postulated pathway to this moiety is illustrated below.

Doubly charged ions abound in the spectra of all the aryl anthraquinones studied, often forming ions of 30% relative abundance. Although common in aromatic systems the frequent



occurrence in these compounds is proof indeed of the high stability of the ions which are formed, since it is only the highly delocalised aromatic systems which can dissipate the the high energy of these species. Metastable ions for doubly charged transitions have been observed for the reaction ;

$$[M\text{-}CO]^{++} \xrightarrow{*} [M\text{-}C_2O_2]^{++} + CO$$

in anthraquinone itself,[52] and similar observations may be

seen in the 1-aryl anthraquinones. The compounds for which transitions have been noted are listed below :

1-o-anisyl anthraquinone $255^{++} \xrightarrow{-HCO} 226^{++}$

* at m/e 100.2

1-phenyl anthraquinone $255^{++} \xrightarrow{-HCO} 226^{++}$

* at m/e 100.2

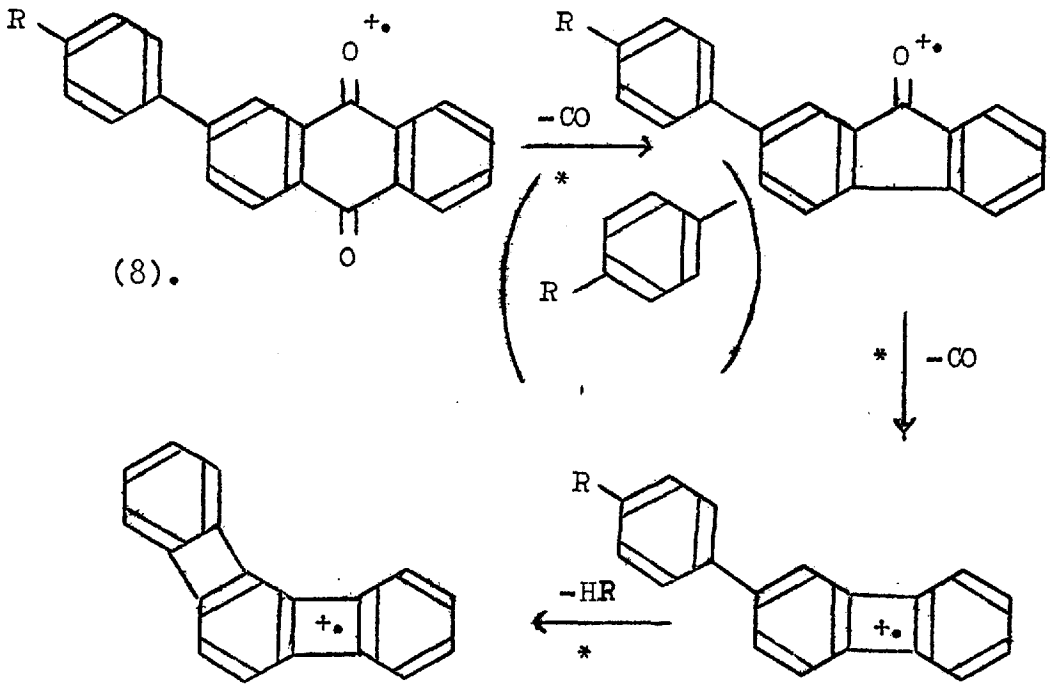
1-m-chlorophenyl anthraquinone $226^{++} \xrightarrow{-C_2H_2} 200^{++}$

* at m/e 88.5

It is assumed that these transitions are accompanied by metastable ions on account of the high intensity of the parent and daughter ions concerned. Similar metastable ions are presumably present in the spectra of other anthraquinones but are too weak to be observed.

For comparative purposes several 2-aryl anthraquinones (8, R = H, Cl, Br) were investigated. (mass spectrum 2 for 8, R = H). These compounds decomposed by successive loss of two molecules of carbon monoxide in the same manner as anthraquinone itself [6] to furnish an ion at m/e 228. This ion is further stabilised by elimination of HR to give the highly conjugated ion at m/e 226 (see below).

Examination of the spectra of the diaryl anthraquinones (9) and (10) gave some insight into the stability of these compounds, and in view of the extensive occurrence of doubly charged ions, some in excess of 25% relative abundance, ions with considerable aromatic character must be formed.

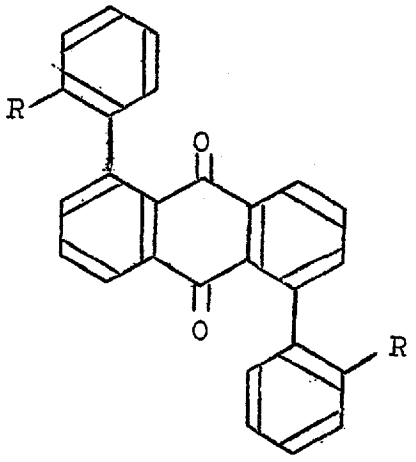


(8).

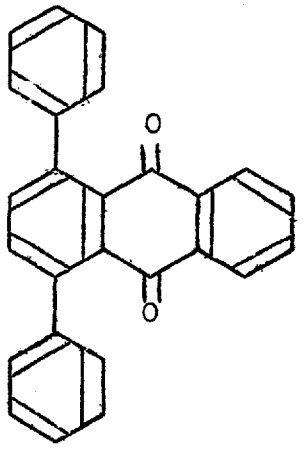
(5). m/e 226

m/e 228 (R = H)

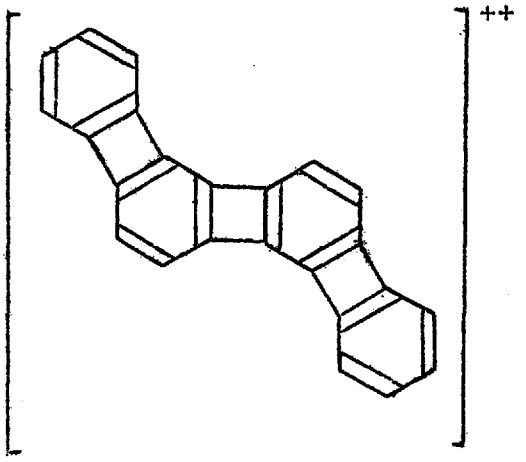
The fragmentation of these diaryl derivatives parallels that of the mono-aryl compounds for singly charged ions, but with further electron abstraction it is possible to remove a second ortho-substituent, the loss of which is followed by two consecutive eliminations of HCO to give an exceptionally stable ion (11) which undergoes no further fragmentation. The formation of these defunctionalised stable ions is in accord with the greater stability associated with even-electron species over the equivalent odd-electron ions.[58]



(9). R = H, Me, NO_2



(10).



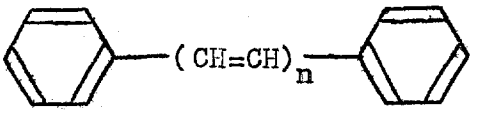
(11).

Part 2.

Terminal Diaryl Polyenes.

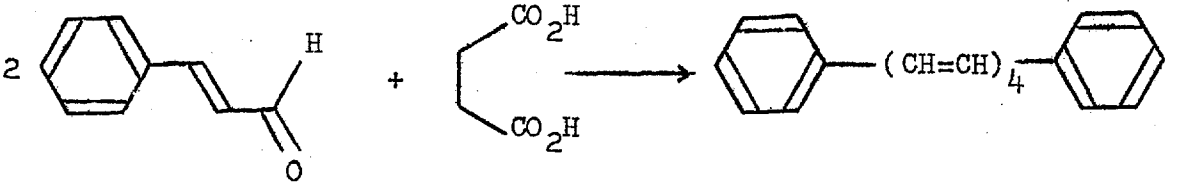
2 , 1 Discussion of Experimental Work.

Structural elucidation of the natural carotenoids has been of interest for many years, and many different approaches have been used with this aim in mind. However, very little constructive mass spectral work has been carried out and it was with this view that several terminal diaryl polyenes were synthesised for use as model compounds. Of all the polyene carotenoids known, only three contain two terminal phenyl rings [59, 60] and four others have only one.[60] All other polyene carotenoids are non-aromatic.



(1). n = 1-9

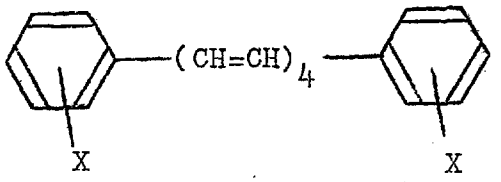
A series of compounds (1) have been prepared by the method of Kuhn and Winterstein,[61] an example of which is the formation of the tetraene (3) by condensation of cinnamaldehyde (2) with succinic acid in the presence of litharge and acetic anhydride.



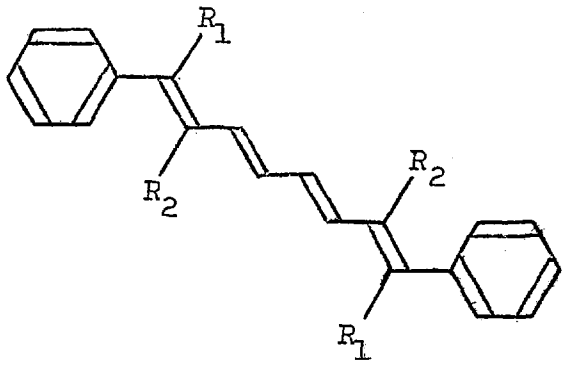
(2). (3).

This reaction usually leads to the production of extensive amounts of polymeric material by self-condensation of the aldehyde, and in consequence gives low yields of the order 3-30% depending on the substituents on the aromatic ring and the length of the polyene chain. However, the insoluble nature of the highly crystalline polyenes leads to their precipitation during formation resulting in relative ease of separation and purification. It has been demonstrated,[62] that the higher polyenes (1, n = 4, 5, 6) on synthesis by different routes gives the same product in each case, and X-ray studies on diphenyl hexatriene (1, n = 3) have shown that this is exclusively the all-trans isomer.[62] From this work it is clear that the all-trans form is the most stable conformation and this stereochemistry is assumed in all the samples prepared. Support of this is obtained from the characteristic u.v. spectra which compare favourably with that of the hexatriene.

As substituted cinnamaldehydes are well-characterised compounds and are simply synthesised by well-known procedures, substituted polyenes of the tetraene type were prepared for comparative purposes. Two distinct types were made, those having substituents in the aromatic ring (4) and those with alkyl or aryl groups replacing hydrogen in the polyene chain (5). Ring substituted cinnamaldehydes were formed by action of the appropriately substituted aryl Grignard reagent on

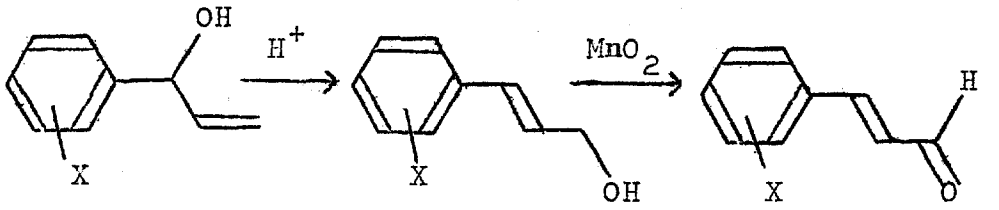


(4). X = m, p, OMe, Me, Cl, Br, F
o, Me



(5). R_1 = H ; R_2 = Me, Et
R_2 = H ; R_1 = Me, Ph

acrolein generating the phenylallyl alcohol (6), which on anionotropic rearrangement forms the cinnamyl isomer (7) in quantitative yield. Oxidation of (7) with manganese dioxide then gives the aldehyde quantitatively.



(6) (7)

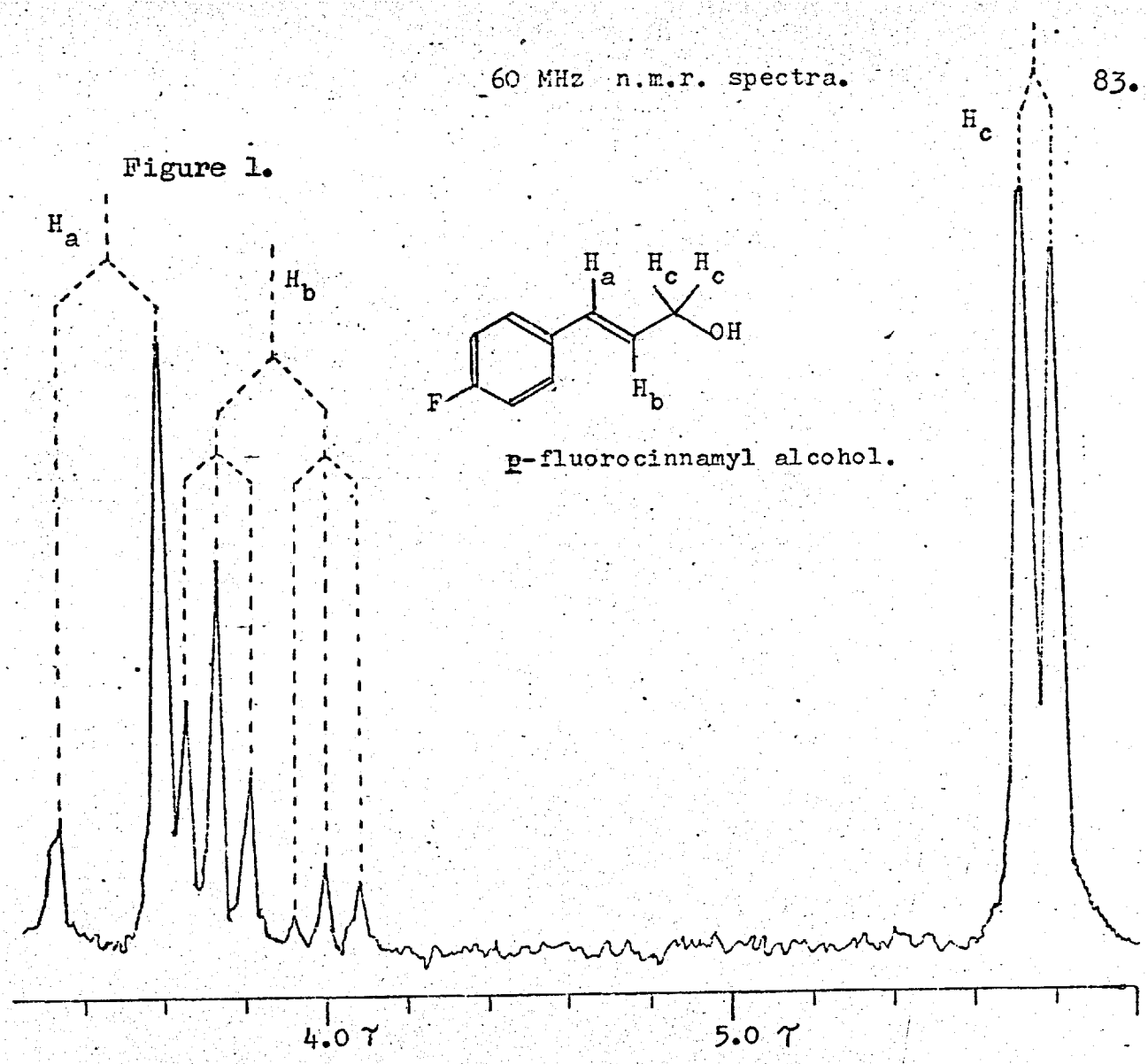
The effect of the substituent on the isomerisation of the 1-phenylallyl alcohol (6) is such that it governs the conditions under which the procedure must be carried out. Unsubstituted, alkyl and alkoxy substituted alcohols isomerise

readily, the procedure involving formation of the acetate with acetic anhydride followed by alkaline hydrolysis. The acetic acid present in the anhydride is sufficient to cause rearrangement to the cinnamyl acetate (shown by n.m.r.) which is simply hydrolysed to the cinnamyl carbinol. Similar treatment of the halogeno derivatives leads to the formation of unrearranged acetate. These derivatives are therefore isomerised with 0.2N hydrochloric acid in 60% aqueous acetone by prolonged refluxing. Mineral acid treatment of the alkyl and alkoxy compounds results in extensive polymerisation and is not advised.

The n.m.r. spectrum of the 1-phenylallyl and cinnamyl systems show characteristic differences in the vinylic region (see for example the p-fluoro derivatives in Figure 1.) and it is these differences which allow unambiguous differentiation even though u.v. and i.r. may also be used.

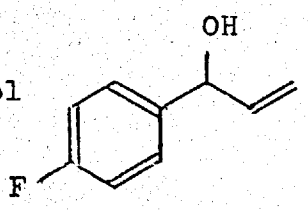
Attempts to prepare 1,8-di-(o-nitrophenyl)-octatetraene (4) proved abortive, the red crystalline product exhibiting carbonyl bands in the i.r. spectrum typical of an anhydride, ν_{max} 1795, 1755 cm^{-1}. Moreover, the u.v. spectrum had maxima at 253.0 mμ and 296.0 mμ suggesting a conjugated chain. On the basis of this evidence the structure of this compound is postulated to be (8). Attempts to hydrolyse and decarboxylate this compound all failed. It is suggested that the nitro groups stabilise the presumed dicarboxylic acid

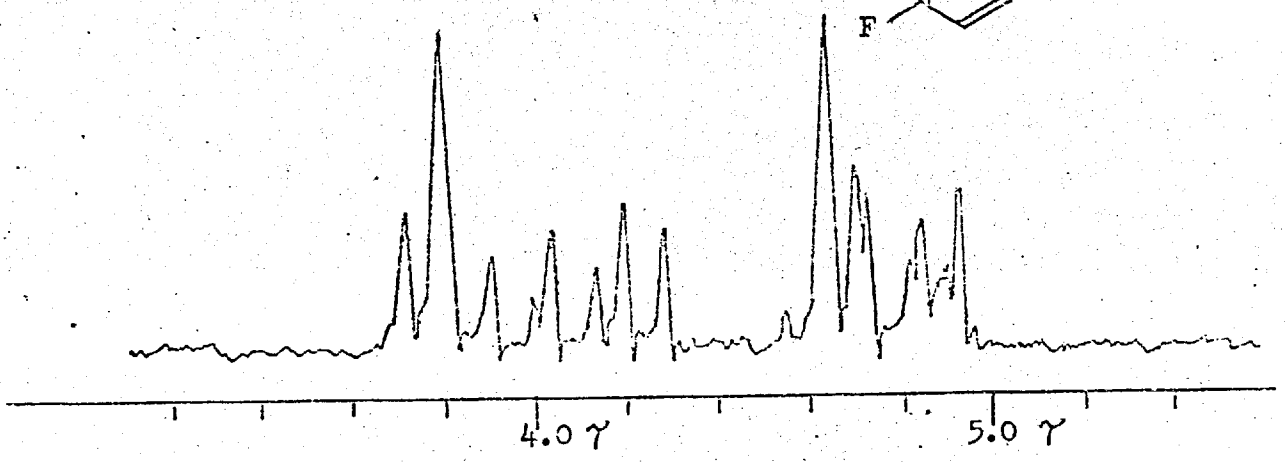
Figure 1.

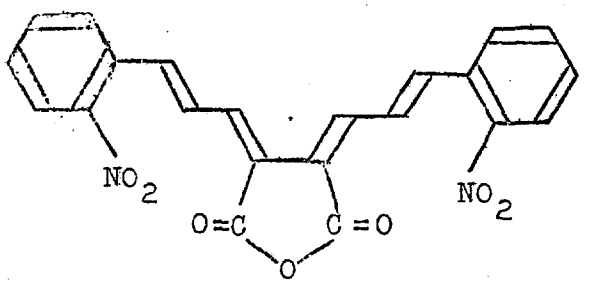


p-fluorocinnamyl alcohol.

I-(p-fluorophenyl)-allyl alcohol



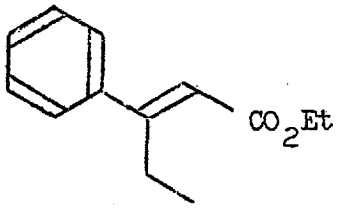




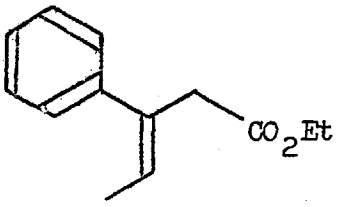
(8).

intermediate (8 with vicinal dicarboxylic acid in place of the anhydride) by electron withdrawal, making the competitive anhydride formation favourable.

Cinnamaldehydes with substituents on the α-carbon atom were prepared by Aldol condensation of benzaldehyde and the appropriate aliphatic aldehyde, and those with β-substituents were prepared by the Reformatski reaction. Somewhat unexpected results were obtained during the attempted synthesis of ethyl-β-ethyl cinnamate (9) by Reformatski reaction of propiophenone and ethyl bromoacetate followed by dehydration. Instead of a single product the i.r. spectrum showed two carbonyl bands at ν_{max} 1730 and 1710 cm^{-1} corresponding to a saturated and an unsaturated ester respectively. Lithium aluminium hydride reduction of the dehydrated ester gave a mixture of alcohols which n.m.r. and g.l.c. showed to be 85% of the non-conjugated alcohol and only 15% of the expected conjugated isomer. Compound (10) thus constitutes the bulk of the Reformatski dehydration product.



(9).



(10).

These results are in disagreement with those of Barltrop *et al.*[63] who claim isomer (9) as the sole product. Structural identification by these authors was effected by reduction and also by hydrolysis to the acid which was compared with an authentic sample. Since reduction of (9) and (10) leads to an identical product this procedure could not possibly distinguish these two isomers, and it is also conceivable that acid hydrolysis might convert (10) to the more stable acid of (9). It is thought therefore that the product isolated by Barltrop and his co-workers[63] was in fact a mixture of the two isomers (9) and (10) with the latter predominating.

Several substituted and deuteriated stilbenes (1, n = 1) were also prepared by well-established routes and will not be discussed further.

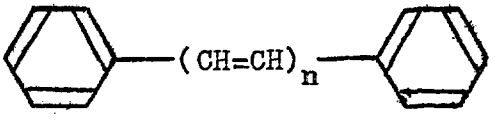
2 , 2 Discussion of Mass Spectra.

The mass spectrum of stilbene (1, n = 1) has been investigated by numerous workers [64, 65] and it is suggested that successive loss of two hydrogen atoms leads to the cyclic phenanthrene ion. As this is the first member of the polyene group (discounting biphenyl (1, n = 0) which is an atypical first member) it was considered necessary to investigate this molecule further and confirm that hydrogen elimination was indeed consecutive. Both cis- and trans-stilbene (mass spectra 11 and 12 respectively) exhibit substantial loss of 1 and 2 m.u. from the molecular ion and metastable ion evidence suggests that this is undoubtedly a two step process. Furthermore, in [2,4,6-$^{2}H_{3}$]-cis-stilbene metastable ion analysis indicated only the following transitions.

$$183\text{m.u.} \xrightarrow[-H]{*\ 181.0\text{m.u.}} 182\text{m.u.} \qquad 182\text{m.u.} \xrightarrow[-D]{*\ 178.0\text{m.u.}} 180\text{m.u.}$$

$$183\text{m.u.} \xrightarrow[-D]{*\ 179.0\text{m.u.}} 181\text{m.u.} \qquad 181\text{m.u.} \xrightarrow[-H]{*\ 179.1\text{m.u.}} 180\text{m.u.}$$

No metastable ion corresponding to loss of HD was observed proving that hydrogen elision is indeed a consecutive process.

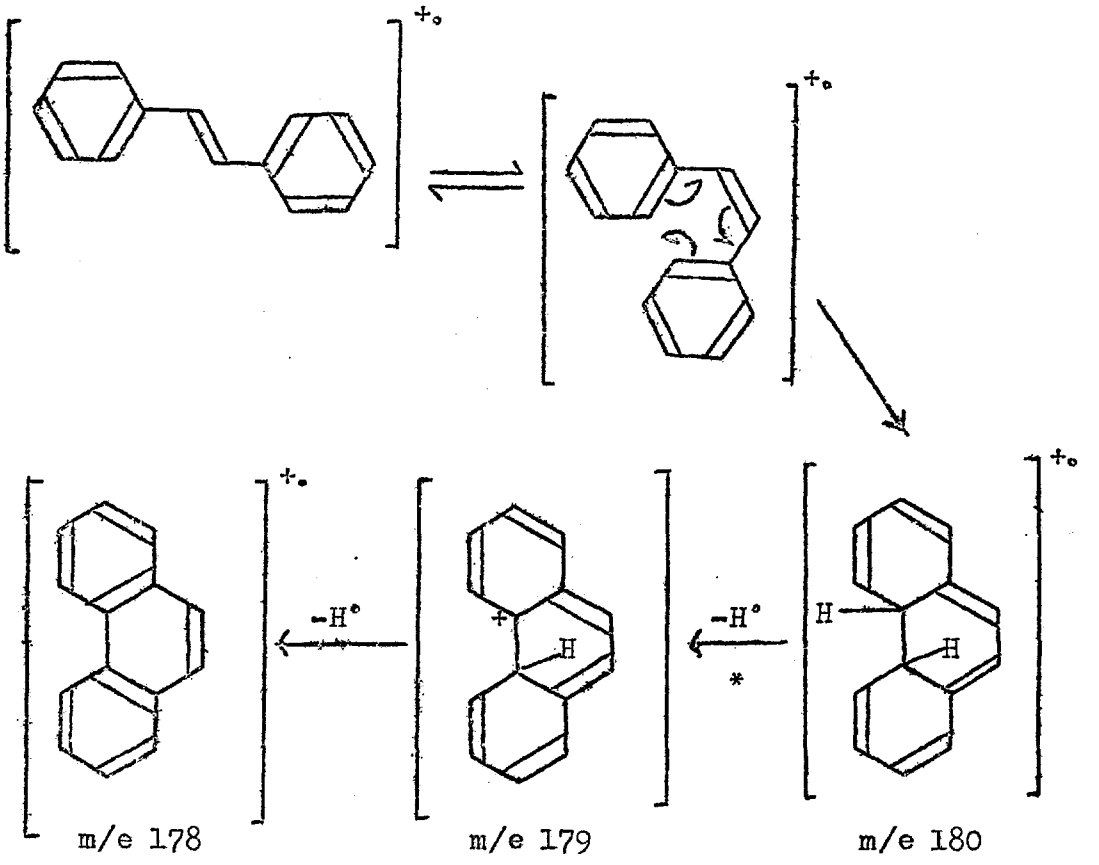


(I). n = 1-9

Above 120°C the mass spectra of *cis* and *trans*-stilbene are identical on account of their ready thermal isomerisation [66] to give an equilibrium mixture consisting of about 20% *trans*- and 80% *cis*-forms (shown by g.l.c.). The mass spectra 11 and 12 were consequently obtained at *ca.* 100°C at which temperature isomerisation is slow. As the fragmentation of stilbenes has been adequately discussed previously [64] no further mention of this will be made, although it is interesting to note that 2,2'-dimethoxy stilbene, which is necessarily *trans* because of steric hindrance between the two methoxyl groups, does not exhibit any loss of hydrogen from the molecular ion. This is strong support for cyclic ions being formed in the unsubstituted stilbenes. The reluctance of 2,2'-dimethoxy stilbene to eliminate hydrogen would also suggest that *cis-trans* isomerism is essential prior to hydrogen loss from *trans*-stilbene, a consideration which is more readily appreciated in the higher homologues (*vide infra*). A plausible explanation of this is that bond formation between the 2,2' positions is necessary before hydrogen loss is energetically favourable. (see Scheme 3).

Proceeding to higher members of the polyene class (1, n = 2-9) the above discussion forms some basis on which to explain the mass spectra of these compounds. These derivatives all have important $[M-1]^+$ and $[M-2]^+$ ions along with smaller $[M-3]^+$ and $[M-4]^+$ ions. Furthermore, metastable ions are

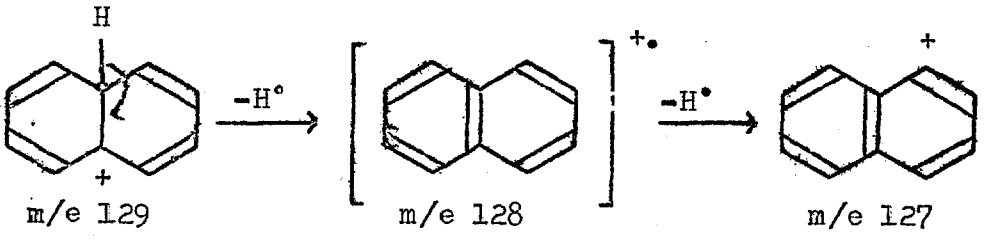
Scheme 3.



observable for a concerted loss of H_2. As both consecutive and concerted mechanisms appear to be in operation simultaneously it is suggested that these are the products of two distinct fragmentation pathways, one involving a Cope cyclisation within the side-chain - henceforth termed chain cyclisation - and the other involving cyclisation of the chain onto one of the phenyl rings - called ring cyclisation. By analogy with the consecutive elimination of hydrogen from stilbene it is tentatively suggested that concerted loss

is observed in the chain cyclisation and consecutive loss from ring cyclisation, both of which occur concurrently.

Besides H_2 elision, fragments corresponding to styrenes, benzenes, biphenyls, stilbenes, phenyl butadienes and naphthalenes as shown in Scheme 4 for 1,8-diphenyl octatetraene (1, n = 4, mass spectrum 14) are also observed. These fragments are products from competitive decompositions and are formed to extents dependent on their relative stabilities (vide infra). Since all these ions are odd-electron species, known to be less favourable than their even-electron counterparts,[58] they are often accompanied by extensive ions one mass unit higher or lower which are necessarily even-electron moieties. For example, the naphthalene ions at m/e 128 are formed along with large associate ions at m/e 129 and 127.



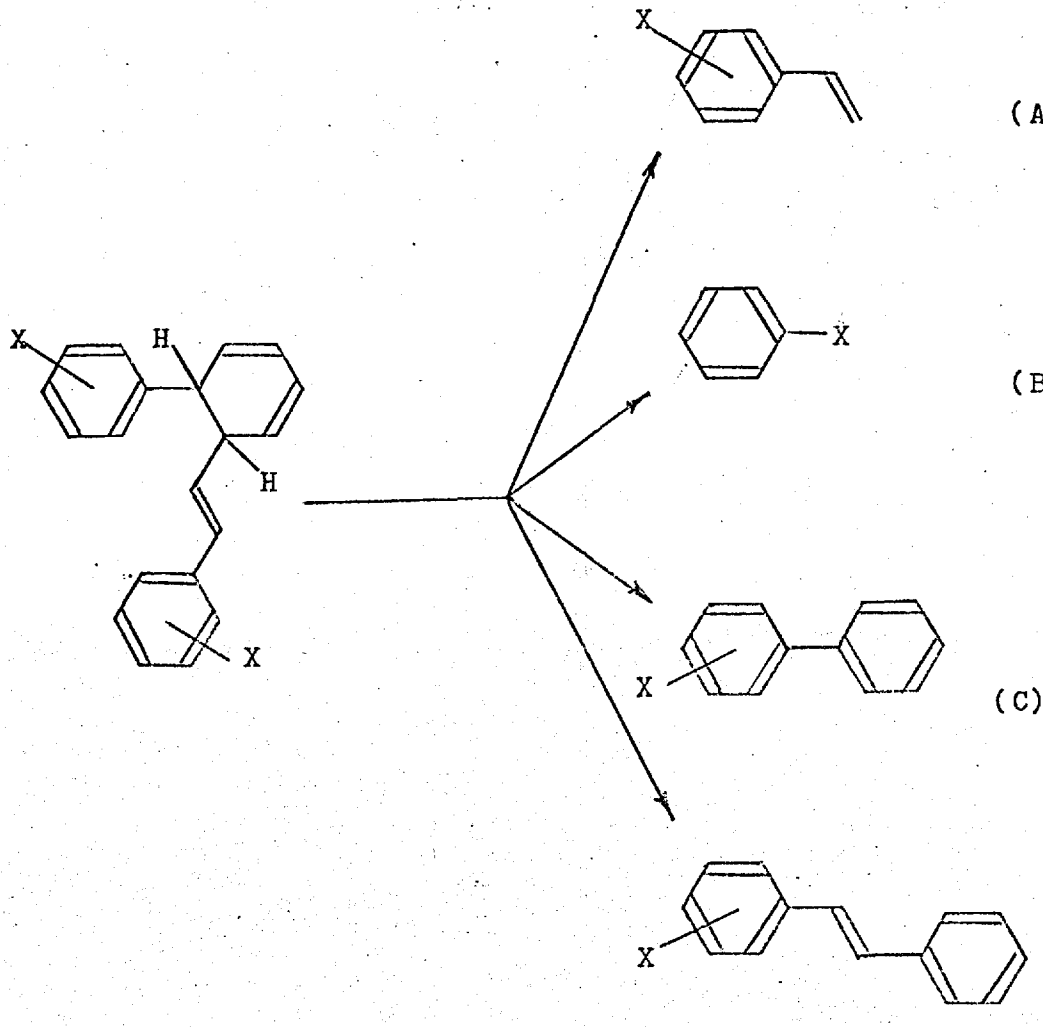
Other major fragments are the tropylium ion, m/e 91, and the $[M-91]^+$ ion (at m/e 167 in this example).

As the value of n increases the molecular ion becomes progressively less plentiful with a concomitant increase in the ion at m/e 78 attributed to benzene. This trend is clearly

Scheme 4.

Chain and ring cyclisation products of terminal diaryl tetraenes.

Chain cyclisation products.



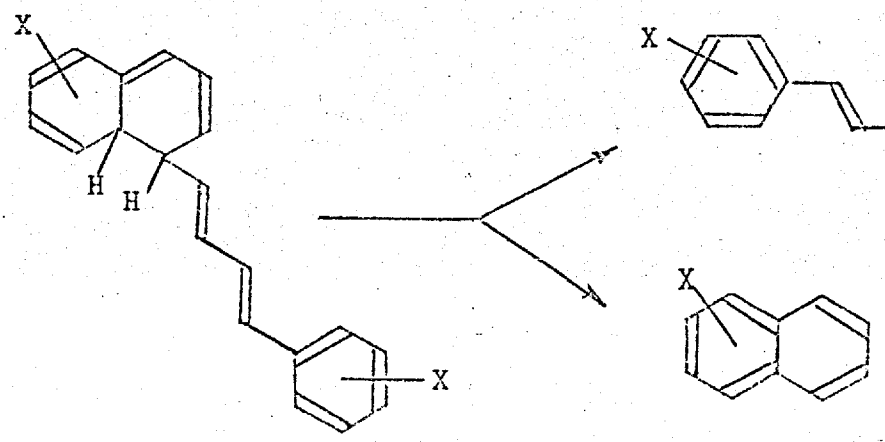
(A). C_8H_7X

(B). C_6H_5X

(C). $C_{12}H_9X$

(D). $C_{14}H_{11}X$

Ring cyclisation products.



(E). $C_{10}H_9X$

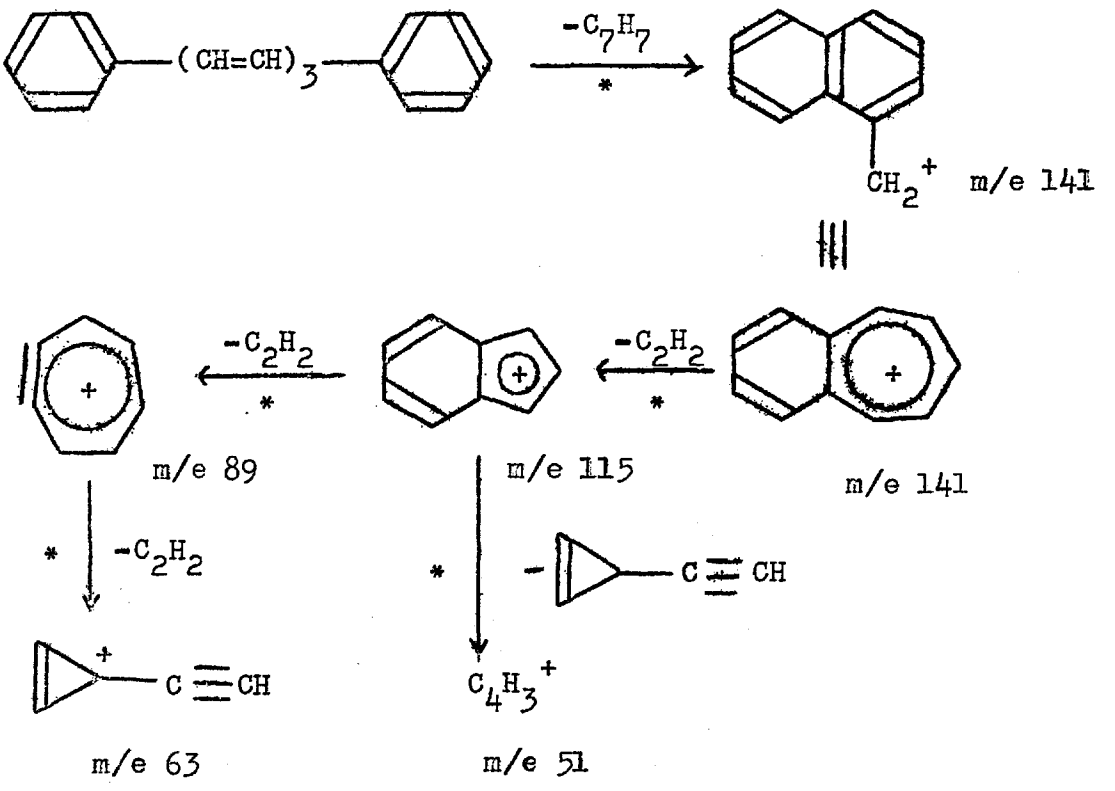
(F). $C_{10}H_7X$

seen in the tri-, tetra-, and penta-enes (mass spectra 13, 14, and 15 respectively) in which the M^+ ion decreases from 100% to 35% relative abundance, and the m/e 78 ion increases from 5% to 100%. Moreover, in the derivatives having n = 7, 8, and 9, the intensity of the benzene ion dwarfs all others to less than 26% relative abundance. The tropylium ion is a prominent ion in all the spectra and is shifted to a strong ion at m/e 121 in the anisyl derivatives. All major ions in the mass spectra have been unambiguously assigned by accurate mass measurement of the 1,8-di-p-anisyl octatetraene fragments.

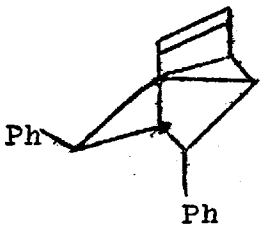
Also important are fragments derived from alkyl naphthalenes [67] by ring expansion and subsequent cleavage, whereby ions at m/e 141, 115, 89, 63, and 51 are rationalised. 1,6-Diphenyl hexatriene (mass spectrum 13) is given as an example in Scheme 5 below. All the transitions shown in the scheme are adequately substantiated by metastable ions.

Pyrolysis of 1,8-diphenyl octatetraene at 700°C and 10^{-2} mm./Hg pressure yielded a mixture of hydrocarbons from which trans-stilbene, biphenyl, and 1-phenyl phenanthrene were isolated, and the presence of naphthalene demonstrated by comparative g.l.c. on two different columns. The presence of these compounds in the pyrolysate constitutes good evidence for the fragmentation pathway proposed in Scheme 4. Furthermore the recent work of Marvell and Seubert [133] has

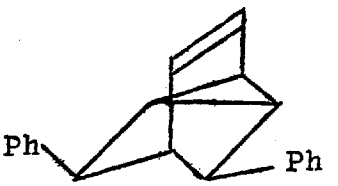
Scheme 5.



shown that thermolysis of 1,8-diphenyl-*trans*-1, *cis*-3, *cis*-5, *trans*-7-octatetraene at 175°C over several hours leads to a complex mixture of electrocyclisation products. Notable amoung these products were *cis*- and *trans*-stilbenes and 2-styryl-1,2-dihydrobiphenyls of the type suggested prior to formation of fragment ions A, B, C, and D in Scheme 4. No naphthalene derivatives were observed by these authors although the more complex tricyclo-octenes (2) and (3) were obtained in greater than 20% yields.



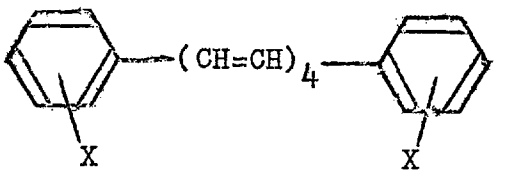
(2)



(3)

Substitution of methyl and phenyl groups in to the 2 and 7 positions of 1,8-diphenyl octatetraene completely prevented loss of hydrogen from the M^+ ion and effectively diminished all fragmentation. This would suggest that little hydrogen elision occurs by ring cyclisation, (since this would not be hindered by substitution in the 2 and 7 positions) but that chain cyclisation predominates. The latter course is completely blocked by this substitution, and leads to the conclusion that with any substituent other than hydrogen in these positions then fragmentation is virtually quenched. However, with alkyl groups in the 3 and 6 positions normal fragmentation is followed even though no elimination of hydrogen from the molecular ion is observed.

Most interesting, however, are the results obtained from aryl polyenes with substituents on the aromatic rings (4), when it is again possible to classify the major ions according to Scheme 4. Table 9 shows the abundances of the characteristic ions A - F expressed as a percentage of the total ion current (% Σ_{30}). From the table it is evident that the



(4). X = m-, p-, OMe, Me, Br, Cl, F
o-, Me

most abundant ion is the substituted biphenyl ion (C) formed by chain cyclisation with elision of a substituted styrene. For ring cyclisation the naphthalene ion (F) is most prominent. Mass spectrum 16 of 1,8-di-p-anisyl octatetraene typifies the fragmentation.

It is interesting that the ratio of M^+ to $[M-2]^+$ in o- and p-tolyl octatetraenes is dependent on both the duration in the heated inlet system and the pressure of air in the instrument before insertion. This is suggestive of an air oxidation reaction proceeding in the 'hot-box' by virtue of both the temperature (ca. 180-220°C) and the air present. Figure 2 illustrates the variation of $M^+/(M^+ + [M-2]^+)$ and $[M-2]^+/(M^+ + [M-2]^+)$ with time at 210°C for the p-derivative from which it may be seen that on insertion about 93% exists as the molecular ion whereas after 80 mins., this declines to only 20%. An equivalent rise in the $[M-2]^+$ ion occurs simultaneously, the two ratios becoming equal after 25 mins. Although this effect was observed with other substituents it

Table 9.

Table of % Σ_{30} values for the ions A-F of substituted 1,8-diphenyl octatetraenes.

Compound	A	B	C	D	E	F	Σ_{30}*	M-PhH
p-OMe	1.50%	0.41%	2.39%	1.36%	0.19%	0.68%	1468	3.20%
p-Me	0.61%	0.42%	2.18%	0.84%	0.17%	0.84%	1306	1.26%
p-F	1.69%	0.77%	6.13%	0.90%	0.28%	2.28%	886	1.35%
p-Cl	0.66%	0.16%	2.32%	0.90%	0.75%	0.32%	1231	1.62%
p-Br	0.89%	nil	1.51%	0.89%	nil	nil	338	0.30%
H	1.25%	1.78%	6.40%	1.96%	0.60%	2.42%	2812	as D
m-OMe	2.05%	0.51%	3.83%	1.00%	0.19%	1.61%	527	1.61%
m-Me	1.08%	0.33%	4.80%	1.32%	0.25%	1.20%	1210	2.32%
m-F	1.41%	0.49%	8.45%	0.97%	0.26%	4.46%	569	1.88%
m-Cl	0.96%	0.38%	5.75%	0.77%	0.72%	0.61%	871	1.52%
m-Br	0.57%	nil	4.31%	0.78%	0.15%	0.19%	1058	2.13%

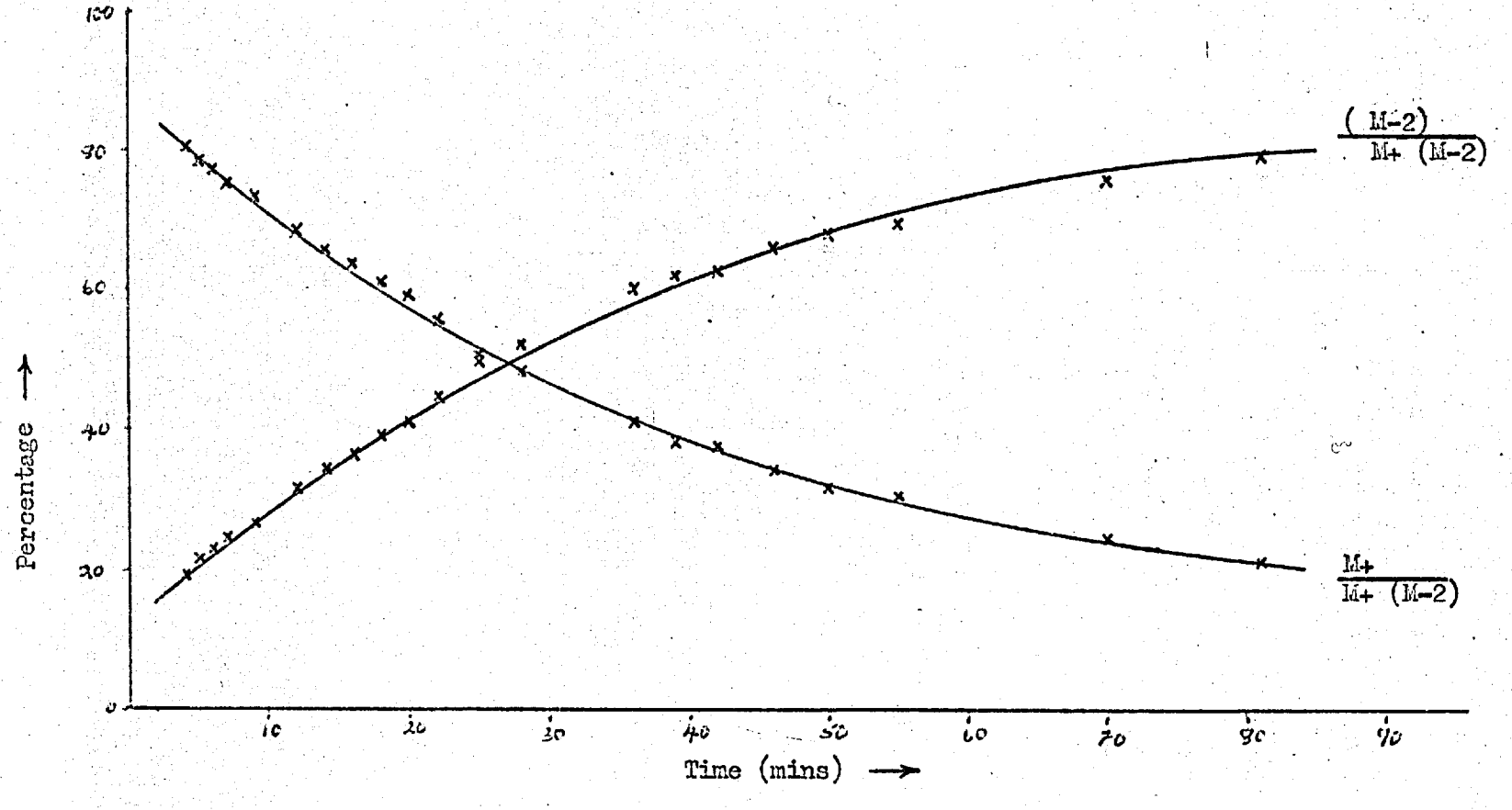
* Arbitrary units.

All isotopes of bromine and chlorine are taken into account.

was much less noticeable, the fluoro compound taking over an hour for the M^+ ion to reduce by 10% of its initial value. Consideration of this effect was made in all quantitative measurements.

Figure 2.

Thermal Loss of (H_2) fron 1, 8 - di - (p-tolyl) octatetraene at 210° C.



Ions A - F show considerable variation with the nature and position of the substituent and consequently the reaction site must be influenced by the electron donating or withdrawing character of the substituent. Plotting log Z/Zo against the Hammett substituent constant as in the method of McLafferty,[68] did not lead to any correlation of the ion (C) intensity with the electronic properties of the substituent, but, adoption of the procedure of Johnstone and Payling [69] lead to a reasonable correlation. In this procedure the difference between the appearence potential (AP) and ionisation potential (IP) is plotted against the substituent constant and results in the graph shown in figure 3. A better correlation, however, was obtained using the Brown substituent constants (see figure 4) which also take into account resonance contributions of the substituent. The AP of type (C) ions was taken throughout this work on account of their greater abundance, allowing easier and more accurate measurement. Allowing for fundamental errors in the results of both IP and AP measurements (shown in Table 10) due to energy spread of the bombarding electrons and the internal energy of the molecule prior to ionisation, these values have an accuracy of $\pm$ 0.2 ev. resulting in an error of $\pm$ 0.4 ev. for the difference, ΔE = AP - IP. Correction for this error - which does not include errors arising from experimental measurement - effectively brings most points on a common straight line in

Table 10.

Table of physical characteristics relating to Figures 3 and 4.

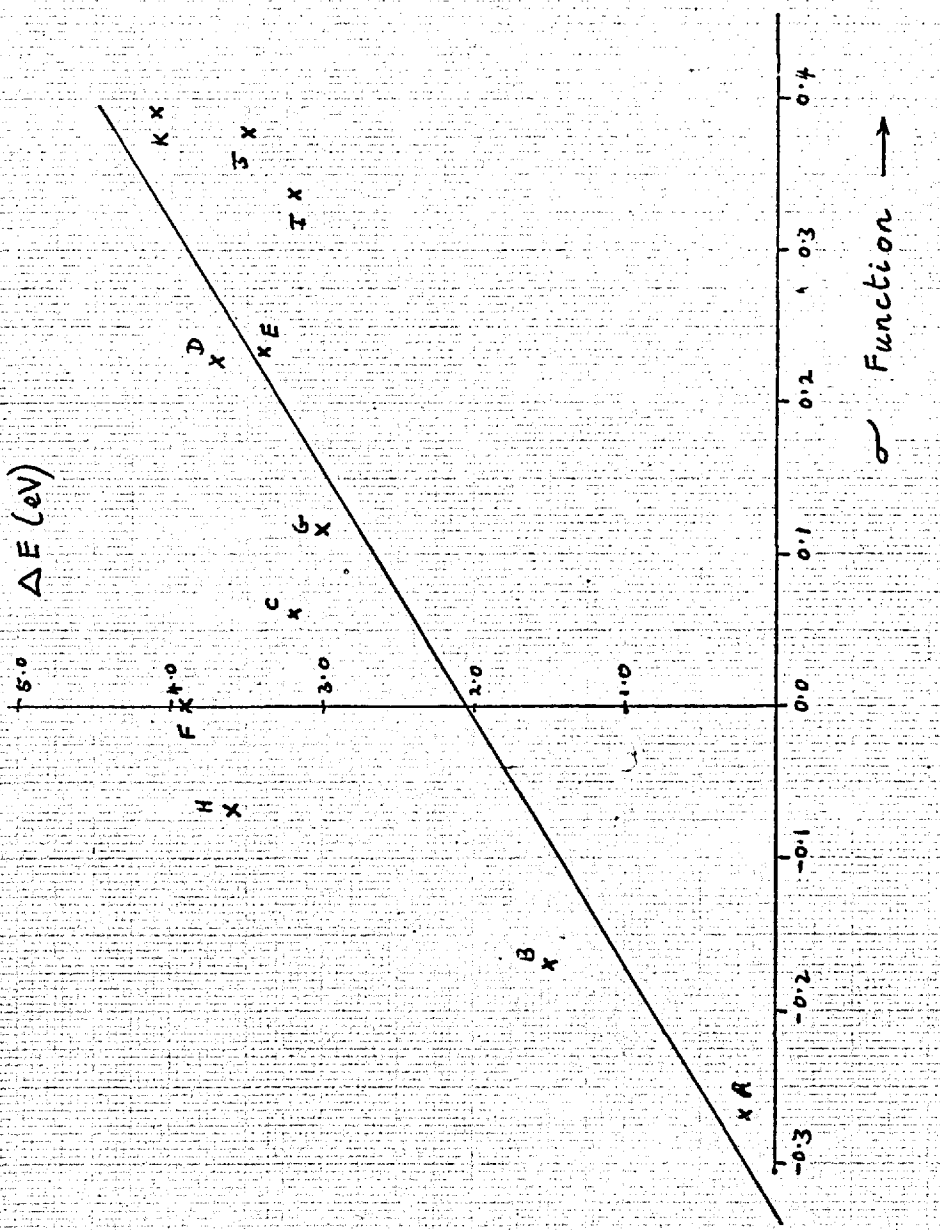
Compound	Hammett Function	Brown Function	IP.*	AP.*	ΔE.†	point
p-OMe	-0.268	-0.78	7.9	8.1	0.2	A
p-Me	-0.170	-0.31	11.4	12.7	1.5	B
p-F	0.062	-0.07	7.2	10.4	3.2	C
p-Cl	0.227	0.11	6.1	9.8	3.7	D
p-Br	0.232	0.15	5.8	9.2	3.4	E
H	0.000	0.00	7.4	11.3	3.9	F
m-OMe	0.115	0.05	7.0	10.0	3.0	G
m-Me	-0.069	-0.07	7.0	10.6	3.6	H
m-F	0.337	0.35	6.8	10.0	3.2	I
m-Cl	0.373	0.40	6.8	10.3	3.5	J
m-Br	0.391	0.40	5.8	9.9	4.1	K

* All results corrected to absolute values using benzene and methyl iodide as standards. Error ± 0.2 ev.

† Error ± 0.4 ev.

Figure 4 and represents good correlation. As the value ΔE is related to the activation energy for the formation of (C) the positive slope of the graph indicates that the formation of (C) is facilitated by electron repelling substituents and

Figure 3.



Graph of $\Delta E = AP - IP$ versus σ for m and p Substituted Polyenes.

Graph of $\Delta E = AP - IP$ versus σ^* for m and p Substituted Polyenes.

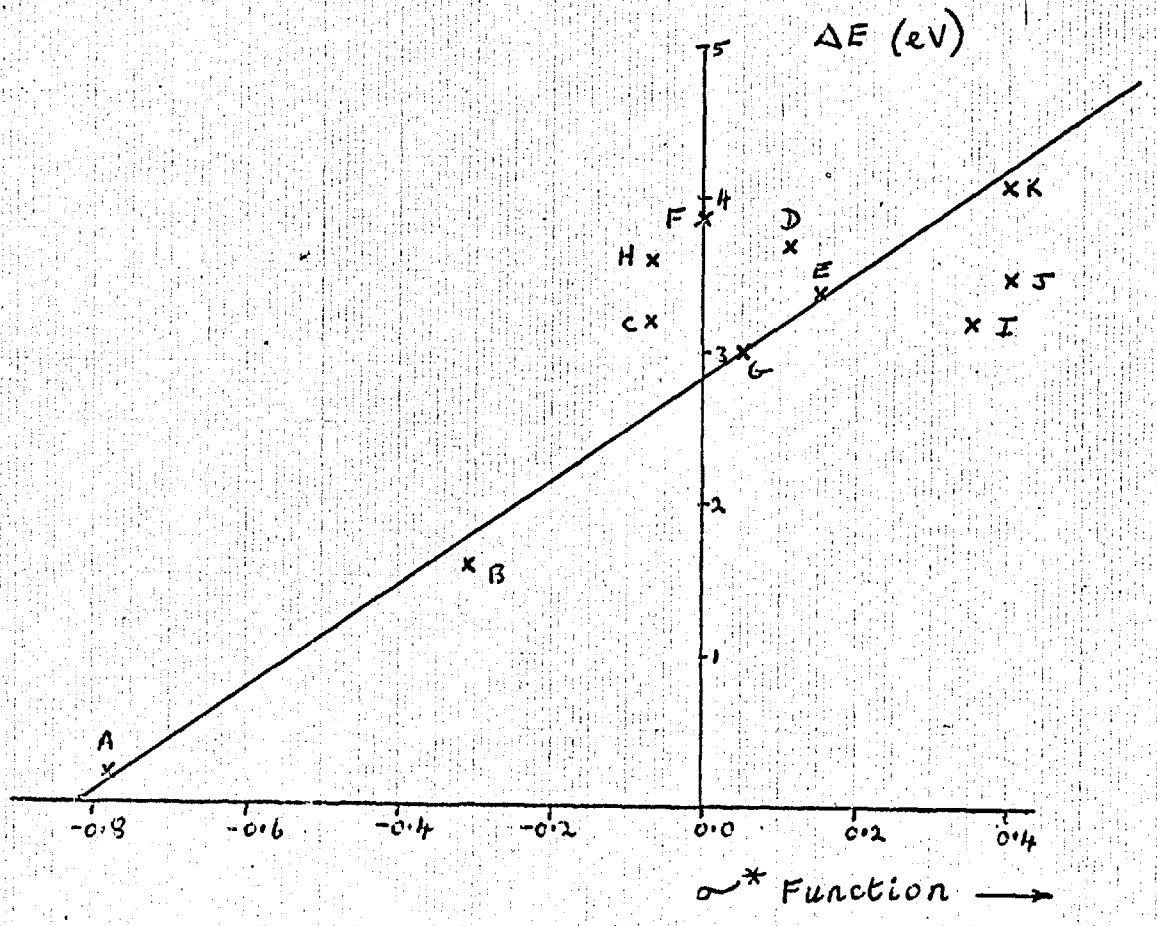
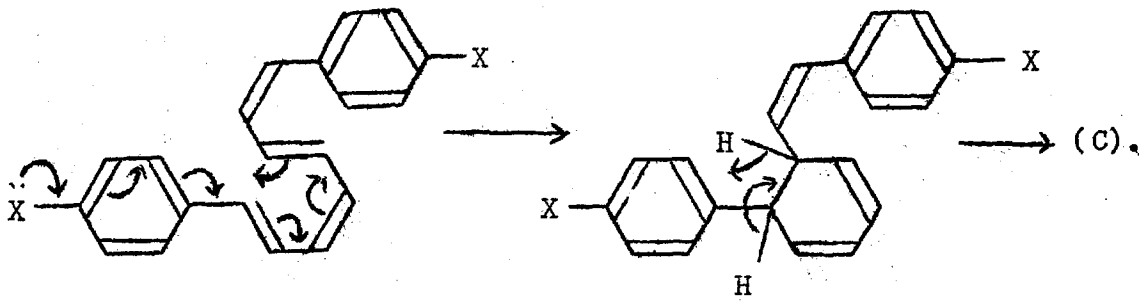
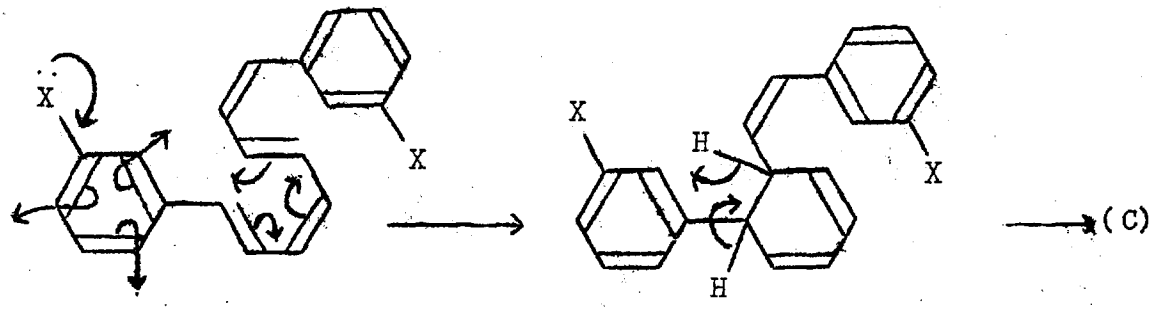


Figure 4.

retarded by those which are electron withdrawing.[70] This is in agreement with electronic considerations and is consistent with the requirement of a high electron density at the reaction site. Thus a <u>para</u>- electron donating substituent will give electron density to the reaction site and thereby reduce the activation energy for the transformation, whereas in the <u>meta</u>-position the effect on the reaction site is much reduced since the resonance effect distributes the electron density towards the <u>ortho</u>- and <u>para</u>- sites and not in the chain where the reaction is proceeding. This is demonstrated for all electron donating substituents, X, (<u>m</u> or <u>p</u>) in the diphenyl tetraene below.



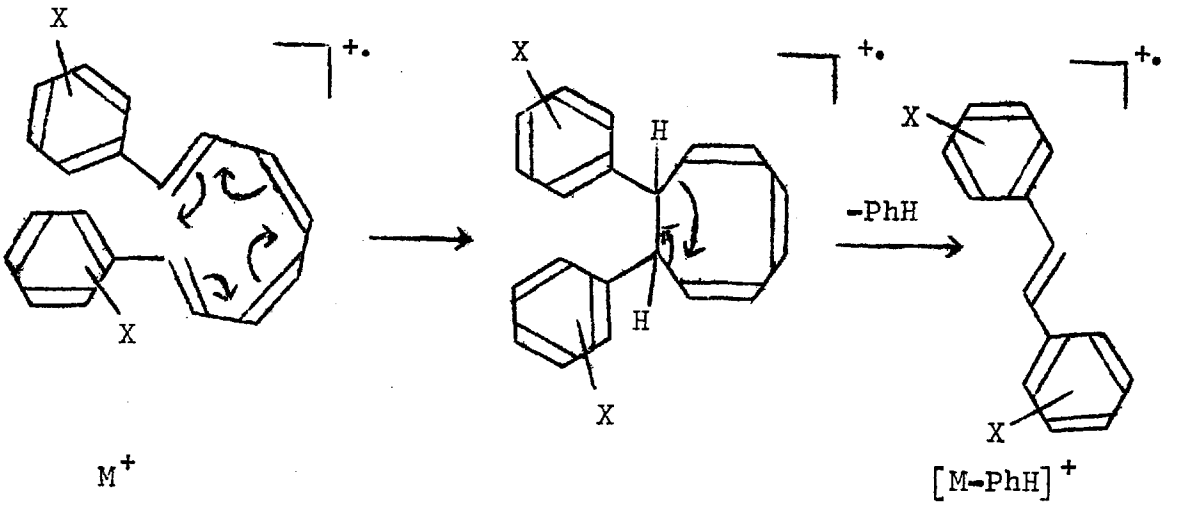


Conversely a meta-nitro group for example would increase the activation energy considerably more than a para-nitro group by virtue of the directional effect of this powerful electron withdrawing group.

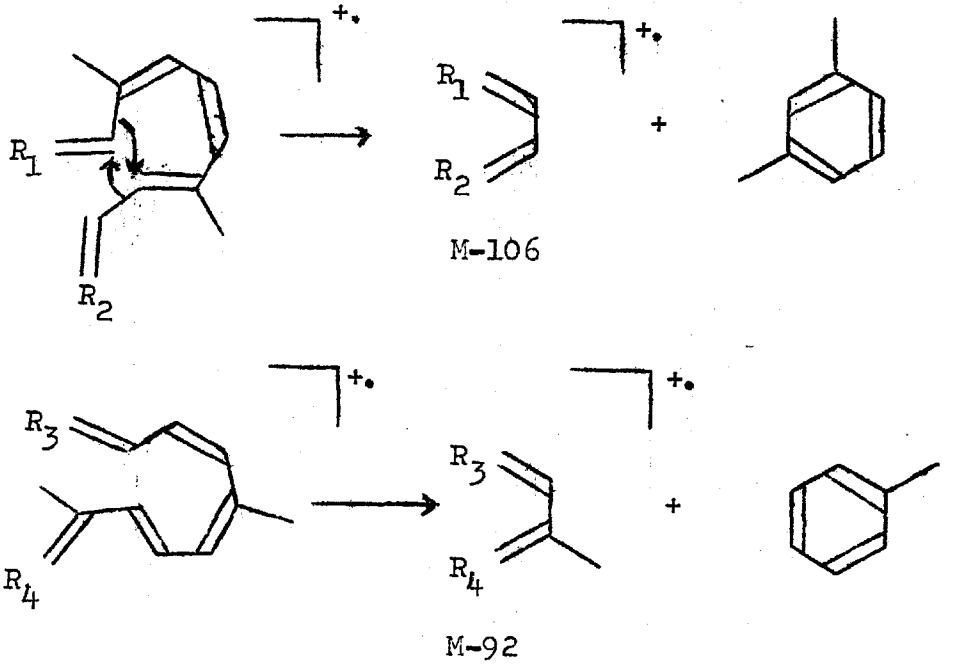
The effect of the second X group is not known with certainty as there appear to be few examples of this type in the literature.[70] Since it acts in the same direction as the other substituent, however, one would expect only an additive increase or decrease of the electron density at the reaction site. It has been shown in solution chemistry [70] that Hammett constants are additive to a considerable degree so it would seem reasonable that two like substituents would be an advantage by increasing the magnitude of the effect.

It is interesting that loss of benzene should still be an important process in ring substituted derivatives (see Table 9), often appearing as great as 3% of the total ion current. A plausible mechanism of formation of the $[M-PhH]^+$ ion is shown in Scheme 6, where a cyclic eight-membered transition state is proposed followed by ring contraction with elimination of benzene. This is consistent with the loss of toluene and xylene from natural polyene carotenoids [71] in which these fragments are suggested to originate in the polyene chain and arise by a concerted six-ring transition state. (Scheme 7). Because the mechanism in Scheme 7 necessitates cleavage of a doubly vinylic linkage, the mechanism proposed in Scheme 6 is thought preferable.

Scheme 6.



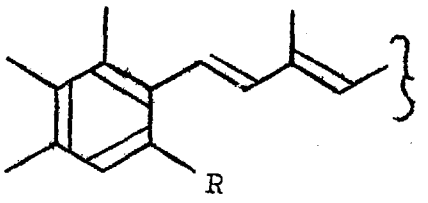
Scheme 7.



Enzell et al.[71] have utilised the ratio $[M-92]^+/[M-106]^+$ to correlate chain length in polyene carotenoids on account of

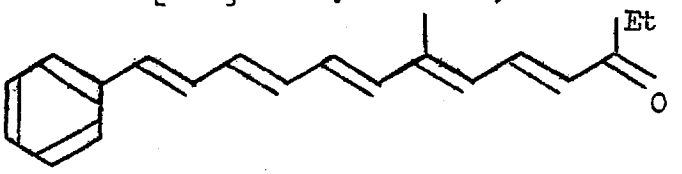
its gradual decrease on increasing the number of olefinic linkages. The usefulness of this ratio, however, is rather doubtful.

Further, it has been found that the mass spectra of terminal diphenyl polyene carotenoids exhibit two distinct modes of fragmentation depending on the aromatic substitution.[72] Thus derivatives of type (5) where R = H cleave to naphthalene fragments (i.e. 129, 128, 127 m.u.), and show naphthalene loss, whereas those having R = alkyl do not.



(5). R = H, alkyl

This is in good agreement with the model compounds prepared which give fairly abundant naphthalene fragments (see Table 9, ions of type F) and $[M-naphthalene]^+$ fragments (phenyl butadienes, ions of type E). The latter ions readily cyclise with hydrogen elimination to give naphthalene ions. Moreover, the spectrum of the natural product asperenone (6) [73] is rationalisable on the basis of ions of type A - F which are superimposed on the spectrum of the ketonic moiety. This compound does not exhibit an $[M-2]^+$ ion, however, which is rather surprising.



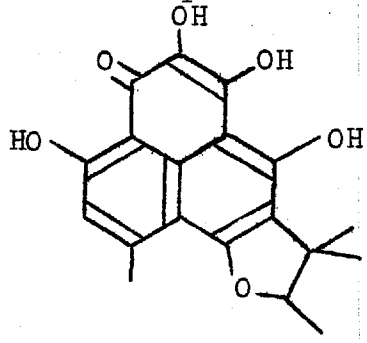
(6).

Part 3.

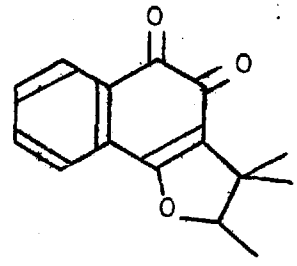
Atrovenetin and its Model Compounds.

3 , 1 Discussion of Experimental Work.

The mould metabolite atrovenetin (isolated from penicillium Atrovenetum in 1956 [74]) has been shown by X-ray crystallographic studies on the trimethyl ether ferrichloride [75] to have the phenalenone structure (1).



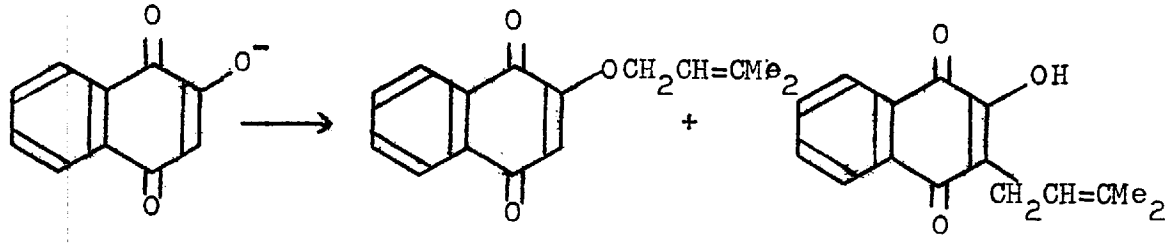
(1).



(2).

In order to investigate the electron impact induced fragmentation of this highly stable natural product model compounds in which deuterium could be specifically incorporated were examined, since little or no labelling experiments are possible on atrovenetin itself. For this reason dunnione (2), itself a natural product isolated from the orange deposit on the leaves, stems and flowers of Streptocarpus Dunnii Mast.[76] was chosen for extensive study. Dunnione (2) has been previously synthesised both by Fieser [77] and by Cooke [78] via 2-(3,3-dimethylallyloxy)-1,4-naphthoquinone (3) which is formed together with the C-alkylated product, lapachol (4), by reaction of a salt of 2-hydroxy naphthoquinone with 3,3-dimethylallyl bromide.

The method of Fieser [77] involves alkylation of the silver



(3) (4)

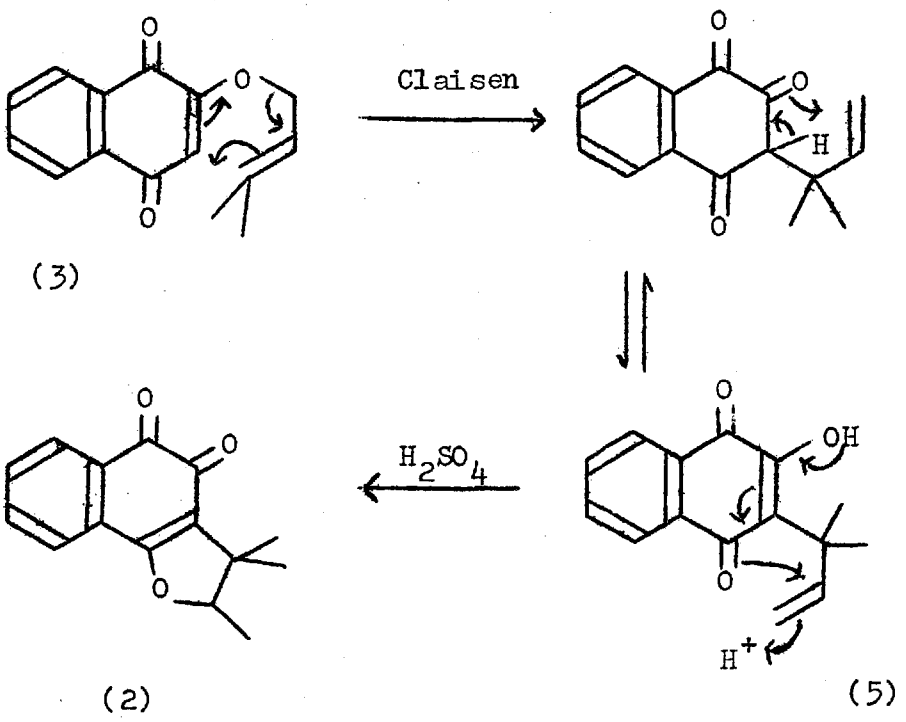
salt of 2-hydroxy naphthoquinone with 3,3-dimethylallyl bromide in diethyl ether which gives (3) and (4) in 3% and 5% yields respectively. The improved procedure of Cooke [78] uses the potassium salt in dry acetone to give 12% and 14% yields respectively. This prompted repetition of the alkylation in an aprotic solvent with a high dielectric constant such as dimethyl formamide in view of the remarkable rate enhancement shown when nucleophilic displacement reactions are conducted in these solvents. [79]

It has been shown [79] that although there is no correlation of rate of S_n2 reactions with any common physical property of the solvent, there is an empirical relationship with solvent polarity. It appears that the only requirement for a 'fast' reaction is that the solvent should be unable to donate hydrogen bonds, since it is found that if the solvent is able to do this then the S_n2 anion-polar molecule reaction is slow. S_n2 reaction appears to be faster in aprotic solvents with high dielectric constants due to little solvation and a high degree of polarity. Because of the

rate increase under these conditions the alkyl halides exhibit less competitive side-reactions e.g. hydrolysis, and give increased yields. Invariably the alkyl bromide is employed in preference to the chloride in view of the better displacement properties of bromine over chlorine. An excellent review exists on the factors influencing S_n2 reaction on alkyl halides. [80]

Very little is known of the criteria affecting C- and O- alkylation, but that aprotic solvents such as dimethyl formamide (d.c. 37) and dimethyl sulphoxide (d.c. 45) strongly enhance the latter is shown by the absence of C-alkylated products from the reaction of sodium β-naphthate and benzyl bromide in either of these solvents. [81]

Reaction of the potassium salt of 2-hydroxy naphthoquinone in anhydrous dimethyl fomamide at room temperature for several days gave the O- and C- alkylated products (3) and (4) in 28% and 30% yields respectively, more than doubling those previously obtained in less favourable solvents. Separation of these isomers by alkali extraction gave the allyl ether (3) in high purity direct from the reaction and was used in this form for the next stage. Claisen rearrangement to the enolic compound (5) followed by strong acid cyclisation to the furan (2) ensued quantitatively for each step giving a synthesis of dl-dunnione (2) in 28% yield from 2-hydroxy naphthoquinone.



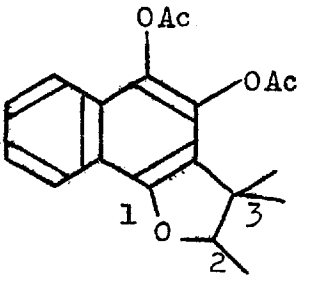
(3) (2) (5)

The kinetic product of the concentrated acid cyclisation is the ortho-quinone (2) but as prolonged treatment rearranges this to the thermodynamically more stable para counterpart [82] the reaction time is kept to a minimum, usually of 15 mins.

Reduction of the red ortho-quinone (2) with sulphurous acid leads to a colourless solution of the hydroquinone, which defies isolation by spontaneous air oxidation to the quinone. Accordingly the quinone was reductively acetylated to generate the stable, crystalline diacetate (6) hereafter called hydrodunnione diacetate* which was the derivative

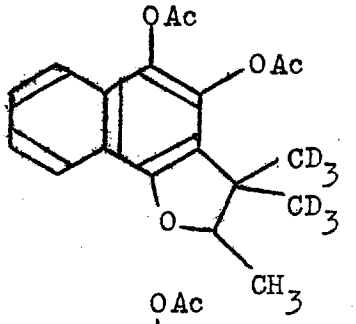
* Systemic name : 4,5-diacetoxy-2,3-dihydro-2,3,3-trimethyl-naphtho-[1,2-b]-furan.

used for mass spectrometry.

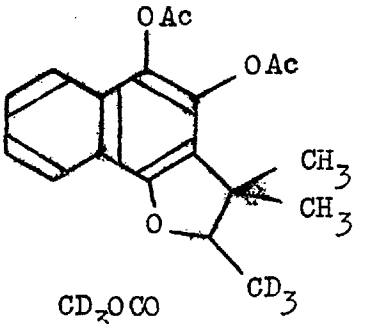


(6)

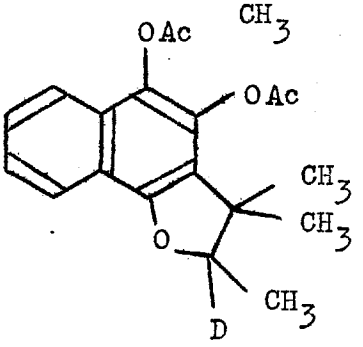
Selective deuteriation of this molecule was then effected using the appropriately labelled 3,3-dimethylallyl bromides, to give compounds (6a-d).



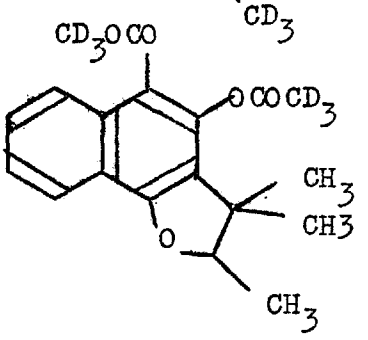
(6a)



(6b)



(6c)



(6d)

Table 11 shows the incorporation achieved in these derivatives as determined by mass spectrometry. The selectivity of deuteriation was ascertained from the n.m.r. spectra of the products and labelled precursors.

The preparation of (6b) is of especial interest because of the necessity of incorporating the label in two distinct

Table 11.

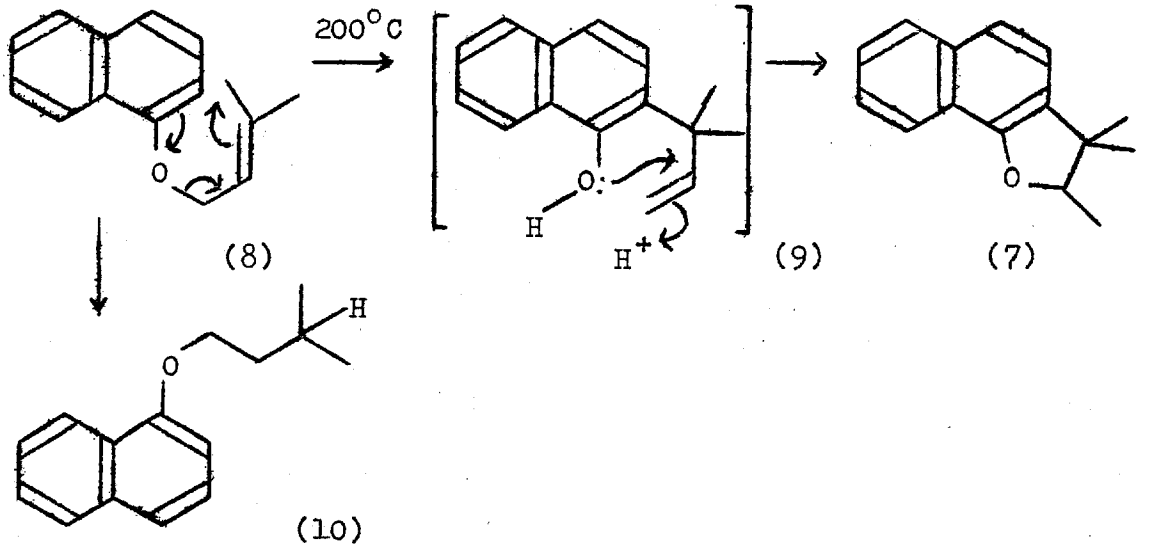
Incorporation of [^{2}H] in hydrodunnione diacetates.

Compound	Number of [^{2}H]-atoms						
	6	5	4	3	2	1	0
6a	71.9%	18.3%	2.6%	-	-	-	-
6b	-	-	-	92.1%	7.9%	-	-
6c	-	-	-	-	-	73.0%	27.0%
6d	97.2%	2.8%	-	-	-	-	-

steps. Two deuterium atoms are derived from lithium aluminium deuteride on reduction of 3,3-dimethyl acrylic acid, and these are carried through without amendment to the Claisen product (5). Successive washing with deuterium oxide removes the active hydrogen atom to give the deuteriated enol, which on cyclisation in concentrated deuteriosulphuric acid gives (6b) with high label content (see Table 11). All other derivatives were prepared in the conventional manner.

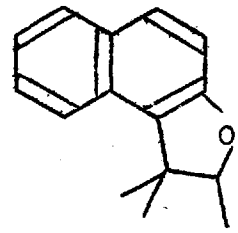
Having successfully produced one selectively labelled model compound it was of interest to prepare several more simple models to investigate the extent of methyl loss. In consequence, 1,2-dihydro-2,3,3-trimethyl naphtho-[1,2-b]-furan (7) was chosen on account of this being the most simple compound having the desired structural characteristics.

Reaction of α-naphthol with 3,3-dimethylallyl bromide in methanolic sodium methoxide under the prescribed conditions for naphthyl ether formation gave only small yields of the required product, presumably due to etherification of the halide by methoxide ion. Using the sodium salt, prepared by the action of sodium hydride on α-naphthol in anhydrous dimethyl formamide, however, gave excellent yields of the pentenyl ether (8) along with some C-alkylated product (23%).



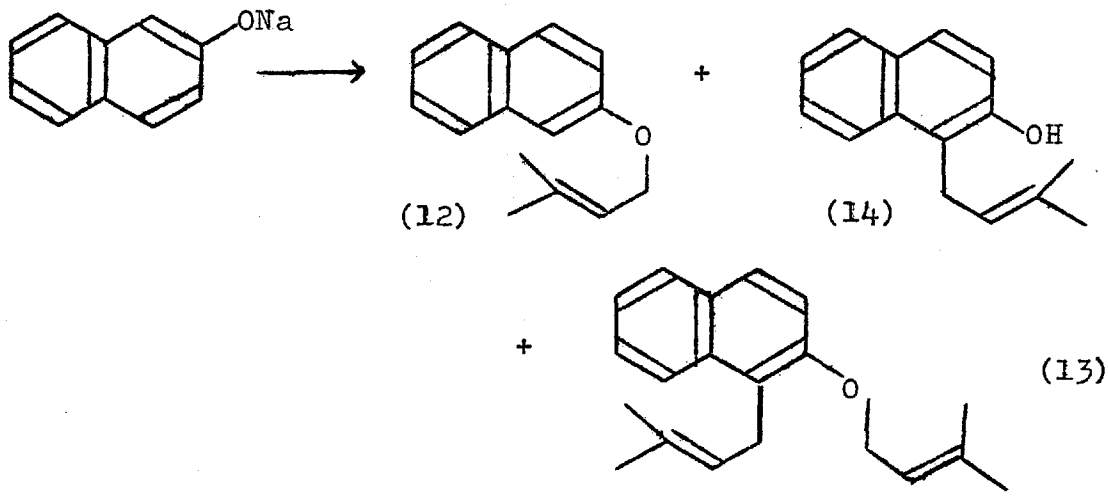
Pyrolysis of (8) under vacuo in a sealed tube at 200°C for 6 hrs. gave the furan (7) in 46% yield along with the saturated pentyl ether (10) in 18% yield. No good explanation for the formation of (10) can be found. All structures were assigned using n.m.r. spectroscopy coupled with analysis and mass spectrometry. An indication of the stability of (8) may be gathered from its rearrangement and cyclisation even on prolonged distillation.

No Claisen rearrangement product (9) was isolated, presumably because of the known inclination of these derivatives to cyclise to the furan.[84]



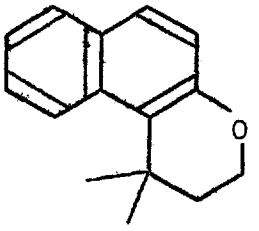
(11)

As an appendage to the [1,2-b] furan (7), preparation of the isomeric 1,2-dihydro-1,1,2-trimethyl-naphtho-[2,1-b]-furan (11) was attempted. Reaction of sodium β-naphthate in dimethyl formamide with 3,3-dimethylallyl bromide as above gave the pentenyl ether (12) in good yield together with a small amount of the dialkylated product (13). The latter compound is unique in that it represents both C- and O-alkylation in a single step. A plausible mechanism for this involves initial C-alkylation followed by further alkylation of the phenol with the excess allyl bromide present.

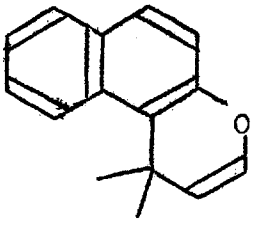


(12) (14) (13)

The structure of (13) was confirmed by n.m.r., elemental analysis and mass spectrometry. N.m.r. spectroscopy was particularly definitive on account of the close similarity to that of a 1 : 1 mixture of (12) and the C-alkylated product (14). Thus protons were observed at τ = 6.22 (d, J = 6.5 Hz, 2H) and τ = 4.80 (t with allylic splitting, J = 6.5 Hz, 1H) for the methylenic and vinylic protons of the C-alkyl side-chain, and at τ = 5.43 (d, J = 6.5 Hz, 2H) and τ = 4.51 (t with allylic splitting, J = 6.5 Hz, 1H) for the methylenic and vinylic protons of the O-alkyl side-chain. Furthermore, the aromatic protons, six in number, were proof of a single naphthalene nucleus.

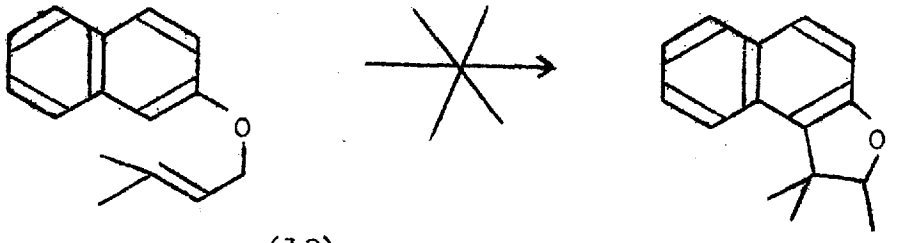


(15)



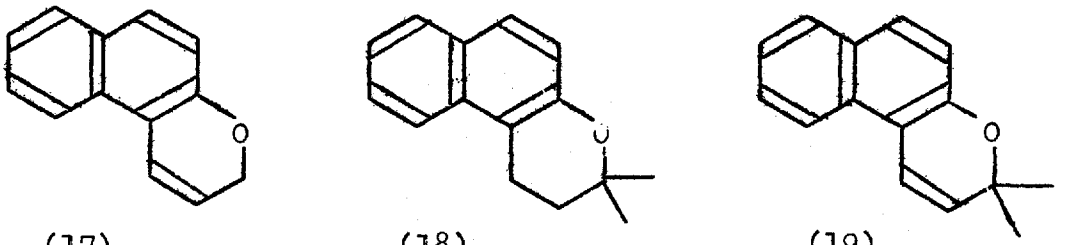
(16)

Pyrolysis of the pentenyl ether (12) gave a compound at first thought to be the pyran (15) on the basis of its n.m.r. spectrum, and its method of formation, even though the latter requires anti-Markownikoff addition of the phenolic oxygen to the double bond. Repetition of the pyrolysis under numerous precisely controlled conditions, with and without radical scavengers, sealed and unsealed tubes, different temperatures and various solvents, did not at any time lead to the desired product (11).



(12) (11)

Moreover, pyrolysis in quinoline yielded a compound thought to be (16), and which on hydrogenation with 20% Pd/C gave the saturated compound (15). The u.v. spectrum of (16) was a little inconclusive but was essentially identical to that of the benzochromene (17) prepared by Iwai and Ide.[85] Here a bathochromic shift of the region 260 - 290 mμ. in the saturated compound to 290 - 320 mμ. in (17) together with the appearance of a peak at 340 mμ. occurs just as in the compounds (15) and (16).

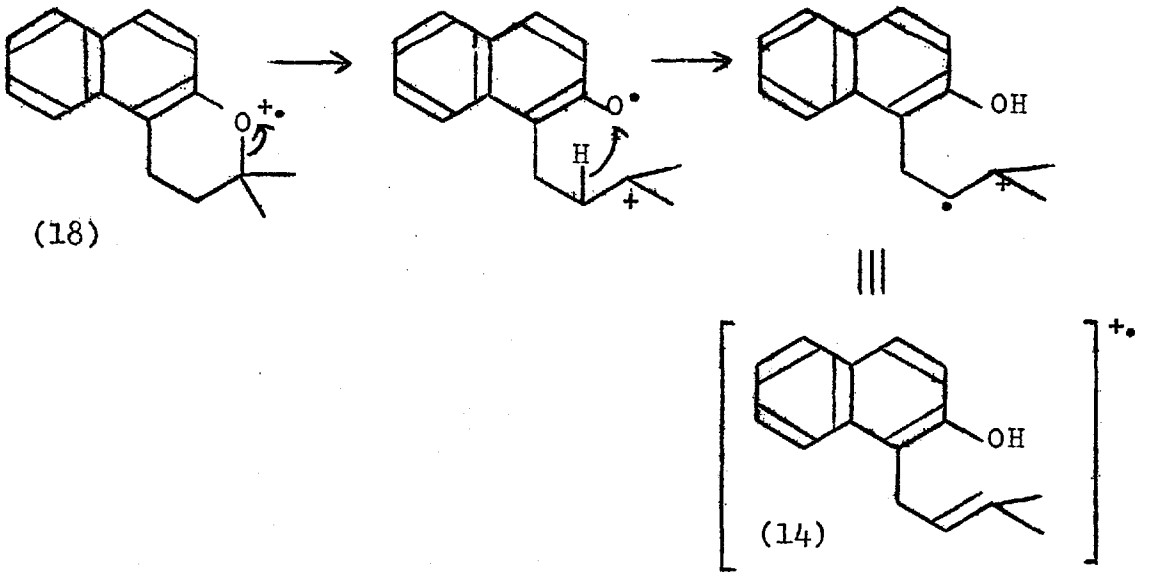


(17) (18) (19)

Furthermore, the mass spectrum of (15) was identical in all respects to that of the phenol (14). The combined u.v. and m.s. results were consistent therefore not with structures (15) and (16) but with the isomeric compounds (18)* and (19).

* Systemic name : 1,2-dihydro-3,3-dimethyl naphtho-[2,1-b]pyran.

respectively. The similarity of the mass spectra of (18) and (14) can be rationalised by the mechanism illustrated below which is more fully discussed in the following section.



(18)

(14)

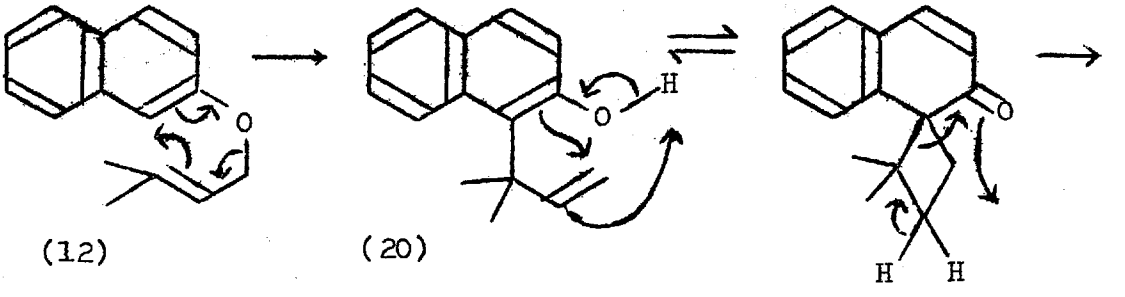
The n.m.r. spectrum is also in agreement with this new formulation since the methylene group adjacent to a phenyl moiety is calculated to resonate at τ = 7.10 and that alpha to an ether function at τ = 6.5. The value observed for the benzochroman is at τ = 7.01 and is consequently in better agreement with formula (18).

As further proof of these revised structures was required, differentiation by chemical means was adopted. A benzochromene such as (16), which is a vinylic ether, would be expected to cleave on treatment with 1 : 1 hydrochloric acid, whereas (19), which is not a vinylic ether, should remain unaffected. After several hours of acid treatment no change was observed

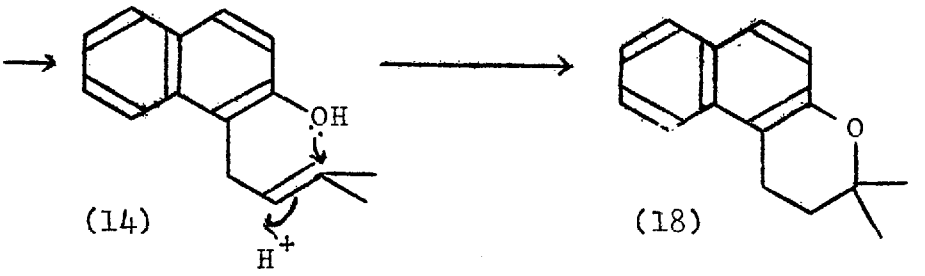
in the n.m.r. spectrum. Moreover, an authentic sample of (18) was prepared by normal Markownikoff cyclisation of the C-alkylated product (14), which from its melting and mixed melting point of 78°C proved to be identical with the product isolated from pyrolysis of the naphthyl ether (12). On this evidence the structures of the benzochroman and benzochromene may now be unambiguously assigned to (18) and (19) respectively.

Having identified the existence of a unique rearrangement on pyrolysis of (12) it is now necessary to elucidate the mechanism by which this takes place, although it may be assumed that (19) is formed directly from the saturated analogue (18) by quinoline dehydrogenation. Abnormal Claisen rearrangements are common-place in the literature and two excellent reviews exist concerning this.[86] However, isomerisation of the type observed for β-naphthol pentenyl ether (12) seems unprecedented. Two feasible pathways may be postulated for this rearrangement :

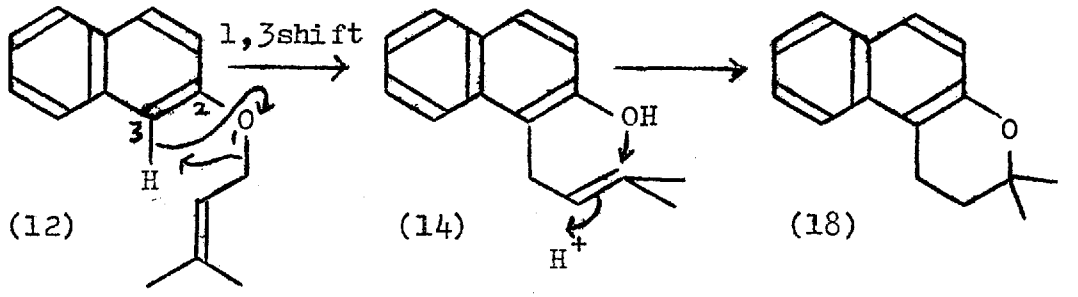
(A). Formation of a four-membered ring preceded by normal Claisen rearrangement.



(12) (20)

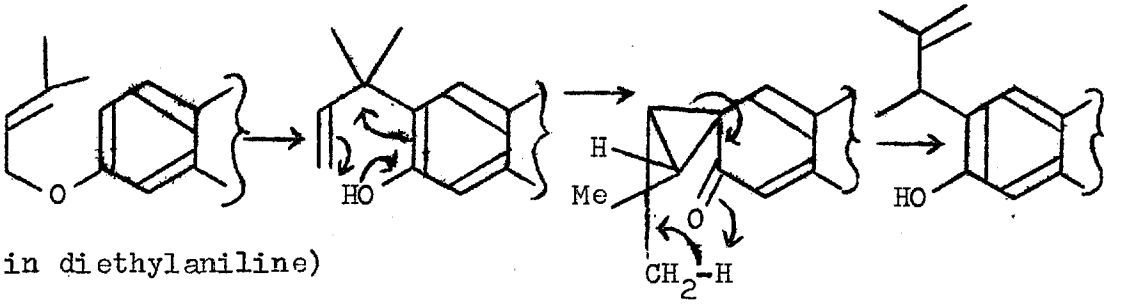


(B). A 1,3 alkenyl shift to give the phenol (14) direct.



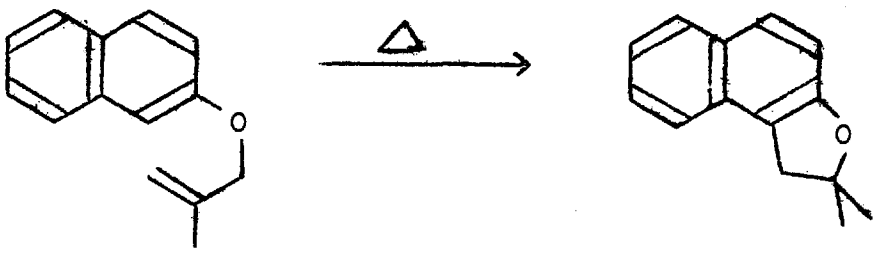
In both (A) and (B) mechanisms the observations can be accounted for on steric grounds. The normal product (20) has the gem-dimethyl group severely hindered by the C_8 hydrogen atom, which molecular framework models show to be spatially orientated between the two methyl groups. In mechanism (A) the relief of steric strain in forming the four-membered ring intermediate followed by alternative and more energetically favourable opening to the C-alkylated compound (14) is postulated to be the driving force for the rearrangement. Compound (14) is then able to cyclise in a normal Markowmikoff manner to the benzochroman (18). Alternative intermediates

involving three-membered rings have been considered, but none of these would be able to afford the observed results. For mechanism (B) the transition state leading to a 1,3 sigmatropic shift would be energetically favourable compared to the hindered Claisen product. However, the Woodward-Hofmann rules do not permit a transition of this kind without inversion [87] which then suggests that (A) is the most likely mechanism. Support for (A) comes from the work of Jefferson and Scheinmann [88] who postulate a three-membered transition state for the abnormal rearrangement of oestrone 3,3-dimethyl allyl ether as illustrated below.



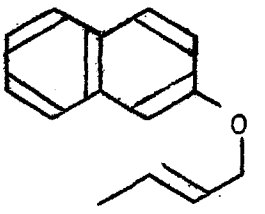
(in diethylaniline)

Chemical evidence for the steric effect in the normal Claisen product (20) comes from the preparation of 1,2-dihydro-2,2-dimethyl naphtho-[2,1-b]-furan (21) which is formed in good yield without trace of abnormal rearrangement products by pyrolytic cyclisation of the isobutenyl ether.

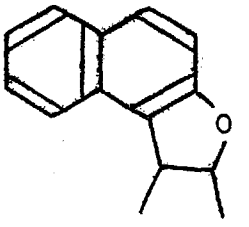


(21)

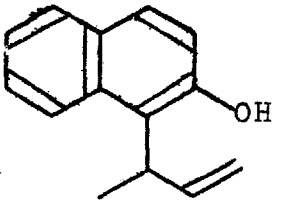
Furthermore, the n-butenyl ether (22) on pyrolysis gave only an intractable mixture from which only low yield, unstable products could be isolated. The n.m.r. spectrum of the most stable fraction (itself a mixture of t.l.c. inseparable components) obtained by chromatography suggested the presence of a small amount of the expected cyclisation product (23).



(22)



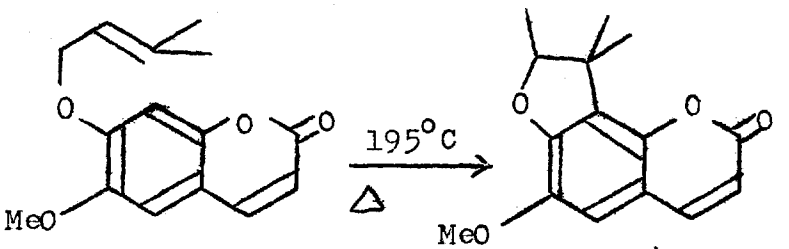
(23)



(24)

The complexity of the product from this pyrolysis may be explained on the assumption that the intermediate (24) is sufficiently hindered between the C_8 proton and the methyl group, to have the choice of either normal or abnormal cyclisation and would appear to be capable of both.

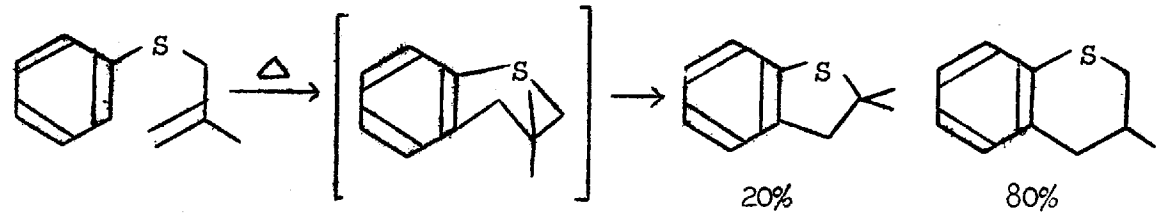
One other reaction relavent to the problem of steric hindrance between the gem-dimethyl group at C_1 and the C_8 proton is to be found in the work of Ballantyne et al.[107] who have isolated Nieshoutin (26) in 21% yield by the pyrolysis of the 3,3-dimethylallyl ether (25).



(25) (26)

The product in this example, a coumarin, has no proton equivalent to that on C_8 in the β-naphthol derivatives and is thus able to form the normal rearrangement product without difficulty.

Mixtures of benzochromans and benzocoumarans such as observed by Kwart and Cohen [89] for thiobutenyl ethers, were not at any time detected. These authors postulate a thiirane intermediate as illustrated below.

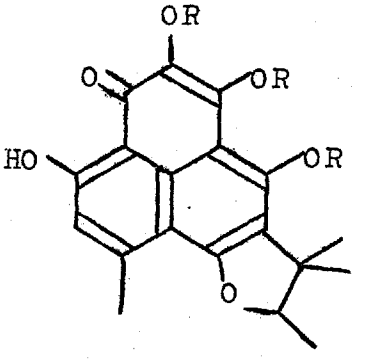


(in quinoline) thiirane thiacoumaran thiachroman

Further support of mechanism (A) is obtained by Claisen rearrangement and cyclisation in the presence of acetic anhydride and quinoline which afforded the intermediary phenol as its acetate. The presence of quinoline was found necessary to avoid cleavage of the ether prior to rearrangement giving β-naphthol acetate, presumably by virtue of the acetic acid present. By this procedure it was possible to isolate the normal rearrangement product (20) as the acetate thus proving conclusively that rearrangement must occur in this molecule prior to cyclisation. A four-membered ring molecule thus seems probable as the intermediate in the formation of the benzochroman (18) from the pentenyl ether (12).

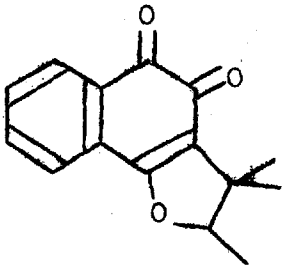
3 , 2 Discussion of Mass Spectra.

The most abundant ion in the mass spectrum of the mould metabolite atrovenetin (1, R = H), has been shown to arise by elimination of a methyl radical from the molecular ion.[18] This loss is most expected from one of the three methyl groups attached to the dihydrofuran ring, since the resulting ions would then be stabilised by resonance (vide infra).

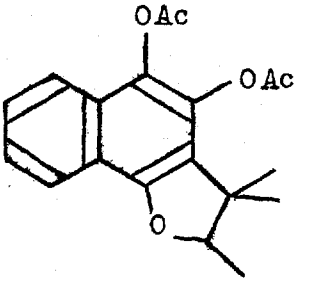


(1)

To confirm this suggestion and elucidate the extent to which methyl loss occurs from the positions α and β to the hetero atom, the mass spectra of dunnione (2) and hydrodunnione diacetate (3) together with their specifically deuteriated analogues were examined in the hope that these would serve as suitable model systems.

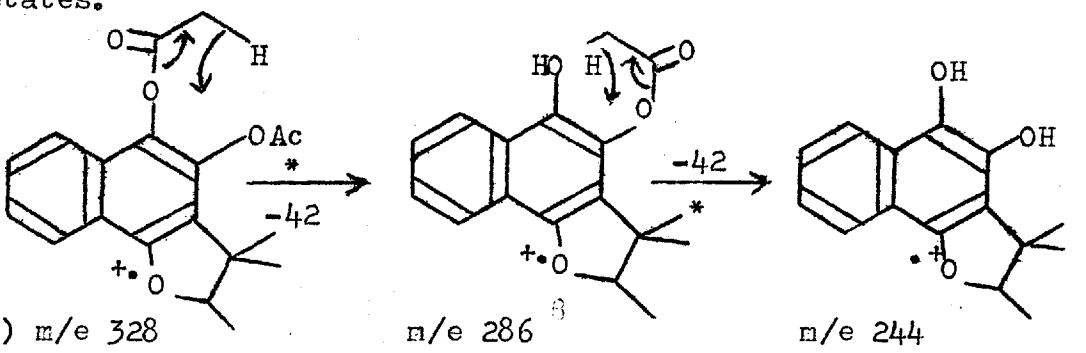


(2)



(3)

Successive loss of two molecules of ketene from the molecular ion of hydrodunnione diacetate (3) leads to the most abundant ion at m/e 244, which is postulated to be the molecular ion of dihydrodunnione. (see mass spectrum 17). It is assumed that this elimination proceeds by way of a cyclic four-membered transition state as suggested for sugar acetates.[90]

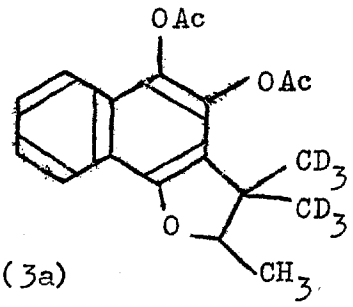


(3) m/e 328 m/e 286 m/e 244

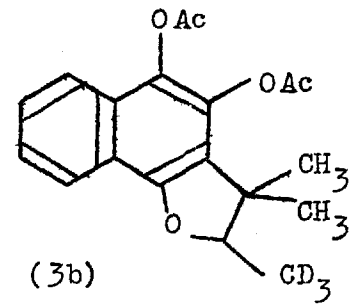
Similarly the mass spectrum of atrovenetin triacetate (1, R = Ac) exhibits the strongest ion at m/e 342, corresponding to elision of three molecules of ketene from the molecular ion. This differs from atrovenetin itself (1, R = H) in that the base peak is shifted 15 m.u. to higher mass. In accordance with expectation the ion at m/e 244 in dihydrodunnione diacetate loses a methyl radical to afford an ion at m/e 229 which represents 14% of the base peak. The low abundance of the m/e 229 ion is to be expected and is attributed to reduced energy of the m/e 244 ion due to its formation by ketene elimination from the molecular ion. This energy loss is better illustrated in atrovenetin itself where the m/e 342 ion is 43.5% as intense as the ion at m/e 327, whereas in the triacetate the intensity orders are reversed,

the ion at m/e 327 being only 50% that at m/e 342.

Examination of the mass spectra of the deuteriated compounds (3a) and (3b) (see Table 12) unambiguously demonstrates that the origin of the eliminated methyl group is in the gem-dimethyl group of the benzylic carbon atom C_3.



(3a)



(3b)

By analogy it is therefore suggested that the methyl radical lost in the fragmentation of atrovenetin comes from the benzylic carbon atom and not that alpha to the furanoid oxygen.[91]

Table 12.

Mass spectra of deuteriated dihydrodunnione diacetate derivatives.

Only peaks greater than 2% are listed.

Compound (3a). (partial spectrum)

m/e	335	334	293	292	291	251	250	249	248	233
%	1.4	7.2	4.6	26	6.1	15	100	35	7.3	3.1
m/e	232	231	215	214	189	188				
%	12	6.1	2.1	6.0	3.5	3.0				

Compound (3b). (partial spectrum)

m/e	332	331	290	289	288	248	247	246	232	231
%	2.1	10.2	6.0	30.5	3.2	15	100	21	9.1	4.8

cont.

m/e	214	189	188	187
%	4.1	2.0	2.3	2.3

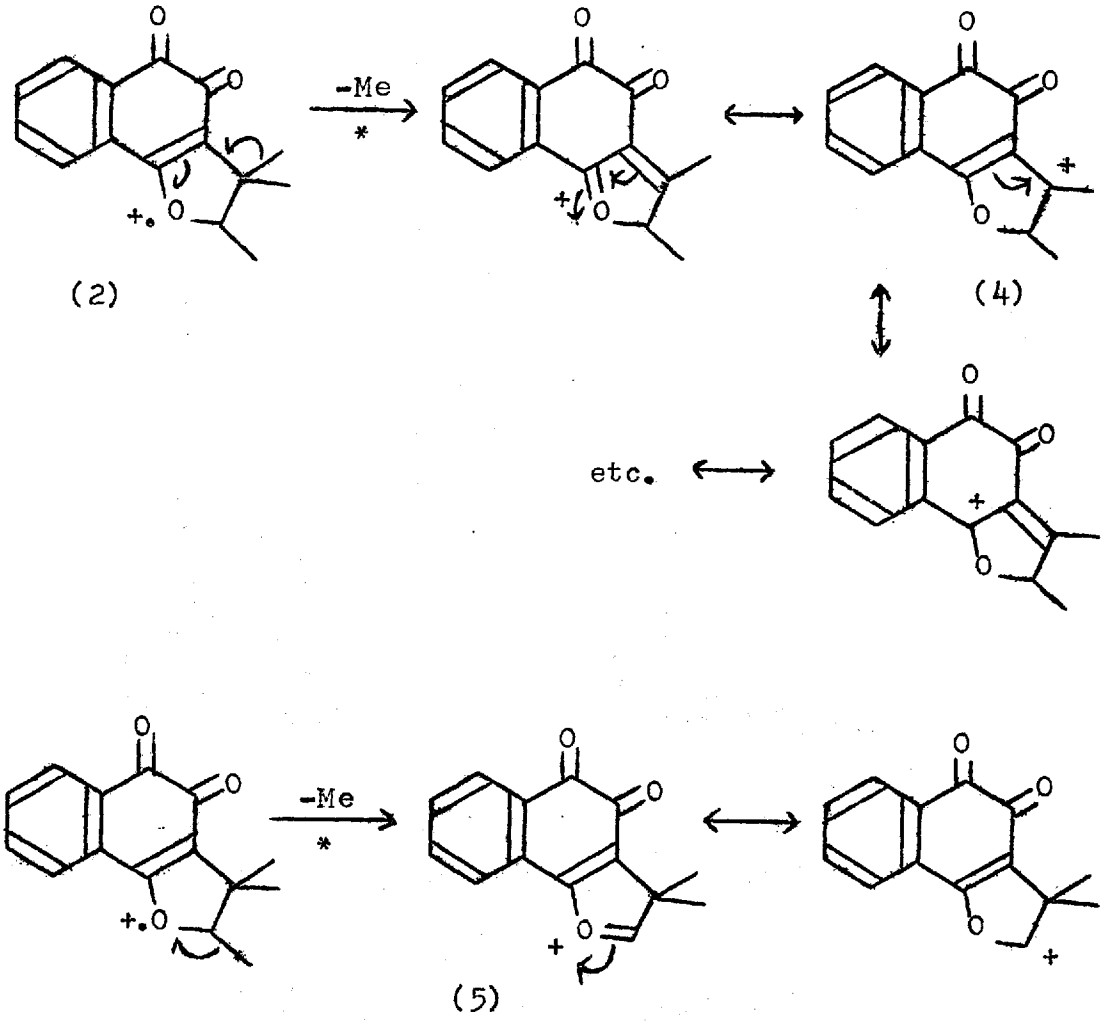
Compound (3c). (partial spectrum)

m/e	335	334	291	290	247	246	245	244	231	229
%	1.5	10.6	6.0	30	16	100	5.3	17	11.5	5.8
m/e	211									
%	5.8									

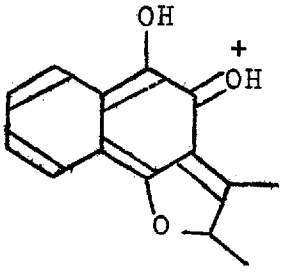
Compound (3d). (partial spectrum)

m/e	330	329	328	288	287	286	246	245	244	243
%	1.4	8.6	2.3	4.8	28	9.7	16	100	51	6.5
m/e	230	229	228	214	212	211				
%	11.5	11	5.0	5.0	5.4	3.4				

The parent compound, dunnione (2) (mass spectrum 18), also loses the methyl radical from its molecular ion (m/e 242), as does the $[M-CO]^+$ ion - shown by a metastable ion at m/e 185.2. Further, the spectra of the deuteriated dunniones also show the loss to be exclusive to the C_3 carbon atom. This specific methyl elimination from the benzylic carbon atom is evidence for the greater stability of the fragment ion (4) over fragment ion (5) formed by loss of a methyl radical from C_2 of the molecular ion. In (4) the positive charge can be delocalised over the aromatic nucleus as well as the furanoid ring, whereas in (5) no such stabilisation is possible.



The $[M-15]^+$ ion of dihydrodunnione has a further resonance form (6) involving hydroxyl participation in addition to those of (4).

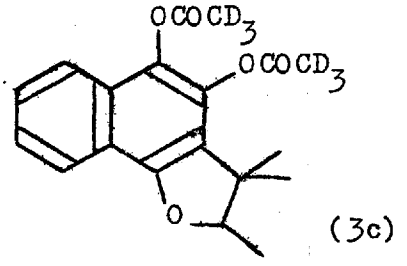


(6)

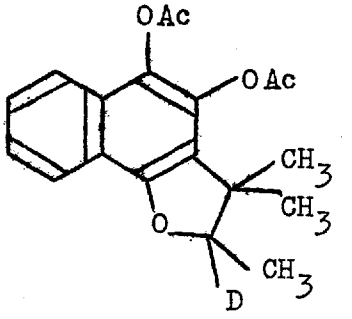
Further, it is of interest to note that the molecular ion of all dunnione samples exhibited small $[M+2]^+$ peaks which

are attributable to ion-molecule reactions in the mass spectrometer (see mass spectrum 18, for example), an effect which is well-authenticated for ortho-quinones.[92]

The ion at m/e 244 derived from dihydrodunnione diacetate (3), is observed to lose an hydrogen atom, removal of which is characterised by a metastable ion. This fragmentation, which has an analogy in atrovenetin, is shown by the elision of deuterium in the bis-deuterioacetate (3c) to be derived from the acetate moiety.

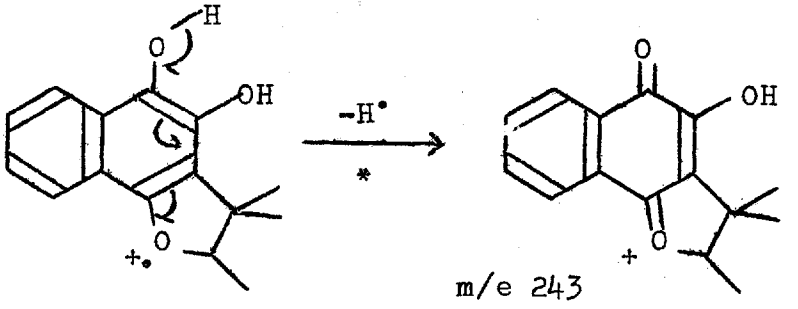


(3c)



(3d)

A plausible mechanism for this fragmentation is shown below.

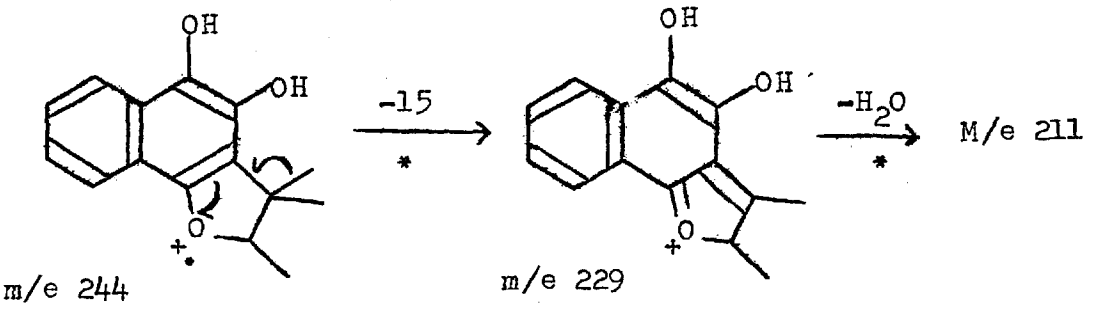


m/e 244 m/e 243

Loss of a second hydrogen atom to give the dunnione molecular ion does not seem to be important.

One other decomposition of the diacetate (3) is of importance and this concerns elimination of water from the ion at m/e 229, formed by loss of a methyl radical from the

dihydrodunmione ion :

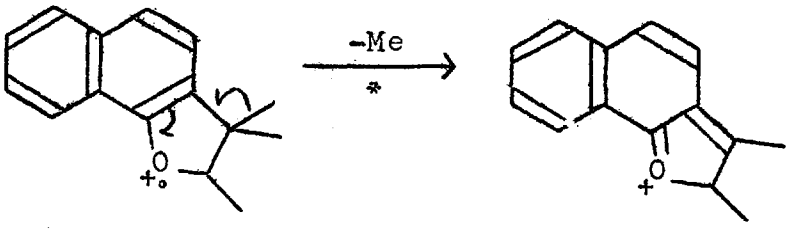


m/e 244 m/e 229

Elimination of deuterium oxide from the bis-deuterioacetate (3c) confirms that the elements of water come exclusively from the vicinal diol system. All other deuteriated analogues show only loss of water. The molecular ion of catechol [93] loses water to afford an ion of medium intensity, although the nature of this is unknown.

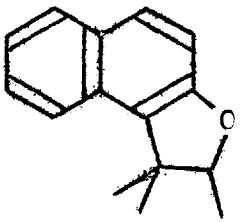
Finally, in common with most acetates, compound (3) has large peaks at m/e 43 and m/e 60 both of which are shifted 3 m.u. to higher mass in the bis-deuterioacetate. These ions represent $[CH_3CO]^+$ and $[CH_3CO_2H]^+$ respectively.

Additional studies on other model compounds have corroborated the results found above, and many have also shown other interesting characteristics. Thus in 1,2-dihydro-2,3,3-trimethyl naphtho-[1,2-b]-furan (7), in which the furan ring substitution is identical to that of both atrovenetin and dunmione, the sole fragmentation is the elimination of a methyl radical from the molecular ion. By analogy with dunnione the resultant ion at m/e 197 is postulated to arise by loss of one of the benzylic methyl groups.



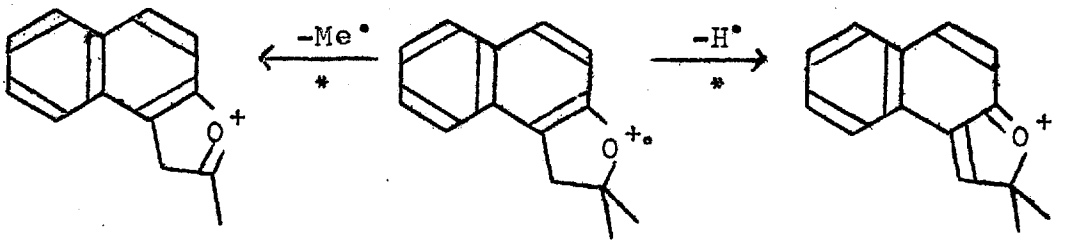
(7). m/e 212 (97%) m/e 197 (100%)

Attempts to prepare the isomeric 1,2-dihydro-1,1,2-trimethyl naphtho-[2,1-b]-furan (8) were abortive, although the homologue (9) was successfully isolated using a similar procedure. The latter compound exhibited little fragmentation, the main ions being M^+, $[M-1]^+$ and $[M-15]^+$. Postulated structures for these ions are illustrated in Scheme 8.



(8)

Scheme 8.



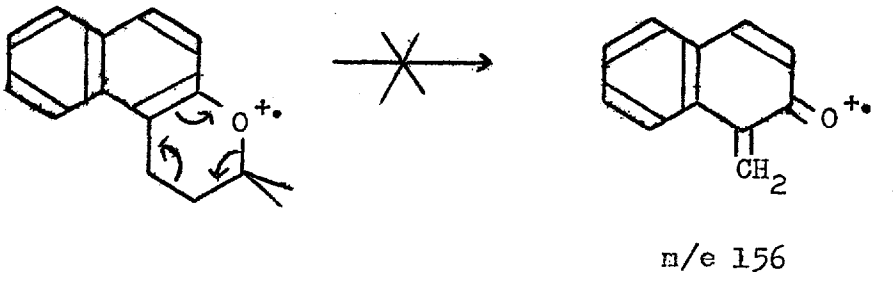
m/e 183 (59%) (9) m/e 198 (100%) m/e 197 (10%)

Loss of the methyl radical from the naphthofuran (9) is not surprising in view of the known stability of aromatic compounds with few functional groups, but it is interesting

to compare the extent of methyl loss with that from the molecular ion of (7). The large difference, ca. 40%, is attributed to the increased stability of the product ion from (7) over that from (9) on account of resonance contributions similar to those in dunnione. (vide supra.) Furthermore, elision of an hydrogen atom is important in (9) since this generates an ion of similar electronic disposition to that formed by loss of a methyl radical from (7). Elimination of H• from the molecular ion of dunnione or of (7) is unimportant.

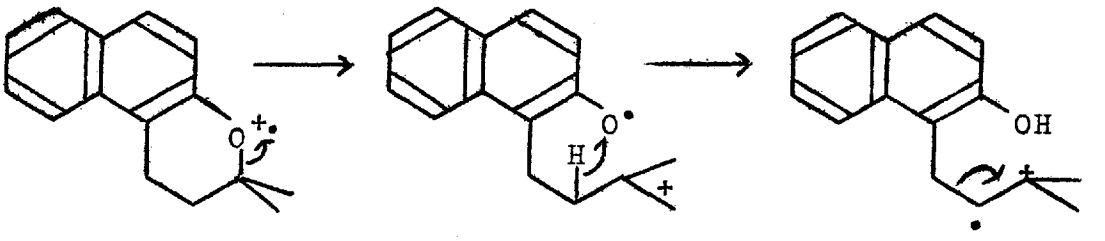
The molecular ion of 1,2-dihydro-3,3-dimethyl naphtho-[2,1-b]-pyran (10) did not exhibit methyl loss, but afforded a spectrum identical in every respect with that of the pentenyl phenol (11). This characteristic, coupled with the consistency of the fragmentation pattern with the latter, suggests that the molecular ion of the pyran rearranges to (11) via transfer of the β-hydrogen atom to the oxygen radical formed by cleavage of the C-alkyl bond. The facility of this rearrangement is consistent with the known ease of hydrogen atom migration to radical sites.[67a] (see Scheme 9).

Had the molecular ion of (10) remained in the pyran form retro-Diels-Alder decomposition to give an ion at m/e 156 might have been expected. However, no fragmentation of this kind was observed.



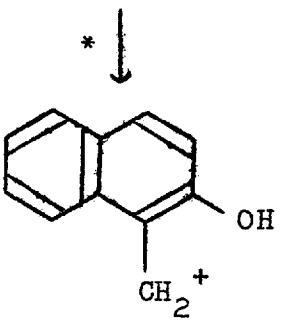
m/e 156

Scheme 9.

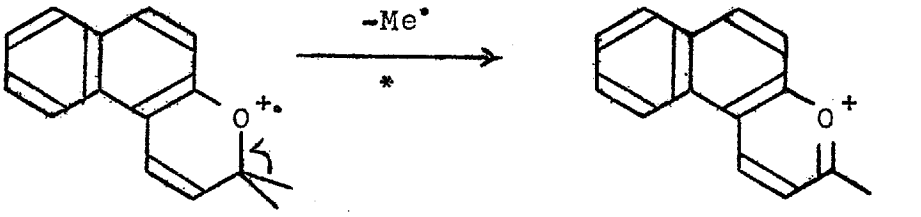


(10) m/e 212 (55%)

(11) m/e 212 (55%)



Finally one other compound is of interest, the benzochromene (12), which loses a methyl radical with exceptional ease to form the most abundant ion at m/e 195. This rapid and facile elision is consistent with the allylic disposition of the gem-dimethyl group and with resonance stabilisation of the product ion. No other fragments are observed in the mass spectrum of (12), presumably due to the great stability of the aromatic ion at m/e 195.



(12) m/e 210 (21%) m/e 195 (100%)

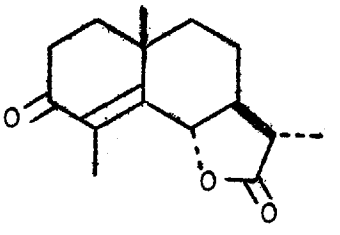
From the results cited above it may be concluded that the importance of methyl loss from the furan ring is exceptionally dependent on the stability of the product ion, since the greater the charge delocalisation in this ion the more facile is alkyl elimination.

Part 4.

Cyclohexenone Derivatives.

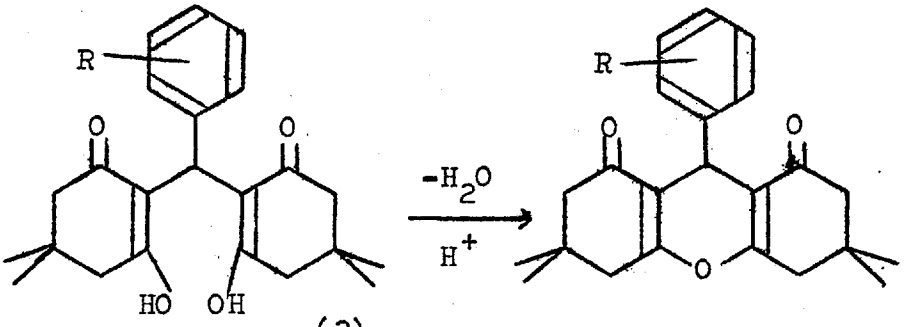
4 , 1 Discussion of Experimental Work.

A prominent ion at m/e 192 in the mass spectrum of 1,2-dihydro santonin (1) has been shown to arise by a single step loss of C_3H_4O from the molecular ion.[94] Because of the singularity of this fragmentation in compounds containing a Δ^2-cyclohexeneone ring several model compounds have been prepared in an attempt to define the structural requirements necessary for it to occur.



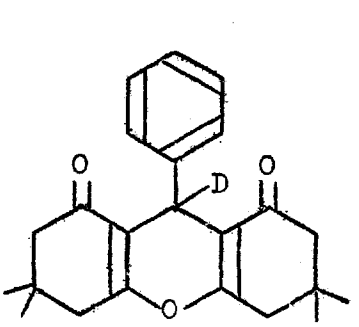
(1)

The first class of compound to be examined were the anhydrodimedones of aromatic aldehydes (3), which were all prepared by acid cyclisation of the dimedone derivative (2), itself made according to the analytical procedure of Horning and Horning involving condensation of the aldehyde with 5,5-dimethyl cyclohexane-1,3-dione in the presence of a catalytic amount of piperidine.[95]

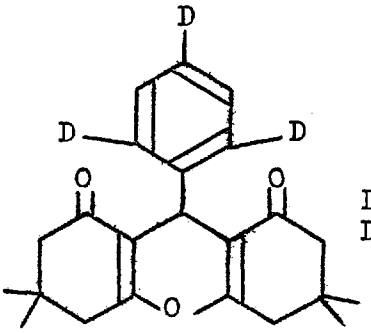


(2) (3)

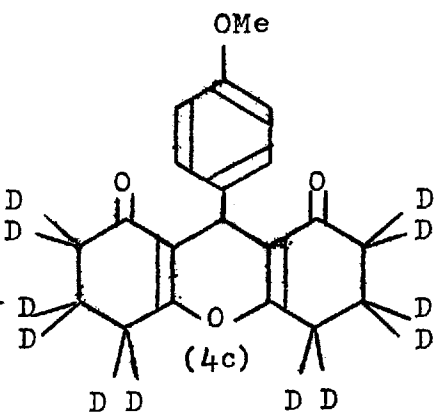
Compounds of type (3) with R = o-, m-, and p- OMe, o- and p- NO_2, o- Br, Me, NO_2, Cl, and H were prepared. Clarification of the fragmentation modes of (3) was assisted by the deuteriated analogues (4 a, b, and c), a and b of which were synthesised from the appropriately labelled aldehyde according to the above method. Compound (4c), however, was obtained by direct exchange of the anisaldehyde derivative with deuterium oxide in anhydrous dimethyl formamide using triethylamine as the base. The extent of deuteriation achieved in these compounds is listed in Table 13.



(4a)



(4b)



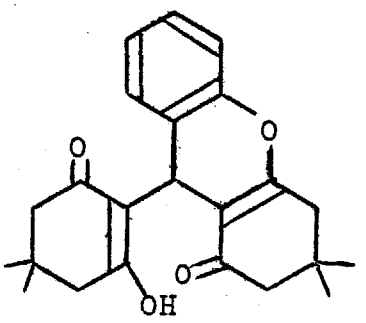
(4c)

Table 13.

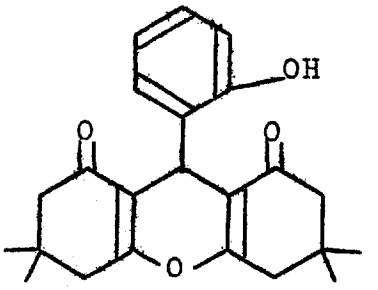
Proportion of deuterium in labelled anhydrodimedone derivatives.

Compound	Number of ^{2}H-atoms								
	8	7	6	5	4	3	2	1	0
4a	-	-	-	-	-	-	-	95.4%	4.6%
4b	-	-	-	-	-	83.0%	16.4%	0.9%	-
4c	75.0%	22.5%	1.7%	1.0%	-	-	-	-	-

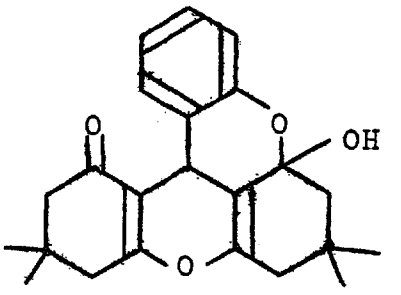
A search of the literature has shown that considerable ambiguity surrounds the structure of the salicylaldehyde dimedone adduct which has been reported by different authors to be either the abnormal cyclisation product (5) [96] or the normal product (6).[97] In view of the activity of the phenolic hydroxyl compared to that of the enolic form of the dione system it would seem probable that the former is the most likely structure, but the chemical evidence put forward by Desai [97] would appear to dispute this.



(5)



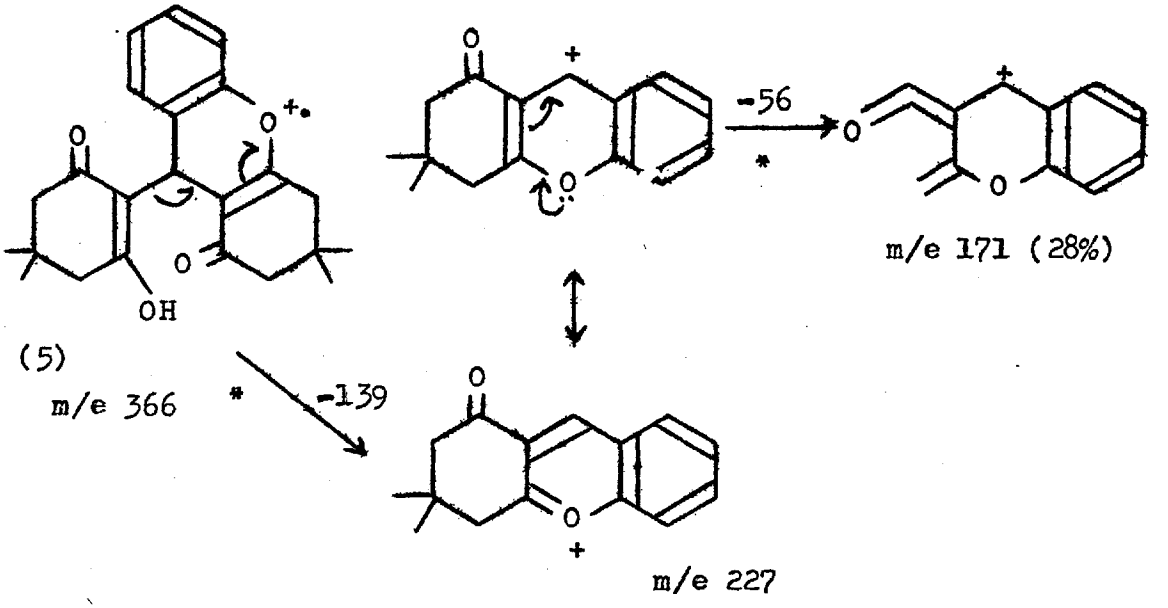
(6)



(7)

The n.m.r. spectrum of the adduct, however, clearly shows the methylene groups as two broad singlets at τ = 7.54 (2H) and τ = 7.83 (6H) which is inconsistent with structure (6) which demands that the methylenic protons exist as two singlets of equal intensity. Moreover, a third possibility (7) stems from the n.m.r. since the methylene group adjacent to the hemi-ketal linkage in this compound might resonate at the same position as the allylic methylene groups at τ = 7.83, thus giving the observed ratio of 2 : 6 for the overall number of

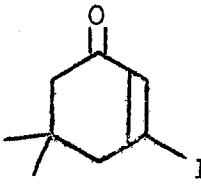
methylenic protons. Adequate distinction between forms (5) and (7), however, is obtainable from the mass spectrum (mass spectrum 19) which vindicates structure (5) on account of the formation of an ion at m/e 227 (98%) consistent with the fragmentation :



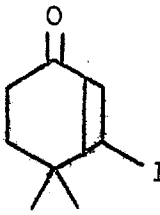
A compound having formula (6) would be expected to undergo the characteristic anhydrodimedone fragmentation (vide infra) leading to a stable ion at m/e 273. A similar conclusion has recently been reached by Baldas and Porter.[98]

Following on from the anhydrodimedones, which also exhibit the unique cyclohexenone ring fracture being investigated, several cyclohexenones of more fundamental nature were prepared in the hope that these would serve as more suitable models for elucidation of the minimal structural features. Two general types were prepared; those having gem-

dimethyl groups in the 3-position (8) (c.f. anhydrodimedones) and those with the gem-dimethyl group in the 4-position (9) (c.f. dihydrosantonin).



(8).

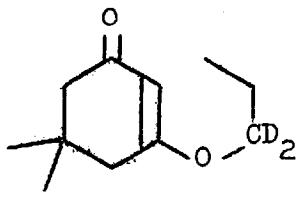


(9).

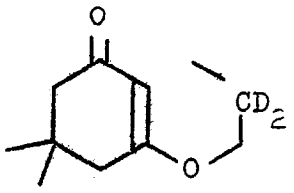
R = OH, OMe, OEt, O-nPr, O-iPr, OAc, Me, Cl, Ph, p-OMePh, N-Ph, N-nBu,

R = Me, OEt, Ph,

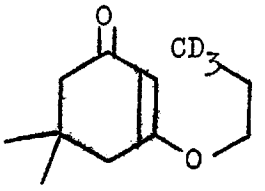
Those derivatives having the dimedone nucleus were prepared from dimedone itself either by direct action, e.g. OMe, OEt, OnPr, OiPr, OAc, Cl, NPh, NnBu or by action of the appropriate Grignard reagent on the ethoxy or methoxy derivative followed by acid removal of the enol ether protecting group. These reactions are possible because of the symmetry of dimedone, a compound which can only form a single product on reaction of one of the carbonyl functions. The deuteriated derivatives 8a, b, and c, caused more of a problem because enol ethers are usually prepared by refluxing dimedone in the appropriate alcohol solvent in the presence of a trace of p-toluenesulphonic acid. Obviously this procedure is impractical for small amounts of deuteriated alcohols which necessitated a modified approach. The technique finally adopted utilised a minimum of benzene as a solvent and water removal was effected by the use of activated



(8a)



(8b)



(8c)

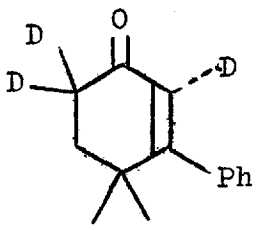
molecular sieves (grade 3A) retained in a Soxhlet extractor thimble. This method gave excelent results on 1g. quantities, but began to fail on 100mg. amounts on account of the excessive amount of solvent necessary. Table 14 shows the deuterium incorporation for these n-propyl compounds and for 4,4-dimethyl-3-phenyl cyclohex-2-ene-1-one (9a) after exchange with deuterium oxide.

Table 14.

Proportion of deuterium in labelled cyclohexenones.

Compound	Number of ^{2}H-atoms.			
	3	2	1	0
8a	-	98.8%	1.2%	-
8b	-	98.5%	1.5%	-
8c	95.2%	4.8%	-	-
9a	36.9%	58.0%	3.4%	2.3%

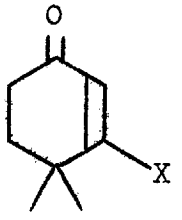
It will be seen that in the latter compound (9a) extensive



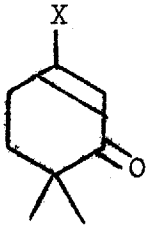
(9a).

vinylic deuteriation has accompanied exchange of the α-methylene group thereby reducing the specificity of deuterium incorporation.

For the cyclohexenones of type (9) the technique utilised for the symmetrical dimedone derivatives could no longer apply since equimolar mixtures of (10a) and (10b) are formed owing to lack of differentiation between the two carbonyl groups. These derivatives are not easily separated because of their similar polarities.



(10a)

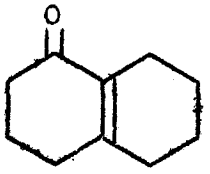


(10b)

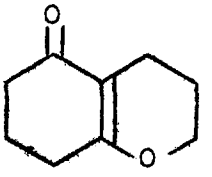
In order to overcome this difficulty, advantage is taken of the knowledge that 4,4-dimethyl cyclohexan-1,3-dione reacts with isobutanol to give the ketone (10b, X = O-iBu) exclusively.[99] The nuclear magnetic resonance spectrum confirmed the absence of the alternative isomer (10a, X = O-iBu). It is suggested that steric hindrance induced by the gem-dimethyl group prevents formation of the (10a) isomer.

Having obtained the isobutoxy derivative (10b), Grignard reaction followed by dilute acid work-up to remove the enol-ether protecting group enables both alkyl and phenyl derivatives to be prepared. Strangely it was not possible to prepare the p-methoxyphenyl derivative in this manner. The ethoxy compound (10, X = OEt) was prepared as for dimedone and the mixture separated by preparative g.l.c.

Finally the series was extended to include the bicyclic ketones (11) and (12).



(11)



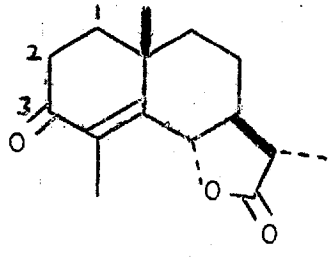
(12)

The route to (11) involved lithium in ethylamine reduction of naphthalene to a mixture of $\Delta^{1,2}$ and $\Delta^{9,10}$ octalenes which isomerised almost completely to the latter olefin on phosphorous pentoxide treatment. N-Bromosuccinimide treatment followed by Na_2CO_3/H_2O/THF hydrolysis then gave (11) directly. It is thought that the intermediate allylic alcohol is oxidised by dissolved peroxides under the reaction conditions.

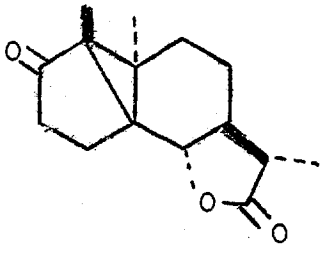
The dihydropyran (12) was the final member of this series and was synthesised in a single step by alkylation of dimedone with trimethylene bromohydrin followed by cyclisation on a silica column.

4 , 2 Discussion of Mass Spectra.

The mass spectrum of 1,2-dihydrosantonin (1) has an abundant ion at m/e 192 (ca. 58%) which has been shown by the presence of an accompanying metastable ion to owe its existance to a one-step loss of C_3H_4O from the molecular ion.[94] This elimination has been investigated with the aid of deuterium labelling experiments from which it is possible to conclude that this fragment has its origin in the C_1, C_2, and C_3 atoms of the cyclohexenone ring. Fragmentation of this kind is unusual for this system which usually undergoes retro-Diels Alder reaction either exclusively or in combination with ketene elision.[67a] Moreover, the mass spectrum of the lumi-product (2), formed on photolysis of (1)[101] shows an almost identical fragmentation, differing only in the relative abundance of the peaks at lower mass.



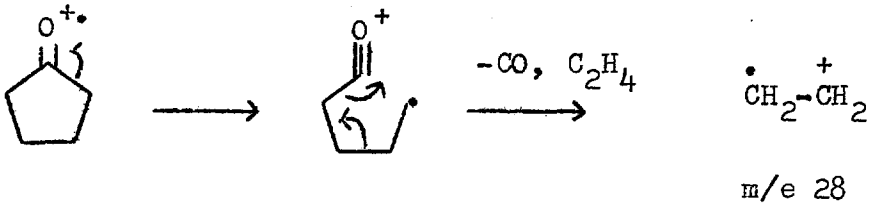
(1)



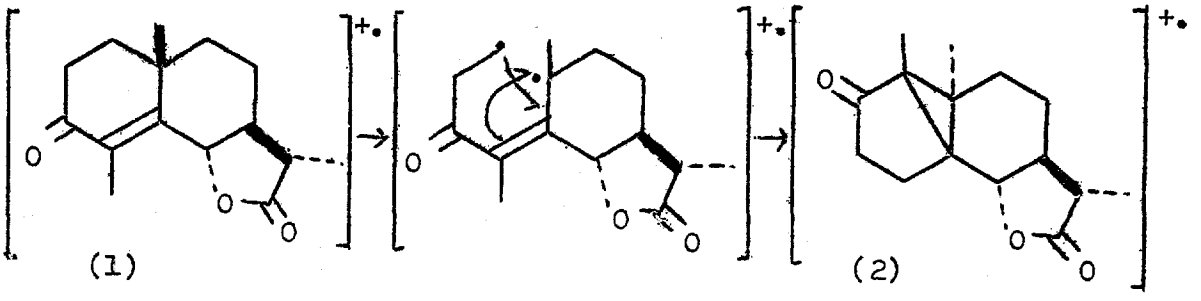
(2)

The elimination of C_3H_4O, which has been substantiated by accurate mass measurement, is a characteristic of compounds containing a cyclopentanone ring system and it is evident in cyclopentanone itself.[102] A plausible mechanism for this

fragmentation is given below :

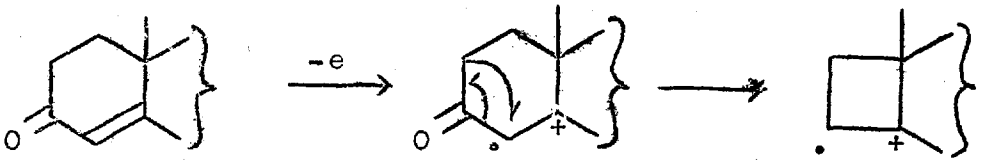


Mass measurement has proved that the product ion at m/e 28 is indeed ethylene and not carbon monoxide. On the basis of the similarity in the mass spectra of isomers (1) and (2) it has been suggested [94] that interconversion between **(1)** and the lumi-product occurs in the mass spectrometer, and that it is the molecular ion of (2) which is able to fragment with loss of C_3H_4O. A plausible mechanism for this isomerisation involves homolytic allylic cleavage followed by recyclisation by radical attack on the double bond as shown.

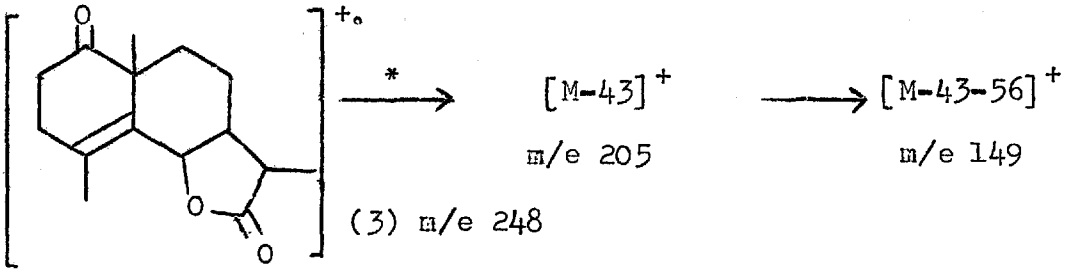


It is a characteristic of steroids containing the cyclohexenone system in ring A that they lose ketene from the molecular ion to give a large $[M-42]^+$ ion, [103] a fission which has been rationalised by Djerassi et al. as ionisation by π electron removal from the olefinic bond followed by concerted homolytic elimination of ketene to form an

ionised butene.

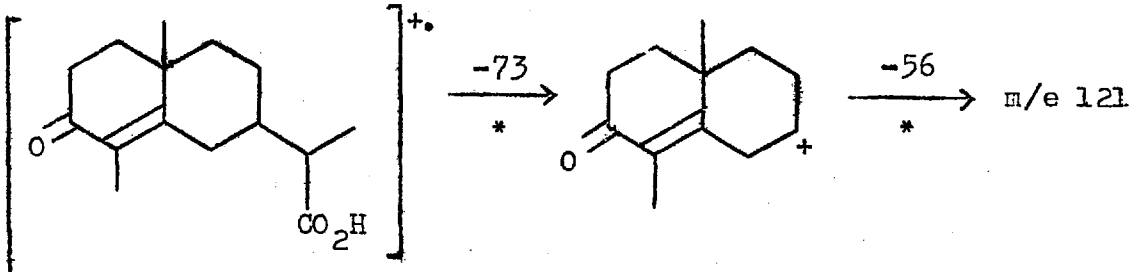


Because of this fundamentally different fragmentation compared to 1,2-dihydrosantonin (1) it is of interest to compare the structures of both Δ^1 and Δ^4 3-keto steroids with that of (1) to discern any salient features existing to explain this difference. The only conspicuous dissimilarity is the degree of olefinic bond substitution in (1) which is absent in most steroids on account of their biogenetic make-up from isoprenoid units. In view of this it is tentatively suggested that tetrasubstitution of the double bond is an essential prerequisit to loss of C_3H_4O from the molecular ion. A considerable volume of information now exists to support this hypothesis, both in santonin type systems and others. For example, the mass spectrum of 8-deoxy-ψ- santonin (3) although not exhibiting elimination of this unit (56m.u. in this instance) from the molecular ion does so from the $[M-43]^+$ moiety and is characterised by a metastable ion at m/e 108.3.



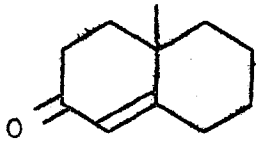
Further, santonic acid (4) also loses this fragment from the

$[M-73]^+$ ion, again supported by a small but distinct metastable ion at m/e 82.7.

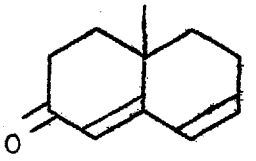


(4) m/e 250 m/e 177

It will be noticed that both compounds (3) and (4) possess a tetrasubstituted double bond. Several similar compounds not possessing the methyl group at C_4 have been examined and it is of interest that these show no metastable ion for elision of C_3H_4O at all. Thus the octalenone (5) and the bicyclic ketone (6) [104] do not show this loss from their M^+, but exhibit only retro-Diels Alder reaction followed by loss of carbon monoxide.



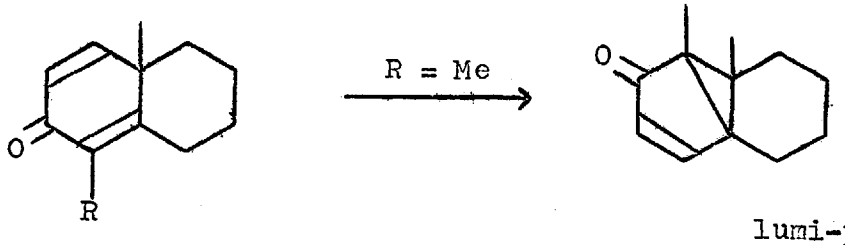
(5)



(6)

This observation bears some analogy with photochemistry where it has been observed that the bicyclic ketone (7, R = Me) forms a lumi-product on u.v. irridation whereas for the homologue, R = H under identical conditions only a complex mixture of products is obtained.[105]

It is noteworthy also that of the two double bonds



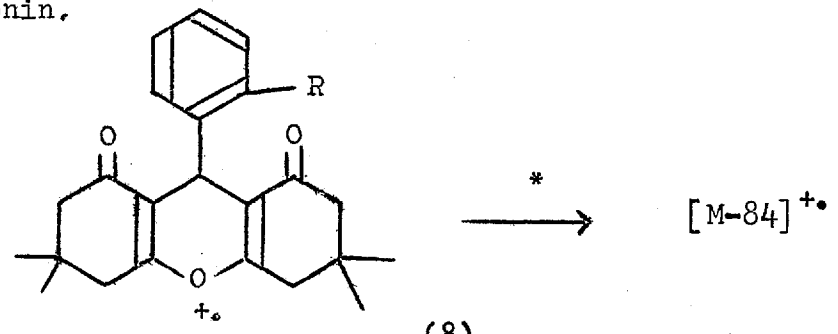
lumi-product

(7) R = H, Me

available for reaction that bearing the greater substitution is affected. This appears to be typical of all cases investigated and is consistent with the greater electron density of the tetra-alkyl substituted olefinic bond over that of the dialkyl substituted. We thus have a not inconsiderable amount of evidence in favour of lumi-product formation in the mass spectrometer prior to fission in the manner expected of cyclopentanones. However, the situation is not so straightforward as presented so far, since there are now available several examples of steroids such as 4-cholestene-3-one which form lumi-derivatives on photolysis[106] even though the olefinic bond is only trisubstituted. It is also found that these compounds have no tendency to lose C_3H_4O in the mass spectrometer, but lose the characteristic ketene fragment instead.[103]

On the basis of this photochemical data it is suggested that the energy required for lumi-compound formation in the mass spectrometer is insufficient unless the olefinic bond concerned is sufficiently activated. The minimum conditions would then appear to be a tetra-substituted double bond.

Examination of the mass spectra of several anhydrodimedone derivatives (8) where R = H, o-, m-, p-, OMe, o-,p-, NO_2, o-, Br, CH_3, Cl, lead to the observation that the molecular ions of these compounds also appear to lose a fragment from the cyclohexenone ring comparable to that lost from 1,2-dihydrosantonin.

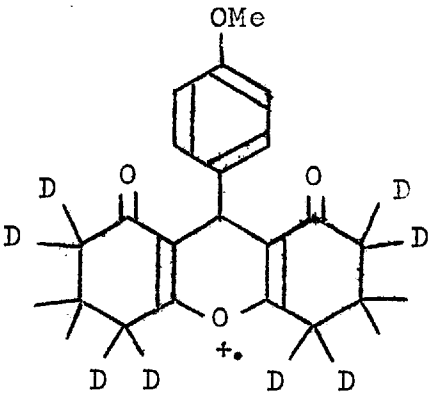


(8)

This fragmentation, which results in the elimination of C_5H_8O from the M^+ (as shown by accurate mass measurement), was characterised by a metastable ion in all cases except for the o- NO_2 and halogeno compounds which exhibited an alternative fragmentation.

A shift of the m/e 296 ion ($[M-84]^+$) in anisaldehyde anhydrodimedone (mass spectrum 20) to six mass units higher in the deuteriated derivative (9) (mass spectrum 21) demonstrated that the C_5H_8O moiety was lost exclusively from the C_1, C_2, and C_3 positions of the cyclohexenone ring, as is the C_3H_4O fragment from 1,2-dihydrosantonin.

The extent to which the C_5H_8O unit is lost from the anhydrodimedones is listed in Table 15 from which it may be seen that the most significant ejection occurs in the



$\xrightarrow{*}$ m/e 302

$-C_5H_6D_2O$

(9) m/e 388

Table 15.

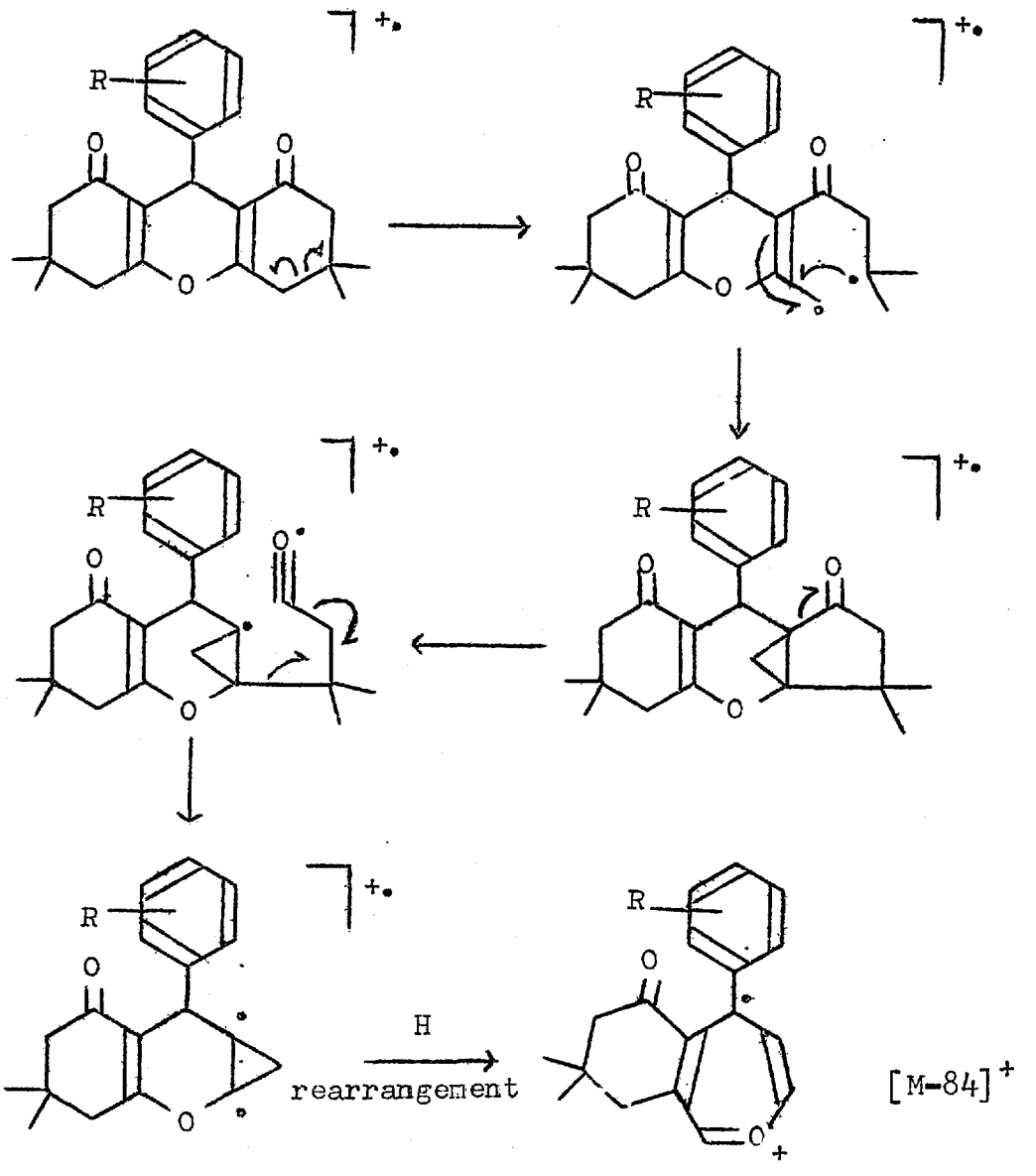
Relative abundance of $[M-84]^+$ ions in substituted anhydrodimedones

R	% Relative abundance $[M-84]^+$
H	4.3%
o-Br	0.0%
o-Cl	0.0%
o-Me	5.5%
o-OH	100.0%
o-NO_2	0.0%
p-NO_2	1.6%
o-OMe	9.1%
m-OMe	5.0%
p-OMe	21.7%

salicylaldehyde derivative where the $[M-84]^+$ ion represents the most abundant ion. However, since this compound has been shown not to possess the structure given as (8) (vide supra)

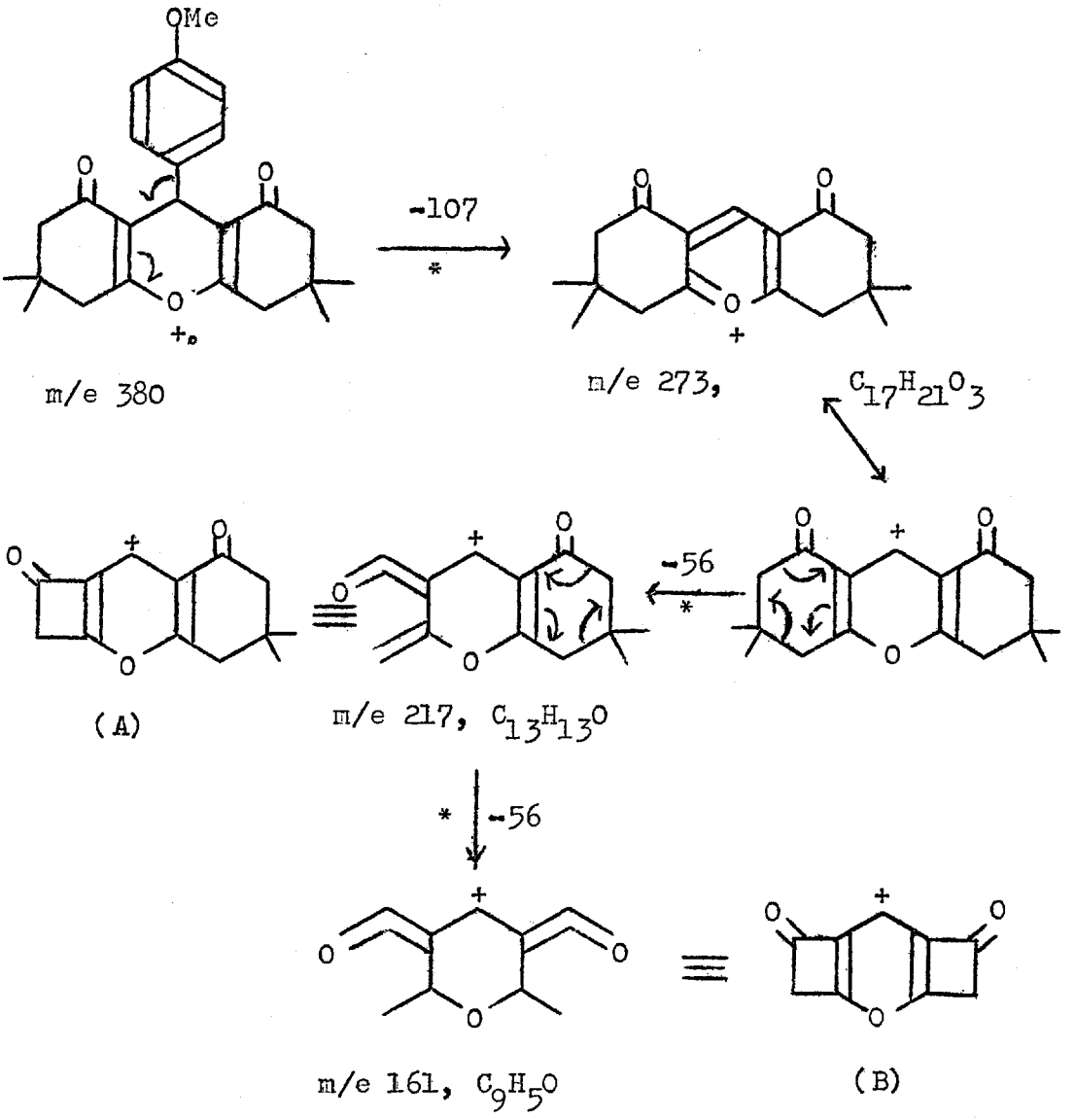
the true importance of this result cannot be evaluated. The second most substantial $[M-84]^+$ ion is observed in the p-anisyl derivative where it represents 22% of the base peak.

It would appear from the table that those derivatives with electron repelling substituents enhance formation of the $[M-84]^+$ fragment whilst others reduce it. Furthermore, substituents such as Br, Cl, and NO_2 which are known to undergo facile elimination themselves from aromatic nuclei suppress the formation altogether. However, the bromo compound does show signs of losing C_5H_8O from the $[M-Br]^+$ ion to the extent of 2.1% but no metastable ion is evident. As non-aromatic anhydrodimedones do not appear to exhibit this fragmentation to any marked extent the above factors suggest that the aromatic ring increases the extent of $[M-84]^+$ formation, especially when electron repelling substituents are present, by increasing the probability of ionisation in the aromatic nucleus. This will have the effect of increasing the electron density of the olefinic double bond by reducing ionisation in the enone unit, with the consequence of promoting rearrangement. A mechanism similar to that proposed for santonin rearrangement is suggested for the loss of C_5H_8O. (see below). The oxatropylium ion suggested as the product would account for the disinclination of this ion to undergo retro-Diels Alder fragmentation as the cyclohexenone double bond is now incorporated into the delocalised oxepine system.



The general fragmentation of anhydrodimedones has been discussed in two recent papers [20,98] and mechanisms given, but little work appears to have been carried out on the aromatic derivatives and no labelling studies have been presented. Since deuterium labelled compounds were needed to elucidate the origin of C_5H_8O loss from these aromatic compounds a resumé of the major fragmentation pathway will be

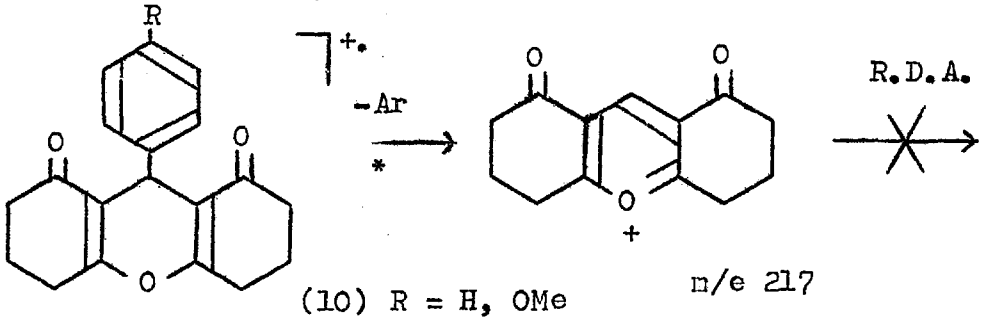
given along with the confirmative labelling evidence. Mass spectrum 20, of p-anisaldehyde anhydrodimedone is typical of the decomposition and will be used to describe the mechanistic route shown below.



Ions (A) and (B) are those suggested by Baldas and Porter.[98] All the decompositions are accompanied by well-defined metastable ions and accurate mass measurement has been employed

to determine the molecular formulae given. Using the [$^2H_8$]-derivative (9), appropriate shifts of m/e 273 to m/e 281, m/e 217 to m/e 223 and of m/e 161 to m/e 165 were observed (see mass spectrum 21) along with a corresponding change in the metastable ion. Moreover, in the derivative derived from α-[$^2H_1$]-benzaldehyde, a shift of 1m.u. to higher mass in all ions was observed confirming that this atom is retained throughout. It is noteworthy that although retro-Diels Alder reactions dominate the fragmentation no loss of isobutylene is observed from the molecular ion. This appears to be due to the greater facility with which the doubly allylic bond joining the aromatic portion to the pyran ring is broken.

In order to investigate the effect of the gem-dimethyl group on fragmentation of the cyclohexenone ring two cyclohexane-1,3-dione derivatives (10) were prepared. These compounds behaved rather unexpectedly in that the molecular ions showed extensive elimination of the aryl fragment as in anhydrodimedones, but these did not then undergo retro-Diels Alder elision of ethylene.

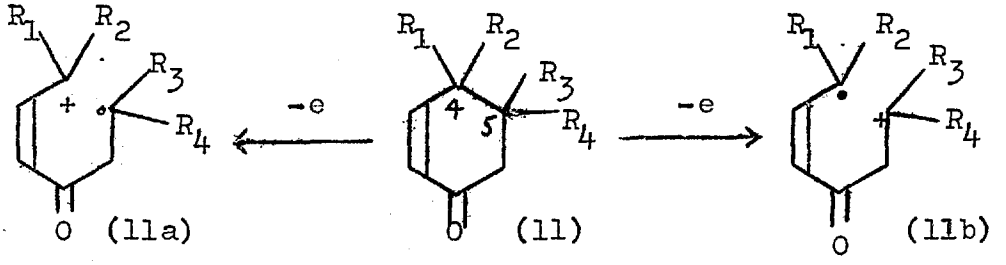


(10) R = H, OMe

m/e 217

In explanation, this is believed to result from the relative

stability of the radicals generated during the elimination, but to consider this fully some description of the mechanism of the retro-Diels Alder reaction is necessary. Consider the cyclohexenone (11) which may be ionised by heterolytic fission of the allylic bond to give either (11a) or (11b). Predominance of either of these depends on the substituents R_1, R_2, R_3, and R_4 since these are the stabilising factors of the ionised compound.[67a]



Ion (11a) is prefered if C_5 is a secondary or tertiary carbon atom, i.e. R_3 = H, R_4 = H or alkyl, and $R_1 = R_2$ = H or alkyl, while (11b) is prefered if C_5 is a quaternary centre, i.e. $R_3 = R_4$ = alkyl and $R_1 = R_2$ = H.

In the anhydrodimedone system C_5 is a quaternary centre leading to an ion of type (11b), $R_3 = R_4$ = Me, $R_1 = R_2$ = H , on ionisation. This ion then fragments by cleavage of the C_{1-6} bond with elimination of isobutylene. However, in the cyclohexane-1,3-dione homologue both the substituents at C_4 and C_5 are H, i.e. $R_1 = R_2 = R_3 = R_4$ = H, making ions of type (11a) preferable. On account of this decomposition with elision of ethylene is not a favoured process. In consequence it can be seen that if stabilisation of a positive charge at

C_5 is not possible then elimination of a neutral fragment via retro-Diels Alder reaction in this system is unlikely. Similar results are seen in steroids [103] where ketene elimination is often favoured to retro-Diels Alder fragmentation.

Elision of C_3H_4O (56m.u.) is an important process in type (10) compounds, representing 4.4% of the base peak in the benzaldehyde adduct and 15.1% in that from anisaldehyde. Furthermore, since the product ion undergoes facile loss of an hydrogen atom the true figures should be considerably higher than these values. (ca. 22.9% in anisyl and 12.1% in benzaldehyde). Because these compounds fragment with loss of C_3H_4O so readily it is clear that the gem-dimethyl group is not necessary for the proposed lumi-compound isomerisation.

Elimination of the hydroxyl radical (37.4% in 10 R = OMe see Table 16 for mass spectrum) is important in these compounds possibly due to enolisation prior to electron impact. This is substantiated in the benzaldehyde adduct which can lose a further 2 m.u. presumably to form an aromatic type ion.

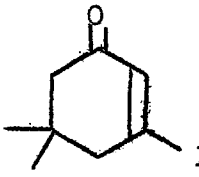
Table 16.

Partial mass spectrum of anisaldehyde anhydrocyclohexanedione.*

m/e	325	324	323	308	307	306	294	293	268
%	21%	100%	39%	9%	38%	5%	11%	52%	15%
m/e	267	218	217						
%	8%	11%	81%						

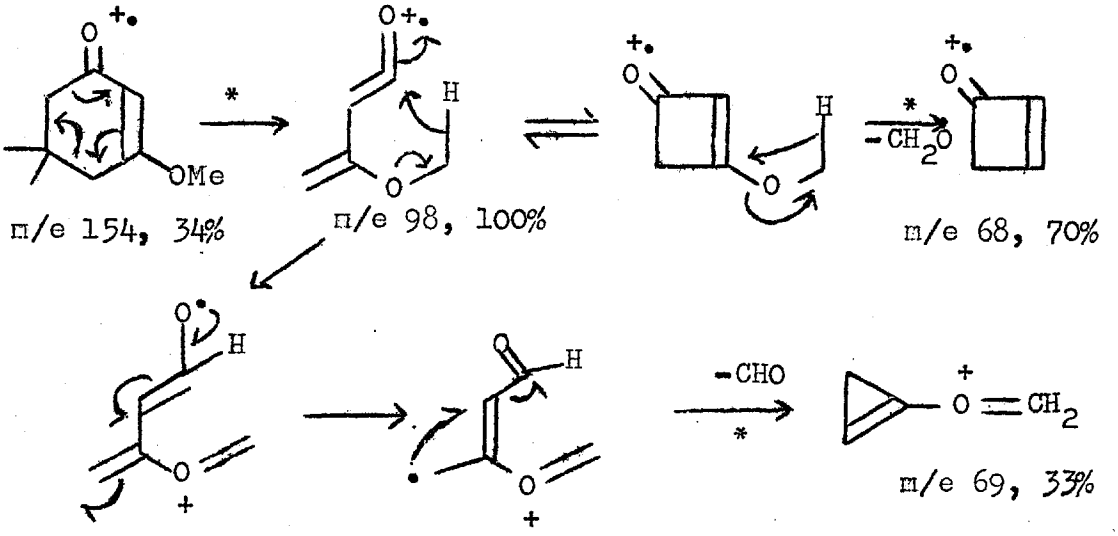
* Only values $\geq$ 5% are quoted.

Examination of the mass spectra of the more elementary cyclohexenyl models (12) reveals several interesting fragmentation modes which because of their dependence on specific structural features could be of importance when differentiating between isomeric compounds.



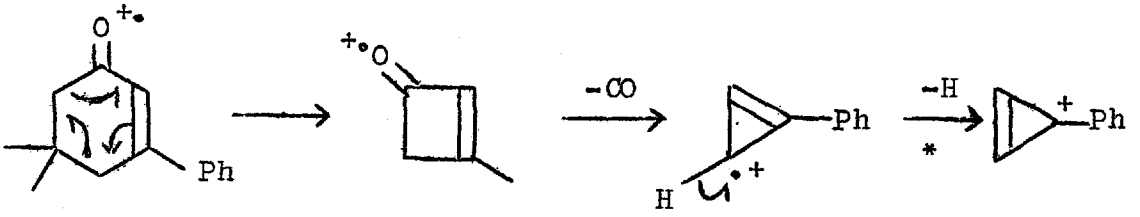
(12)

In the mass spectrum of the methoxy derivative (11, R = OMe, mass spectrum 22) the primary fragmentation consists of retro-Diels Alder reaction followed by loss of either HCO or H_2CO, as shown by accurate mass measurement, to form ions at m/e 69 (C_4H_5O) and m/e 68 (C_4H_4O) respectively. These decompositions are well characterised by metastable ions and are depicted in the scheme below.



Fragmentation of the phenyl and p-methoxy phenyl analogues (12, R = Ph and p-OMePh) parallels this sequence in so far as

isobutylene is lost via retro-Diels Alder reaction but in these cases the resulting ion is stabilised by elision of carbon monoxide to form ions at m/e 116 (34%) and m/e 146 (43%) respectively. The former then loses an hydrogen atom to generate the highly stable π-aromatic cyclopropenyl ion at m/e 115 (32%).



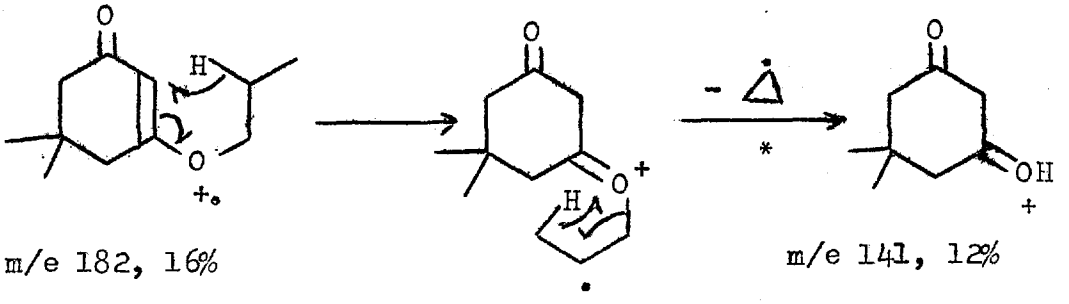
m/e 200, 23% m/e 144, 100% m/e 116 (34%) m/e 115

The anisyl derivative does not form an ion equivalent to that at m/e 115 in the phenyl analogue due to alternative fission of the methoxyl substituent.

In the 3-chloro compound (12, R = Cl) retro-Diels Alder reaction is again observed but the resulting ion does not lose carbon monoxide on account of the ready ejection of the Cl° radical to produce an ion at m/e 67 (33%).

The mass spectrum (number 23) of 5,5-dimethyl-3-ethoxy-cyclohexenone (12, R = OEt) is interesting in that along with the expected retro-Diels Alder reaction followed by CO loss there is also a metastable ion at m/e 42.5 characterising a one-step loss of 84 m.u. (C_5H_8O by mass measurement) from the molecular ion. As this ion corresponds to that from consecutive loss of isobutylene and carbon monoxide the extent of this decomposition mode is unknown, but its

similarity to fragmentation in anhydrodimedones makes it of notable importance. It is thought that the ethoxy group supplies sufficient extra electron density to the olefinic bond to enable rearrangement to a cyclopentanone prior to elimination of C_5H_8O. This is consistent with the absence of a similar metastable transition in the methoxy homologue which would be expected to have a less activated double bond. To check this hypothesis the n-propoxy homologue was examined (mass spectrum 24a) but this revealed no ion at all corresponding to loss of C_5H_8O. Also absent were ions derived by retro-Diels Alder reaction and other normally observed fragmentations. Instead a unique decomposition involving elimination of a 41 m.u. fragment (mass measured as C_3H_5) and well characterised by a metastable ion at m/e 109.2 was taking place. The facility of this process is assumed to account for the disinclination to form an $[M-84]^+$ ion. A plausible mechanism for this fragmentation is suggested below.

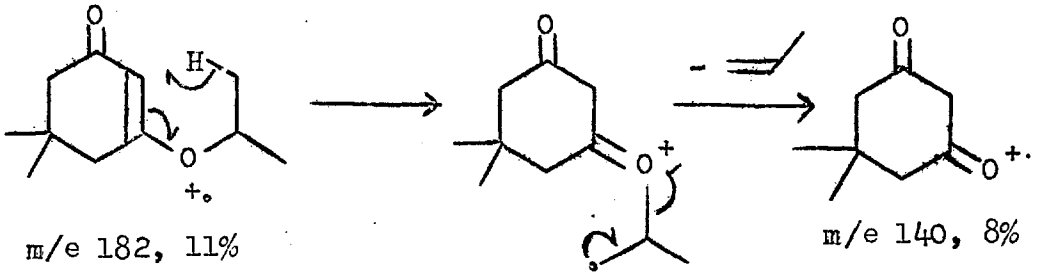


m/e 182, 16%

m/e 141, 12%

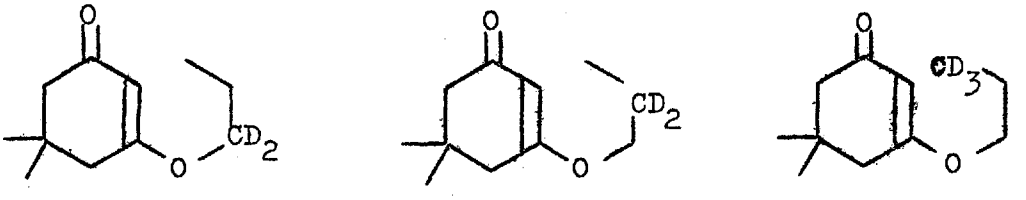
The singularity of this fragmentation pathway stems from the double hydrogen transfer which is believed to have no precedence in the literature. Support of the above mechanism comes from the isopropxy compound (12, R = O-iPr)

which loses 41 m.u. to a negligible extent (less than 1%), the pathway ensuing through elimination of 42 m.u. (not ketene as shown by mass measurement). This is consistent with the ability of the first hydrogen atom transfer to occur but not the second, thus ;



m/e 182, 11% m/e 140, 8%

Similarly the ethoxy homologue is incapable of the second hydrogen transfer consequently losing ethylene to form the m/e 140 ion (4%, mass spectrum 23). However, as has been mentioned, preferable alternative decomposition modes are available in this molecule. Conclusive evidence in support of this mechanism, however, was forthcoming only from the deuteriated n-propoxy compounds (13a, b, and c) the mass spectra of which are given (24b, c, and d respectively).



(13a) (13b) (13c)

In derivative (13a) the peak at m/e 141 remains unaltered, but in the other deuteriated compounds (13b and c) it is shifted 1 m.u. higher consistent with two separate

proton shifts from the 2 and 3 positions of the propyl side-chain. Furthermore, metastable ions exist for the loss of the C_3 moiety from these deuteriated derivatives and their positions are recorded in Table 17.

Table 17.

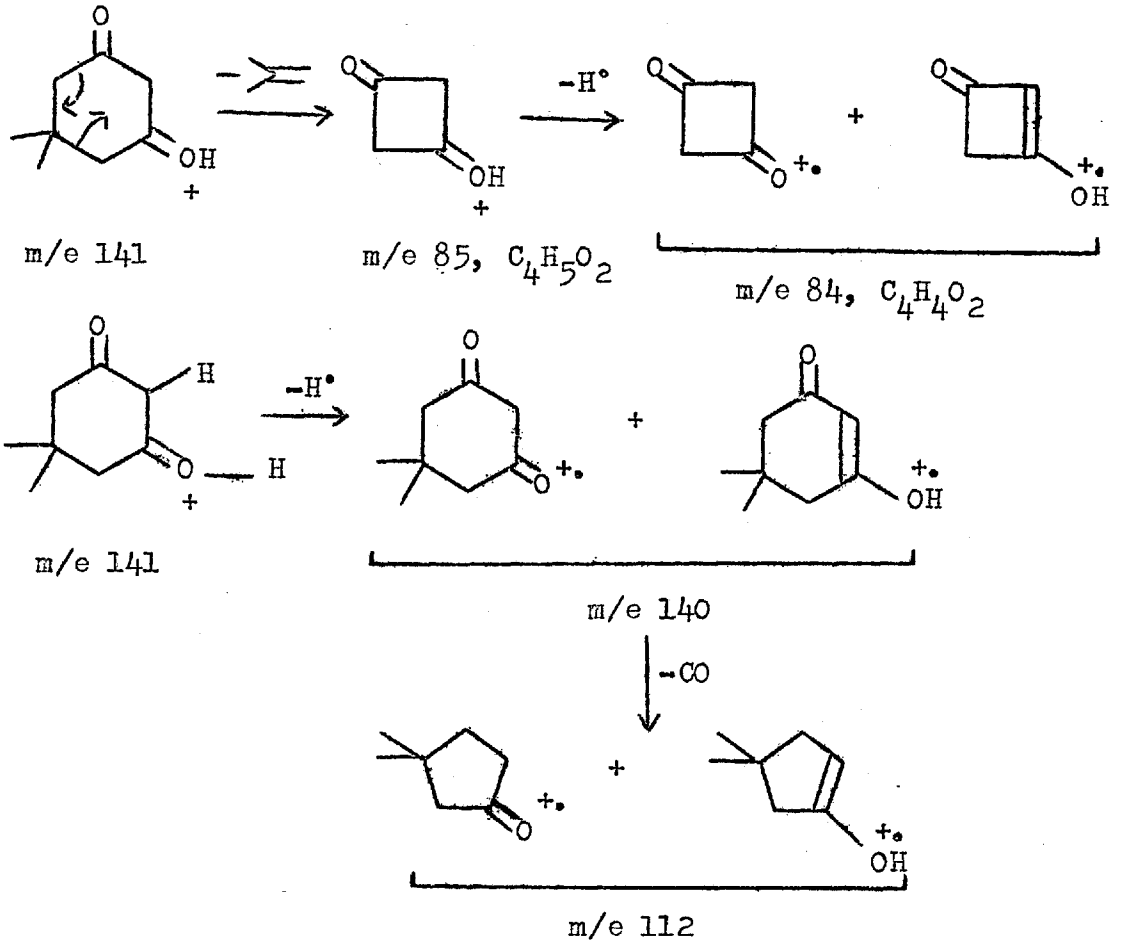
Metastable ions observed for elision of the C_3 fragment from deuteriated n-propoxy cyclohexenones.

Compound	Metastable ion		Transition
	Observed	Calculated	
12, R= nPr	m/e 109.2	m/e 109.1	182-141 (-41)
13a	m/e 108.1	m/e 108.0	184-141 (-43)
13b	m/e 109.7	m/e 109.7	184-142 (-42)
13c	m/e 109.0	m/e 109.0	185-142 (-43)

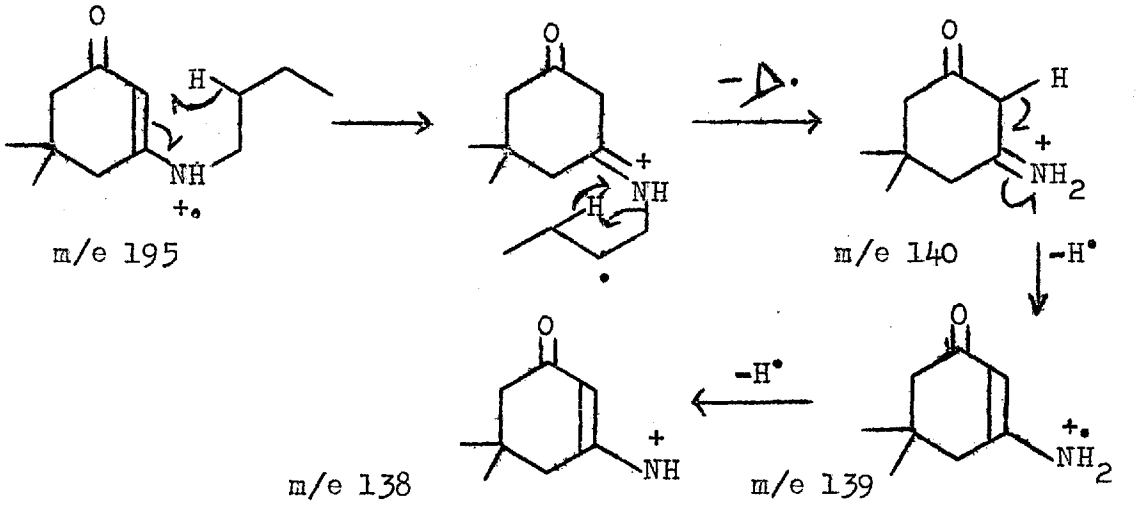
Moreover, from the spectra of the deuteriated analogues it is postulated that the complete fragmentation pathway, which proceeds *via* the m/e 141 fragment is as shown in the scheme below. A paucity of metastable ions in the spectra, however, does not allow confirmation of the transitions although all ions have been accurately mass measured to ensure the atomic composition suggested.

The generality of this two proton transfer is demonstrated in 3-N-butylamino-5,5-dimethyl cyclohexenone (12, R = N-butyl, mass spectrum 25) which forms ions at m/e 153 and 139 corresponding to loss of C_3H_5 and C_4H_7 followed by $H^{\bullet}$

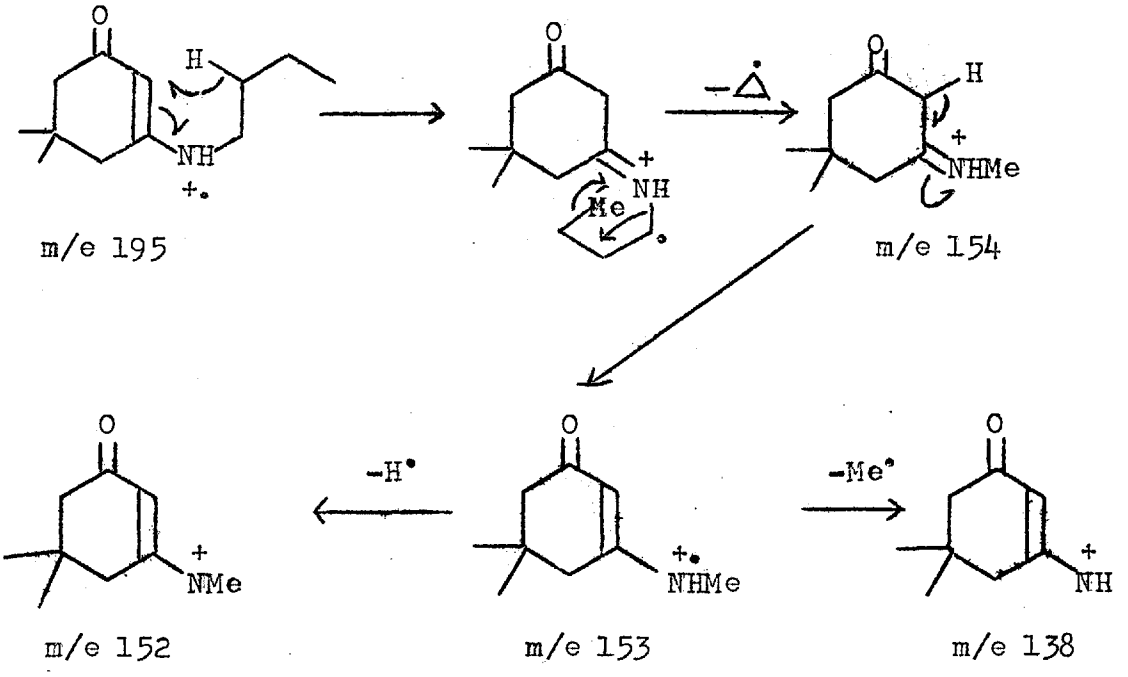
from M^+. The mechanistic route is illustrated in Scheme 10.



Scheme 10.

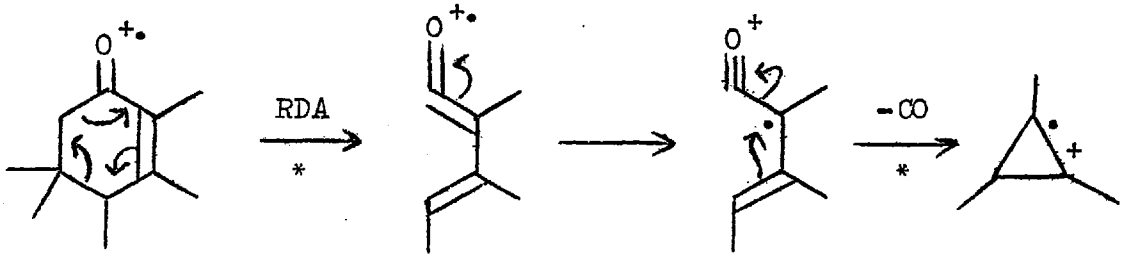


Scheme 10 continued.



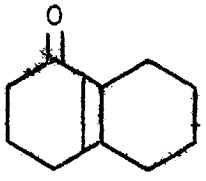
The mass spectrum of isophorone (12, R = Me) has been studied by Bowie[108] who observed only retro-Diels Alder reaction in the molecular ion followed by elimination of carbon monoxide to give an ion at m/e 54. No metastable ion for the direct transition $M^+ \rightarrow [M-84]^+$ was recorded. In view of this the mass spectrum of the homologue (14) was investigated in the expectation that two methyl groups on the double bond would be sufficiently activating to bring about direct loss of C_5H_8O. However, this was not the case since once again only consecutive elision of isobutylene and carbon monoxide was observed.

More rewarding results were found in the $\Delta^{9,10}$-octalenone (15) which besides undergoing retro-Diels Alder

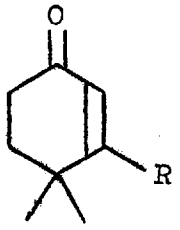


(14), m/e 166 (80%) m/e 110, (55%) m/e 82, (100%)

type fragmentation also fractured with loss of C_3H_4O in a single-step process as shown by the presence of a small metastable ion at m/e 58.9. This suggests that the equivalent of two ethyl groups on the olefinic bond should be sufficient to initiate isomerism and unique fragmentation of the cyclohexenone ring.



(15)



(16)

In order to complement the series of compounds governed by (12) several 4,4-dimethyl cyclohex-2-ene-1-ones (16) were examined with the object in mind of discerning the importance, if any, of the gem-dimethyl position. The trimethyl ketone (16, R = Me)(mass spectrum 26) showed no metastable ion for the transition $M^+ - [M-56]^+$ but decomposed by two competing pathways, one with the elimination of ketene and the other with elimination of ethylene. An abundant ion at m/e 110 was suggestive of the latter mode and was proved by accurate mass

measurement to result almost exclusively by loss of ethylene from the molecular ion. A narrow scan spectrum at high resolution indicated the presence of a second peak at m/e 110, found to be ca. 4% of the larger ion, and which mass measurement confirmed to be the $[M-CO]^+$ ion. The low abundance of the $[M-CO]^+$ ion is consistent with the relative ease of the alternative fragmentations. Reduction of the electron voltage to 15 ev. resulted in a considerable increase in the loss of ketene (see Table 18) which suggests that ketene elimination is a comparatively low energy process. A similar result has recently been observed in other compounds of this type. [109]

Table 18.

Dependence of ketene loss on ev. in 3,4,4-trimethylcyclohexenone.

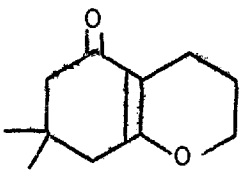
M^{+} *	$[M-28]^+$	$[M-42]^+$	Ionising voltage
14.5	12	19	70 ev.
22	8.5	26	15 ev.

* Arbitrary units.

Ketene loss was confirmed to come from C_1 and C_2 atoms by deuteriation of the α-protons in the phenyl derivative (16, R = Ph) whereby loss of 44 m.u. was observed. The phenyl and ethoxyl compounds of (16) were both found to have no metastable ion corresponding to the transition $M^+ - [M-56]^+$, but fragmented in a similar manner to the methyl analogue by

ketene; ethylene competition. This type of compound is known to exhibit facile ketene loss, the minimum conditions required having been determined by Burlingame et al. to be the presence of at least one alkyl group at C_4.[110] On account of this no further discussion of ketene elimination will be made.

One final compound investigated was the cyclic ether (17) which it was hoped would possess a metastable ion at m/e 41.2 corresponding to the concerted loss of isobutylene and carbon monoxide. Unfortunately none was observed, but it is thought that metastable defocussing experiments might demonstrate the occurrence of this transition.



(17)

In conclusion it is suggested that the postulated isomerisation to a cyclopentanone is only possible when the olefinic bond is tetrasubstituted (with the exception of 5,5-dimethyl-3-ethoxy cyclohexenone) and only then if sufficient electron density is being transferred from the substituents to the carbon atoms bearing the double bond. This is consistent with the photochemical analogies mentioned above, and the known greater activity of high electron density double bonds.

Part 5.

Experimental Section.

General.

The infra-red spectra were recorded using a Unicam SP 200 spectrometer, with the sample in the form of a liquid film (l.f.), nujol mull (mull), or in solution in a 0.1 mm. cell using polystyrene as a reference marker. Ultra violet spectra were obtained on a Unicam SP 800 instrument with an Holmium filter standard.

Nuclear magnetic resonance spectra were recorded on either the Varian Associates 100 MHz., HA-100 or 60 MHz., A-60 spectrometer, tetramethyl silane being used as an internal standard.

The purity of all compounds was checked by t.l.c. on silica gel or for volatile liquids by gas chromatography using a Perkin-Elmer F 11 fitted with a 2 metre Carbowax 1500 on Chromosorb W column.

Melting points were determined on a Kofler Micro Heating Stage, and are quoted without correction.

5, 1 Anthraquinone Derivatives.

2-Ethyl bromobenzene. (Gatterman procedure)

2-Ethyl aniline (30.3g. ; 0.25mole) in 48% aqueous hydrogen bromide (85ml.) cooled to 5°C in ice-salt was diazotised by gradual addition of sodium nitrite (18.3g.) in water (25ml.). After each addition the flask was stoppered and shaken until all the red fumes had dissolved, keeping the temperature between 5-10°C. When diazotisation was complete copper powder (1g.) was added and the mixture gently refluxed on a steam bath until nitrogen evolution commenced when it was immediately cooled in ice to moderate the reaction. Decomposition was completed by warming on a steam bath for 30mins. after which the solution was diluted with water (200ml.) and steam distilled. The distillate was made alkaline with 10% sodium hydroxide and the organic layer separated, washed with water, dried ($CaCl_2$) and distilled. Yield 16.8g. (36%), b.p.60°/0.5mm.; n_D^{23} 1.5470.

2,6-Dimethyl bromobenzene.

This was prepared according to the procedure of von-Schwectem[112] for hindered aryl bromides involving formation of the mercury complex of diazotised 2,6-dimethyl aniline (18.8g.) and decomposition with sodium bromide. Yield 15.7g. (49%); b.p.64°/7mm.; n_D^{20} 1.5552.

p-Nitro cumene.

A mixture of nitric acid (s.g.1.42, 20.75g.) and sulphuric

acid (s.g.1.84, 31.25g.) was slowly added to cumene (25g.) stirred at 40-50°C. Stirring was continued for 2hrs. and the product poured into ice-water (1 litre). After extraction with ether the product was washed, dried (Na_2SO_4) and distilled to a yellow oil. Yield 27.9g. (82%); b.p.135°/13mm.; (lit.[113] b.p.128°/12mm.)

2-Bromo-4-nitro cumene.[114]

4-Nitro cumene (16.5g.), silver sulphate (17g.), concentrated sulphuric acid (90ml.) and water (10ml.) were stirred with gradual addition of bromine (5.2ml.). After addition was complete the mixture was stirred for a further 2hrs. and poured into a dilute solution of sodium bisulphite (500ml.). The oil which separated was extracted with ether, dried (Na_2SO_4) and distilled. Yield 18.37g. (76%); b.p. 145-155°/13mm. (lit. b.p.155-160°/15mm.)

4-Amino-2-bromo cumene.[114]

In a three necked flask fitted with a reflux condenser and stirrer were placed the above nitro compound (15g., 0.125 mole), iron filings (11g., 0.375mole) and 50% aqueous ethanol (15ml.). The stirred mixture was heated to boiling and a solution of concentrated hydrochloric acid (0.9ml., 0.01mole) in 50% ethanol (3.5ml.) was slowly added. After refluxing for 2hrs. the solution was made basic with 2N sodium hydroxide and filtered hot to remove iron. The residue was washed with ethanol and the filtrate diluted with water and ether extracted.

The brown extracts were washed, dried (Na_2SO_4) and distilled. Yield 9.01g. (69%); b.p.143-144°/12mm. This mixture of amines was chromatographed on SiO_2 eluting with chloroform whereby both 4-amino-2-bromo cumene, b.p.155-156°/12mm. (second fraction) and 2-amino-4-bromo cumene, b.p.140-2°/12mm. (first fraction) were obtained.

2-Bromo cumene.[114]

4-Amino-2-bromocumene (3.6g.) was added to concentrated hydrochloric acid (6.7ml.) and water (13.4ml.) and the mixture warmed on a steam bath to effect partial solution of the hydrochloride, and then poured onto ice (17g.). An aqueous solution of sodium nitrite (1.17g. in water (2.5ml.)) was slowly added to the cold ($<2°C$) stirred solution and the filtered diazonium solution treated with 50% hypophosphorous acid (25ml.) at 0°C. The mixture was left at 0°C overnight and the oil extracted with ether. The extracts were dried (Na_2SO_4) and distilled. Yield 2.35g. (70%); b.p.82-83°/14mm.; $n_D^{19.5}$ 1.5422. (lit. b.p.90°/15mm.)

tert-Butyl benzene.

This was prepared by alkylation of benzene according to the method of Schramm.[115] Yield 44% ; b.p.165-168°/760mm.

4-Nitro-tert-butyl benzene.

This was made by the procedure of Shoesmith and Mackie[116] by nitration of tert-butyl benzene (37.4g.). Yield 37.7g. (76%); b.p.128-136°/13mm. (lit. b.p.125-130°/10mm.)

2-Bromo-4-nitro-tert-butyl benzene.[114]

Was prepared according to Crawford and Stewart[114] from 4-nitro-tert-butyl benzene (23.2g.). Yield 18.7g. (56%); m.p.89-93°, (lit. m.p.94°).

4-Amino-2-bromo-tert-butyl benzene.

This was prepared by the method of Shoesmith and Mackie[116] from 2-bromo-4-nitro-tert-butyl benzene (15g.). Yield 4.9g. (32%) of the hydrochloride.

2-Bromo-tert-butyl benzene.

Again prepared by the method of Crawford and Stewart[114] from the above hydrochloride (4.8g.). Yield 2.7g. (69%); b.p.103°/15mm.; $n_D^{20.5}$ 1.5441; (lit. b.p.96-98°/12mm.)

Phenyl propenyl carbinol.[117]

Bromobenzene (15.7g.; 0.1mole) was introduced to a stirred suspension of magnesium (2.64g.; 0.11mole.) and ethyl bromide (0.2ml.) in anhydrous ether (50ml.) at such a rate that the solution gently refluxed. When the reaction was complete, the solution was cooled to -10°C in an ice-salt mixture and freshly distilled crotonaldehyde (7.0g.; 0.1mole, b.p.104°) in anhydrous ether (20ml.) was added with stirring over 1hr. Stirring was continued at 0°C for 3hrs. and saturated aqueous ammonium chloride (150ml.) added. The ethereal solution was separated and the aqueous phase ether extracted. The combined ether layers were washed with water, dried (K_2CO_3), and distilled from a trace of potassium

carbonate. Yield 11.2g. (75.5%); b.p.79-80°/0.3mm.; n_D^{20} 1.5410; ν_{max}(l.f.) 3400,1670,1603 $cm.^{-1}$ n.m.r. ($CDCl_3$) τ 8.37 (d, J=4.6Hz. 3H, vinylic methyl), 6.69 (broad singlet, 1H, hydroxyl), 5.10 (m, 2H, vinylic protons), 2.82 (s, 5H, aromatics).

1-Phenyl butadiene.[117]

Phenyl propenyl carbinol (7.4g.; 0.05mole) was heated at 60°C under 10^{-2}mm. pressure with 1/10th of its weight of anhydrous potassium bisulphate until the vigorous rearrangement process ceased (ca. 10mins.) and distilled. Fractionation of the product then gave the diene as a colourless oil. Yield 3.2g. (49%); b.p.44-46°/0.04mm.; n_D^{20} 1.6101; ν_{max}(l.f.) 1630,1600,1010, and 910 $cm.^{-1}$ n.m.r. (CCl_4) τ 4.59-5.04 (m, 2H, methylene), 3.90-3.18 (m, 3H, vinylic protons), 2.85-2.59 (m, 5H, aromatics).

The substited 1-phenyl butadienes shown in Table 19 were similarly prepared from the bromobenzene via the propenyl carbinol, although the anisyl derivatives were protected by a nitrogen atmosphere. Invariably the carbinol was rearranged and dehydrated without isolation so that yields in Table 19 refer to the overall yield from the substituted bromobenzene. All products were structurally confirmed by i.r. and n.m.r. spectra.

Table 19.

Substituted 1-aryl butadienes.

substituent	% Yield	n_D^*	b.p. °C	m.p.
m-Me	40%	1.5930(22°)	67-70°/0.001mm.	
p-Me	42%	-	78°/0.005mm.	26°
m-OMe	40%	1.6040(23°)	90°/0.02mm.	
p-OMe	56%	-	-	46°
o-Cl	42%	1.5847(20°)	57-60°/0.001mm.	
m-Cl	34%	1.5868(20°)	65-67°/0.001mm.	
p-Cl	39%	1.6210(18°)	49°/0.002mm.	18°
o-Br	29%	1.6109(22°)	55-60°/0.001mm.	
m-Br	37%	1.6048(21°)	50°/0.001mm.	
p-Br	38%	-	88°/0.001mm.	29°
m-F	56%	1.5827(24°)	34°/0.001mm.	
p-F	49%	1.5788(22°)	37°/0.001mm.	16-16.5°
o-Et	41%	1.5850(19°)	50°/0.07mm.	
2,6-dimethyl	32%	1.5678(25°)	85-90°/0.03mm.	
o-isopropyl	25%	-	80°/0.1 mm.	
o-t-butyl	18%	1.5622(19°)	76-78°/0.02mm.	

* Temperature in parenthesis.

1-Chloro-4-(p-nitrophenyl)but-2-ene.[117,118]

p-Nitroaniline (20g.) was warmed for 10mins. with 12N hydrochloric acid (34ml.) and water (30ml.) on a steam bath

to form the pink hydrochloride, the solution of which was cooled in ice and sodium nitrite (10g.) in water (17ml.) was slowly added to the stirred solution during 1hr. at 0°C. The diazotised solution was filtered and maintained at 0°C while gradually added to a stirred mixture of butadiene (17ml.), acetone (143ml.), sodium acetate solution (11.4g. in water (14ml.) and cupric chloride solution (4.2g. in water (7ml.)) cooled in ice-salt. The reaction mixture was stirred at room temperature overnight to yield a brown, oily upper layer and a green aqueous layer. The two phases were separated and the aqueous phase extracted with ether. The combined organic layers were washed, dried (Na_2SO_4) and evaporated to afford the crude but-2-ene. Yield 24.6g.

1-p-Nitrophenyl butadiene.[40,118]

The crude but-2-ene (24.6g) was dissolved in methanol (60ml.) and a solution of potassium hydroxide (15.8g.) in methanol (85ml.) added to the stirred solution, the temperature being kept between 20-30°C by occassional cooling. After 2hrs. the solution was filtered to isolate the product as a brown crystalline solid. Addition of water to the filtrate produced a further crop of crystals. Recrystallisation from methanol gave a yellow-orange solid. Yield from p-nitroaniline 15.2g. (60%); m.p.77-78°, (lit. m.p.78-78.8°).

1-m-Nitrophenyl butadiene.[119]

This was made as above from m-nitroaniline (20g.), but

required ether extraction and distillation to isolate the diene. Yield 13.0g. (51%); Recrystallisation from methanol gave a pale yellow solid; m.p.52°, (lit.[119] m.p.53°).

1-o-Fluorophenyl butadiene.[119]

This was prepared from the chlorobut-2-ene (made as above) by refluxing with a three fold excess of powdered potassium hydroxide in dioxan for 15mins. The solution was poured into ice-cold water and ether extracted. The extracts were washed with water, dried (Na_2SO_4) and distilled. Yield 27% overall; b.p.70-76°/3mm.; n_D^{21} 1.5675; ν_{max}(l.f.) 1630,1590, 1560, 1230, 1010 and 760 $cm.^{-1}$

Attempted preparation of 1-(p-anisyl) butadiene without distillation.

In an attempt to reduce polymerisation p-anisyl propenyl carbinol (1.0g.) was warmed to 60°C on an oil bath at 0.9×10^{-2}mm. for 10mins. and extracted with ether. The extracts were washed, dried (K_2CO_3) and evaporated to a white solid. After recrystallisation from methanol and then from petrol (b.p.40-60) it melted at 108-110°; ν_{max}(mull) 1603, 1262, 980 and 825 $cm.^{-1}$ n.m.r.($CDCl_3$) τ 8.73 (d, J=6Hz. 6H, methyls), 6.19 (s, 6H, methoxyls), 5.84(q, J=6Hz. 2H, O-CH), 4.32-3.35 (m, 4H, vinylics), 2.29 (s, 8H, aromatics).; (Found: C,77.78%; H,7.69%; $C_{22}H_{26}O_3$ requires: C,78.00%; H,7.69%); λ_{max}(EtOH) 263.5, 294.0, 305.0mμ (log ε , 4.69, 3.96, 3.76). Physical data is in agreement with formula 4 (section 1 , 1).

1-Phenyl anthraquinone.

To a solution of 1-phenyl butadiene (1.3g., 0.01mole) in anhydrous benzene (15ml.) was added recrystallised naphthaquinone (1.58g., 0.01mole) and the mixture refluxed overnight. Evaporation of the solvent gave a dark brown solid which after treatment with refluxing 10% ethanolic potassium hydroxide (30ml.) through which air was drawn for 2hrs. yielded a yellow crystalline solid. The ethanolic solution was poured into water (30ml.) and the solid filtered off. Purification was effected either by sublimination or by recrystallisation from ethanol. Yield 1.93g. (68%); m.p.178°, (lit.[42] m.p. 177-178°); ν_{max}(mull) 1669 cm.$^{-1}$ The n.m.r. ($CDCl_3$) showed only aromatic protons at τ 2.82-1.51 (m).

Apart from the nitro derivatives the anthraquinones shown in Table 20 were prepared by an identical procedure, the o-ethyl and fluoro derivatives being accompanied by the dihydro compounds were purified by chromatography on silica gel eluting with chloroform.

1-(p-Nitrophenyl) anthraquinone.

1-p-Nitrophenyl butadiene (1.0g.), naphthaquinone (1.0g.) and nitrobenzene (5ml.) were heated at 150°C for 2hrs. on an oil bath and the deep red liquid diluted with ethanol (2-5ml.). The ginger solid precipitated was filtered off, washed with ethanol and sublined to a bright yellow solid. Yield 0.93g. (58.5%); m.p.273-273.5°.

Table 20.

1-Aryl anthraquinones.

Compound	Yield	m.p.	u.v. ($CHCl_3$) λ_{max} mμ
m-Me	19%	164-165°	256(4.74),274(4.29),333(3.39)
p-Me	15%	178.5-179.5°	256(4.65),278(4.25),331(3.60)
m-OMe	18%	155-156°	255(4.72),274(4.31), 335(3.73)
p-OMe	27%	196°	256(4.70),274(4.28)*,314(3.79)
m-NO_2	38%	248°	260(5.03), 330(4.11)
p-NO_2	59%	273-273.5°	255(4.66),271(4.46)
o-Cl	29%	212°	256(4.69),273(4.26),332(3.68)
m-Cl	32%	187-189°	255(4.72),273(4.30),334(3.76)
p-Cl	36%	199.5-200.5°	256(4.60),277(4.19),334(3.61)
o-Br	19%	222-224°	257(4.64),274(4.26),334(3.69)
m-Br	18%	202-203°	256(4.70),274(4.30),334(3.73)
p-Br	21%	212-213°	265(4.61),278(4.18),333(3.58)
o-F	32%	215-217°	255(4.70),275(4.34)*,334(3.58)
m-F	22%	206°	255(4.71),273(4.31),333(3.72)
p-F	27%	194°	256(4.70),274(4.28),336(3.70)
o-Et	64%	151.5-152.5°	256(4.53),274(4.25),332(3.72)
2,6-dimethyl	10%	179-180°	256(4.71),274(4.26),333(3.73)
o-isopropyl	28%	191-192.5°	
o-t-butyl	29%	206-207	

* Inflection.

Analyses.

Found: C,84.22, H,4.75, $C_{21}H_{14}O_2$ requires: C,84.45, H,4.70.

Found: C,84.28, H,4.66, $C_{21}H_{14}O_2$ requires: C,84.45, H,4.70.

Found: C,79.99, H,4.39, $C_{21}H_{14}O_3$ requires: C,80.24, H,4.49.

Found: C,79.98, H,4.56, $C_{21}H_{14}O_3$ requires: C,80.24, H,4.49.

Found: C,72.86, H,3.43, N,3.95, $C_{20}H_{11}NO_4$ requires: C,72.95, H,3.37, N,4.25.

Found: C,72.76, H,3.42, N,4.01, $C_{20}H_{11}NO_4$ requires: C,72.95, H,3.37, N,4.25.

Found: C,75.51, H,3.78, Cl,11.17, $C_{20}H_{11}ClO_2$ requires: C,75.36, H,3.48, Cl,11.13.

Found: C,75.26, H,3.32, Cl,11.05, $C_{20}H_{11}ClO_2$ requires: C,75.36, H,3.48, Cl,11.13.

Found: C,75.49, H,3.40, Cl,11.25, $C_{20}H_{11}ClO_2$ requires: C,75.36, H,3.48, Cl,11.13.

Found: C,65.91, H,3.23, Br,21.53, $C_{20}H_{11}BrO_2$ requires: C,66.12, H,3.05, Br,22.00.

Found: C,66.00, H,3.20, Br,21.95, $C_{20}H_{11}BrO_2$ requires: C,66.12, H,3.05, Br,22.00.

Found: C,66.10, H,3.06, Br,21.84, $C_{20}H_{11}BrO_2$ requires: C,66.12, H,3.05, Br,22.00.

Found: C,79.39, H,3.82, F,6.55, $C_{20}H_{11}FO_2$ requires: C,79.47, H,3.67, F,6.29.

Found: C,79.58, H,3.62, F,6.28, $C_{20}H_{11}FO_2$ requires: C,79.47, H,3.67, F,6.29.

Found: C,79.64, H,3.88, F,6.31, $C_{20}H_{11}FO_2$ requires: C,79.47, H,3.67, F,6.29.

Found: C,84.35, H,5.14, $C_{22}H_{16}O_2$ requires: C,84.55, H,5.16.

Found: C,84.33, H,5.05, $C_{22}H_{16}O_2$ requires: C,84.55, H,5.16.

Found: C,84.21, H,5.56, $C_{23}H_{18}O_2$ requires: C,84.49, H,5.85.

1-(m-Nitrophenyl) anthraquinone.

This was prepared as above from m-nitrophenyl butadiene (1g.). Yield 0.70g. (38%), m.p. 248°.

Attempted preparation of 1-(p-nitrophenyl) naphthaquinone.

1-p-nitrophenyl butadiene (1g.), benzoquinone (0.62g., slight excess), and nitrobenzene (10ml.) were heated at 150-160°C for 2hrs. and the red liquid cooled and diluted with an equal volume of ethanol. Filtration gave a yellow solid which after washing with ethanol and sublimation had m.p. 326°. Yield 0.21g., ν_{max}(mull) 1669,1600,1580,1520,1350 and 1270 $cm.^{-1}$ Shown to be the di-adduct, 1,5-di-(p-nitrophenyl) anthraquinone. (Found: C,69.43%, H,3.33%, N,5.97%, $C_{26}H_{14}N_2O_6$ requires: C,69.34%, H,3.13%, N,6.22%.)

[2,4,6,N,N,N-$^2H_6$]-Anilinium bromide.

Aniline hydrobromide (13g.) and deuterium oxide (6.5ml.) were refluxed for 24hrs. and the water removed under reduced pressure. This procedure was repeated twice more and the deuterio anilinium bromide isolated. Yield 11.55g. (85%).

[2,4,6-$^2H_3$]-Bromobenzene.

[2,4,6,N,N,N-$^2H_6$]-Anilinium bromide (11.55g.) was converted to the deuteriated bromobenzene according to the method of Akawie et al.[50] Yield 4.05g. (39%), b.p.154-158°/760mm.; n_D^{23} 1.5598

[2,4,6-$^2H_3$]-Phenyl propenyl carbinol.

The Grignard reagent from [2,4,6-$^2H_3$]-bromobenzene (3.54g.)

and magnesium (0.545g.) was treated with crotonaldehyde (2.02g.) under the conditions given for the undeuteriated compound. Yield 2.04g. (62%); b.p.60°/0.09mm.; n_D^{22} 1.5402; ν_{max}(l.f.) 3400,2280,1665, and 1620 $cm.^{-1}$ The nmr showed only 2 protons at τ 2.82(s).

1-[2,4,6-$^2H_3$]-Phenyl butadiene.

The propenyl carbinol above (1.82g.) was rearranged and dehydrated as for the undeuteriated compound with anhydrous potassium bisulphate. Yield 0.4g. (25%); b.p.40-45°/0.09mm.; ν_{max}(l.f.) 2260,1630,1600 $cm.^{-1}$

1-[2,4,6-$^2H_3$]-Phenyl anthraquinone.

The above deuteriated butadiene (0.371g.) underwent Diels Alder reaction with naphthaquinone (0.44g.) according to the procedure of the unlabelled analogue. Yield 0.351g. (44%); m.p.180.5-181.5°; mass spectrum shows D_3,65.0%, D_2,25.9%, D_1,9.3%. Total deuteriation 85.4%.

[3,5-$^2H_2$]-Bromobenzene.

This was prepared from [2,4,6,N,N,N-$^2H_6$]-anilinium bromide (8.5g.) following the method of Akawie et al.[50] Yield 2.02g.(27%); b.p.156-158°/760mm.; n_D^{22}1.5572.

[3,5-$^2H_2$]-Phenyl propenyl carbinol.

The Grignard reagent formed from [3,5-$^2H_2$]-bromobenzene (2.06g.) and magnesium (0.313g.) was treated with crotonaldehyde (0.91g.) in the described manner. Yield 0.63g. (32%); b.p.70°/0.75mm.; n_D^{19} 1.5458; ν_{max}(l.f.) 3390,2290,

1670,1585, and 1445 cm.$^{-1}$ n.m.r. showed only 3 aromatic protons at τ 2.82(s).

1-[3,5-$^{2}H_2$]-Phenyl butadiene.

Dehydration of the above carbinol (0.62g.) with potassium hydrogen sulphate gave the title compound. Yield 0.545g.(21%); b.p.60-61°/0.3mm.; ν_{max}(l.f.) 2260,1625, 1598,1585,1440,910 and 810 cm.$^{-1}$

1-[3,5-$^{2}H_2$]-Phenyl anthraquinone.

This was prepared from the diene (0.113g.) according to the general procedure. Yield 0.122g.(50%); m.p.179-180°; ν_{max}(mull) 1669 cm.$^{-1}$; mass spectrum gives D_2,57.0%, D_1,36.0%, D_0,7.0%; total deuteriation, 75%.

2-Bromobenzoic acid.

2-Bromotoluene (12.5g.) was oxidised by alkaline potassium permanganate (32.5g. 40% excess) by the method of Bigelow,[120] to give the title compound on acidification. Yield 9.87g.(67%); m.p.147-8°, (lit. m.p.150°).

Ethyl-2-bromobenzoate.

2-Bromobenzoic acid (5.04g.) was refluxed 24hrs. with an excess of ethanolic hydrogen chloride (20ml.), and the alcohol evaporated. The residue was taken up in ether and washed successively with saturated aqueous sodium carbonate and water, dried ($MgSO_4$) and distilled. Yield 3.65g.(64%); b.p.109°/3mm.; n_D^{24} 1.5440; ν_{max}(l.f.) 1725 cm.$^{-1}$

2-Bromobenzyl alcohol.

2-Bromobenzoic acid (0.97g.) in anhydrous ether (20ml.) was added to a slurry of lithium aluminium hydride (0.515g. 10% excess) in ether (10ml.) over 20mins. After stirring for 1.5hrs., water was cautiously introduced followed by 10% aqueous sulphuric acid. The mixture was ether extracted, dried ($MgSO_4$) and evaporated to a white crystalline solid which was recrystallised from ethanol. Yield 0.35g.(39%); m.p.80°, (lit.[121] m.p.80°); ν_{max}(mull) 3300-3200,1590, and 1570 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 7.67(broad s, 1H, hydroxyl), 5.29 (s, 2H, methylene), 3.04-2.38(m, 4H, aromatics).

2-Bromobenzyl tosylate.

2-Bromobenzyl alcohol (300mg.) in anhydrous ether (2.2ml.) was added to a 50% dispersion of sodium hydride (0.079g.) and refluxed for 22hr. The mixture was cooled to -20°C in card-ice/ethanol and a solution of tosyl chloride (0.32g.) in ether (2.2ml.) added over 1hr. with stirring. Stirring was continued for 2hrs. at -10°C and for a further 1hr. at room temperature. The suspension was filtered, the filtrate cooled to -78°C and the tosylate filtered off and dried in vacuo. Recrystallise from pentane. Yield 0.405g.(74%); m.p.80-81°C; ν_{max}(mull) 2200,1598,1485,1450,1362,1175,828 and 775 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 7.59(s, 3H, methyl), 4.88(s, 2H, methylene), 2.95-2.07(m, 8H, aromatics). (Found: C,49.59%, H,3.86%, Br,23.57%, S,9.09%, $C_{14}H_{13}BrO_3S$ requires: C,49.28%,

H,3.84%, Br,23.42%, S, 9.38%.)

2-Bromo-[α,α-$^2H_2$] benzyl alcohol.

To a slurry of stirred lithium aluminium deuteride (0.31g. 10% excess) in anhydrous ether (10ml.) was added ethyl-2-bromobenzoate (2.96g.) in ether (10ml.) at such a rate that the solution gently refluxed. After refluxing for 2hrs. water (1ml.) and 10% aqueous sulphuric acid (15ml.) were introduced and the ethereal layer withdrawn and dried ($MgSO_4$). Evaporation gave a white solid, yield 2.05g.(84%); m.p.80°; n.m.r. showed no signal at τ 5.29.

2-Bromo-[α,α-$^2H_2$] benzyl tosylate.

This was prepared from the [$^2H_2$]-alcohol (2.05g.) prepared above according to the procedure used for the unlabelled analogue. Yield 2.60g.(70%); m.p. 80-81°; n.m.r. showed the absence of a signal at τ 4.88.

2-Bromo-[$^2H_3$] toluene.

The tosylate (2.39g.) in anhydrous ether (25ml.) was added to lithium aluminium deuteride (310mg.) in ether (25ml.) and the mixture stirred for 2hrs. at room temperature. Water (2ml.) and aqueous 10% sulphuric acid (20ml.) were added, the ethereal solution separated, washed with water and dried. Distillation gave the title compound. Yield 0.75g.(61%); b.p.181°/760mm.; n_D^{20} 1.5548; ν_{max}(l.f.) 2250, 1598, 1570, and 750 $cm.^{-1}$; no methyl protons shown in the n.m.r. spectrum.

1-o-[$^2H_3$-Methyl]-phenyl anthraquinone.

This was prepared according to the procedure for 1-phenyl anthraquinone from 2-bromo-[$^2H_3$]-toluene (700mg.). Yield 0.182g.(15% overall); m.p.149°(ethanol), (lit.[43] m.p.149°); ν_{max}($CHCl_3$) 1670 $cm.^{-1}$; mass spectrum, D_3,99.8%, D_2,0.2%.

Reduction of 1-phenyl anthraquinone.

1-Phenyl anthraquinone (1.0g.), granulated tin (0.7g.) and glacial acetic acid (5.3ml.) were heated to boiling and concentrated hydrochloric acid (2.0ml.) added in 0.1ml. portions over 2hrs. to the refluxing mixture. The solution was filtered, water added (1ml.) and the mixture cooled in ice. The precipitated pale-yellow solid was filtered off, washed well with water and dried in vacuo over phosphoric oxide. Yield quantitative, t.l.c.(benzene/silica) showed only one spot although n.m.r. indicated the presence of a 1:1 mixture of the anthra-9 and -10-ones, A and B respectively. Fractional crystallisation from methanol gave 1-phenyl anthra-9-one (A) as the least soluble isomer, m.p.190-191.5°; ν_{max} (mull) 1650 $cm.^{-1}$; n.m.r.($CDCl_3$) τ 5.61(s, 2H, methylene), 2.91-2.38(m, 11H, aromatics), 2.00-1.72(m, 1H, low field proton), λ_{max}($CHCl_3$) 254,262(inf),267,310, (log ϵ , 4.17,4.19,4.21, 3.68). (Found: C,88.72%, H,5.13%, $C_{20}H_{14}O$ requires: C,88.86%, H,5.22%.)

The more soluble isomer, 1-phenyl anthra-10-one (B), was isolated from the mother liquors and recrystallised from

ethyl acetate, m.p.139°; ν_{max}(mull) 1650 cm,$^{-1}$; n.m.r.($CDCl_3$) τ 5.87(s, 2H, methylene), 2.84-2.40(m, 10H, aromatics.), 1.80-1.50(m, 2H, low field protons); λ_{max}($CHCl_3$) 258,269, 310mμ (log ε , 4.23,4.25,3.61). (Found: C,88.70%, H,5.12%, $C_{20}H_{14}O$ requires: C,88.86%, H,5.22%.)

An identical mixture was obtained on alkaline sodium dithionite reduction.

β-Phenyl propionic acid.[122]

A suspension of freshly crystallised cinnamic acid (83.5g. m.p.133°) in ethanol (200ml) was hydrogenated in the presence of Adam's catalyst (0.90g.) until the uptake of hydrogen ceased. Filtration and evaporation then afforded the title compound which was recrystallised from petroleum ether(60-80°). Yield 79.5g.(93%); m.p.53°, (lit. m.p.48.5°).

1-Indanone.[122,123]

90% Syrupy phosphoric acid (103ml.) was added to phosphoric oxide (174g.) and the mixture homogenised on a steam bath for 2hrs. To this was introduced β-phenyl propionic acid (34.5g.) and the mixture rapidly stirred at 80°C for 80mins. after which it was quenched by pouring into ice-cold water and ether extracted. The extracts were washed with water, 10% aqueous sodium bicarbonate, water and dried(Na_2SO_4). Distillation gave the product as a white crystalline solid which was recrystallised from ligroin (40-60°). Yield 18.3g. (60%); m.p.41-42°, (lit. m.p.42°).

2-Benzal-1-indanone.[124]

1-Indanone (14.3g.) was dissolved in benzaldehyde (11.4g.) and 4% ethanolic potassium hydroxide (16ml.) slowly added to the stirred solution at 0°C. After 30mins. the mixture solidified although it was maintained at 0°C until the alkali addition was complete. The solid was filtered off, washed with water and dried in vacuo. Purification was effected by washing with hot aqueous methanol (100ml. of 50%) and recrystallisation from ethanol. Yield 22.1g.(94%); m.p.110°, (lit. m.p.109-111°).

1,2,3,4,-Tetrahydro-3-oxo-1-phenyl fluorene.[125]

2-Benzylidine indan-1-one (21g.), ethylacetoacetate (12.6g.) and ethanol (105ml.) containing sodium ethoxide (from sodium (2.1g.)) were refluxed for 3hrs. and poured into ice-cold water (420ml.) containing acetic acid (6.3ml.). The product was extracted with ether, and the extracts washed with 10% aqueous sodium bicarbonate and water and dried (Na_2SO_4). Evaporation gave a yellow solid from which the product was isolated by extraction with ligroin (60-80°), and recrystallised from the same. Yield 17.0g.(54%); m.p.130°, (lit.[125] m.p.133°). This ester (10.3g.) was boiled for 40mins under reflux with acetic acid (41ml.), water (10ml.) and concentrated sulphuric acid (20.6ml.) and poured into cold water. Ether extraction followed by washing of the extracts with aqueous sodium bicarbonate and water gave the title compound on evaporation.

Yield 4.56g.(57%); m.p.115°(ligroin b.p.60-80°), (lit. m.p. 117-118°).

1,2,3,9a-Tetrahydro-3-hydroxy-1-phenyl fluorene.[125]

This compound was prepared by lithium aluminium hydride reduction of the above compound (4.05g.) according to the method of Anderson et al.[115] Yield 3.36g.(82%); m.p.100-101°, (lit. m.p. 100-101°).

1-Phenyl fluorene.[125]

Aromatisation of the above alcohol (2.4g.) again by the method of Anderson et al.[125] gave the title compound. Yield 1.68g.(76%); m.p.48°, (lit. m.p.48°).

1-Phenyl fluorenone.

1-Phenyl fluorene (0.5g.) was dissolved in boiling acetic acid (1.5ml.) and a solution of chromium trioxide (0.5g.) in acetic acid (2ml.) was added. After refluxing for 1hr. the mixture was poured into ice and the product extracted with chloroform. The chloroform layer was washed with water, dried ($MgSO_4$) and evaporated. Chromatography on silica gel eluting with benzene gave the fluorenone as the second fraction and was recrystallised from ethanol. Yield 0.25g.(47%); m.p.120°, (lit.[125] m.p.120°); ν_{max}($CHCl_3$) 1704 $cm.^{-1}$

4-Phenyl benzophenone-2'-carboxylic acid.

This was prepared by alkylation of biphenyl (7.5g.) with phthalic anhydride (17.5g.) according to the method of Scholl and Neovius[126]. Yield 10.8g.(74%); m.p.230-232°(glacial

acetic acid), (lit.[126] m.p.225-226°); ν_{max}(mull) 2690,2570, 1692,1673 and 1577 cm.$^{-1}$

2-Phenyl anthraquinone.

4-Phenyl benzophenone -2'-carboxylic acid (2g.) was cyclised with zinc chloride (10g.) by the procedure of Scholl and Neovius.[126] The product was purified by chromatography on silica eluting with chloroform whereby the first yellow fraction was collected and recrystallised from methanol in pale-yellow needles. Yield 0.75g. (40%); m.p.160-161°, (lit. 160-161°); ν_{max}(mull) 1673 and 1590 cm.$^{-1}$; λ_{max}($CHCl_3$) 252, 275, and 340mμ (log ϵ , 4.39, 4.59 and 3.80).

4-Chloro diphenyl.

Prepared according to Organic Syntheses [127] from p-chloroaniline (32g. 0.25mole). Yield 13.6g.(29%); m.p.76°, (lit.[128] m.p.76°).

4"-Chloro-4'-phenyl-2-benzoyl benzoic acid.

This was made by the method of Groggins[128] from 4-chloro diphenyl (5g.)and phthalic anhydride (3.93g.). Yield 8.26g. (93%); m.p.251-2°(glacial acetic acid), (lit. m.p.251°); ν_{max}(mull) 1688, and 1665 cm.$^{-1}$

2-(p-Chlorophenyl) anthraquinone.

The above keto acid (2.0g.) was cyclised with concentrated sulphuric acid as described by Groggins.[128] Yield 1.70g.(90%); Recrystallised from toluene in pale-yellow needles, m.p.208-9°, (lit. m.p.210°); ν_{max}(mull) 1668 cm.$^{-1}$; λ_{max}($CHCl_3$) 247,

275, and 344mμ, (log ε , 4.40,4.57, and 3.82).

4"-Bromo-4'-phenyl-2-benzoyl benzoic acid.

This was prepared from 4-bromodiphenyl (5g.) in the same manner as for the chloro compound. Yield 7.35g.(90%); m.p.237-238°(glacial acetic acid); ν_{max}(mull) 3500-2500, 2680,2580,1686,1666, and 1603 cm.$^{-1}$. (Found: C,63.01%, H,3.62%, Br,20.72%, $C_{20}H_{13}BrO_3$ requires: C,63.03%, H,3.44%, Br,20.96%).

2-(p-Bromophenyl)anthraquinone.

The above keto acid (1.5g.) was treated with concentrated sulphuric acid and heated to 125°C on a Wood's metal bath for 2hrs. The deep red solution was poured into water (75ml.) and the yellow solid formed was boiled for 1hr. with 2N sodium hydroxide to remove sulphonic acids, and then washed free of alkali. Recrystallisation from toluene gave yellow crystals. Yield 1.24g.(87%); m.p.224-5°; ν_{max}(mull) 1670,1590,875,838, and 830 cm.$^{-1}$; $\lambda_{max}(CHCl_3)$ 245,275, and 345mμ(log ε , 4.43, 4.58, and 3.85). (Found: C,66.18%, H,3.08%, Br,21.74%, $C_{20}H_{11}BrO_2$ requires: C,66.12%, H,3.05%, Br,22.00%).

4"-Methoxy-4'-phenyl-2-benzoyl benzoic acid.

This was prepared as for the chloro derivative from 4-methoxy diphenyl (5g.) and phthalic anhydride (4.02g.). Yield 0.26g. This reaction could not be repeated. m.p.219-222°; ν_{max}(mull) 1689,1669, cm.$^{-1}$; (Found: C,75.51%, H,5.04%, $C_{21}H_{16}O_4$ requires: C,75.86%, H,4.85%.)

Attempted cyclisation of the above keto acid.

Concentrated sulphuric acid treatment of this acid gave only sulphonated products. Cyclisation with alternative reagents such as ferric or zinc chlorides was not attempted.

Pyrolysis of 1-phenyl anthraquinone.

The quinone (1.5g.) was pyrolysed by slowly distilling through a silica tube 9" long and maintained at 700°C under a pressure of 0.8mm. The pyrolysate was collected in a cold-trap at -78°C as a brown oily solid. Extraction with chloroform followed by chromatography on silica eluting with benzene gave 1-phenyl fluorenone, R_f,0.42, as a yellow solid (50mg.). Recrystallised from ethanol, m.p.120°, (lit.[125] m.p. 120°); $\nu_{max}(CHCl_3)$ 1705 $cm.^{-1}$. The ratio $[M-1]^+/M^+$ of 1.69 was consistent with that of an authentic sample and not the alternative 4-phenyl fluorenone isomer which would not be expected to lose an hydrogen atom from the M^+. 1-Phenyl anthraquinone was also isolated (1.3g.), but the hydrocarbon fractions issuing from the column were not analysed.

5 , 2 1,8-Diaryl polyenes.

α-Phenyl cinnamic acid.[129]

Benzaldehyde (10.6g.), phenyl acetic acid (13.7g.), anhydrous triethylamine (1 ml.) and freshly distilled acetic anhydride (20ml.) were reacted according to Organic Syntheses[129] to afford the title compound. Yield 12.7g.(58%); m.p.172-174° (aqueous ethanol), (lit. m.p.172-173°).

cis-Stilbene.[130]

α-Phenyl cinnamic acid (5.75g.) was decaboxylated with copper chromite (0.5g.) in quinoline (35ml.) at 212-215°C for 1.25hrs. until evolution of carbon dioxide ceased. The dark mixture was worked up according to the procedure of Buckles and Wheeler.[130] Yield 2.3g.(50%); b.p.95-97°/1mm.; n_D^{22} 1.6210. (lit. b.p.95-97°/1mm.; n_D^{20} 1.6212).

1,8-Diphenyl octatetraene[61] - General method.

A mixture of redistilled cinnamaldehyde (26.4g. 0.2mole), succinic acid (11.8g. 0.1mole), lead oxide (22.3g. 0.1mole) and acetic anhydride (28.5ml.) was heated to 140°C for 10mins. with frequent shaking and then refluxed for 3hrs. The solution was cooled to 40°C and the yellow, crystalline tetraene filtered off and washed successively with acetic anhydride/acetic acid, ethanol and water. After drying in vacuo the product was recrystallised from chloroform. Yield 4.0g.(16%); m.p.232°, (lit. m.p.232°).

Dichloromuconic acid.[131,132]

Mucic acid (41.7g.) and phosphorous pentachloride (250g.) were ground together and heated to 80°C for 20mins. The bright coloured reaction mixture was then heated at 100°C so that simultaneous distillation of phosphorous oxychloride ensued as it was formed. Final traces of the oxychloride were removed in vacuo and the product poured into water (200ml.) with vigorous stirring. After cooling to -10°C the solid was filtered off and dried in vacuo. Yield 17g.(40%); Recrystallised from acetone to afford a white compound which decomposes at 295°; ν_{max}(mull) 3080,2660,1689, and 1575 $cm.^{-1}$

Dihydromuconic acid.[61,132]

Dichloromuconic acid (8g.) was dissolved in 5% aqueous potassium hydroxide (65ml.) and cooled to 0°C in ice-salt. Small portions of 5% sodium amalgam (138g.) were then added over a period of 6-7hrs. with vigorous stirring, the temperature being kept below 3°C. The solution was neutrallised with 12N hydrochloric acid, filtered to remove mercury and cooled to -10°C. Filtration gave the desired acid which was recrystallised from water. Yield 4.4g.(82%); m.p.196-198°, (lit. m.p.195°).

1,10-Diphenyl decapentaene.[61]

This was prepared as for the octatetraene from β-dihydromuconic acid (2g.) and cinnamaldehyde (7.5g.). Recrystallised from chloroform. Yield 0.28g.(7%); m.p. 253-4° (lit. m.p.253°).

5-Phenyl penta-2,3-dienal.[61]

Aldol condensation of cinnamaldehyde (75g.) and 50% aqueous acetaldehyde (75g.) gave the dienal as a yellow oil after ether extraction and distillation. Yield 12.3g.(15%), b.p.124-126°/1.5mm.; (lit. b.p.124°/3mm.), ν_{max}(l.f.) 1680 cm.$^{-1}$

1,12-Diphenyl dodecahexane.[61]

A mixture of the above aldehyde (4g.), succinic acid (1.56g.), litharge (2.94g.) and acetic anhydride (3.76ml.) were treated by the method utilised for the octatetraene to produce the title compound. Recrystallised from chloroform in orange crystals. Yield 1.01g.(26%); m.p.272-274°, (lit. m.p. 267°).

1,14-Diphenyl tetradecaheptaene.[61]

Dihydromuconic acid (1.38g.) and 5-phenyl pentadienal (3.03g.) were condensed with lead oxide (2.14g.) and acetic anhydride (6ml.). The brick-red solid was recrystallised from chloroform. Yield 0.225g.(7.6%); m.p.279°, (lit. m.p.279°).

7-Phenyl heptatrienal.[61]

This was prepared according to the procedure of Kuhn and Winterstein[61] by Aldol condensation of 5-phenyl pentadienal (4g.) and acetaldehyde (2g.). The product was isolated without distillation as a red oil. Yield 1.69g.(39%).

1,16-Diphenyl hexadecaoctaene.[61]

The above aldehyde (1.69g.) and succinic acid (0.56g.)

were condensed as for the octatetraene above. Yield 0.16g. (9.5%); decomposes 285°, (lit. decomposes 285°).

2-Methoxy benzyl cyanide.

2-Methoxy benzyl alcohol (13.8g. 0.1mole) and 12N hydrochloric acid (24.8ml.) were vigorously stirred for 20mins. after which time the mixture was transferred to a separating funnel and the lower layer (the chloride) was taken off and dried ($CaCl_2$, 2g.) for 30mins. A solution of the unstable, crude chloride in acetone (50ml.) was added to finely powdered sodium cyanide (7.36g. 0.15mole) and the heterogeneous mixture heated under reflux with vigorous stirring in the presence of sodium iodide (1.0g.) for 20hrs. The mixture was cooled and filtered and the solid washed with dry acetone, after which the combined filtrates were evaporated to a pale yellow oil. On dissolution of the oil in benzene (30ml.) followed by washing with hot water (3x10ml.), the dried benzene phase afforded a white solid on evaporation. Yield 14.7g. (50%); m.p.72-73°(ligroin b.p.60-80°), (lit.[134] m.p.68°); ν_{max}(mull) 2290, 1605, and 1599 $cm.^{-1}$

2-Anisyl acetic acid.

Hydrolysis of the above nitrile (6.8g.) with 25% aqueous potassium hydroxide (50ml.) afforded the acid after 20hrs. of refluxing. The colourless product was recrystallised from water. Yield 3.84g.(45%); m.p.123-124°, (lit.[134] m.p.124°).

α-(2'-Anisyl)-2-methoxy cinnamic acid.

2-Methoxy benzaldehyde (0.82g.), 2-methoxyphenyl acetic acid (1g.), anhydrous triethylamine(0.6ml.) and acetic anhydride (1.2ml.) were refluxed under anhydrous conditions for 19hrs. and steam distilled until the distillate was no longer cloudy. After cooling the yellow solid remaining in the still pot was filtered off and dissolved in ethanol (25ml.). Addition of the aqueous mother liquors and charcoalisation afforded the title compound on acidification with 6N hydrochloric acid. A small sample was recrystallised from aqueous ethanol. Yield 1.23g.(72%); m.p.199° and 213-214° (cis- and trans- forms), ν_{max}(mull) 3300-2400,2620,1677, 1610,1290,1260,765, and 758 $cm.^{-1}$; n.m.r.($CDCl_3$+DMSO) τ 6.30 (s, 3H, methoxyl), 6.19(s, 3H, methoxyl), 3.68-2.46(m, 9H, aromatics and vinylic proton), 1.93(s, 1H, acid proton). (Found: C,71.69%, H,5.69%, $C_{17}H_{16}O_4$ requires: C,71.81%, H,5.67%).

2,2'-Dimethoxy stilbene. (trans-form).

To a solution of the above acid (0.70g.) in quinoline (5ml.) was added copper chromite (0.07g.) and the mixture was heated to 210-220°C in an ethyl benzoate constant boiling bath until effervescence ceased (1.25hrs.). The mixture was cooled and acidified with hydrochloric acid to remove quinoline, after which the dark solution was extracted with ether. The extracts were washed with saturated aqueous sodium carbonate and water and dried ($MgSO_4$). Evaporation

and charcoalisation from petroleum ether (b.p.60-80°) gave a white crystalline solid which was recrystallised from ethanol. Yield 0.23g.(39%); m.p.82-83°; $\nu_{max}(CCl_4)$ 3050, 3000,2930,2810,1601,1582,1255, and 945 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 6.22(s, 6H, methoxyls), 3.50-2.30(m, 10H); λ_{max}(EtOH) 275.4, and 311mμ (log ϵ, 3.99, and 3.99). (Found: C,79.93%, H,6.73%. $C_{16}H_{16}O_2$ requires: C,79.99%, H,6.71%.)

2,4,6-[$^2H_3$]-Benzonitrile.[8]

2,4,6-[$^2H_3$]-Aniline (5.13g., prepared as in section 5,1) in concentrated hydrochloric acid (14.1ml.) and water (14.1ml.) was diazotised below 5°C with sodium nitrite (4.1g.) in water (19.3ml.). After filtration the diazonium solution was added to cuprous cyanide solution (prepared from copper sulphate (16.7g.) according to Vogel[135]) at 60-70°C in small amounts with stirring. When the addition was complete the reaction was completed by heating on a steam bath for 20mins. and the product steam distilled until no more yellow oil discharged. The nitrile was extracted from the distillate with ether and the extracts washed with 2N sodium hydroxide (10ml.) - to remove phenol- then with 2N sulphuric acid - to remove isocyanide- and finally with water. After drying ($MgSO_4$), evaporation gave the desired product as a yellow oil. Yield 3.74g.(66%); b.p.188-191°/760mm.; ν_{max}(l.f.) 2250, 1578, and 1388 cm.$^{-1}$; mass spectrum gives, D_3,83.2%, D_2,16.9%, D_1,0%.

2,4,6-[$^2H_3$]-Benzaldehyde.

Anhydrous stannous chloride[135](13.1g.) was added to dry ether (50ml.) and saturated with dry hydrogen chloride for 2hrs. when two layers formed. A solution of 2,4,6-[$^2H_3$]-benzonitrile (3.6g.) in ether (100ml.) was added and the mixture vigorously stirred for 24hrs. Water (100ml.) was introduced and sodium bicarbonate added until the solution was neutral to congo red. Steam distillation and ether extraction of the distillate afforded the aldehyde as a yellow oil. Yield 2.18g.(59%); ν_{max}(l.f.) 1696 cm.$^{-1}$

α-Phenyl-2,4,6-[$^2H_3$]-cinnamic acid.

This was prepared as for the unlabelled compound from the above deuteriated aldehyde (1.7g.). Yield 1.4g.(41%).

2,4,6-[$^2H_3$]-Stilbene.

Decarboxylation of the above acid (1.4g.) in the manner described for the undeuteriated derivative gave the title compound. Yield 0.27g.(24%); b.p.100-108°/0.5mm.; n.m.r.($CDCl_3$) τ 3.49(s, 2H, vinylics), 2.88(s, 7.5H, aromatics), mass spectrum, D_3,82.0%, D_2,16.6%, D_1,1.5%, D_0,0%.

β-Methyl cinnamyl alcohol.

A suspension of lithium aluminium hydride (1.1g.) in dry ether (250ml.) was slowly added to a stirred solution of ethyl β-methyl cinnamate (10.4g., kindly supplied by Dr.D.J.Blythin) in ether (30ml.) at -10°C over 2.5hrs., and then allowed to stand at room temperature overnight. Water

(50ml.) and 10% aqueous sulphuric acid (270ml.) were added and the aqueous phase ether extracted. The combined extracts were washed with saturated aqueous sodium bicarbonate and dried (Na_2SO_4). Evaporation and distillation gave the desired alcohol. Yield 5.37g.(68%); b.p.97°/1.5mm.; n_D^{25} 1.5654; (lit.[136] b.p.127-128.5°/6mm.; n_D^{25} 1.5654.)

β-Methyl cinnamaldehyde.

A solution of β-methyl cinnamyl alcohol (3g.) in dry carbon tetrachloride (150ml.) was stirred for 3hrs. with activated manganese dioxide (30g.) at ambient temperature. Filtration and evaporation afforded the product as a pale yellow oil. Yield 1.55g.(52%); b.p.89-94°/1.5mm.; n_D^{24} 1.5824, (lit.[136] b.p.117-119°/6mm.; n_D^{23} 1.5876.) n.m.r.(CCl_4) showed this to be a mixture of cis- (25%) and trans- (75%) isomers.

trans. τ 7.51(d, J=1.5Hz, 3H, methyl), 3.75(d.q. J=1.5 and 7.5Hz, 1H, vinylic), 2.92-2.39(m, 5H, aromatics), -0.05(d, J=7.5Hz, 1H, CHO).

cis. τ 7.75(d, J=1.5Hz, 3H, methyl), 4.00(d.q. J=1.5 and 7.5Hz, 1H, vinylic), 2.92-2.39(m, 5H, aromatics), 0.62(d, J=7.5Hz, 1H, CHO).

1,8-Dimethyl-1,8-diphenyl octatetraene.

A mixture of β-methyl cinnamaldehyde (1.03g.) and succinic acid (0.356g.) were condensed as for the unsubstituted 1,8-diphenyl octatetraene above. The product was recrystallised from acetone in yellow plates. Yield 0.10g.(10%); m.p.141-143°;

$\nu_{max}(CCl_4)$ 3030,2920,2870,1620,1600,1500,1450,1385,995 and 705 cm.$^{-1}$; λ_{max}(EtOH) 373.0mμ (log ε, 4.83); n.m.r.($CDCl_3$) HA-100, τ 7.84(s, 6H, methyls), 3.50,3.41(s, 6H, vinylics), 2.86-2.48(m, 10H, aromatics). (Found: C,92.21%, H,7.51%, $C_{22}H_{22}$ requires: C,92.23%, H,7.74%).

1,1,8,8-Tetraphenyl octatetraene.

This was prepared according to the general method (p.189) from 3,3-diphenyl prop-2-en-1-al (1.12g., supplied by Dr.T.C. Smale). Recrystallised from ligroin (b.p.60-80°) in pale yellow needles. Yield 0.64g.(65%); m.p. 198-199°, (lit.[137] m.p.198-199°), n.m.r.($CDCl_3$) HA-100, τ 3.71-3.58(m, 6H, vinylics), 2.98-2.50(m, 20H).

Ethyl 3-hydroxy-3-phenyl-pent-2-enoate.

This was prepared by Reformatski reaction on propiophenone (31.5g.) according to the method of Barltrop et al.[63] yield 35.7g.(69%); b.p.86-94°/0.3mm., (lit. b.p.95-105°/0.1mm.) ν_{max}(l.f.) 3490,2960,2920,1708,1340,1200,1180,770 and 708 cm.$^{-1}$ n.m.r.(CCl_4) τ 9.26(t, J=7Hz, 3H, chain methyl), 8.94(t, J=7Hz, 3H, ester CH_3), 8.26(q, J=7Hz, 2H, chain CH_2), 7.24(d, J=2.5Hz, 2H, CH_2 next to ester), 6.05(q, J=7Hz, 2H, ester CH_2), 5.98(broad s, 1H, hydroxyl), 2.98-2.60(m, 5H, aromatics).

Ethyl β-ethyl cinnamate.

Dehydration of the above ester both with phosphorous pentoxide and phosphorous oxychloride gave a mixture of ethyl β-ethyl cinnamate (15%) and ethyl 3-phenyl-pent-2-enoate (85%),

as shown by n.m.r. which exhibits a vinylic methyl group along with a vinylic ethyl group. No attempt at separation was made.

α-Methyl cinnamaldehyde.

A mixture of freshly distilled benzaldehyde (12.5g.), potassium hydroxide (0.75g.) and dry ethanol (17g.) was treated over 5hrs. at 10°C with propionaldehyde (5g.). The yellow product was poured into water (100ml.), acidified with glacial acetic acid and ether extracted after saturating with sodium chloride. The extracts were washed with saturated aqueous sodium carbonate and water and dried (Na_2SO_4/K_2CO_3). Evaporation and distillation afforded the aldehyde as a pale yellow oil. Yield 8.8g.(70%); b.p.142-145°/27mm.; ν_{max}(l.f.) 1678,1624,760 and 702 $cm.^{-1}$; n.m.r.(CCl_4) τ 7.98(d, allylic splitting, 3H, methyl), 2.92-2.09(m, 6H, vinylic + aromatics), 0.45(s, 1H, CHO).

2,7-Dimethyl-1,8-diphenyl octatetraene.

This was prepared from α-*m*-ethyl cinnamaldehyde (2.5g., 0.5g. excess) according to the general procedure (p.189). The crude product was purified by chromatography on silica eluting with chloroform followed by recrystallisation from acetone. Yield 0.2g.(10%); m.p.173-4°, (lit.[138] m.p.174°).

α-Ethyl cinnamaldehyde.

Freshly distilled benzaldehyde (14.4g.), butyraldehyde (9.9g.) and 60% aqueous ethanol (100ml) were treated with a

solution of sodium hydroxide (0.85g.) in water (8.5ml.) over 24hrs. with stirring. After working up in the same manner as given for the α-methyl homologue the product was isolated as a yellow oil. Yield 6.1g.(28%); b.p.92-100°/1mm.; n_D^{24} 1.5895, ν_{max}(l.f.) 1680,1625,760 and 705 cm.$^{-1}$; n.m.r.(CCl_4) τ 8.89(t, J=7.5Hz, 3H, CH_3), 7.48(q, J=7.5Hz, 2H, CH_2), 3.00-2.45(m, 6H, vinylic + aromatics), 0.51(s, 1H, CHO).

2,7-Diethyl-1,8-diphenyl octatetraene.

Condensation of α-ethyl cinnamaldehyde (2g.) with succinic acid (0.74g.) according to the general procedure (p.189) afforded the title compound as large yellow plates (from acetone). Yield 0.1g.(5%); m.p.155-157°; ν_{max}(mull) 1598, and 995 cm.$^{-1}$; (Found: C,91.62%, H,8.19%, $C_{24}H_{26}$ requires: C,91.66%, H,8.34%).

1-p-Methyl phenylallyl alcohol.

p-Bromotoluene (17.1g., 0.1mole) was added to a stirred suspension of dry magnesium (2.6g., 0.11mole) and ethyl bromide (0.2ml.) in anhydrous ether (50ml.) at a rate such that the ether gently refluxed. When the reaction was complete, the solution was cooled in ice-salt and freshly distilled acrolein (6.72g., 0.12mole) in ether (20ml.) was introduced over 1hr. Stirring was continued at room temperature for 2hrs. and saturated ammonium chloride (150ml.) added. The ethereal layer was separated, washed with water, dried (K_2CO_3) and distilled. Yield 8.15g.(55%); b.p.84-90°/2mm.; n_D^{18} 1.5370;

ν_{max}(l.f.) 3400,1645,1618, and 830 cm.$^{-1}$;

The substituted 1-phenylallyl alcohols shown in Table 21 were prepared by the same method. The n.m.r. spectra are similar to that shown in Figure 1.

Table 21.

Derivatives of 1-phenylallyl alcohols.

substituent	% yield	n_D^*	b.p.
o-Me	52%	1.5410(23)	74-76°/0.8mm.
m-Me	57%	1.5380(20)	80-83°/1.0mm.
m-OMe	53%	1.5445(21)	88-92°/0.4mm.
p-OMe	55%	1.5470(21)	96-98°/0.4mm.
m-Cl	72%	1.5540(22)	80°/0.6mm.
p-Cl	67%	1.5556(18)	86-88°/0.4mm.
m-Br	38%	1.5798(20)	104-108°/1.3mm.
p-Br	46%	1.5752(21)	106-110°/1.0mm.
m-F	72%	1.5166(23)	66-68°/0.6mm.
p-F	56%	1.5152(23)	73-74°/2.0mm.

* Temperature in parenthesis.

p-Chlorocinnamyl alcohol. - Method (A).

1-p-Chlorophenylallyl alcohol (6.8g.) in 60% aqueous acetone (500ml.) was made 0.2N with concentrated hydrochloric acid and refluxed for 3days. The product was evaporated to small bulk under reduced pressure and ether extracted. On drying (Na_2SO_4) and evaporation the ether phase afforded a

white crystalline solid which was recrystallised from ligroin (b.p.40-60°). Yield 5.3g.(78%), m.p.57°, (lit.[139] m.p.57°); ν_{max}(mull) 3320,1650,1590,1500 and 855 cm.$^{-1}$

o-Methyl cinnamyl alcohol. - Method (B).

1-o-Methyl phenylallyl alcohol (5.5g.) and acetic anhydride (5.6ml.) were refluxed for 6hrs. and distilled. The cinnamyl acetate (b.p.106-108°/1.0mm.) was refluxed for 3hrs. with 5% ethanolic potassium hydroxide (115ml.), neutrallised with concentrated hydrochloric acid and evaporated to small bulk. After pouring into water (200ml.) the cinnamyl alcohol was isolated by ether extraction followed by distillation. Yield 5.5g.(72%); b.p.102-104°/0.9mm.; n_D^{22} 1.5686 ; ν_{max}(l.f.) 3340, 979, and 759 cm.$^{-1}$

Table 22 shows the method used and the yields obtained in the preparation of other cinnamyl alcohols. The n.m.r. spectra of all the products were determined and are characterised by Figure 1 (p.83).

o-Nitrocinnamaldehyde.

This was prepared by nitration of cinnamaldehyde (28g.) by the method described in Organic Syntheses.[140] Yield 14g. (38%); m.p.127-128.5°, (lit. 126-127°).

Table 22.

Derivatives of cinnamyl alcohols.

Substituent	yield	n_D^*	m.p./b.p.	Method of preparation	Lit.[139] m.p.
m-Cl	100%	1.5942(19)	102-104°/0.3mm	A	
p-Br	100%	-	m.p.67°	A	67°
m-Br	100%			A	
p-F	70%	-	m.p.57-58°	A	57°
m-F	90%	1.5498(20)	95-97°/0.7mm.	A	
p-Me	60%	-	m.p.50-51°	B	50-1°
m-Me	70%		110-120°/1.2mm	B	
p-OMe	70%	-	m.p.80°	B	80°
m-OMe	69%	1.5790(18)	115°/0.3mm.	B	

* Temperature in parentheses.

p-Fluoro cinnamaldehyde.

p-Fluoro cinnamyl alcohol.(3.18g.) was dissolved in dry carbon tetrachloride (160ml) and stirred in the presence of acivated manganese dioxide for 2hrs. at ambient temperature. The solution was filtered and the filtrate evaporated under reduced pressure to a pale yellow crystalline solid which melted below room temperature. Yield 2.51g.(80%); ν_{max}(l.f.) 1680,1628,1603,1242,1135,985, and 830 $cm.^{-1}$; n.m.r. ($CDCl_3$) τ 3.22(d.d, J=16Hz, 7.2Hz, 1H, proton adjacent to CO), 2.27

(d, J=16Hz, 1H, benzylic proton), 3.02-2.09(m, 4H, aromatics), 0.30(d, J=7.2Hz, 1H, CHO). Semicarbazone, m.p.210-212°(ethanol). (Found: C,58.08%, H,4.85%, F,9.23%, N,20.09%, $C_{10}H_{10}FN_3O$ requires: C,57.98%, H,4.86%, F,9.17%, N,20.29%).

m-Fluoro cinnamaldehyde.

This was prepared from m-fluoro cinnamyl alcohol (5.7g.) as above in quantitative yield, b.p.83-84°/0.5mm.; n_D^{20} 1.5907; ν_{max}(l.f.) 1678,1628,1130,985 and 795 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 3.28(d,d, J=16 and 7.2Hz, 1H, proton adjacent to CO), 2.50 (d, J=16Hz, 1H, benzylic proton), 2.98-2.41(m, 4H, aromatics), 0.23(d, J=7.2Hz, 1H, CHO). Semicarbazone, m.p.204-205°. (Found: C,57.82%, H,5.07%, F,9.06%, N,20.00%, $C_{10}H_{10}FN_3O$ requires: C,57.98%, H,4.86%, F,9.17%, N,20.29%).

m-Bromo cinnamaldehyde.

This was prepared as for the p-fluoro derivative from m-bromo cinnamyl alcohol (2.7g.) and was isolated in quantitative yield. ν_{max}(l.f.) 1680,1625,1130,980, 788, and 682 cm.$^{-1}$; n.m.r.($CDCl_3$)τ3.26(d.d, J=15.5Hz, and 7Hz, 1H), 2.52(d, J=15.5Hz, 1H), 2.68-2.18(m, 4H,), 0.23(d, J=7Hz, 1H). Semicarbazone, m.p. 210-212° (ethanol). (Found: C,45.02%, H,3.84%, Br,29.87%, N,15.67%, $C_{10}H_{10}BrN_3O$ requires: C,44.79%, H,3.76%, Br,29.81%, N,15.67%.)

All other substituted cinnamaldehydes were prepared by the same method and are listed in Table 23. For the less soluble alcohols chloroform was added until dissolution was complete.

Table 23.

Table of substituted cinnamaldehydes.

Substituent	Yield	b.p.	m.p.	Literature values
o-Me	100%	94°/0.9mm.	-	91°/0.4mm. [143]
m-Me	100%	96°/0.7mm.	-	
p-Me	76%	-	42°	41.5° [141]
p-Br	100%	-	80-81°	81° [142]
m-OMe	100%	110°/0,5mm.	37°	37° [146]
p-OMe	100%	-	59°	59° [141]
m-Cl	100%	103-4°/0.2mm.	39°	39° [145]
p-Cl	100%	-	61°	62-62.5° [144]

1,8-Diaryl octatetraenes.

These were all prepared by the general procedure on p.189 and their yields and physical properties are listed in Table 24.

Table 24.

Substituted i,8-diaryl octateraenes.

substituent	yield	m.p.	$\lambda_{max}^{m}\mu(CHCl_3)$
1. o-Me	14%	151-2°	368*(4.86), 371(4.90), 400*(4.70)
2. m-Me	10%	180°	363(4.85), 381(5.00), 403(4.92).
3. p-Me	14%	231-2°	358(4.78), 373(4.88), 403(4.87).
4. m-OMe	6%	147-9°	
5. p-OMe	20%	259-260°	lit.[147] m.p.266-7°

Table 24 (continued).

substituent	yield	m.p.	$\lambda_{max}^{m}\mu(CHCl_3)$
6. m-Cl	6%	198-9°	348*(4.54), 363(4.83), 381(4.99), 403(4.89).
7. p-Cl	8.5%	237-238.5°	350*(4.59), 367(4.84), 385(4.99), 408(4.89).
8. p-Br	9%	250°	370(4.83), 388(4.94), 410(4.90).
9. m-Br	6%	205-206.5°	346*(4.56), 364(4.84), 382(5.00), 404(4.90).
10. p-F	7%	222-223°	359(4.81), 376(4.93), 398(4.88).
11. m-F	4%	179-181°	360(4.82), 379(4.99), 401(4.90).

* Point of inflection.

Analyses.

1. Found: C,92.07%, H,7.55%, $C_{22}H_{22}$ requires: C,92.26%, H,7.74%.

2. Found: C,92.11%, H,7.69%, $C_{22}H_{22}$ requires: C,92.26%, H,7.74%.

3. Found: C,92.38%, H,7.57%, $C_{22}H_{22}$ requires: C,92.26%, H,7.74%.

4. Found: C,82.86%, H,7.00%, $C_{22}H_{22}O_2$ requires: C,82.96%, H,6.96%.

5. Found: C,82.83%, H,6.93%, $C_{22}H_{22}O_2$ requires: C,82.96%, H,6.96%.

6. Found: C,73.33%, H,5.11%, Cl,21.76%, $C_{20}H_{16}Cl_2$ requires: C,73.40%, H,4.93%, Cl,21.67%.

7. Found: C,73.09%, H,5.19%, Cl,21.71%, $C_{20}H_{16}Cl_2$ requires: C,73.40%, H,4.93%, Cl,21.67%.

8. Found: C,57.64%, H,3.71%, Br,38.21%, $C_{20}H_{16}Br_2$ requires: C,57.72%, H,3.88%, Br,38.40%.

9. Found: C,57.82%, H,4.08%, $C_{20}H_{16}Br_2$ requires: C,57.72%, H,3.88%,

10. Found: C,81.64%, H,5.39%, F,12.81%, $C_{20}H_{16}F_2$ requires: C,81.62%, H,5.48%, F,12.91%.

11. Found: C,81.85%, H,5.60, $C_{20}H_{16}F_2$ requires: C,81.62%, H,5.48%.

1,8-Di-(o-nitrophenyl) octatetra-1,3,5,7-ene-4,5-dicarboxylic acid anhydride.

o-Nitro cinnamaldehyde (1.0g.) was treated with succinic acid (0.51g.), litharge (1.13g.) and acetic anhydride (1.4ml.) and refluxed for 3hrs. On working up as for the general method (P.189) a red crystalline solid was isolated which is suggested to be the title compound. Yield 56mg. (1.6%); m.p.259-260°(methylene dichloride); ν_{max}(mull) 1805,1797, 1760,1603,1520,1350 and 990 $cm.^{-1}$; $\lambda_{max}(CHCl_3)$ 253 and 296mμ. (Found: C,60.60%, H,3.47%, N,6.35%, $C_{22}H_{14}N_2O_7$ requires: C,63.16%, H,3.37%, N,6.70.)

This compound defied all attempts to hydrolyse and decarboxylate. Moreover, sublimation causes extensive decomposition.

Pyrolysis of 1,8-diphenyl octatetraene.

Recrystallised 1,8-diphenyl octatetraene (2g.) was pyrolysed at 700°C by passing through a silica tube 9" long maintained at this temperature under 10^{-2}mm pressure. The dark brown pyrolysate was collected at -78°C in a card-ice

cooled receiver and taken up in hot chloroform. Chromatography on grade 3 alumina eluting with petroleum ether (b.p.40-60°) yielded four fractions which were individually analysed. Each fraction was separated on a Pye series 105 preparative gas chromatograph using a 30ft. methyl silicone gum E 30 column at 180°C, three pure samples being isolated and the presence of two others conclusively shown.

Compound A.(Naphthalene), molecular weight 128 (mass spectrum). This was isolated only as a mixture with other aromatic components, but its presence was proved beyond doubt by its retention time on two separate g.l.c. columns, apiezon and carbowax, compared to that of an authentic sample. This product represented ca. 5% of the total pyrolysate.

Compound B. (Biphenyl), molecular weight 130 (mass spectrum). Biphenyl was isolated as a pure fraction from the preparative separation and represented ca. 20% of the pyrolysate mixture. m.p.70°; (ethanol), mixed m.p. 70°; λ_{max}(EtOH) 249mμ (4.24); the i.r. spectrum was coincident with that of an authentic biphenyl sample.

Compound C. (trans-stilbene). This product constituted by far the most extensive portion of the pyrolysate bulk, ca. 50% and was easily isolated in a pure state. m.p.124°, mixed m.p.124°; molecular weight 180 (mass spectrum); λ_{max}(EtOH) 229, 295, 308 and inf. 320mμ (logε, 4.2, 4.4, 4.4, and 4.2). Comparative i.r. with an authentic sample gave identical spectra.

Compound D. (Dihydro-1-phenyl phenanthrene). Molecular weight 256 (mass spectrum,) λ_{max}(EtOH) 256 and 300mμ, with peaks in the ratio 5 : 4 respectively, ν_{max}(CCl_4) 3050, 1600,1495 and 1450 $cm.^{-1}$. The alternative structure, 1-phenyl-4-(α-naphthyl) buta-1,3-diene,[148] was ruled out on the basis of the u.v. spectrum which does not compare at all with that of the compound isolated. This compound represented ca. 15% of the total pyrolysate and was a white crystalline solid.

Compound E. (Biphenylene) . The presence of this component was only determined by comparative glc as for naphthalene. This compound represented only ca.1-2% of the total pyrolysate.

Two other compounds were present in average abundance in the mixture but these were not identified.

5 , 3 Atrovenetin models.

3-Methyl but-2-enol.[149]

3,3-Dimethyl acrylic acid (50g.) in dry ether (270ml.) was added (N_2 atmosphere) over 3hr. to a cooled (0°C) stirred mixture of lithium aluminium hydride (20.9g., 10% excess) in ether (330ml.) and the mixture stirred at room temperature for 18hrs. Water (40ml.) followed by 20% sulphuric acid (650ml.) was added and the ether layer separated. The aqueous phase was ether extracted and the combined ethereal solutions were washed successively with water, saturated aqueous sodium bicarbonate, and water, and dried (Na_2SO_4). After distillation the alcohol 29.7g.(69%), had b.p.52-4°/16mm. n_D^{17} 1.440, (lit.[150] b.p.139-140°/760mm.; n_D^{20} 1.4410); and contained by g.l.c. ca. 5% of an impurity, probably 3-methyl butanol. ν_{max}(l.f.) 3370,1665, and 845 cm.$^{-1}$; n.m.r.(CCl_4) τ 8.36(s, 3H, trans-CH_3), 8.29(d, J=1.2Hz, 3H, cis-CH_3), 7.02 (s, 1H, hydroxyl), 6.03(d, J=7.5Hz, 2H, CH_2), 4.72(t.q. J=7.5 and 1.2Hz, 1H, vinylic proton).

3-Methyl but-2-enyl bromide.[149]

A solution of 3-methyl but-2-enol (5.5g.) in petroleum ether (13ml., b.p.40-60°) was introduced during 30mins. to a solution of phosphorous tribromide (6.25g.) and pyridine (0.95g.) in petroleum ether (15ml.) at -15°C. Stirring was continued at -15°C for 2hrs. and overnight at 20°C, after which the

product was distilled direct from the reaction flask. Yield 5.2g.(55%); b.p.78-84°/145mm., (lit.[149] b.p.77-78.5°/135mm.) ν_{max}(l.f.) 1656,1456,1382,1205 and 848 cm.$^{-1}$; n.m.r.(CCl_4) τ 8.27(s, 3H, trans-CH_3), 8.22(d, J=1.2Hz, 3H, cis-CH_3), 6.12(d, J=8.5Hz, 2H, CH_2), 4.52(t.q. J=8.5 and 1.2Hz, 1H,).

Potassium salt of 2-hydroxy naphthaquinone.

The quinone (10g.) was suspended in hot water (150ml.) containing potassium hydroxide (3.22g.) and the red liquid heated to boiling. Sufficient water to effect solution was added and the liquid clarified by filtration. After evaporation to small bulk (ca.15ml.) under reduced pressure the product was cooled and the red crystalline solid filtered off and washed sparingly with ice-cold water. The solid was dried in vacuo over phoshoric oxide. Yield 8.59g.(70%).

2-(3-Methylbut-2-enyloxy)-naphtha-1,4-quinone.

The potassium salt of 2-hydroxy-1,4-naphthaquinone (2.84g.) was suspended in dry NN-dimethylformamide (40ml.) and a solution of 3-methylbut-2-enyl bromide (2.0g.) in dry NN-dimethylformamide (10ml.) was added with stirring over 30mins. The mixture was further stirred at 20°C for 2-3days while precipitation of potassium bromide occurred. The pale red supernatant liquid was poured into aqueous hydrochloric acid and extracted with benzene. The benzene layer was washed with 2N sodium hydroxide until the alkaline layer was no longer red, then with water, and dried (Na_2SO_4). The pale

yellow solid obtained after removing benzene was recrystallised (benzene/ligroin) to give long floculent yellow needles. Yield 0.89g.(28%); m.p.149.5-150.5°, (lit.[77,78] m.p.149-150°, 148-149°), ν_{max}(mull) 1680,1650,1609,1579,1456,1259,1220, 793 and 730; $cm.^{-1}$; n.m.r.($CDCl_3$) τ 8.22(s, 6H, gem-dimethyl), 5.42(d, J=6.5Hz, 2H, CH_2), 4.52(t with allylic splitting, J=6.5Hz, 1H, side chain vinylic), 3.85(s, 1H, ring vinylic), 2.42-2.15(m, 2H), 2.12-1.79(m, 2H).

2-Hydroxy-3-(3-methylbut-2-enyl)-naphthaquinone. - (Lapachol).

The alkaline extract obtained above, was filtered and the pH adjusted to 7.1 with glacial acetic acid. The orange precipitate was filtered off, washed with water and dried in vacuo over phosphoric oxide. After crystallisation (ethanol) the product, 1.02g.(31.5%), had m.p.138-140°,(lit.[78] m.p.140-1°), ν_{max}(mull) 3360,1660,1644,1591,1464,1383,1360,1278,1244, and 731 $cm.^{-1}$; n.m.r.($CDCl_3$) τ 8.32(s, 3H, trans-CH_3), 8.22 (s, 3H, cis-CH_3), 6.70(d, J=7.5Hz, 2H, CH_2), 4.80(t.m. J=7.5Hz, 1H, vinylic), 2.66(s, 1H, hydroxyl), 2.44-2.21(m, 2H), 2.08-1.79(m, 2H).

Acidification of the mother liquors gave reclaimed 2-hydroxy naphthaquinone (26%).

2-Hydroxy-3-(1,1-dimethylprop-2-enyl)-naphthaquinone.[78]

2-(3-Methylbut-2-enyl)-naphthaquinone (0.79g.) was refluxed overnight in ethanol (40ml.) to afford an orange solution. Evaporation under reduced pressure gave a yellow

residue which was extracted with 0.5% sodium hydroxide (45ml.) and the extract filtered. Acidification with glacial acetic acid and filtration gave the Claisen rearrangement product. Yield 0.72g.(91%), m.p.69-70°,(ethanol), (lit.[78] m.p.70-71°), ν_{max}(mull) 1667,1640,1618,.585,1465,1365,1332,1293,910 and 728 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 8.42(s, 6H, gem-dimethyl), 5.04 (2H), 3.70(1H),(ABC system, H_a trans, H_b cis to alkyl substituent, J_{ab}=17.5, J_{ac}=10.0, J_{bc}=1.0Hz,), 2.15(s, 1H, hydroxyl), 2.44-1.84(m, 4H, aromatics).

dl-Dunnione.[78]

2-Hydroxy-3-(1,1-dimethylprop-2-enyl)-naphthaquinone (0.62g.) was dissolved in concentrated sulphuric acid (6.2ml.) and the dep red solution allowed to stand for 15mins. at 20°C. On pouring into water (120ml.) dunnione separated as an orange solid which after filtration was dried in vacuo over phosphoric oxide. Yield 0.534g.(86%); m.p.91-93°(ligroin, b.p.40-60°), (lit.[78] m.p.93-94°); ν_{max}(mull) 1692,1635, 1611,1589,1572,1230, and 730 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 8.75(s, 3H, CH_3), 8.57(s, 3H, CH_3), 8.52(d, J=6.5Hz, 3H, single CH_3), 5.33(q, J=6.5Hz, 1H, proton adjacent to single CH_3), 2.51-2.29 (m, 3H), 2.12-1.88(m, 1H).

Reduction of dunnione with sulphurous acid.

Dunnione (5mg.) was suspended in water (5ml.) and sulphur dioxide passed through the stirred solution. After 1hr. the colourless liquid was extracted with ether and the extracts washed with water. Reoxidation to the quinone was apparent

immediately from reddening of the ethereal phase and it was not possible to isolate the hydroquinone.

Reductive acetylation of dunnione.

Dunnione (0.1g.) and zinc dust (0.1g.) were suspended in acetic anhydride (0.5ml.) containing a little pyridine and the mixture warmed on a steam bath for 30mins. Glacial acetic acid (0.5ml.) was added and the mixture filtered hot to remove unreacted zinc dust. Water (10ml) was added (to hydrolyse the acetic anhydride) and the mixture stirred for 30mins. The white solid which separated was extracted with chloroform and the extracts washed and dried (Na_2SO_4). Evaporation afforded dl-hydrodunnione diacetate, 0.129g.(92%), which had m.p.145.5-146.5°(methanol), (lit.[76] m.p.143-144° for d-isomer), ν_{max}(mull) 1763,1583,1521,1458,1390,1380, 1213,1195, and 770 $cm.^{-1}$; n.m.r.($CDCl_3$) τ 8.81(s, 3H, CH_3), 8.61(s, 3H, CH_3), 8.55(d, J=6.5Hz, 3H, single methyl), 5.43 (q, J=6.5Hz, 1H, proton adjacent to single methyl), 7.67,7.62 (s, 6H, acetate CH_3), 2.80-2.28(m, 3H), 2.28-1.92(m, 1H); λ_{max}(EtOH) 246,310,317,331mμ (logε, 4.63,3.79,3.80,3.77).

1,1-[$^2H_2$]-3-Methylbut-2-enol.

This was prepared from 3,3-dimethyl acrylic acid (3.14g.) as for the unlabelled derivative but using lithium aluminium deuteride. Yield 1.38g.(50%); b.p.50-54°/16mm.; n_D^{18} 1.441. The n.m.r. showed no signal at τ 6.03 and a broad singlet at τ 4.61.

1,1-[$^2H_2$]-3-Methylbut-2-enyl bromide.

The above alcohol (1.34g.) was brominated according to the procedure of Bolleter et al.[149]. Yield 1.26g.(55%); b.p.89-91°/140mm. The n.m.r. showed a broad singlet at τ 4.54 and no signal at τ 6.12.

2-(1,1-[$^2H_2$]-3-Methylbut-2-enyloxy)-naphthaquinone.

This was prepared from the above bromide (1.21g.) and the potassium salt of 2-hydroxy naphthaquinone (1.71g.) according to the method given for the undeuteriated analogue. Yield 0.556g.(28.2%); m.p.149-150.5°. The n.m.r. showed no protons at τ 5.42 and the triple multiplet at τ 4.52 has now collapsed to a broad singlet.

From the alkaline extract [$^2H_2$]-lapachol, 0.456g.(23%), m.p.140-141° was isolated.

2-Hydroxy-3-(3,3-[$^2H_2$]-1,1-dimethylprop-2-enyl)-naphthaquinone.

Claisen rearrangement of the above ether (0.485g.) afforded the title compound. Yield 0.43g.(89%), m.p.69°. The n.m.r. showed that the ABC system had now condensed to a broad singlet at τ 3.70.

2,3-Dihydro-2-[$^2H_3$-methyl]-3,3-dimethylnaphtho-[1,2-b]-furan-4,5-dione. or Mono-[$^2H_3$-methyl]-dunnione.

The above quinone (0.39g.) was dissolved in anhydrous chloroform and shaken with deuterium oxide (3x2ml) to exchange the acidic proton. After evaporation of the solvent and drying (P_2O_5 in vacuo) the solid was dissolved in

concentrated [$^2H_2$]-sulphuric acid and allowed to stand for 15mins. at 20°C before pouring into water (80ml.). The precipitated solid was filtered off and dried. Yield 0.245g. (63%), m.p.91-92°. The n.m.r. showed a singlet at τ 5.33 and no signal at τ 8.52.

Mono-[$^2H_3$-methyl]-hydrodunnione diacetate.

The above quinone (0.1g.) was reductively acetylated with acetic anhydride (0.5ml.) and zinc dust (0.1g.) as for the unlabelled sample. Yield 0.129g.(92%); m.p.142-144°. The n.m.r. spectrum showed that the label was specific. D_3,92.1%, D_2,7.9%, D_1,0%.(mass spectrum).

Ethylidene cyclohexylamine.[151]

Acetaldehyde (21.2g.) was slowly added to stirred cyclohexylamine (47g.) at 0°C and the mixture allowed to remain at this temperature for 30mins. After warming to room temperature dry potassium carbonate was added to destroy the complex and the mixture stirred for a further 24hrs. The aqueous phase was separated and the organic layer dried (BaO). Yield 41.5g.(70%); b.p.57-58°/30mm.; n_D^{20} 1.4580, (lit.[151] b.p.54°/18mm.; n_D^{15} 1.4646), ν_{max}(l.f.) 1663 (C=N) $cm.^{-1}$

Lithium diisopropylamine.[152]

To a solution of diisopropylamine (7.9g.) in ether (20ml.) was added freshly prepared phenyl lithium (97ml. of a 1molar solution in ether)[153] at such a rate as to maintain the stirred solution gently boiling. The solution was stirred

for 5mins. after the addition was complete and the yield was assumed quantitative. Yield 8.35g.

3,3-Di-[$^2H_3$-methyl]-acrolein.

The ethereal solution of lithium diisopropylamine (8.35g.) prepared above was cooled to 0°C and ethylidene cyclohexylamine (9.7g.) in ether (15ml.) added over 15mins. After 10mins. the mixture was cooled to -70°C and [$^2H_6$]-acetone (5g.) was introduced. The mixture was allowed to warm to room temperature and water added to hydrolyse the lithium salt. The solution was acidified with oxalic acid and steam distilled, the distillate being extracted with ether. The extracts were dried (Na_2SO_4) and evaporated. Some biphenyl and polar impurities were present in the product. Crude yield 4.13g., ν_{max}(l.f.) 1670 cm.$^{-1}$

3,3-Di-[$^2H_3$-methyl]-allyl alcohol.

The crude aldehyde prepared above (4.13g.) was dissolved in isopropanol (25ml.) and added to a stirred solution of sodium borohydride (0.93g.) in water (60ml.) at 10°C. After the addition was complete the mixture was allowed to attain room temperature and stirred overnight. Saturated aqueous ammonium chloride was added and the mixture extracted with ether. The extracts were dried (Na_2SO_4) after washing with water. Evaporation gave an oil, shown by t.l.c. (benzene-20% acetone on silica) to be essentially the desired alcohol, and which was purified by column chromatography on the same

system, R_f, 0.45. Yield 1.09g.(15.1% based on [$^2H_6$]-acetone), ν_{max}(l.f.) 3370,2910,2860,2220,2200,2120,2060,1658, and 845 cm.$^{-1}$

3,3-Di-[$^2H_3$-methyl]-allyl bromide.

This was prepared from the above alcohol (1.09g.) by the method of Bolleter et al.[149] Yield 1.12g.(61%); b.p.80°/110mm.

2-(3,3-Di-[$^2H_3$-methyl]-prop-2-enyloxy)-naphthaquinone.

Reaction of the potassium salt of 2-hydroxy naphthaquinone (1.50g.) with the above bromide (1.1g.) as before gave the title compound. Yield 0.47g.(27%); m.p.149-150°. The n.m.r. showed no signal at τ 8.22 and the allylic splitting of the proton at τ 4.50 had collapsed.

From the alkaline extract [$^2H_6$]-lapachol, 0.384g.(22%) m.p.139-140°, was isolated.

2-Hydroxy-3-(1,1-di-[$^2H_3$-methyl]-prop-2-enyl)-naphthaquinone.

The deuteriated quinone ether above (0.42g.) was rearranged on refluxing in ethanol overnight and the product isolated as for the unlabelled analogue. Yield 0.372g.(89%), m.p.69-70°. The n.m.r. indicated the absence of a signal at τ 8.42.

2,3-Dihydro-3,3-di[$^2H_3$-methyl]-prop-2-enyl)-naphthaquinone. or - di-[$^2H_3$-methyl]-dunnione.

The above Claisen product (0.33g.) was cyclised with concentrated sulphuric acid (3.3ml.) according to the method of Cooke.[78] Yield 0.32g.(97%); m.p.92-93°.

Di-[$^2H_3$-methyl]-hydrodunnione diacetate.

Reductive acetylation of di-[$^2H_3$-methyl]-dunnione (0.1g.) afforded the title compound. Yield 0.128g.(92%); m.p.145.5-146.5°. The n.m.r. spectrum showed the absence of protons at τ 8.81 and 8.61; D_6,79.1%, D_5,18.3%, D_4,2.6%, D_3,0%.

[$^2H_3$]-Acetaldehyde.[154]

A solution of dry ($CaSO_4$) acetaldehyde (22g., 0.5mole) in deuterium oxide (50ml.) was heated in a **Carius** tube at 90°C for 12hrs. in the presence of pyridine (4g., 0.05mole.). The product was distilled (N_2 atmosphere) through a 10" column packed with Fenske helices and collected at -78°C. The distillate was retreated twice to yield 14.27g.(61%) of labelled aldehyde, b.p.22°/760mm.; D_3,93%, D_2,7%, D_1,0%.

2-[$^2H_1$]-3,3-dimethyl acrolein.

The [$^2H_3$]-acetaldehyde (9.31g.) was condensed with cyclohexylamine (19g.) by the method of Tiollais,[151] and then treated consecutively with lithium diisopropylamine and acetone as for the [$^2H_6$]-analogue to afford [$^2H_1$]-acrolein. Yield of crude product 4.59g.

3,3-Dimethyl-2-[$^2H_1$]-allyl alcohol.

The crude aldehyde above (4.50g.) was reduced with sodium borohydride)1.02g.) to afford the desired alcohol which was purified by chromatography on silica eluting with 20% acetone in benzene. Yield 0.81g.(12% from the Schiff base), b.p.66°/20mm.

3,3-Dimethyl-2-[$^2H_1$]-allyl bromide.

The above alcohol (0.74g.) was converted to the bromide by the method described by Bolleter et al.[149] Yield 0.637g. (50%); b.p.87°/170mm.

2-(2-[$^2H_1$]-3-Methylbut-2-enyoxy)-naphthaquinone.

This was prepared from 3,3-dimethyl-2-[$^2H_1$]-allyl bromide (0.63g.) in the same manner as for the unlabelled compound. Yield 0.295g.(29%), m.p.149.5-150.5°. The n.m.r. showed only a small signal at τ 4.52 and the triplet at τ 5.42 had now condensed to a broad singlet.

[$^2H_1$]-Lapachol, 0.27g.(27%), m.p.140-141°, was isolated from the alkaline extracts.

2-Hydroxy-(2-[$^2H_1$]-3-methylbut-2-enyl)-naphthaquinone.

Prepared by Claisen rearrangement of the above allyl ether (0.238g.). Yield quantitative, m.p.69-70°.

2,3-Dihydro-2-[$^2H_1$]-2,3,3-trimethyl-naphtho-[1,2-b]-furan-4,5-dione.

The above compound (0.17g.) was cyclised in concentrated sulphuric acid (1.7ml.) as before. Yield 0.161g.(95%); m.p.93°. The n.m.r. spectrum showed no signal at τ 5.33 and the methyl signal at τ 8.56 had collapsed to a singlet.

[$^2H_1$]-Hydrodunnione diacetate.

Reductive acetylation of the above quinone (0.1g.) gave the title compound. Yield 0.126g.(90%); m.p.143-145°. A very small signal at τ 5.43 in the n.m.r., D_1,73.0%, D_0,27%.

Hydrodunnione-[$^2H_6$]-diacetate.

Dunnione (0.05g.) was reductively acetylated with [$^2H_6$]-acetic anhydride (0.3ml.), zinc dust (0.05g.) and a trace of pyridine. Yield 55mg.(77%); m.p.142-144°. The n.m.r. showed no signals at τ 7.67, 7.62; D_6,97.2%, D_5,2.8%,(mass spectrum).

1-(3-Methylbut-2-enyloxy)-naphthalene.

α-Naphthol (8.8g.) was dissolved in anhydrous DMF (120ml.) and a 50% dispersion of sodium hydride (3.0g.) added with caution. The pale green solution was allowed to regain room temperature and a slight excess of 3,3-dimethylallyl bromide (10.8g.) in DMF (10ml.) added over 1hr. The reaction mixture was stirred for several days at 20°C then poured into water (700ml.) and acidified. The product was extracted with ether and the extracts washed well with 10% aqueous sodium hydroxide (200ml.) and water and dried (Na_2SO_4). Evaporation gave a red oil which t.l.c. showed to be ca. 95% pure. Yield 7.2g.(55%).

2,3,3-Trimethyl naphtho-[1,2-b]-furan.

The above ether (1g.) was degassed and sealed in a pyrex tube under vacuum. Pyrolysis at 190-200°C for 6hrs. afforded a red liquid which was chromatographed on silica eluting with benzene. The first fraction was shown to be 1-(3-methyl-butyloxy)-naphthalene, 0.175g.(18%), and was distilled in a bent-tube at 0.08mm, n_D^{21} 1.5684, ν_{max}(l.f.) 1620,1590,1580,1510,1272,1240,1102,800 and 780 cm.$^{-1}$; n.m.r. ($CDCl_3$) τ 8.97(d, J=5Hz, 6H, gem-dimethyl), 8.17(t, J=6Hz, 3H,

CH_2 adjacent to gem-dimethyl and tertiary proton.), 5.87(t, J=6Hz, 2H, CH_2 adjacent to ether link), 3.33-1.61(m, 7H,). (Found: C,83.77%, H,8.52%, $C_{15}H_{18}O$ requires: C,84.07%, H,8.47%).

The second fraction yielded the title compound. Yield 0.42g.(42%); b.p.105°/0.08mm.; n_D^{22} 1.5959; ν_{max}(l.f.) 1592, 1582,1522,1380,1287,1138,1087,815 and 750 $cm.^{-1}$; n.m.r.($CDCl_3$) τ 8.73(d, J=7Hz, 3H, CH_3 adjacent to ether.), 8.60, 8.46 (s, 3H each, gem-dimethyl), 6.68(q, J=7Hz, 1H, solitary proton), 2.92-1.95(m, 6H, aromatics.). (Found: C,84.84%, H,7.50%, $C_{15}H_{16}O$ requires: C,84.87%, H,7.53%).

2-(3-Methylbut-2-enyloxy)-naphthalene.

3,3-Dimethylallyl bromide (10g.) was added to a well stirred mixture of β-naphthol (8.8g.) and sodium methoxide (3.27g.) together with potassium iodide (0.184g.) in methanol (60ml.) with ice cooling. The mixture was stirred at room temperature for several days, poured into water (700ml.) and ether extracted. The extracts were washed with 10% aqueous sodium hydroxide (3x50ml.), water, and dried (Na_2SO_4). Removal of the solvent afforded a red oil which was chromatographed on silica eluting with benzene/5% acetone.

The first fraction, obtained in low yield, 200mg., was distilled in a bent-tube to a pale yellow oil shown to be the dialkylated product; 1-(3-methylbut-2-enyl)-2-(3-methylbut-2-enyloxy)-naphthalene, ν_{max}(l.f.) 1670,1623,1265,1245, 818 and 752 $cm.^{-1}$; n.m.r.($CDCl_3$) τ 8.36(broad s, 6H, gem-

dimethyl), 8.29(s with side splitting, cis-CH_3 of C-alkyl chain), 8.17(s, trans-CH_3 of C-alkyl chain), 6.21(d, J=6.5Hz, 2H, CH_2 of C-alkyl chain), 5.43(d, J=6.5Hz, 2H, CH_2 of O-alkyl chain), 4.80(t with side splitting, J=6.5Hz, 1H, vinylic of C-alkyl chain), 4.51(t with side splitting, J=6.5Hz, 1H, vinylic of O-alkyl chain), 3.01-1.99(m, 6H, aromatics). (Found: C,85.60%, H,8.56%, $C_{20}H_{24}O$ requires: C,85.67%, H,8.63%).

The second fraction was the desired ether. Yield 3.2g. (24.6%); b.p.130°/0.3mm.; m.p.47-47.5°; ν_{max}(l.f.) 1670, 1630,1602,1399,1260,1220,1182,1125,1010,850,825 and 755 $cm.^{-1}$ n.m.r.($CDCl_3$) τ 8.26(broad s, 6H, gem-dimethyl), 5.42(d, J=6.5Hz, 2H, CH_2), 4.45(t, J=6.5Hz, 1H, vinylic proton), 2.96-2.16(m, 7H, aromatics). (Found: C,85.06%, H,7.77%, $C_{15}H_{16}O$ requires: C,84.87%, H,7.53%).

The third fraction was the C-alkylated product. Yield 3.9g.(30%); b.p.132°/0.07mm.; n_D^{21} 1.6180; ν_{max}(l.f.) 3450, 1660,1625,1600,1382,1362,1290,1210,820 and 755 $cm.^{-1}$; n.m.r. ($CDCl_3$) τ 8.29(s with side splitting, 3H, cis-CH_3), 8.12(s, 3H, trans-CH_3), 6.27(d, J=7.2Hz, 2H, CH_2), 4.75(split t, J=7.2Hz, 1H, vinylic proton), 4.75(s, 1H, hydroxyl), 3.12-1.98 (m, 6H, aromatics). (Found: C,84.78%, H,7.35%, $C_{15}H_{16}O$ requires: C,84.87%, H,7.53%).

Repetition of this reaction in DMF as for α-naphthol afforded 58% yield of the O-alkylated product. The presence of a dialkylated product under these conditions was not observed.

Pyrolysis of 2-(3-methylbut-2-enyloxy)-naphthalene.

1/. Pyrolysis of the naphthyl ether (2g.) under nitrogen for 6hrs. at 200°C afforded a dark oil which was chromatographed on silica eluting with benzene to remove charcoalised residues. The white solid isolated was recrystallised from petroleum ether (b.p.40-60°). Yield 1.48g.(74%), m.p.77-79°. This was shown by mixed melting point of 78.5° with an authentic sample to be 1,2-dihydro-3,3-dimethyl naphtho-[2,1-b]-pyran, ν_{max}(l.f.) 1630,1602,1400,1380,1245,830,762, and 698 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 8.63(s, 6H, gem-dimethyl), 8.09(t, J=6.7Hz, 2H, CH_2 β-to ether link), 7.01(t, J=6.7Hz, 2H, benzylic CH_2), 3.12-2.12(m,6H, aromatics). λ_{max}(EtOH) 239,259(inf.),268,278,289,332,336,mμ (log ε ,4.77,3.46,3.61, 3.67,3.52,3.30,and 3.37). (Found: C,84.62%, H,7.64%, $C_{15}H_{16}O$ requires: C,84.87%, H,7.53%).

2/. Pyrolysis ina sealed tube under vacuo gave the same result as above.

3/. The pyrolysis was repeated in the presence of hydroquinone but the same product was isolated.

4/. Pyrolysis of the naphthyl ether (300mg.) in quinoline (1ml.) with a trace of hydroquinone at 160°C afforded a product which after chromatography on silica eluting with benzene : 20% acetone and recrystallisation (ligroin, b.p. 40-60°) had m.p.42°. Yield 70mg.(23%); This was shown to be 3,3-dimethyl-naphtho-[2,1-b]-pyran, ν_{max}(l.f.) 1625, 1598,1520,1382,1245,818, and 750 cm.$^{-1}$; λ_{max}(EtOH) 238(inf.),

245,261,289,301,314,346, and 360mμ, (log ε, 4.66,4.71,3.72, 3.54,3.65,3.68,3.57, and 3.54), n.m.r. $CDCl_3$, τ8.57(s, 6H, gem-dimethyl), 4.40(d, J=10Hz, proton β- to ether link), 3.05 (d, J=10Hz, 1H, benzylic hydrogen), 3.08-2.00(m, 6H, aromatics). (Found: C,85.58%, H,6.54%, $C_{15}H_{14}O$ requires: C,85.68%, H,6.17%).

Hydrogenation of 3,3-dimethyl-naphtho-[2,1-b]-pyran.

The pyran (20mg.) was dissolved in absolute ethanol (20ml.) and hydrogenated in the presence of 20% Pd/C (5mg.) till no further uptake ensued. Filtration and evaporation gave a product with m.p. and mixed m.p. with 1,2-dihydro-3,3-dimethyl-naphtho-[2,1-b]-pyran of 78°.

Acid treatment of 3,3-dimethyl-naphtho-[2,1-b]-pyran.

The pyran (25mg.) was dissolved in ether (5ml.) and 5N hydrochloric acid (2ml.) was added. The mixture was vigorously stirred at 20°C for 3hrs. and the ethereal layer dried and evaporated. The n.m.r. spectrum showed no change.

1,2-Dihydro-3,3-dimethyl-naphtho-[2,1-b]-pyran.

An authentic sample of this derivative was prepared by pyrolysis of 2-hydroxy-1-(3-methylbut-2-enyl)-naphthalene (180mg,) in a sealed tube at 190°C for 5hrs. Purification was effected by chromatography on silica eluting with benzene : 20% petroleum ether (b.p.40-60°), and recrystallisation (petrol). Yield 165mg.(92%); m.p. 77-78°. The n.m.r. spectrum was identical to that isolated from the pyrolysis of 2-(3-methylbut-2-enyoxy)-naphthalene.

Trapping experiment for the pyrolysis of 2-(3-methylbut-2-enyloxy)-naphthalene.

The ether (200mg.) was dissolved in quinoline (1ml.) to which acetic anhydride (0.5ml.) was added and the solution heated under vacuum at 190°C for 5hrs. Excess acetic anhydride was hydrolysed with water (1ml.) and the mixture acidified. Ether extraction followed by drying of the extracts (Na_2SO_4) and evaporation gave an oil. Chromatography on silica eluting with benzene afforded 2-acetoxy-1-(1,1-dimethylprop-2-enyl)-naphthalene in low yield. $\nu_{max}(CCl_4)$ 1765, 1230 $cm.^{-1}$ The n.m.r. spectrum demonstrated the presence of a vinylic methylene group.

2-Methylallyl bromide.

2-Methylallyl alcohol (12.13g.) in petroleum ether (b.p.40-60°, 30ml.) was brominated with phosphorous tribromide (13.8g.) in the presence of pyridine (2.1g.) as for 3,3-dimethylallyl bromide above. Yield 9.91g.(47%); b.p.70°/135mm.

2-(2-Methylprop-2-enyloxy)-naphthalene.

β-Naphthol (8.8g.) was alkylated with 2-methylallyl bromide (9.91g.) in methanol (60ml.) according to the method of McKusick.[84] The product was purified by chromatography on silica eluting with benzene : 5% acetone. The first fraction gave the title compound as white needles from petroleum ether (b.p.40-60°), yield 5g.(41%); m.p.45°; ν_{max}

(l.f.) 1630,1603,1520,1265,1223,852, and 758 $cm.^{-1}$; n.m.r. ($CDCl_3$) τ 8.16(s, 3H, CH_3), 5.50(s, 2H, CH_2 adjacent to ether), 5.02(allylic split s, 1H, proton trans to CH_3), 4.88(s, 1H, proton cis to CH_3), 2.94-2.19(m, 7H, aromatics). (Found: C,84.95%, H,7.12%, $C_{14}H_{14}O$ requires: C,84.80%, H,7.12%).

The second fraction afforded the C-alkylated product as a yellow oil. Yield 1.24g.(10%); b.p.110-112°/0.3mm.; ν_{max}(l.f.) 3480,1642,1600,1270,1150,908,820, and 755 $cm.^{-1}$; n.m.r.($CDCl_3$) τ 8.23(s, 3H, CH_3), 6.29(s, 2H, benzylic CH_2), 5.38(broad s, 1H, vinylic), 5.20(t, J=1.5Hz, 1H, vinylic), 4.61(s, 1H, hydroxyl), 3.13-2.06(m, 6H, aromatics). (Found: C,84.69%, H,7.01%, $C_{14}H_{14}O$ required: C,84.80%, H,7.12%).

1,2-Dihydro-2,2-dimethyl-naphtho-[2,1-b]-furan.

2-(2-Methylprop-2-enyloxy)-naphthalene (3.8g.) was pyrolysed under nitrogen at 200°C for 6hrs. and the product purified by chromatography on silica eluting with benzene.

The first fraction was shown to be the desired product. Yield 1.17g.(31%); b.p.99°/0.2mm.; n_D^{20} 1.6059; m.p.41-42.5° (ligroin b.p. 40-60°); ν_{max}(l.f.) 1632,1601,1270,825 $cm.^{-1}$; n.m.r.($CDCl_3$) τ 8.57(s, 6H, gem-dimethyl), 6.97(s, 2H, CH_2), 3.17-2.23(m, 6H, aromatics); λ_{max}(EtOH) 240,271,281,295, 334,343, and 347mμ (logε, 4.81,3.59,3.66,3.54,3.44, 3.44, and 3.44).

The second fraction was shown to be the Claisen rearrangement product which due to symmetry of the side chain is identical to the C-alkylated product above.

Crotyl bromide.

But-2-enol (6.0g.) in petroleum ether (b.p.40-60°, 10ml.) was brominated by the procedure of Bolleter et al.[149]. Yield 7.9g.(70%); b.p.103-5°/760mm.; n_D^{20} 1.4822; ν_{max}(l.f.) 1663,1460,1445,1215 and 980 cm.$^{-1}$.

2-(But-2-enyloxy)-naphthalene.

β-Naphthol (3.38g.) in anhydrous DMF (15ml.) was alkylated with crotyl bromide (3.38g.) according to the procedure given for the other halides. The product was purified by column chromatography on silica eluting with benzene. Yield 3.50g.(76%); b.p.123°/0.5mm.; m.p.44°(b.p. 40-60° ligroin); ν_{max}(l.f.) 1675,1635,1603,1265,980,855, and 760 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 8.27(d, J=4.5Hz, 3H, CH_3), 5.48(d, with side splitting, J=4Hz, 2H, CH_2), 4.21(t, J=4Hz, 1H, proton β to oxygen), 4.21(q, J=4.5Hz, 1H, proton α to CH_3), 3.00-2.17(m, 7H, aromatics). (Found: C,84.91%, H,7.09%, $C_{14}H_{14}O$ requires: C,84.81%, H,7.12%).

Pyrolysis of 2-(but-2-enyloxy)-naphthalene.

The ether (0.58g.) was pyrolysed in the usual manner and the product chromatographed. No stable compounds were isolable but from the n.m.r. spectrum traces of the normal cyclisation product were evident.

5, 4 Cyclohexenone derivatives.

Anhydrodimedones.

The anhydrodimedones of the aromatic aldehydes shown in Table 25 were all prepared *via* the dimedone derivatives by the method of Horning and Horning.[95]

Table 25.

Melting points of dimedone and anhydrodimedone derivatives.*

Substituent	Dimedone m.p.	Anhydrodimedone m.p.
o-OMe	187-188°	190-191°
m-OMe		185-187° (a)
p-OMe	144-145°	252-253°
o-NO_2	178-179° (b)	255° (c)
p-NO_2	188-191°	227-228°
o-Br	194-196.5° (d)	224.5-226° (e)
o-Me	166-167°	213-215°
o-Cl	201-203°	227-228°
o-OH	-	204-205°
H	192-195°	204-206°
p-OMe**	196°	203-206° (f)
H**	-	264°

* All precursors apart from the halogeno and tolyl aldehydes were readily available.

** Cyclohexane-1,3-dione adducts.

Analyses.

(a). Found: C, 75.58%, H, 7.39%, $C_{24}H_{28}O_4$ requires: C, 75.75%, H, 7.42%.

(b). Found: C, 66.70%, H, 6.72%, N, 3.31%; $C_{23}H_{27}NO_6$ requires: C, 66.80, H, 6.58%, N, 3.39%.

(c), Found: C, 69.48%, H, 6.47%, N, 3.39%, $C_{23}H_{25}NO_5$ requires: C, 69.83%, H, 6.37%, N, 3.54%.

(d). Found: C, 61.59%, H, 6.06%, Br, 18.00%, $C_{23}H_{27}BrO_4$ requires: C, 61.75%, H, 6.08%, Br, 17.86%.

(e). Found: C, 64.54%, H, 6.06%, Br, 18.75%, $C_{23}H_{25}BrO_3$ requires: C, 64.33%, H, 5.87%, 18.61%.

(f). Found: C, 74.03%, H, 6.29%, $C_{20}H_{20}O_4$ requires: C, 74.06%, H, 6.32%.

o-Bromobenzaldehyde diacetate.

This was prepared by oxidation of o-bromotoluene (10g.) with chromium trioxide in the presence of acetic anhydride (91ml.) according to the method of Organic Syntheses[155] for which the p-derivative is quoted. Yield 11.09g. (66%), m.p. 89-90° (ethanol), (lit.[156] m.p. 84-86°).

o-Bromobenzaldehyde.

Hydrolysis of the above diacetate (5g.) by the method of Organic Syntheses[155] afforded the required aldehyde. Yield 2.21g. (69%); b.p. 62-64°/0.1mm.; n_D^{21} 1.5902; m.p. 22°.

o-Chlorobenzaldehyde diacetate.

Prepared as for the bromo compound from o-chlorotoluene (11.1g.). Yield 13.4g. (63%); m.p. 56-57° (ethanol); ν_{max} (mull) 1748, and 770 $cm.^{-1}$; n.m.r. ($CDCl_3$) τ 7.94 (s, 6H, acetates),

2.71(s, 4H, aromatics), 2.22(s, 1H, benzylic proton). (Found: C,54.65%, H,4.55%, Cl,14.75%, $C_{11}H_{11}ClO_4$ requires: C,54.45%, H,4.55%, Cl,14.61%).

o-Chlorobenzaldehyde.

o-Chlorobenzaldehyde diacetate (8.46g.) was hydrolysed by the method cited in Organic Syntheses.[155] Yield 3.43g. (60%); b.p.54°/0.25mm.; n_D^{22} 1.5600.

o-Tolualdehyde.

Chromyl chloride (13g.) in chloroform (25ml.) was cooled to 0°C in an ice-salt bath and a solution of o-xylene (4.55g.) in chloroform (40ml.) was added over 45mins. with stirring. The mixture was maintained at 0°C for 90mins. and stirred for a further 12hrs. at 20°C after which the red solid complex was cooled in ice and a little sulphurous acid added. Sulphur dioxide was passed until saturated and the product steam distilled. The aldehyde was isolated from the distillate by chloroform extraction. Yield 1.48g.(29%); b.p.82-85°/15mm.; n_D^{22} 1.5451.

2,4,6-[$^2H_3$]-Benzaldehyde anhydrodimedone.

This was prepared by the method of Horning and Horning[95] from 2,4,6-[$^2H_3$]-benzaldehyde, made as on p.195.

2-Phenyl-2-morpholino-acetonitrile.

A solution of benzaldehyde (5.3g.) and morpholine perchlorate (10.3g.) in morpholine (50ml.) was stirred at 60°C for 45mins. After cooling, sodium cyanide (2.7g.) dissolved

in a minimum of water was introduced and the solution warmed to 80°C for 30mins. The mixture was cooled and poured into ice-water, the precipitate being filtered and recrystallised from petroleum ether (b.p.60-80°). Yield 9.73g.(96%); m.p.67.5-68.5°,(lit.[157] m.p.68-70°); n.m.r.($CDCl_3$) τ 5.2 (tertiary hydrogen singlet).

2-Phenyl-2-morpholino-2-[$^2H_1$]-acetonitrile.

53.3% Sodium hydride dispersion (2.7g.) was added to a stirred solution of 2-phenyl-2-morpholino-acetonitrile (6.0g.) in dry DMF (60ml.) under nitrogen, and after 1hr. deuterium oxide (6ml.) was added. After 5mins. the solution was neutralised with solid carbon dioxide, excess water added (200ml.) and the solid filtered off. Yield 4.3g.(71%); m.p.68-69°,(b.p.60-80° petroleum ether). This compound showed no signal at τ 5.2 in the n.m.r. spectrum.

α-[$^2H_1$]-Benzaldehyde.

2-Phenyl-2-morpholino-2-[$^2H_1$]-acetonitrile (2g.) was refluxed with 6N-hydrochloric acid (200ml.) for 1hr. and the solution cooled and extracted with chloroform. Evaporation of the dried (Na_2SO_4) extracts under reduced pressure gave the labelled aldehyde. Yield 0.95g.(90%); ν_{max}(l.f.) 1684 $cm.^{-1}$. The n.m.r. showed only a small signal at τ 0.04.

α-[$^2H_1$]-Benzaldehyde anhydrodimedone.

This was prepared by the literature method[95] from α-[$^2H_1$]-benzaldehyde, and had m.p.192-195°. D_1,95.4%, D_0,4.6%.

[$^{2}H_{8}$]-Anisaldehyde anhydrodimedone.

A solution of anisaldehyde anhydrodimedone (100mg.) in anhydrous DMF (5ml.) was added to deuterium oxide (2ml.) and the mixture refluxed overnight in the presence of a little triethylamine. The solvent was evaporated on an oil pump and the residue retreated. Recrystallisation from ethanol afforded the derivative with a high degree of incorporation. D_8,75.0%, D_7,22.5%, D_6,1.7%, D_5,1.0%, (mass spectrum).

5,5-Dimethyl-3-methoxy cyclohex-2-ene-1-one.

Dimedone (10g.), methanol (100ml.) and concentrated sulphuric acid (1ml.) were refluxed overnight. After cooling barium carbonate was added to neutrallise the acid and the barium salts removed by centrifugation. evaporation under reduced pressure and distillation gave the title compound. Yield 6.37g.(57%); b.p.78-80°/0.8mm.; n_D^{20} 1.4960; ν_{max}(l.f.) 1663,1618,1472,1388,1230,1160,1028, and 838 $cm.^{-1}$; n.m.r. (CCl_4) τ 8.94(s, 6H, gem-dimethyl), 7.94(s, 2H, allylic CH_2), 7.78(s, 2H, CH_2 adjacent to CO), 6.32(s, 3H, methoxyl), 4.80(s, 1H, vinylic proton).

5,5-Dimethyl-3-ethoxy cyclohex-2-ene-1-one.

This was prepared as above from ethanol (50ml.) and dimedone (5g.). Yield 4.1g.(68%); m.p.56-57°(ligroin b.p. 40-60°), (lit.[158] m.p.58.5-59.5°).

5,5-Dimethyl-3-n-propoxy cyclohex-2-ene-1-one.

To a solution of n-propanol (10ml.) in anhydrous benzene

(50ml.) was added dimedone (4g.) and a little p-toluene sulphonic acid (0.2g.) and the mixture refluxed under a Dean and Stark head until no further water was collected. The solvent was removed under reduced pressure and the residual oil distilled to a colourless liquid. Yield 3.91g. (75%); b.p.154°/15mm.; ν_{max}(l.f.) 1660,1612, and 835 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 9.02(t, J=6.5Hz, 3H, CH_3 of propyl group), 8.92(s, 6H, gem-dimethyl), 8.25(sextuplet, J=6.2Hz, 2H, CH_2 adjacent to chain methyl), 7.82(s, 2H, allylic CH_2), 7.73(s, 2H, CH_2 adjacent to CO), 6.22(t, J=6.2Hz, 2H, CH_2 next to ether link), 4.70(s, 1H, vinylic).

5,5-Dimethyl-3-isopropyl cyclohex-2-ene-1-one.

This compound was prepared as above for the ethoxy and methoxy analogues from isopropyl alcohol (40ml.) and dimedone (4g.). Yield 1.5g.(29%); m.p.46-46.5°(b.p.40-60° petroleum ether), (lit.[159] m.p.47°); ν_{max}(mull) 1640 and 1603 cm.$^{-1}$. This compound would have been better prepared as for the n-propyl isomer.

5,5-Dimethyl-3-phenyl cyclohex-2-ene-1-one.

To the Grignard reagent formed from bromobenzene (4.06g.) and magnesium (0.63g.) in anhydrous ether (20ml.) was added the methoxy enol of dimedone (2g.) in ether (5ml.) with stirring. After stirring for 1hr. 2N-hydrochloric acid was introduced and the ether layer separated and washed successively with water, aqueous sodium bicarbonate and

water and dried. Evaporation gave an oil which was purified by chromatography on silica eluting with chloroform. Yield 1.82g.(70%); b.p.122°/0.5mm.; m.p.54-55°(b.p.40-60° petroleum ether), (lit.[160] m.p.54-55.5°) ν_{max}(l.f.) 1665, and 1612 cm.$^{-1}$.

5,5-Dimethyl-3-(p-anisyl)-cyclohex-2-ene-1-one.

This was prepared as for the phenyl derivative from 5,5-dimethyl-3-methoxy cyclohexenone (2.17g.) and the Grignard reagent from p-bromo anisole (5.2g.) using a nitrogen atmosphere. Yield after chromatography 1.26g.(39%); m.p. 44.5-45.5°(b.p.40-60°petroleum ether); ν_{max}(l.f.) 1655,1600, 1370,1255, and 838 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 8.89(s, 6H, gem-dimethyl), 7.69(s, 2H, CH_2 adjacent to CO), 7.49(d, J=1.2Hz, 2H, allylic CH_2), 6.19(s, 3H, methoxyl), 3.65(t, J=1.2Hz, 1H, vinylic proton), 2.83(AB quartet, J=8.7 and 36Hz, 4H,). (Found: C,78.45%, H,7.64%, $C_{15}H_{18}O_2$ requires: C,78.24%, H,7.88%).

3-Chloro-5,5-dimethyl cyclohex-2-ene-1-one.

Dimedone (8.5g.) was suspended in dry chloroform (20g.) and phosphorous trichloride (3.5g.) added. After refluxing the mixture on a steam bath for 3hrs. the chloroform was removed and the residue poured into ice-water and extracted with ether. The extracts were washed well with 2N-sodium hydroxide, dried ($CaCl_2$) and distilled. Yield 5.86g.(65%); b.p.91-92°/13mm.; n_D^{23} 1.4960; (lit.[161] b.p.109-110°/14mm.; n_D^{20} 1.4942); ν_{max}(l.f.) 1680 and 1618 cm.$^{-1}$

3-Anilino-5,5-dimethyl cyclohex-2-ene-1-one.

This was prepared by azeotropic removal of water from a mixture of dimedone (4g.) and aniline (6g.) in benzene (50ml.) in the presence of a trace of p-toluene sulphonic acid. The product was isolated as usual. Yield 5.8g.(93%); m.p.184-5° (benzene); ν_{max}(mull) 3240,1600,1580,1505,1278,1250,780 and 715 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 8.93,(s, 6H, gem-dimethyl), 7.83 (s, CH_2 adjacent to CO), 7.65(s, 2H, allylic CH_2), 4.46(s, 1H, vinylic), 3.02-2.57(m, 6H, aromatics + NH).

3-n-Butylamino-5,5-dimethyl cyclohex-2-ene-1-one.

Condensation of dimedone (4g.) with n-butylamine (2.1g.) as above afforded the required compound. Yield 5.08g.(92%); m.p.123-4°(benzene), (lit.[162] m.p.124-5°) ν_{max}(mull) 3270 and 1598 cm.$^{-1}$

7,7-Dimethyl-5-oxo-5,6,7,8,-tetrahydro-$\Delta^{9,10}$-chroman.

To a solution of dimedone (2.0g.) and sodium ethoxide (from 0.36g. of sodium) in ethanol (20ml.) was added trimethylene bromohydrin (2.0g.) at 5°C . After stirring for 30mins. the mixture was refluxed on a steam bath until precipitation of sodium bromide was complete. The liquid was cooled, and after acidification with concentrated hydrochloric acid was evaporated to small bulk. Water (30ml.) was added to the residue and the product extracted with ether. The extracts were washed with 2N-sodium hydroxide and water and after drying evaporated to a colourless oil. On eluting

through a silica column with benzene : 20% acetone cyclisation was effected and the title compound isolated. Yield 1.32g.(51%); b.p.66-68°/0.1mm.; n_D^{18} 1.5174; ν_{max}(l.f.) 1650,1630,1405 and 1380 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 8.92(s, 6H, gem-dimethyl), 8.26-7.91(m, 2H, CH_2 β to ether link), 7.91-7.58(m, 6H), 5.50(t, J=4.8Hz, 2H, CH_2 adjacent to ether link). Found: C,73.19%, H,8.87%, $C_{11}H_{16}O_2$ requires: C,73.30%, H,8.95%.

2,5,5-Trimethyl cyclohexan-1,3-dione.

Methyl iodide (38.4g.) was slowly added to a cooled solution of dimedone (21g.) in methanolic sodium methoxide (4.32g. of sodium in 50ml. of methanol) and the mixture warmed on a steam bath for 3hrs. The methanol was removed and the residue ether extracted. The ethereal solution was extracted with 10% aqueous sodium bicarbonate and the solid obtained from the alkaline extract on acidification was recrystallised from aqueous ethanol. Yield 12.3g.(53%); m.p.163°,(lit.[163] m.p.163°). From the ether extract 2,2,5,5,-tetramethyl cyclohexan-1,3-dione (2.6g.) m.p.95-96° was isolated, (lit.[163] m.p.99°).

Attempted preparation of 3-ethoxy-2,5,5-trimethyl cyclohex-2-ene-1-one.

The above dione (2.08g.) was added to an ice-cold solution of sodium (0.62g. 2equiv.) in methanol (7ml.) followed by ethyl iodide (4.22g. 2equiv.). The mixture was refluxed for 2.5 hrs., the solvent removed and the residue

added to water (3.5ml.). The aqueous phase was basified to pH 9-10 with 2N-sodium hydroxide and immediately extracted with ether. After washing with water the dried (Na_2SO_4) ethereal solution was evaporated to give a white crystalline solid. Yield 0.5g.(25%); m.p.71-72.5°;(b.p.60-80°ligroin). The n.m.r. and i.r. spectra showed this to be 2-ethyl-2,3,3-trimethyl cyclohexan-1,3-dione, ν_{max}(mull) 1710, and 1692 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 9.20(t, J=6.8Hz, 3H, CH_3 of ethyl group), 9.13(s, 3H, CH_3), 8.93(s, 3H, CH_3), 8.83(s, 3H, CH_3), 8.21(q, J=6.8Hz, 2H, CH_2 of ethyl group), 7.43(AB quartet, 4H, CH_2 adjacent to the carbonyls). (Found: C,72.58%, H,9.91%, $C_{11}H_{18}O_2$ requires: C,72.49%, H,9.95%).

4-Cyano-2,2-dimethyl butaldehyde.

Michael addition of isobutaldehyde (60g.) to acrylonitrile (100ml.) was effected by the method of Born et al.[164]. Yield 66.5g.(64%); b.p.88-98°/1.5mm.; n_D^{20} 1.4378.

2,2-Dimethyl glutaric acid.

The above cyanoaldehyde (64.5g.) was gradually added to a mixture of concentrated sulphuric acid (31g.) and 65% nitric acid (155g.) at 35-40°C after which the mixture was cautiously heated for 2hrs. at 70-80°C. (n.b. As soon as the initial reaction starts cool rapidly until the vigorous reaction dies down and then continue heating. For this scale a 3l. flask was used.) The yellow solution was poured onto crushed ice (70g.) and the white crystalline solid filtered

off and dried in vacuo over $CaCl_2$. Yield 54.8g.(66%); m.p.82-84°(benzene).

2,2-Dimethyl glutaric anhydride.

2,2-Dimethyl glutaric acid (48.5g.) was refluxed with an excess of acetic anhydride (300ml.) for 8hrs. and distilled. Yield 32.1g.(75%); b.p.120°/5.0mm.

1-Carboxyethyl-1,1-dimethyl butyric acid.[165]

2,2-Dimethyl glutaric anhydride (30.3g.) was refluxed with ethanol (50ml) according to the procedure of Champagne et al.[165] . Yield 18.1g.(45%); b.p.132-136°/2.0mm.; n_D^{23} 1.4410; (lit. b.p.120°/1.6mm.; n_D^{24} 1.4395).

1-Carbethoxy-1,1-dimethyl butyryl chloride.

The above mono ester (17g.) and thionyl chloride (14.9g.) were stirred at room temperature for 15hrs. and distilled. Yield 16.1g.(86%); b.p.80-82°/1.7mm.,(lit.[165] b.p.70°/1.2mm.)

2-Carbethoxy-2-methyl-5-oxo-hexane.[165]

This was prepared by the method of Champagne et al.[165] from 1-carbethoxy-1,1-dimethyl butyryl chloride (15.6g.) and the cadmium Grignard reagent from methyl bromide. Yield 11.6g. (83%); b.p.81-87°/2mm., (lit. b.p.72°/2mm.; n_D^{24} 1.4347).

4,4-Dimethyl cyclohexan-1,3-dione.[99]

To a suspension of potassium t-butoxide (from 1.64g. of potassium) in anhydrous ether (50ml.) was added gradually with cooling the keto ester prepared above (10.6g.) in dry

ether (15ml.), and the mixture stirred at room temperature for 12hrs. After refluxing for 1.5 hrs. the solution was decomposed with 2N-hydrochloric acid (45ml.) and the ether phase separated, washed with water and dried (Na_2SO_4). Evaporation afforded the title compound. Yield 6.0g.(75%); m.p.103-104°(b.p.60-80°petroleum ether), (lit.[165] m.p.105°).

2,2-Dimethyl-5-isobutoxy cyclohex-5-ene-1-one.[99]

The above dione (1.65g.) was refluxed under a Dean and Stark head with isobutanol (1.10g.) in benzene (35ml.) containing a little p-toluene sulphonic acid for 8.5 hrs. and the enol ether distilled direct as a colourless oil. Yield 1.94g.(84%); b.p.100-102°/0.8mm.; n_D^{22} 1.4870, (lit. b.p.115°/3mm.; n_D^{21} 1.463). The n.m.r. showed the absence of the alternative isomer.

3,4,4-Trimethyl cyclohex-2-ene-1-one.[99]

This was prepared according to the literature procedure[99] by reaction of methyl magnesium iodide (from 0.90g. methyl iodide) with 2,2-dimethyl-5-isobutoxy cyclohex-5-ene-1-one (0.80g.). The product was purified by chromatography on silica eluting with chloroform. Yield 0.39g.(70%); b.p.105°/15mm.; n_D^{19} 1.4868, (lit. b.p.93-95°/10mm.; n_D^{24} 1.4840). The n.m.r.($CDCl_3$) showed the vinylic methyl group at τ 8.11(d, J=1Hz,); ν_{max}(l.f.) 1670, and 1618 $cm.^{-1}$; λ_{max}(EtOH) 236mμ (log ε ,4.18).

4,4-Dimethyl-3-phenyl cyclohex-2-ene-1-one.

This was prepared as above from phenyl magnesium iodide and 2,2-dimethyl-5-isobutoxy cyclohex-5-ene-1-one (0.8g.). The product was purified by chromatography on silica eluting with chloroform. Yield 0.37g.(45%); b.p.124°/1.5mm.; n_D^{20} 1.5628, (lit.[166] b.p.124-126°/2mm.); ν_{max}(l.f.) 1678, 1610,888,770, and 712 cm.$^{-1}$

6,6-[$^2H_2$]-4,4-Dimethyl-3-phenyl cyclohex-2-ene-1-one.

The above cyclohexenone (15mg.) was refluxed for 24hrs. in deuterium oxide (3ml.) containing sodium metal (5mg.) and stirred in the presence of chloroform for a week. The heterogeneous reaction mixture was acidified with deuterio sulphuric acid and the chloroform layer separated, dried and distilled. Yield 12mg.(80%). The n.m.r. spectrum showed no signal at τ 7.60-7.27(m) and the signal at τ 4.22 was also considerably reduced. D_3,36.9%, D_2,58.0%, D_1,3.4%, D_o,2.3%.

4,4-Dimethyl-3-ethoxy-cyclohex-2-ene-1-one.

4,4-Dimethyl cyclohexan-1,3-dione (1.35g.) was converted to a 50% mixture of the two ethyl enol ethers according to the procedure of Champagne et al.[165]. The two isomers were effectively separated by preparative g.l.c. on a 9metre methyl silicone gum column column at 150°C. The title compound had b.p.84-86°/0.8mm.; ν_{max}(l.f.) 1655,1610 cm.$^{-1}$; n.m.r.($CDCl_3$) τ 8.88(s, 6H, gem-dimethyl), 8.64(t,J=7Hz, 3H, CH_3 of ethyl group), 8.18(t, J=6Hz, 2H, CH_2 β to carbonyl),

7.61(t, J=6Hz, 2H, CH_2 α to carbonyl), 6.08(q, J=7Hz, 2H, CH_2 of ethyl group), 4.73(s, 1H, vinylic proton).

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

Naphthalene (12.8g. 0.1mole) was reduced with lithium (8.3g. 1.2g.atom) in anhydrous ethylamine by the method of Bakeser et al.[167] to a mixture of $\Delta^{1,9}$ and $\Delta^{9,10}$ octalins, 9.2g. Treatment of this mixture with phosphoric oxide (5.3g.) for 2hrs. at 140°C then afforded the $\Delta^{9,10}$ octalin in high purity. Yield 5.0g.(37%); b.p.80-82°/13mm.; n_D^{23} 1.4928, (lit.[167] b.p.192-5°/760mm.)

1-Bromo-$\Delta^{9,10}$-octalin.

$\Delta^{9,10}$-Octalin (5.0g.) was dissolved in anhydrous benzene (20ml.) and a little benzoyl peroxide (0.06g.) was introduced. The solution was brought to a vigorous reflux and N-bromosuccinimide (6.5g., slight excess) together with a little benzoyl peroxide (0.06g.) was added as rapidly as the frothing allowed (ca. 5mins.). After refluxing for a few minuits the solution was cooled in ice and the precipitated succinimide filtered off. The solid was washed with a small amount of cold benzene and the filtrate evaporated to a yellow-brown oil (7.64g., 96%) which was used in this state.

$\Delta^{9,10}$-Octalin-1-one.

The crude bromo compound (3.64g.) in tetrahydrofuran (12.5ml.) was added to a 2molar excess of aqueous sodium bicarbonate and stirred at 25°C for 20hrs. After dilution

with water the product was extracted with ether and the extracts dried (Na_2SO_4). Evaporation gave an oil which t.l.c. showed to consist of three components. Chromatography on silica eluting with benzene : 5% acetone gave the desired compound as a colourless oil. Yield 1.72g.(68%); b.p.62°/0.2mm.; n_D^{20} 1.5308; ν_{max}(l.f.) 1665, and 1630 $cm.^{-1}$,(lit.[168] b.p.67-69°/0.1mm.; n_D^{20} 1.5241).

1,1-[$^2H_2$]-n-Propanol.

To a slurry of lithium aluminium deuteride (1.0g.,10% excess) in anhydrous ether (25ml) was added with stirring a solution of propionic acid (2.14g.) in ether (25ml.) at such a rate that the ether gently refluxed. After the addition was complete the mixture was vigorously stirred overnight and just sufficient water to decompose the complex added (ca. 3ml.). The precipitated alumina was filtered off and the ethereal solution dried (Na_2SO_4) and distilled. Yield 1.38g. (77%); b.p.90-94°/760mm.; ν_{max}(l.f.) 3500 $cm.^{-1}$

3-(1,1-[$^2H_2$]-n-Propoxy)-5,5-dimethyl cyclohex-2-ene-1-one.

[$^2H_2$]-Propanol (1.38g.) prepared as above was refluxed for 8hrs with benzene (25ml.) and dimedone (3.1g.) in the presence of a catalytic amount of p-toluene sulphonic acid, the water being removed by activated type 3A molecular sieves contained in a Soxhlet thimble. Distillation gave the requisit derivative. Yield 0.64g.(16%); b.p.146°/15mm.; n_D^{20} 1.4895. The n.m.r. showed no signal at τ 6.22.

2,2-[$^2H_2$]-n-Propanal.

Propanal (4.5g.) dried over $CaSO_4$, was added to deuterium oxide (15ml.) containing pyridine (0.75g.) and the mixture heated to 100°C in a Carius tube for 15hrs. Distillation under nitrogen through a 5" Vigreux column and collection of the distillate at -30°C afforded the partially labelled aldehyde which was recycled with a further quantity of deuterium oxide (15ml.). Yield 1.62g.(34%); a low yield due to considerable resinification. The n.m.r. showed 97.5% incorporation of deuterium.

2,2-[$^2H_2$]-Propanol.

Reduction of the above aldehyde (1.06g.) with lithium aluminium hydride (0.18g.,10% excess) in ether (20ml) gave the title compound. Quantitative yield, b.p.90-98°/760mm.

3-(2,2-[$^2H_2$]-n-Propoxy)-5,5-dimethyl cyclohex-2-ene-1-one.

Dimedone (2.34g.) was condensed with the above alcohol (1.06g.) according to the procedure cited for the other deuteriated analogue, p.242. Yield 0.210g.(15%); b.p.142-4°/15mm.; n_D^{21} 1.4939. The n.m.r. showed the absence of a signal at τ 8.25. D_2,98.5%, D_1,1.5%, (mass spectrum).

2,2,2-[$^2H_3$]-Ethyl iodide.

[$^2H_4$]-Acetic acid (4.2g.) in anhydrous ether (10ml.) was added slowly to a stirred suspension of lithium aluminium hydride (2.06g., 10% excess) in anhydrous ether (30ml.) and the mixture stirred overnight at 20°C. Sufficient water to

destroy the complex was added and the azeotrope of water/ethanol (b.p.80-100°) distilled out. 55% Aqueous hydrogen iodide (15ml.) was added to the distillate and the mixture refluxed for 1hr. Slow distillation at 60°C through a 15cm. column over 70mins, gave the crude iodide. Yield 2g.(50%).

3,3,-[$^2H_3$]-Propanol.

The above iodide (2g.) was dissolved in ether (10ml.) and added to dry magnesium (0.34g.,10% excess). The Grignard reagent so formed was added to a slurry of solid carbon dioxide (4g.) in ether (10ml.) and allowed to stand for 1hr. Aqueous sulphuric acid (20%, 10ml.) was added followed by silver sulphate (3g. to destroy iodine) and the acid isolated by continuous ether extraction overnight. After drying and evaporation the acid (ca. 2g.) was reduced with lithium aluminium hydride (0.8g.) and worked up as for the other deuteriated alcohols. Yield 0.67g.(85% overall).

5,5-Dimethyl-3-(3,3,3-[$^2H_3$]-n-propoxy) cyclohex-2-ene-1-one.

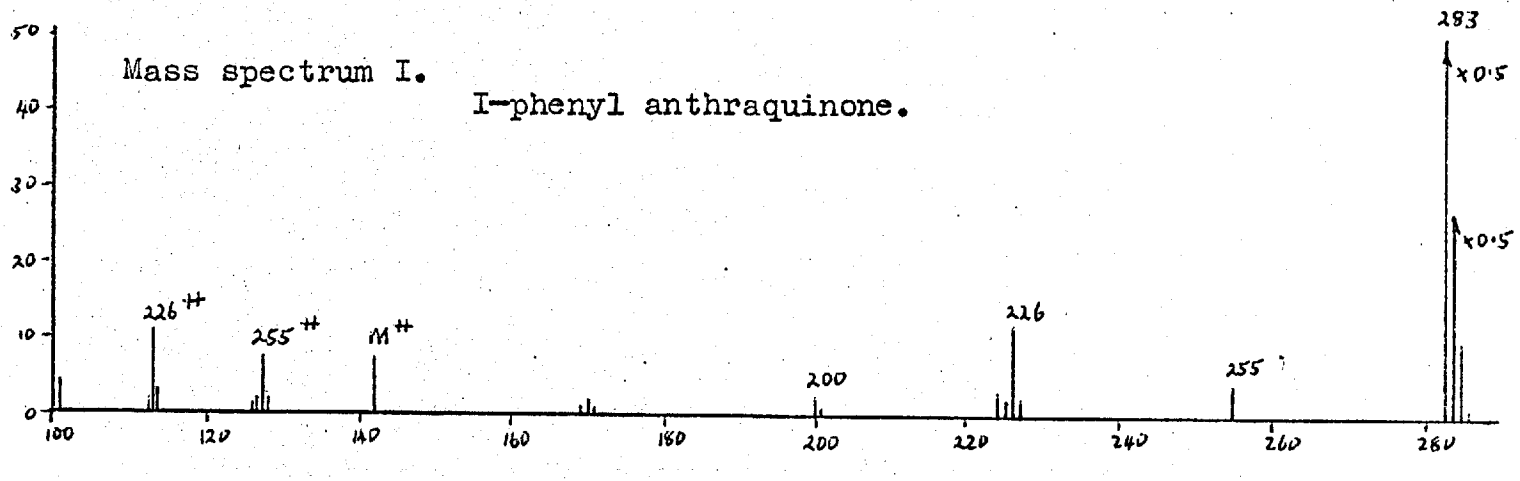
This was prepared as for the other deuteriated derivatives from dimedone (1.34g.) and 3,3,3-[$^2H_3$]-n-propanol (0.67g.) Yield 0.125g.(14%). The n.m.r. spectrum showed no signal at τ 9.02. D_3,95.2%, D_2,4.8%, (mass spectrum).

5 . 5 Mass spectra.

Mass spectra were obtained with an A.E.I. MS 9 double focussing instrument, operated at 8kV accelerating voltage, 70eV ionizing voltage and 100μA trap current. High resolution mass measurements were made using heptacosafluorotri-n-butylamine as a mass standard, with a resolving power of between 7 and 11 thousand. All samples were inserted via the heated inlet system except for the anhydrodimedones which were directly inserted in the ion beam using a ceramic probe, the conditions used being those of minimum temperature sufficient to produce a sufficient vapour pressure in the sample.

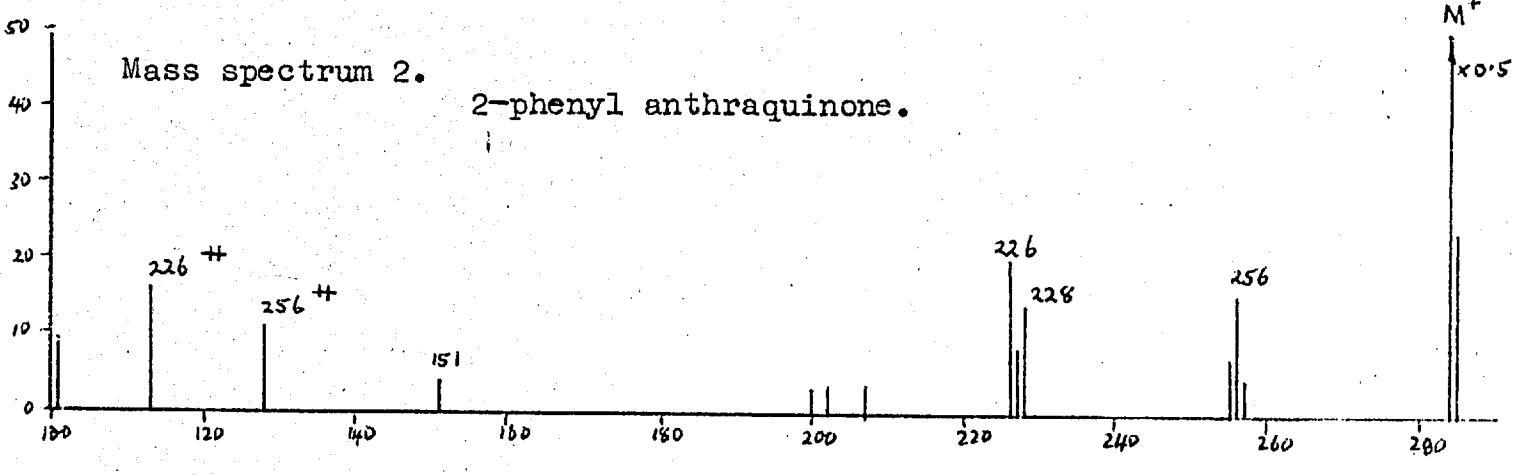
Mass spectrum I.

I-phenyl anthraquinone.



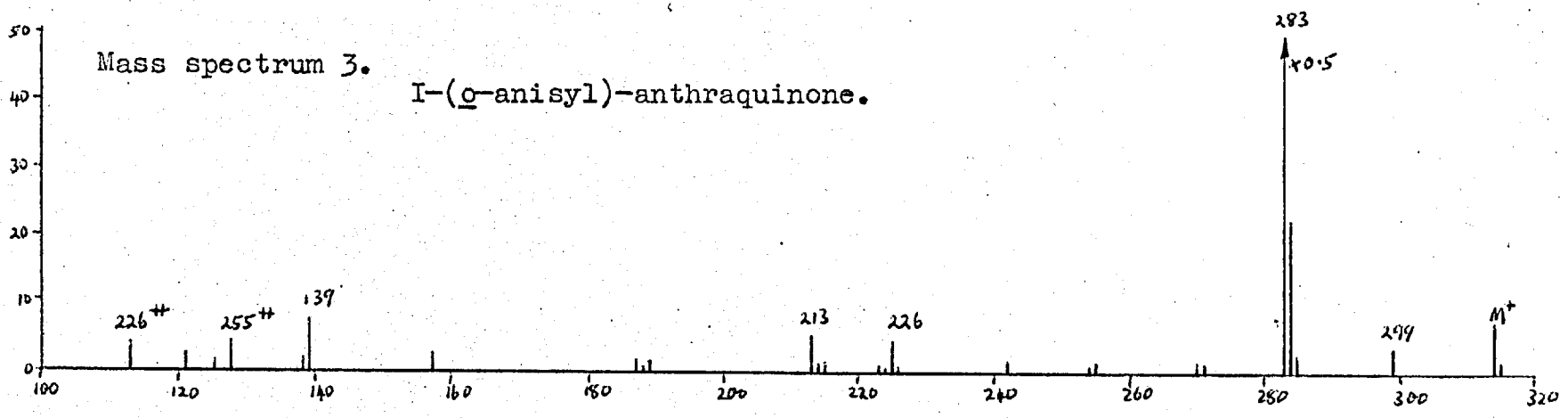
Mass spectrum 2.

2-phenyl anthraquinone.



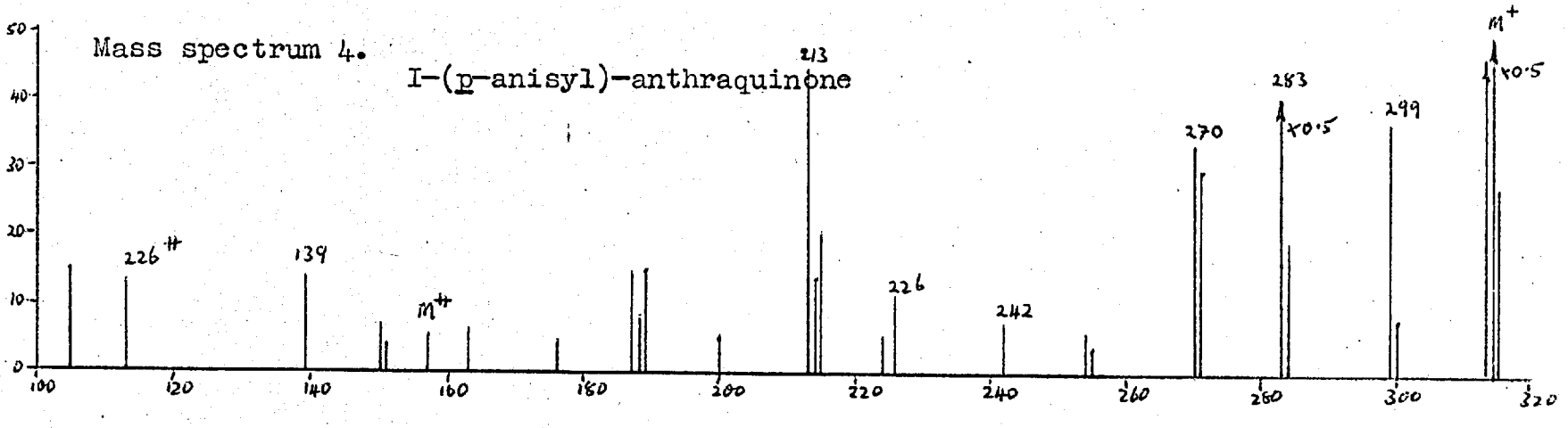
Mass spectrum 3.

I-(o-anisyl)-anthraquinone.



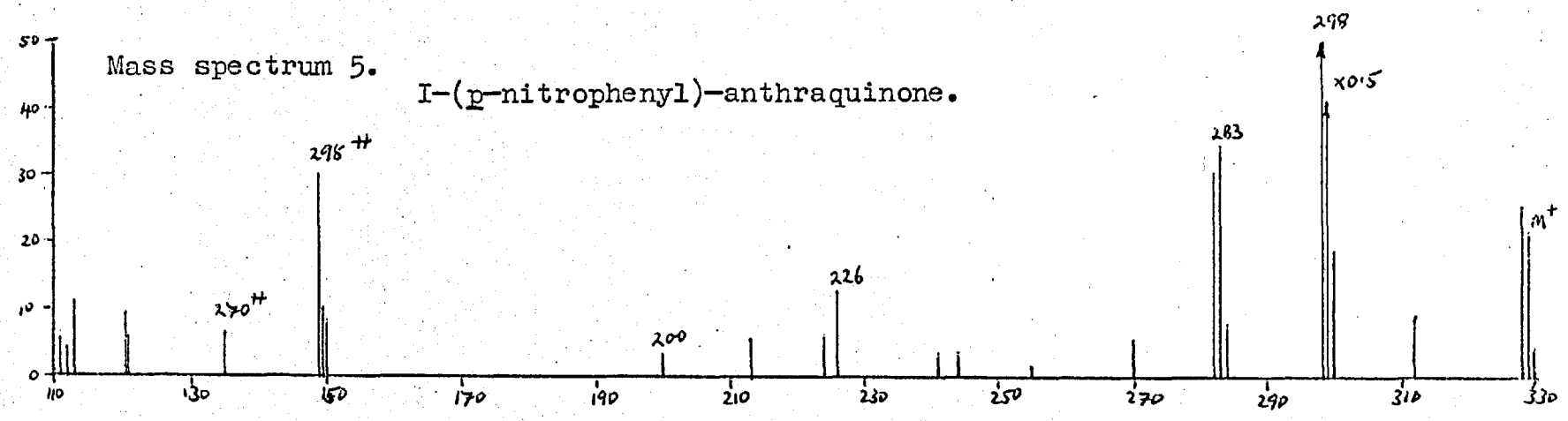
Mass spectrum 4.

I-(p-anisyl)-anthraquinone



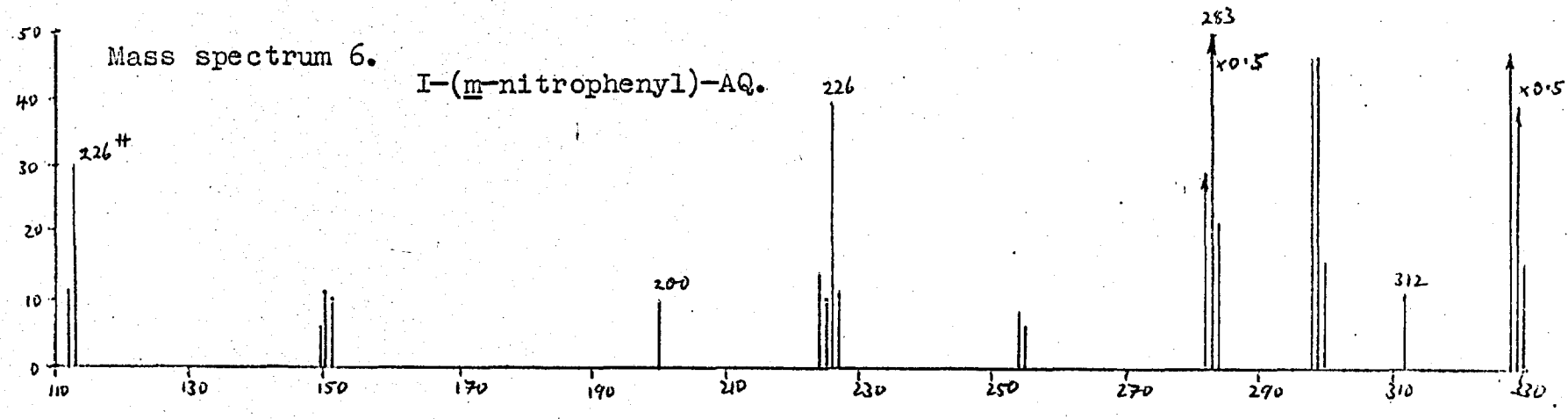
Mass spectrum 5.

I-(p-nitrophenyl)-anthraquinone.



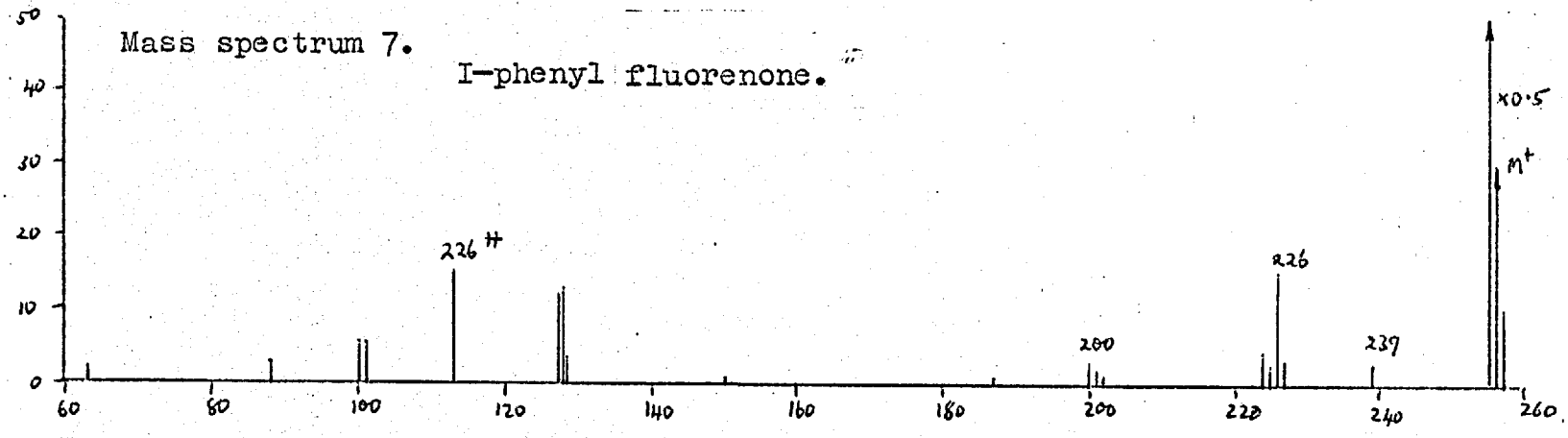
Mass spectrum 6.

I-(m-nitrophenyl)-AQ.



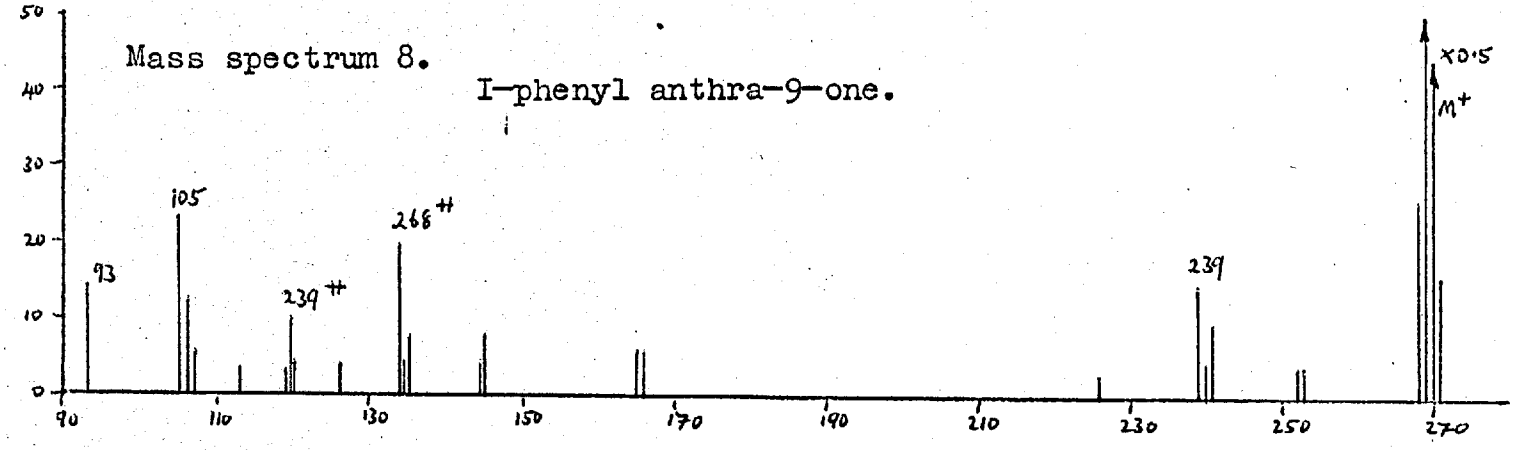
Mass spectrum 7.

I—phenyl fluorenone.



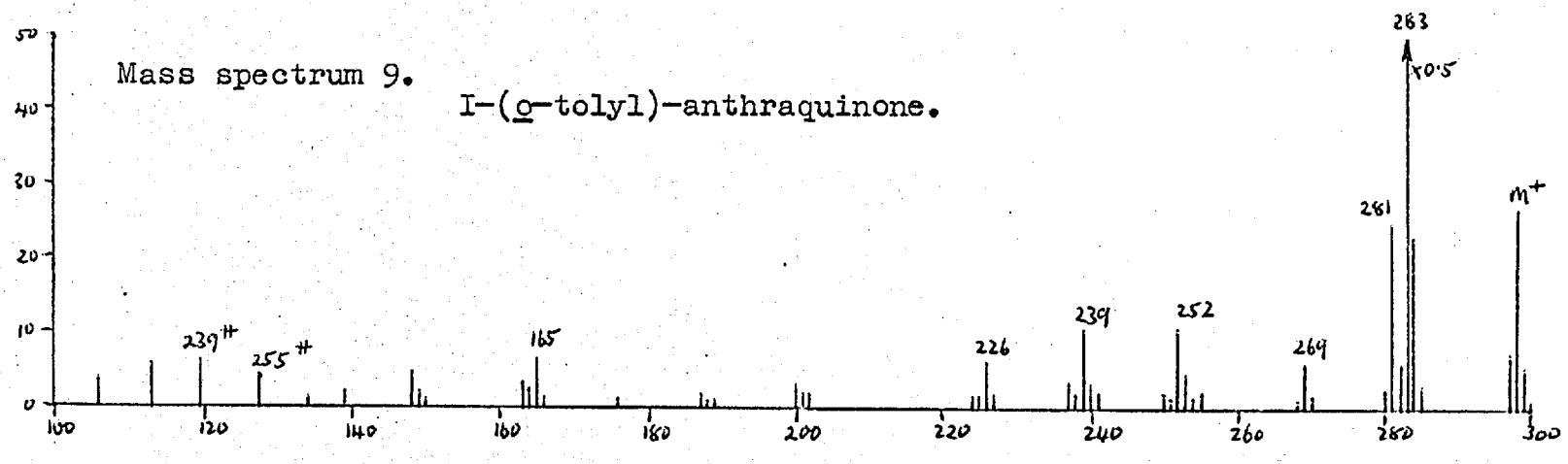
Mass spectrum 8.

I—phenyl anthra—9—one.



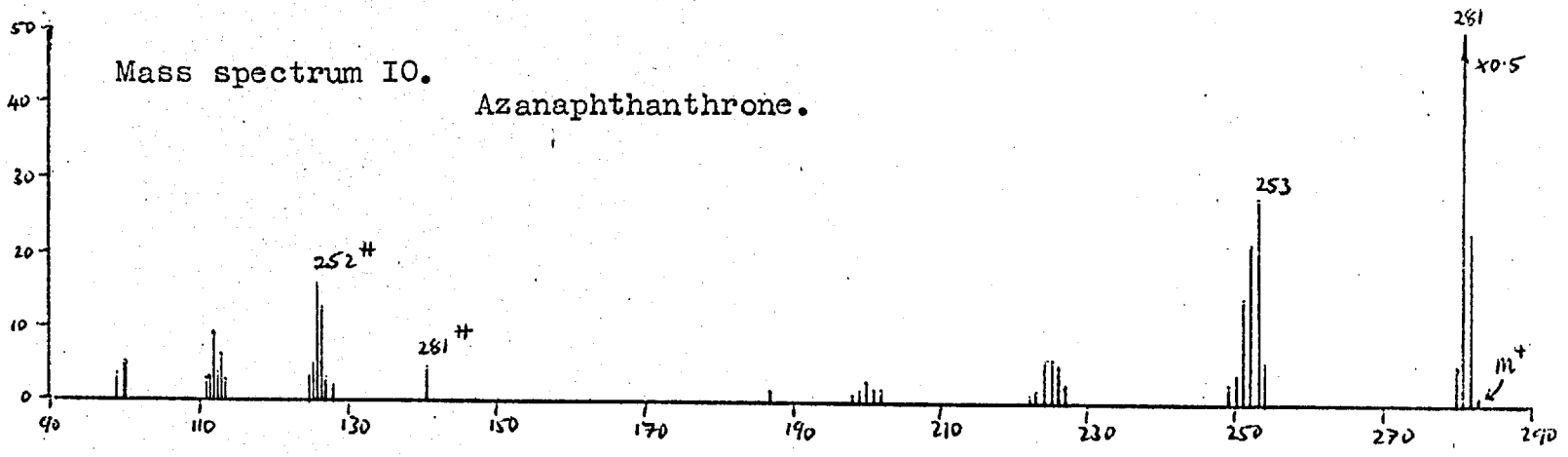
Mass spectrum 9.

I-(o-tolyl)-anthraquinone.



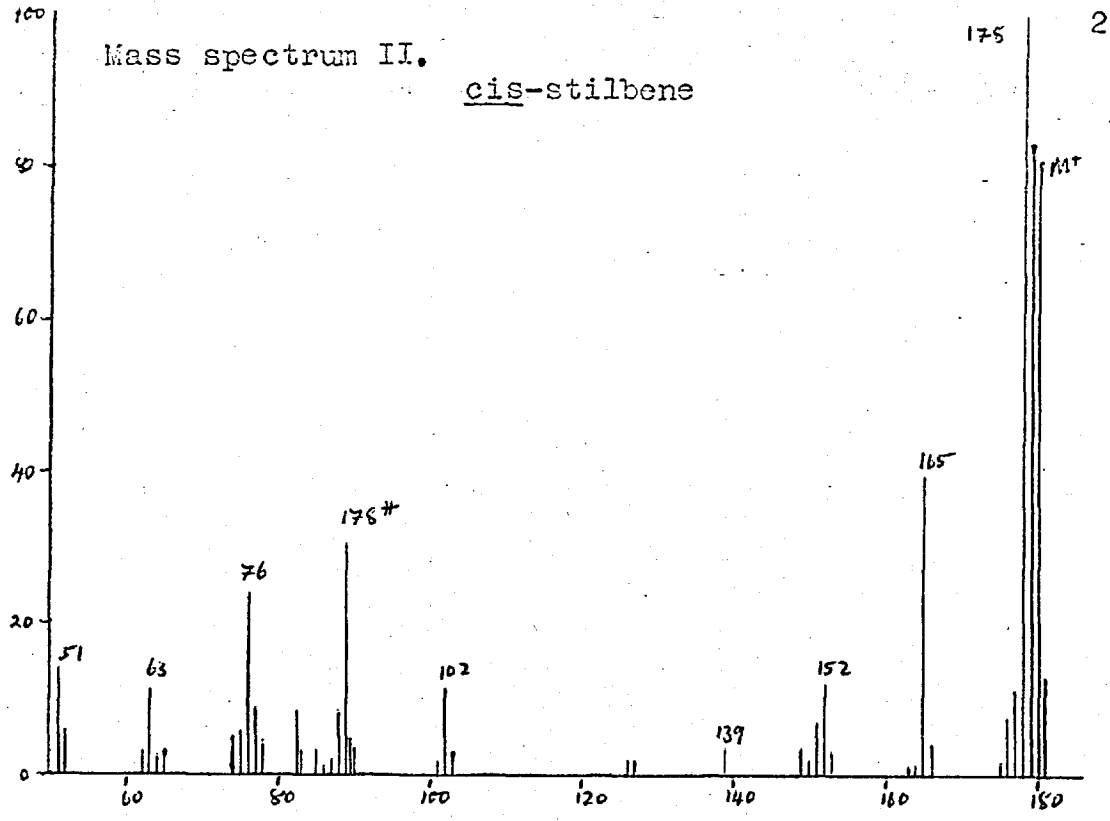
Mass spectrum IO.

Azanaphthanthrone.



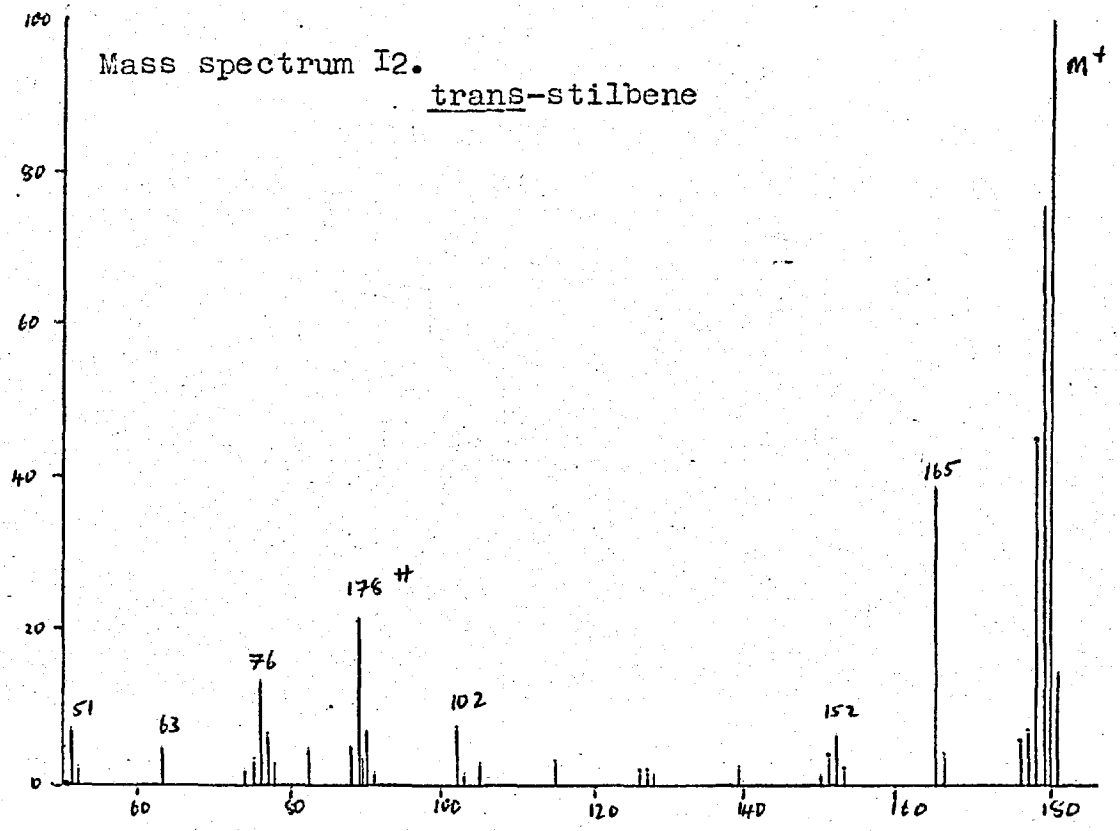
Mass spectrum II.

cis-stilbene

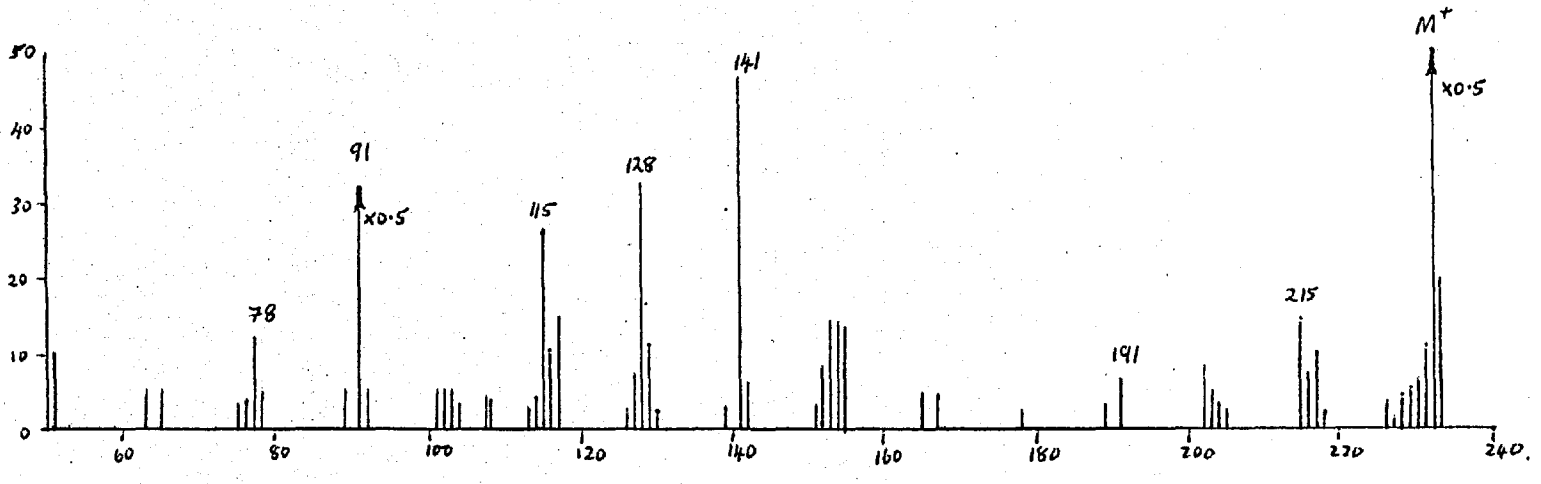


Mass spectrum I2.

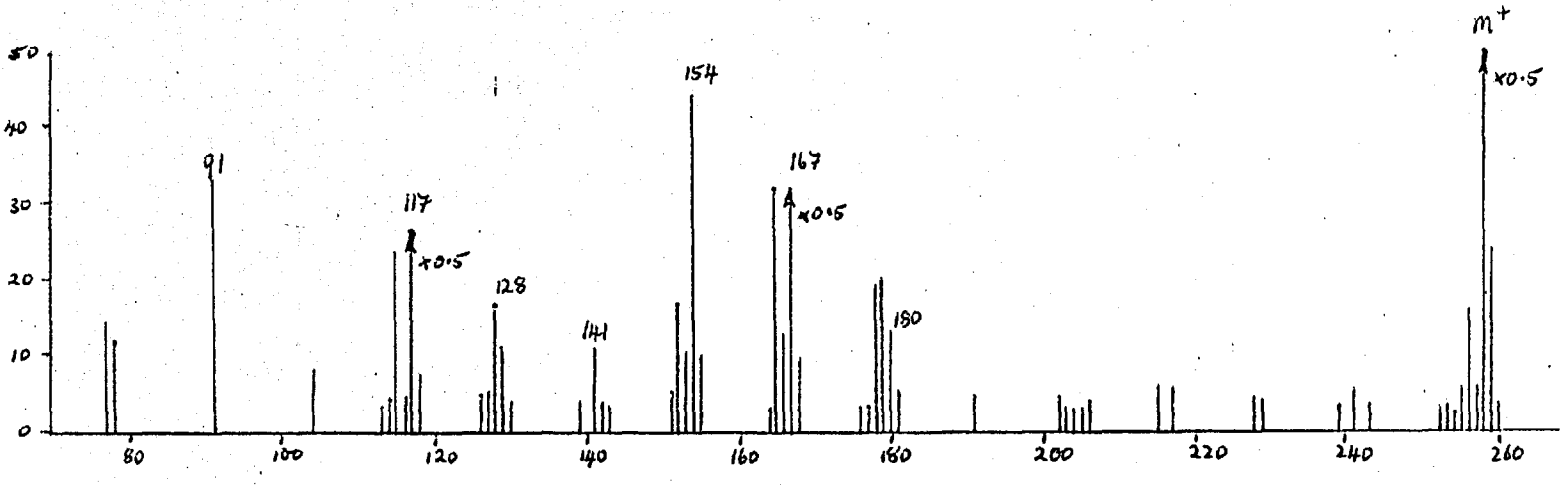
trans-stilbene



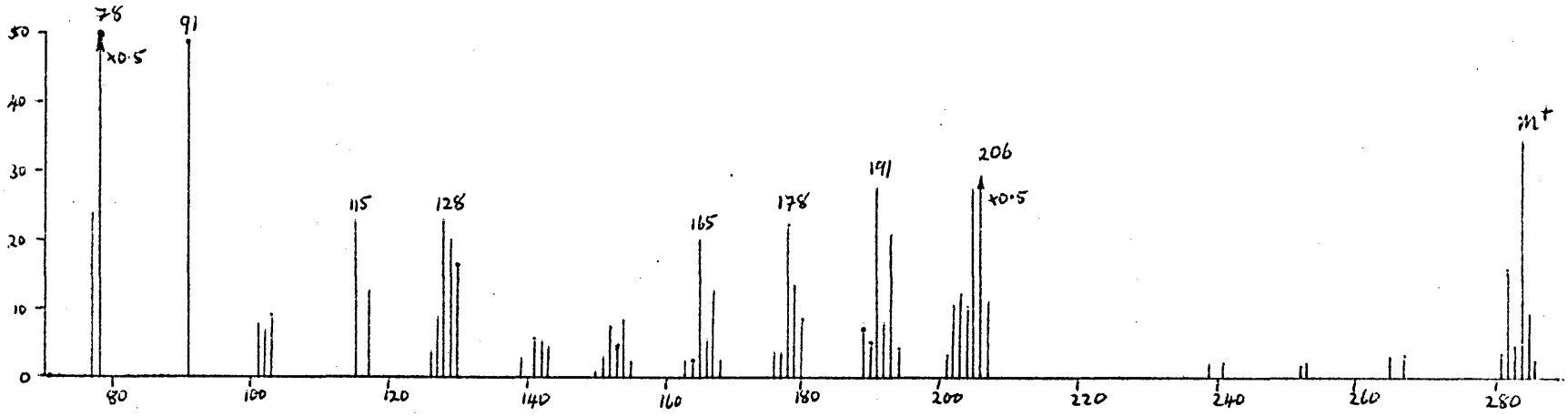
Mass spectrum I3. I,6-diphenyl hexatriene



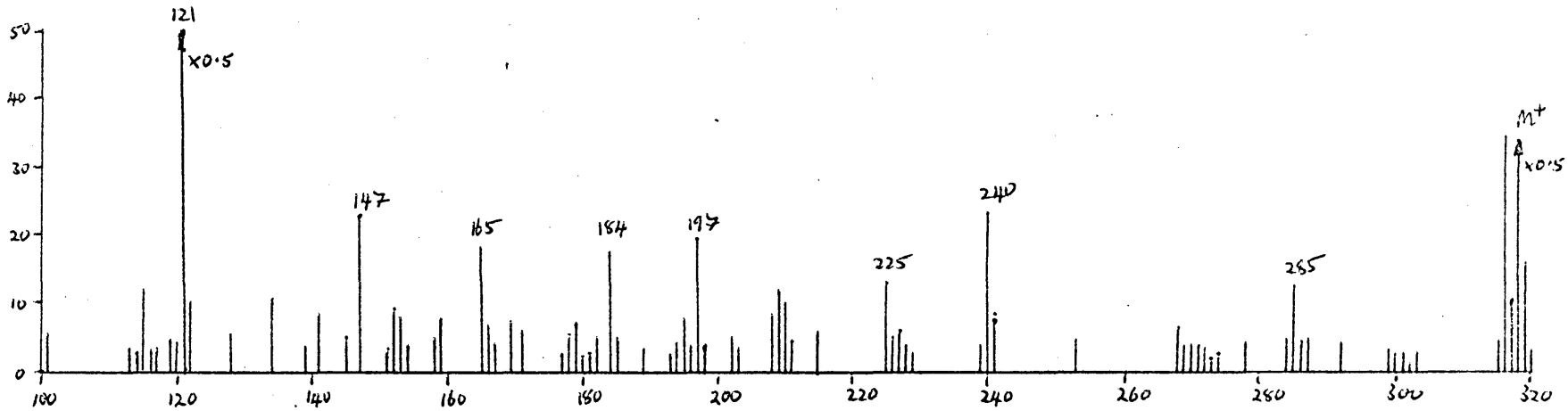
Mass spectrum I4. I,8-diphenyl octatetraene



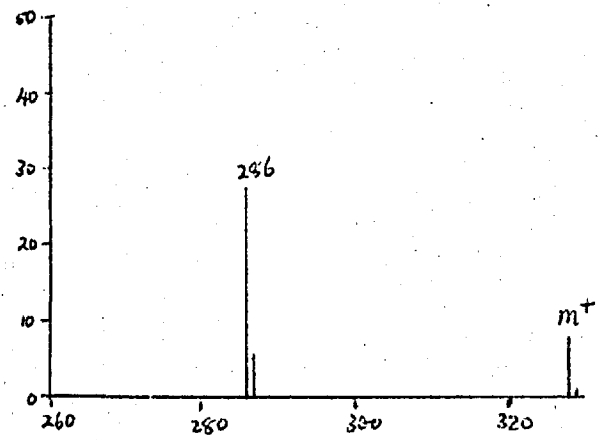
Mass spectrum I5. I,IO-diphenyl decapentaene

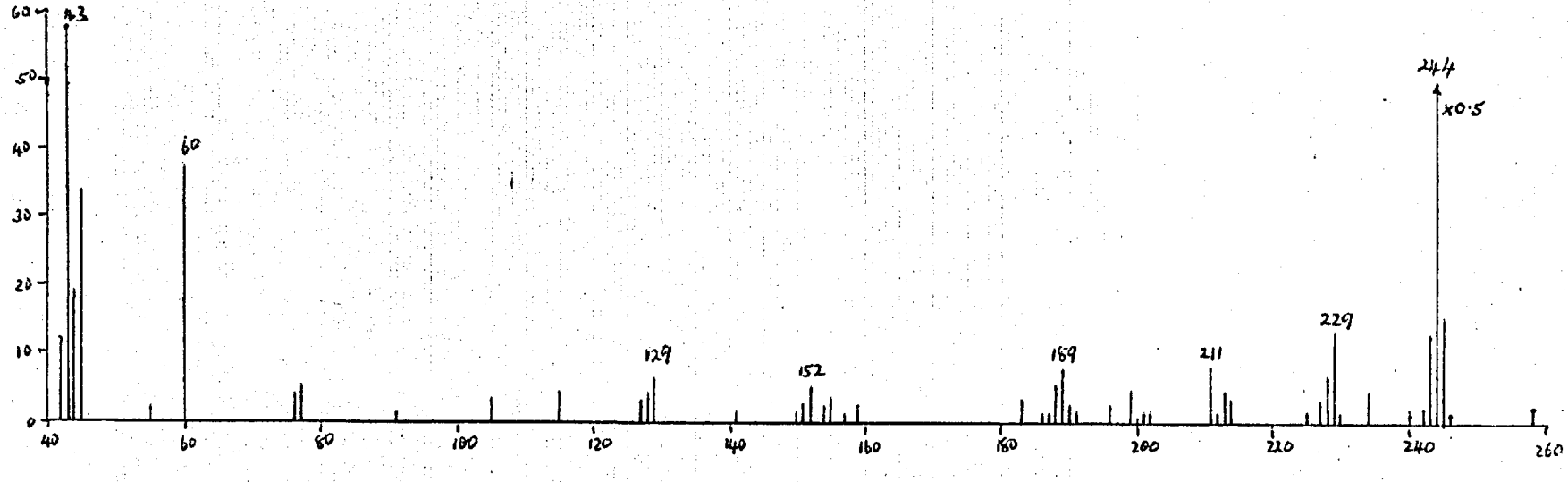


Mass spectrum I6. I,8-di-(p-anisyl)-octatetraene

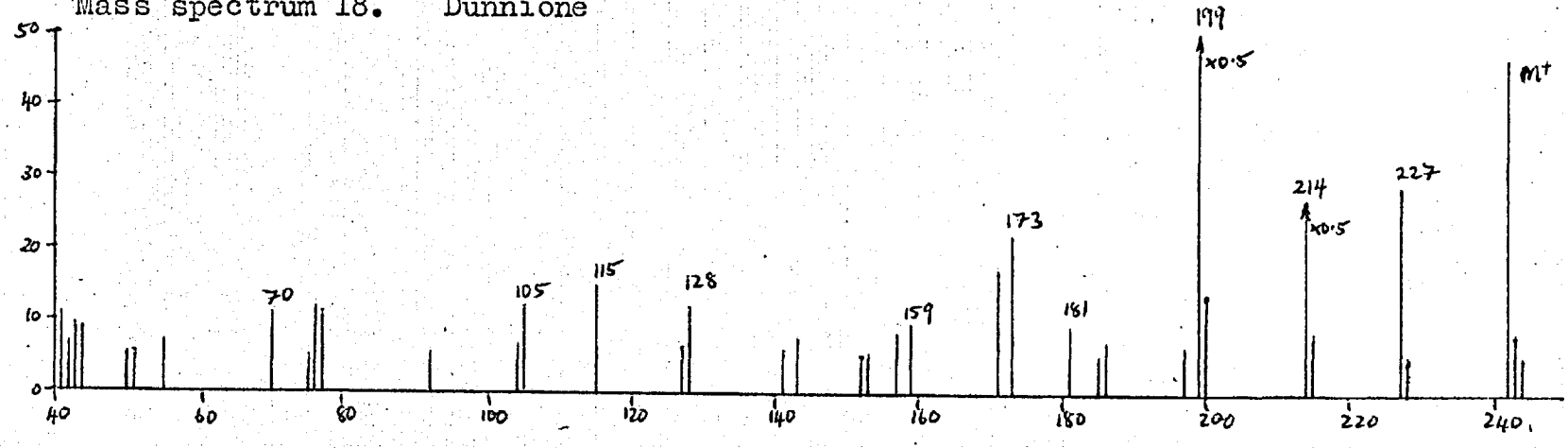


Mass spectrum I7. Hydrodunnione diacetate

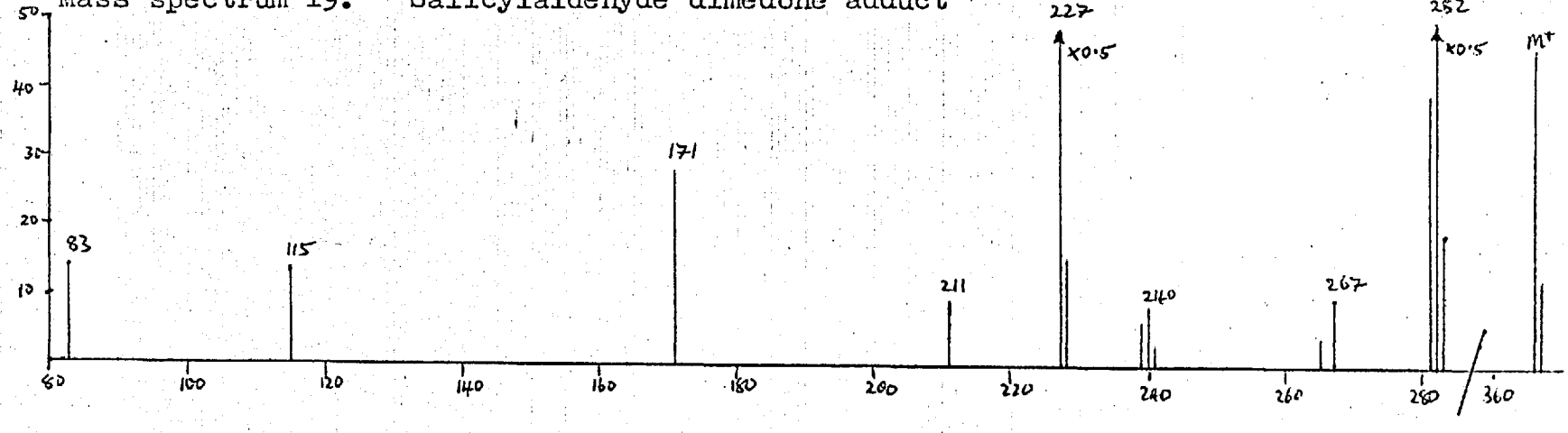




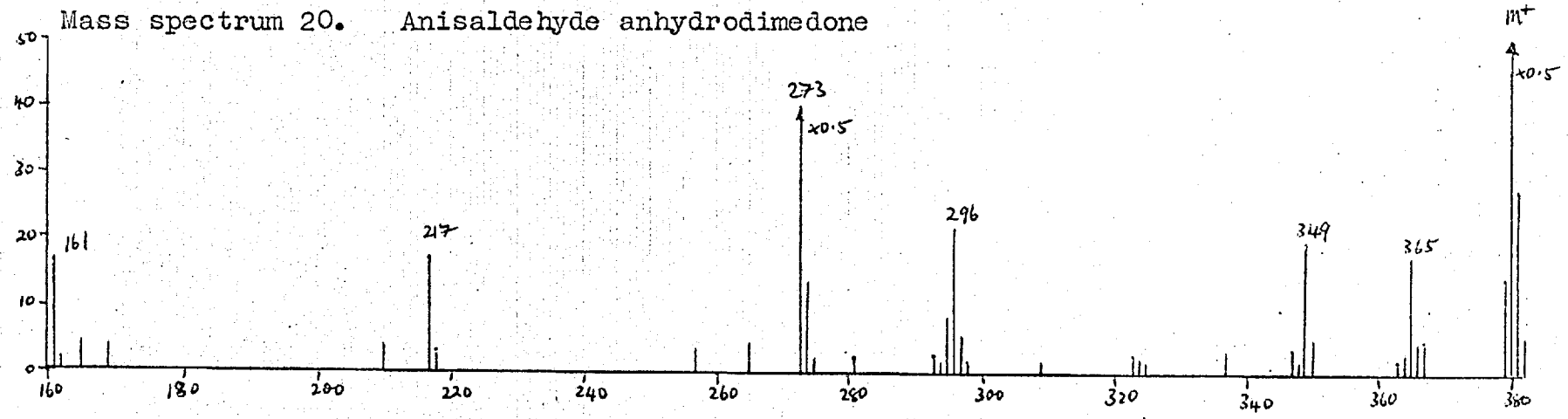
Mass spectrum I8. Dunnione



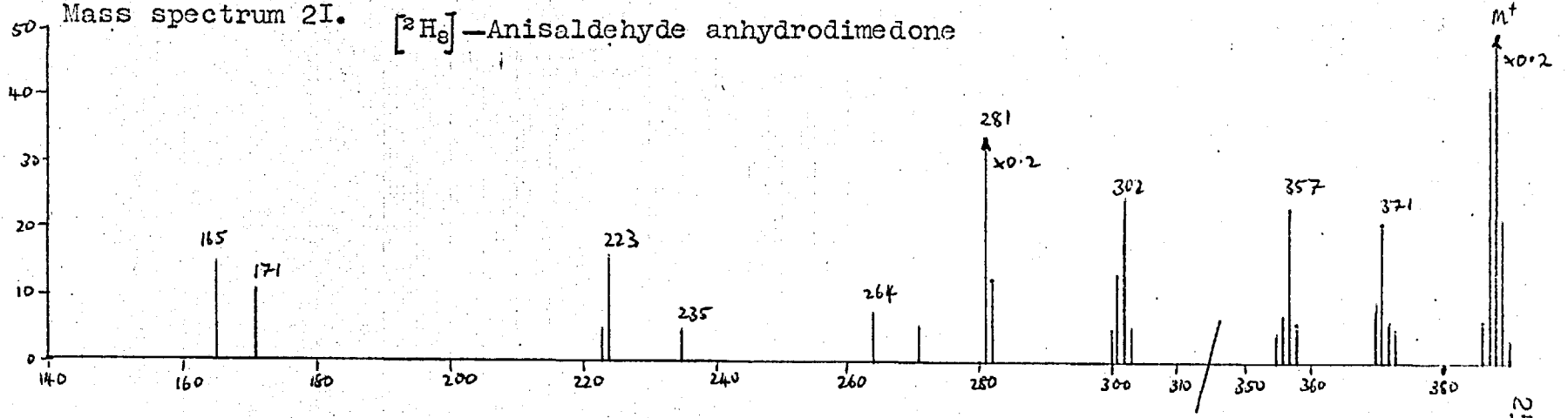
Mass spectrum I9. Salicylaldehyde dimedone adduct



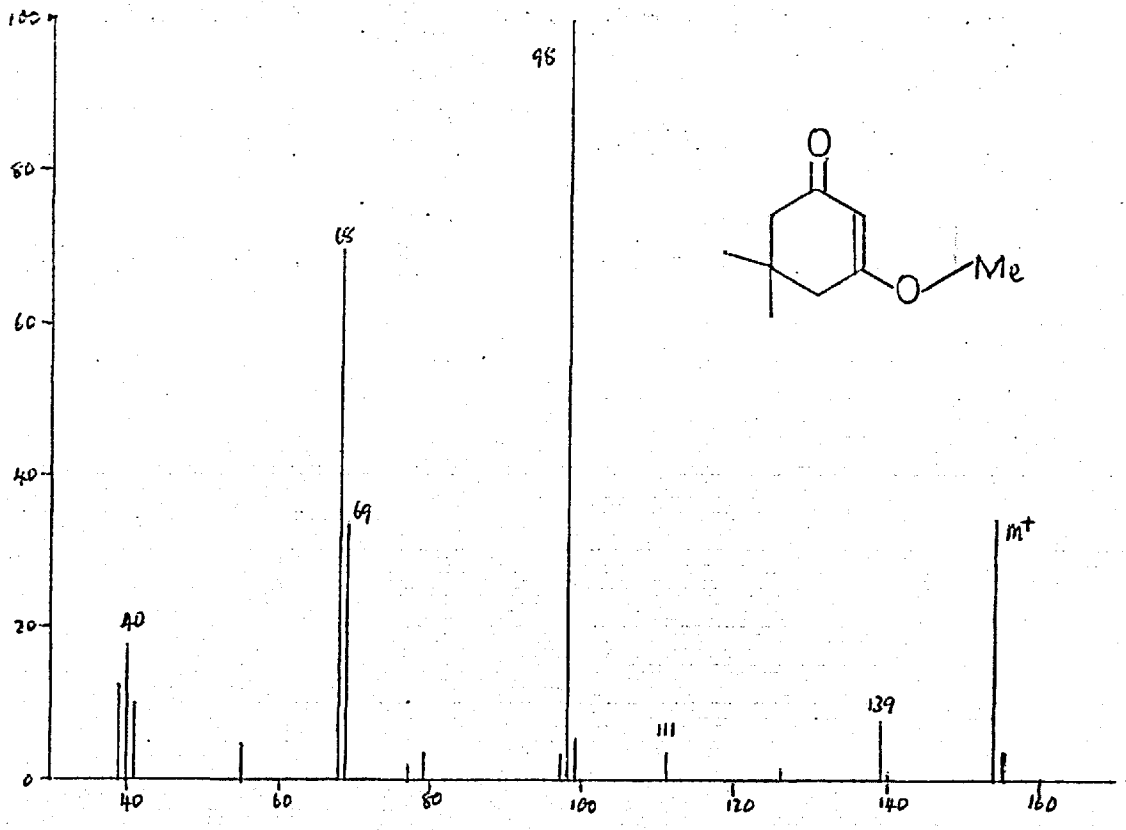
Mass spectrum 20. Anisaldehyde anhydrodimedone



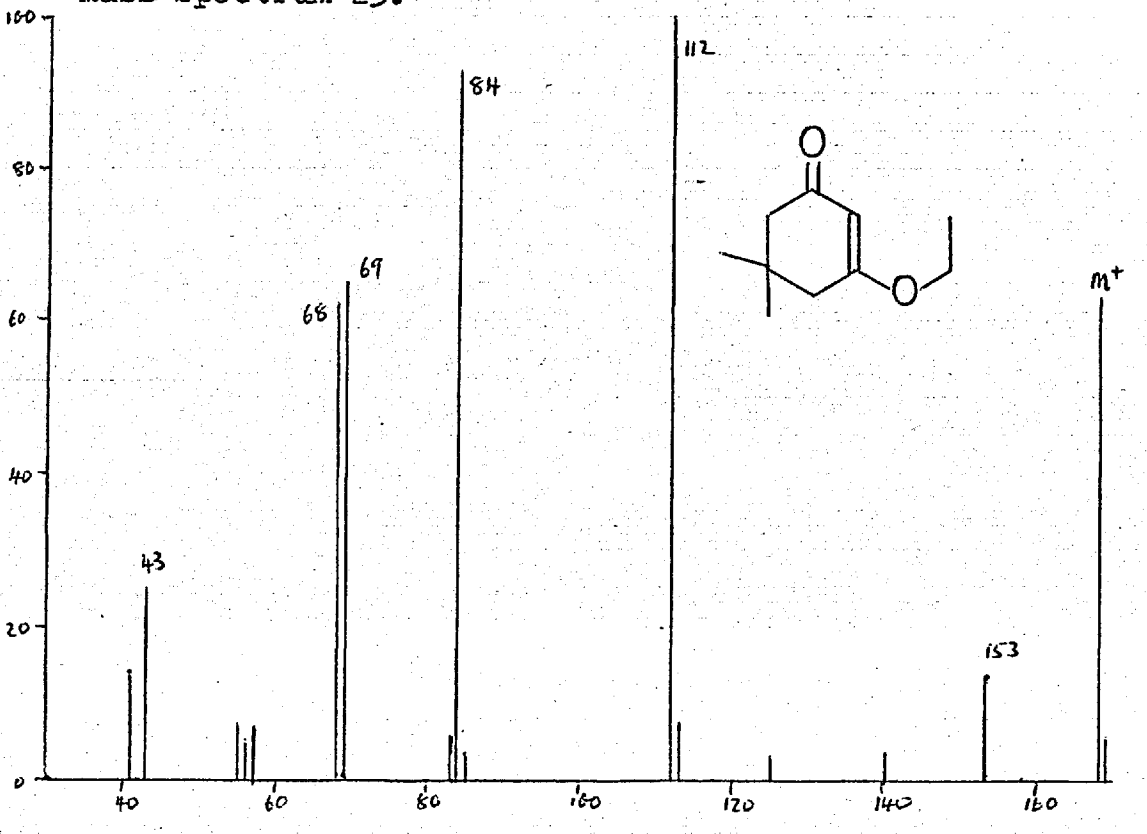
Mass spectrum 2I. [$^2H_8$]—Anisaldehyde anhydrodimedone



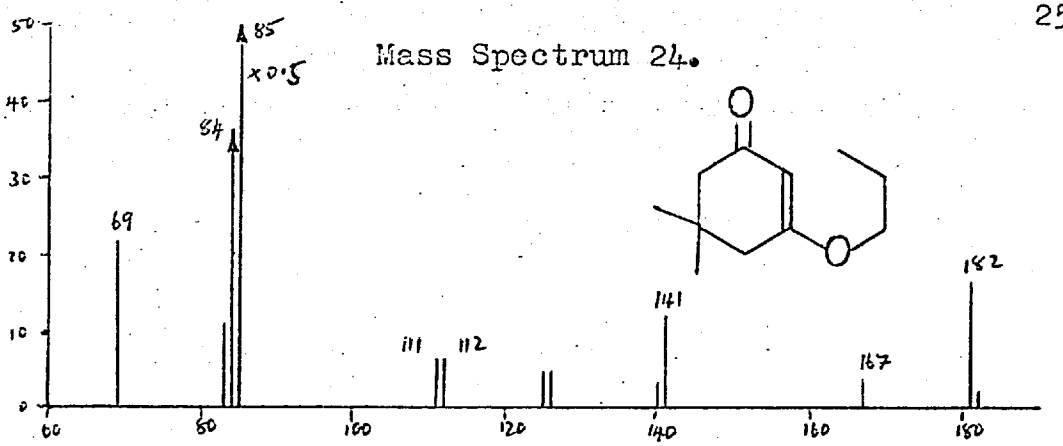
Mass Spectrum 22.



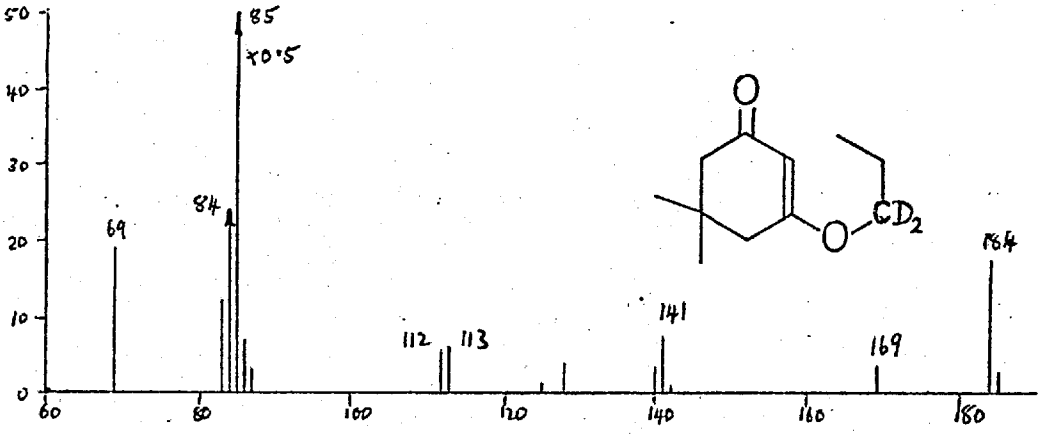
Mass Spectrum 23.



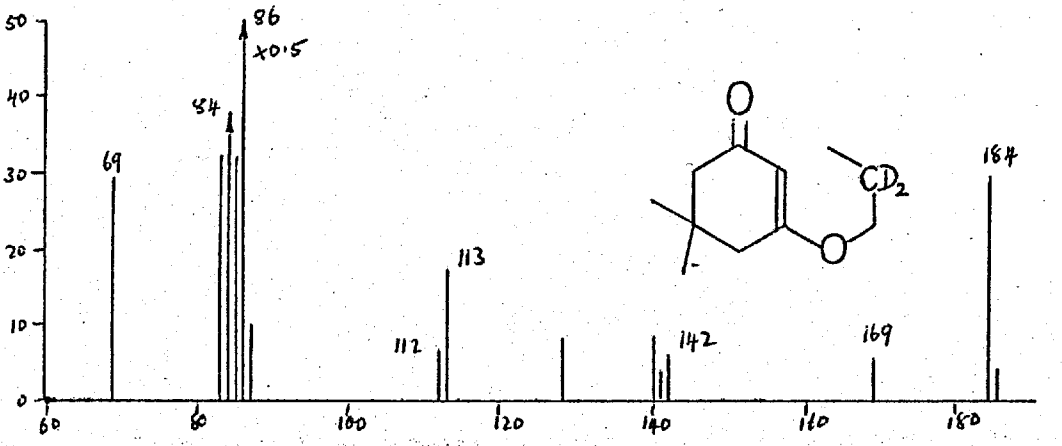
Mass Spectrum 24.



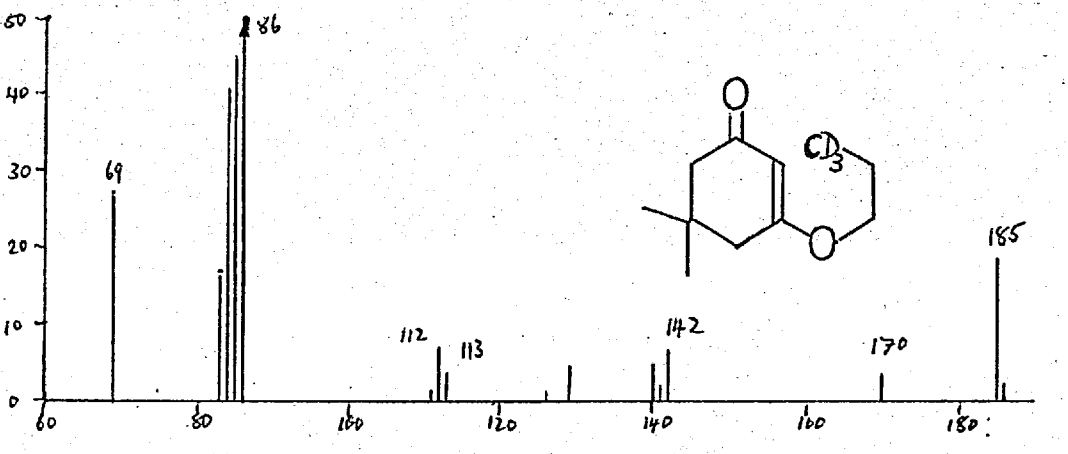
(a)



(b)



(c)



(d)

References.

(1) F.W.Aston, Phil.Mag., 1919, 38, 707 ; F.W.Aston, 'Isotopes', Edward Arnold, London, 1922, p1924.

(2) W.T.Pike & F.W.McLafferty, J.Amer.Chem.Soc., 1967, 89, 5954 ; M.M.Bursey & L.R.Dusold, Chem.Comm., 1967, 712.

(3) J.Momigmy, L.Brakier & L.d'Or, Bull.Class.Sci.Acad.Roy.Belge. 1962, 48, 1002.

(4) J.H.Beynon & A.E.Fontaine, Chem.Comm., 1966, 717.

(5) T.A.Elwood & M.M.Bursey, Org.Mass Spectrom., 1968, 1, 531, 537.

(6) J.H.Beynon, G.R.Lester & A.E.Williams, J.Phys.Chem., 1959, 63, 1861 ; J.H.Beynon, Advan.Mass Spectrom., 1959, 1, 328.

(7) R.I.Reed & J.M.Wilson, Chem. & Ind., 1962, 1428.

(8) J.Ronayne, D.H.Williams & J.H.Bowie, J.Amer.Chem.Soc., 1966, 88, 4980.

(9) Y.Itagaki, T.Kurokawa, S.Sasaki, C-T.Chang & F.-C.Chen, Bull.Chem.Soc.Japan., 1966, 39, 538.

(10) R.I.Reed & V.V.Takhistov, 'Some Newer Physical Methods in Structural Chemistry' R.Bonnett & J.G.Davis, United Trade Press, London, 1967, p39 ; Tetrahedron, 1967, 23, 2807.

(11) E.M.Emery, Anal.Chem., 1960, 32, 1495.

(12) U.Claussen, H.-w.Fehlhaber & F.Korte, Tetrahedron., 1967, 22, 3533.

(13) D.H.Williams, R.G.Cooks, J.H.Bowie, P.Madsen, G.Schroll & S.-O Lawesson, Tetrahedron., 1967, 23, 3173.

(14) J.D.Spence, Personal Communication.

(14a) J.K.MacLeod,J.B.Thompson & C.Djerassi,Tetrahedron., 1967, 23,2095.

(15) J.H.Bowie,D.H.Williams,S.-O.Lawesson & G.Schroll, J.Org.Chem.,1966,31,1384.

(16) S.H.H.Chaston,S.E.Livingstone,T.N.Lockyer,V.A.Pickles & J.S.Shannon,Austral.J.Chem.,1965,18,673.

(17) D.J.Blythin & E.S.Waight,J.Chem.Soc. (B).,1967,583.

(18) E.S.Waight, 'Newer Physical Methods in Structural Chemistry' Oxford 1966.

(19) H.J.Jacobsen,S.-O.Lawesson,J.T.B.Marshall,G.Schroll & D.H.Williams, J.Chem.Soc.(B)., 1966,940.

(20) D.J.Blythin & E.S.Waight, ibid.(C)., 1968,993.

(21) F.W.McLafferty,M.M.Bursey & S.M.Kimball, J.Amer.Chem.Soc. 1966,88,5022.

(22) D.H.Williams, Chem. in Brit., 1968,4,5.

(23) D.H.Williams & R.Ronayne, Chem.Comm., 1967,1129.

(24) R.G.Cooks,R.S.Ward & D.H.Williams, ibid., 1967,850.

(25) L.Kaplan,K.E.Wilzbach,W.G.Brown & S.S.Yang, J.Amer.Chem.Soc., 1965,87,675.

(26) D.Bryce-Smith & H.C.Longuet-Higgins, Chem.Comm.,1966,593.

(27) K.E.Wilzbach & L.Kaplan, J.Amer.Chem.Soc.,1965,87,4004.

(28) K.R.Jennings, Z.Naturforsch., 1967,22a,454.

(29) T.H.Kinstle,O.L.Chapman & M.Sung, J.Amer.Chem.Soc. 1968,90,1227.

(30) A.F.Thomas & B.Willhalm, Tetrahedron Letters., 1967, 5129.

(31) R.G.Cooks, R.S.Ward, D.H.Williams, M.A.Shaw & J.C.Tebby, Tetrahedron., 1968, 24, 3289.

(32) J.M.Wilson, M.Ohashi, H.Budzikiewicz, C.Djerassi, S.Itô & T.Nozoe, ibid., 1963, 19, 2247.

(33) M.A.Baldwin, A.G.Loudon, A.Maccoll, D.Smith & A.Ribera, Chem.Comm., 1967, 350.

(34) A.M.Duffield, C.Djerassi, G.Schroll & S.-O.Lawesson, Acta.Chem.Scand., 1966, 20, 361.

(35) R.Lawrence & E.S.Waight, J.Chem.Soc.(B)., 1968, 1.

(36) B.Sogaard Larsen, G.Schroll, S.-O.Lawesson, J.H.Bowie & R.G.Cooks, Tetrahedron, 1968, 24, 5193.

(37) O.Buchardt, A.M.Duffield & R.H.Shapiro, ibid., 1968, 24, 3139.

(38) E.A.Braude & J.S.Fawcett, J.Chem.Soc., 1951, 3117; 1952, 1528.

(39) E.A.Braude, Quart.Rev., 1950, 4, 404.

(40) E.C.Coyner & G.A.Ropp, J.Amer.Chem.Soc., 1948, 70, 2283; 1950, 72, 3960.

(41) G.Wittig, Organic Synthesis., 1959, 39, 75.

(42) O.Diels & K.Alder, Chem.Ber., 1929, 62, 2337.

(43) E.A.Braude, J.S.Fawcett & A.A.Webb, J.Chem.Soc., 1954, 1049.

(44) P.Montforte & G.Lo Vecchio, Atti. soc. peloritana sci. fis. mat. e nat., 1957-8, 4, 183 , CA., 1960, 54, 5521d.

(45) L.Fieser, J.Amer.Chem.Soc., 1948, 70, 3165.

(46) E.Bergmann, L.Haskelberg & F.Bergmann, J.Org.Chem., 1942, 7, 303.

(47) P.H.Groggins, Ind.Eng.Chem., 1930,22,620.

(48) C.K.Ingold,C.G.Raisin & C.L.Wilson, J.Chem.Soc.,1936,1637.

(49) A.P.Best & C.L.Wilson, ibid., 1946,239.

(50) R.J.Akawie,J.M.Scarborough & J.G.Burr, J.Org.Chem., 1959,24,946.

(51) R.A.Morton & W.T.Earlam, J.Chem.Soc., 1941,159 ; R.H.Peters & H.H.Sumner, ibid., 1953,2101.

(52) J.H.Beynon & A.E.Williams, Appl.Spectroscopy.,1960,14,156.

(53) D.R.Buckle & E.S.Waight, Org.Mass Spectrom., 1968,1,273.

(54) J.H.Beynon,R.A.Saunders & A.E.Williams, Ind.Chim.Belge., 1964,29,311.

(55) J.Harley-Mason,T.P.Toube & D.H.Williams, J.Chem.Soc.,(B). 1966,396.

(56) F.W.McLafferty, Anal.Chem., 1962,34,16.

(57) R.F.C.Brown & R.K.Solly, Austral.J.Chem., 1966,19,1045.

(58) F.W.McLafferty, 'The Mass Spectra of Organic Ions' Academic Press, 1963, p.318.

(59) B.C.L.Weedon, Chem. in Brit., 1967,3,424.

(60) S.L.Jensen, Pure Appl.Chem., 1967,14,227.

(61) R.Kuhn & A.Winterstein, Helv.Chim.Acta., 1928,11,87.

(62) L.Zechmeister, Chem.Rev., 1944,34,335.

(63) J.A.Barltrop,R.M.Acheson,P.G.Philpott,K.E.MacPhee & J.S.Hunt, J.Chem. Soc., 1956,2928.

(64) J.H.D.Eland & G.J.Danby, ibid., 1965,5935.

(65) R.A.W.Johnstone & B.J.Millard, Z.Naturforsch.,1966,21a,604; R.A.W.Johnstone & S.D.Ward, J.Chem.Soc.(C)., 1968,1805.

(66) T.W.J.Taylor & C.E.J.Crawford, J.Chem.Soc., 1934,1130.

(67a) H.Budzikiewicz,C.Djerassi & D.H.Williams, 'Mass Spectrometry of Organic Compounds' Holden)Day, San Francisco, 1967. ;

(67b) R.T.Aplin & S.Safe, Chem.Comm., 1967,140.

(68) F.W.McLafferty & T.Wacks, J.Amer.Chem.Soc.,1967,89,5043.

(69) R.A.W.Johnstone & D.W.Payling, Chem.Comm., 1968,601.

(70) H.H.Jaffé, Chem.Rev., 1953,53,191.

(71) C.R.Enzell,G.W.Francis & S.Liaanen-Jensen, Acta.Chem.Scand. 1968,22,1054.

(72) Professor B.C.L.Weedon Private Communication.

(73) W.E.Jefferson, Biochemistry., 1967,6,3479.

(74) K.G.Neill & H.Raistrick, Chem. in Industry., 1956,551.

(75) I.C.Paul,G.A.Sim & G.A.Morrison, Proc.Chem.Soc.,1962,352; I.C.Paul & G.A.Sim, J.Chem.Soc., 1965,1097.

(76) J.R.Price & R.Robinson, Nature., 1938,142,147. ; J.Chem.Soc., 1939,1522.

(77) L.F.Fieser, J.Amer.Chem.Soc., 1927,49,857.

(78) R.G.Cooke, Austral.J.Sci.Research., 1950,3A,481.

(79) A.J.Parker, Quart.Rev., 1962,16,163.
A.J.Parker, Advances in Physical Organic Chemistry., 1967,5,173.

(80) R.H.De Wolfe & W.G.Young, Chem.Rev., 1956,56,753.

(81) N.Kornblum,P.J.Berrigan & W.J.Le Noble, J.Amer.Chem.Soc., 1963,85,1141.

(82) R.H.Thomson, 'Naturally Occurring Quinones', Academic Press, N.Y. 1957, pp59-72.

(83) G.Wittig & H.Reiff, Angew.Chem.Internat.Edit.,1968,7,7.

(84) B.C.McKusick, J.Amer.Chem.Soc., 1948,70,2196, and references quoted here.

(85) I.Iwai & J.Ide, Chem.Pharmac.Bull.(Japan)., 1962,10,926.

(86) D.S.Tarbell, Chem.Revs., 1940,27,495. ;
A.Jefferson & F.Scheinmann, Quart.Rev., 1968,391.

(87) H.J.Hansen & H.Schmit, Chem. in Brit., 1969,111.

(88) A.Jefferson & F.Scheinmann, Chem.Comm., 1966,239.

(89) H.Kwart & M.H.Cohen, J.Org.Chem., 1967,32,3138, and references quoted.

(90) K.Heyns & D.Muller, Tetrahedron Letters., 1966,6061.

(91) D.R.Buckle & E.S.Waight, Org.Mass Spectrom., 1969,2,367.

(92) R.T.Aplin & W.T.Pike, Chem. & Ind., 1966,2009;
S.Ukai,K.Hirose,A.Tatematsu & T.Goto, Tetrahedron Letters., 1967,49,4999.
R.W.A.Oliver & R.M.Rashman, J.Chem.Soc.(B)., 1968, 1141.

(93) T.Aczel & H.E.Lumpkin, Anal.Chem., 1960,32,1819.

(94) D.G.B.Boocock & E.S.Waight, Chem.Comm., 1966,90;
D.G.B.Boocock, PhD Thesis London, 1967.

(95) E.C.Horning & M.G.Horning, J.Org.Chem., 1946,11,95.

(96) G.C.Chakravarti,H.Challopadhyaya & P.C.Ghosh, J.Indian Inst.Sci., 1931,A14,141.

(97) R.D.Desai, J.Indian Chem.Soc., 1933,10,663.

(98) J.Baldas & Q.N.Porter, Tetrahedron Letters, 1968,1351.

(99) R.P.Gandhi,B.Vig & S.M.Hukherji, J.Indian Chem.Soc., 1959,56,299.

(100) R.A.Benkeser,R.E.Robinson,D.M.Sauve & O.H.Thomas, J.Amer.Chem.Soc., 1955,77,3230.

(101) D.Arigoni,H.Bosshard,H.Bruderer,G.Buchi,O.Jeger & L.J.Krebaum, Helv.Chim.Acta., 1957,40,1732. ;
D.H.R.Barton,P.de Mayo & M.Shafiq, Proc.Chem.Soc., 1957,205, ;
D.H.R.Barton,P.de Mayo & M.Shafiq, J.Chem.Soc.,1958, 140.

(102) P.Natalis, Bull.Soc.Chim.Belge., 1958,67,599.

(103) R.H.Shapiro,J.M.Wilson & C.Djerassi, Steroids.,1963,1,1.;
H.Budzikiewicz,C.Djerassi & D.H.Williams, 'Structural Elucidation of Natural Products by Mass Spectometry', Holden-Day, 1964, p.87. ;
R.L.N.Harris,F.Komitsky & C.Djerassi, J.Amer.Chem.Soc., 1967,89,4765.

(104) Samples kindly supplied by Mr.J.Bilton.

(105) O.L.Chapman, 'Advances in Photochemistry' Vol.1, p.323.
H.Durter,C.Ganter,H.Ryf,E.C.Utzinger,K.Weinberg, K.Schaffner,D.Arigoni & O.Jeger, Helv.Chim.Acta., 1962, 45,2346.

(106) B.A.Shoulders,W.W.Kwie,W.Klyne & P.D.Gardner, Tetrahedron., 1965,21,2973.
P.de Mayo & S.T.Reid, Quart.Rev., 1961,15,393.

(107) M.M.Ballantyne,R.D.H.Murray & A.B.Penrose, Tetrahedron Letters., 1968,4155.

(108) J.H.Bowie, Austral.J.Chem., 1966,19,1619.

(109) C.Fenselau,W.G.Dauben & G.W.Schaffer, J.Amer.Chem.Soc., 1969,91,112.

(110) A.L.Burlingame, C.Fenselau, W.J.Richter, W.G.Dauben, G.W.Schaffer & N.D.Vietmeyer, ibid., 1967,89,3346.

(111) E.N.Marvell & J.Seubert, Tetrahedron Letters, 1969,1333.

(112) H.C.Brown & M.Grayson, J.Amer.Chem.Soc.,1953,75,20.

(113) E.C.Stirling & M.T.Bogert, J.Org.Chem., 1939,4,20.

(114) M.Crawford & F.H.C.Stewart, J.Chem.Soc., 1952,4443.

(115) Schramm, Monatsch., 1888,9,615.

(116) J.B.Shoesmith & A.Mackie, J.Chem.Soc., 1928,2334.

(117) E.A.Braude,E.H.R.Jones & E.S.Stern, ibid., 1947,1087.

(118) E.A.Braude & J.S.Fawcett, ibid., 1951,3113.

(119) A.V.Dombrovski, Doklady Akad.Nauk.SSSR., 1956,111,827. 1957,115,103.

(120) L.A.Bigelow, J.Amer.Chem.Soc., 1922,44,2015.

(121) C.Mettler, Chem.Ber., 1906,39,2938.

(122) C.L.Arcus & G.C.Barrett, J.Chem.Soc., 1958,2740.

(123) R.C.Gilmore Jnr., & W.J.Horton, J.Amer.Chem.Soc., 1951, 73,1411.

(124) A.Hassner & N.H.Cromwell, ibid., 1958,80,893. ; F.S.Kippling, J.Chem.Soc., 1894,65,480.

(125) D.M.W.Anderson,N.Campbell,D.Leaver & W.H.Stafford, ibid., 1959,3992.

(126) R.Scholl & W.Neovius, Chem.Ber., 1911,44,1079.

(127) M.Gomberg & W.E.Bachmann, Organic Synthesis Coll. Vol. 1, p.113

(128) P.H.Groggins, Ind.Eng.Chem., 1930,22, 620,626.

(129) R.E.Buckles & N.G.Wheeler, Organic Synthesis Coll.Vol. 4, p.777.

(130) ibid., p.808.

(131) A.Bayer & H.Rupe, Annalen., 1890,256,1.

(132) F.Bode, ibid., 1864,132,95.

(133) E.N.Marvell & J.Seubert, Tetrahedron Letters., 1969,1333.

(134) R.Pschorr,O.Wolfes & W.Buckow, Chem.Ber., 1900,33,166.

(135) A.I.Vogel, 'Practical Organic Chemistry' Longmans, 1951.

(136) E.Royals & E.R.Covington, J.Amer.Chem.Soc.,1955,77,1697.

(137) G.Wittig & A.Klein, Chem.Ber., 1936,69B,2087.

(138) K.Bernhauer, & I.Skudrzyk, J.Pract.Chem., 1940,155,310.

(139) M.Y.Shandala, PhD Thesis London, 1964.

(140) R.E.Buckles & M.P.Bellis, Organic Synthesis Coll.Vol. 4, p.722.

(141) M.Scholtz & A.Wiedermann, Chem.Ber., 1903,36,845.

(142) J.v.Braun & J.Nelles, ibid., 1933,66,1464.

(143) A.C.Cope,T.A.Liss & D.S.Smith, J.Amer.Chem.Soc., 1957, 79,240.

(144) F.Strauss, Annalen., 1912,393,311.

(145) K.Sirotanovic,M.Bajlon-Rocen & D.Galovic, CA. 59,8635g.

(146) P.Pfeiffer, Annalen., 1917,412,322.

(147) K.Friedrich & W.Hartmann, Chem.Ber., 1961,94,840.

(148) Y.Hirschberg,E.Bergmann & F.Bergmann, J.Amer.Chem.Soc., 1950,72,5120.

(149) A.Bolleter,K.Eiter & H.Schmid, Helv.Chim.Acta., 1951, 34,186.

(150) V.I.Anosov,A.P.Savostin,V.G.Pines,M.A.Miropolskaya, V.I.Fedotova & G.I.Samokhvalov, U.S.S.R.Pat.,1961, 136,344,; CA. 1961, 55, P23343f.

(151) R.Tiollais, Bull.Soc.Chim.France., 1947,708.

(152) M.Hammell & R.Levine, J.Org.Chem., 1950,15,162.

(153) H.G.Gilman,E.A.Zoellner & W.M.Selby, J.Amer.Chem.Soc. 1933,55,1252.

(154) J.E.Baldwin & R.G.Pudńssery, Chem.Comm., 1968, 408.

(155) S.V.Libermann & R.Connor, Organic Synthesis Coll.Vol. 2, p.441.

(156) O.L.Brady,A.N.Cosson & A.J.Roper, J.Chem.Soc.,1925,2429.

(157) L.H.Goodson & H.Christopher, J.Amer.Chem.Soc., 1950, 72,358.

(158) M.Beringer & I.Kuntz, J.Amer.Chem.Soc., 1951,73,364.

(159) L.A.Duncanson,J.F.Grove & P.W Jeffs, J.Chem.Soc., 1958, 2229.

(160) G.F.Woods, J.Amer.Chem.Soc., 1947,69,2549.

(161) R.L.Frank & H.K.Hall ibid., 1950,72,1645.

(162) E.I.Stankervich & G.Vanags, CA. 58, 2430a.

(163) E.G.Meek,J.H.Turnbull & W.Wilson, J.Chem.Soc., 1953,811.

(164) H.Born,R.Pappo & J.Szmuszkovicz, ibid., 1953, 1779.

(165) J.Champagne,H.Favre,D.Vocelle & I.Zbrikowski,
Canad.J.Chem., 1964,42,212.

(166) S.Isoe & M.Nakazaki, Bull.Chem.Soc.Japan., 1964,37(2),151.

(167) R.A.Bakeser,R.E.Robinson,D.M.Sauve & O.H.Thomas,
J.Amer.Chem.Soc., 1955,77,3230.

(168) H.N.A.Al-Jallo, PhD Thesis London, 1964, p.146.