STUDIES IN THE CHEMISTRY OF BENZOBICYCLO SYSTEMS

by

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SUMMARY

Reactions of tetrahalogenobenzynes with certain tertiary arylamines afford products which are derived by both 1,2- and 1,4-cyclo-addition as well as from a betaine. The tetrahalogenobenzynes and benzyne react with eneamines to give benzocyclobutene-derivatives via betaines; the tetrahalogenobenzyne derivatives are readily hydrolysed to 2-tetrahalogenophenyl cycloalkanones.

1-N-alkylamino derivatives of 5,6,7,8-tetrahalogeno-1,4-dihydronaphthalene also undergo cleavage reactions in protic media. Thus, for example, 1-N,N-dimethylamino-tetrafluorobenzobarrelene gives 2,3,4,5-tetrafluoro-4'-N,N-dimethylaminobiphenyl in high yield and 1,2,3,4-tetrafluoro-5,8-dihydro-5,8-N-(-methyl)-iminonaphthalene affords 2'-(2,3,4,5-tetrafluorophenyl)-N-methyl pyrrole.

Apparent similarities between mass spectral and thermal processes have been investigated in connection with retro-Diels-Alder reactions leading to 4,5,6,7-tetrahalogeno-isobenzofurans and 4,5,6,7-tetrafluoro-2-methylisoindole. These derivatives are more stable than the non-halogenated compounds.

The rearrangement reactions of 1-methoxybenzobarrelene derivatives in strong acids have been studied. Various possible mechanistic pathways have been investigated by deuterium labelling methods. Benzobicyclo[3.2.1] derivatives arise via a 2-carbonium ion while a 3-carbonium ion leads to benzobicyclo[2.2.2]dien-2-one derivatives. The solvolyses of certain toluene-p-sulphonates have been used to check mechanistic predictions. The position of protonation and the extent of the rearrangement can be controlled by the use of alkyl substituents. Thus 2,6-dimethyl-1-methoxy-tetrafluorobenzobarrelene affords only derivatives of benzobicyclo[3.2.1]-octadiene while 3,5-dimethyl-1-methoxy-tetrafluorobenzobarrelene gives products derived by rearrangement to the benzobicyclo[2.2.2] system.

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Lastly I sincerely acknowledge the help and understanding of my wife at all stages of this work.

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GENERAL

INTRODUCTION

Introduction

The chemistry of orthodehydrobenzene (benzyne) has been studied extensively over the past thirty years.[1] Although the structure of benzyne has been the subject of much controversy, it is now generally accepted that it is a neutral species derived by the removal of two ortho substituents from the benzene aromatic system. The removal of the substituents leaves two carbon sp^2-orbitals with two electrons distributed between them; the orbitals being orthogonal to the molecular orbitals of the aromatic ring. The two carbon sp^2-orbitals can interact to give a singlet or a triplet state. However, calculations[2] show that benzyne exists in a symmetric singlet ground state.

The chemistry of this species, in summary, can be regarded as a highly electrophilic intermediate with a half life of ca. 10^{-4} sec..[3]

Benzyne undergoes cycloaddition reactions with olefins and strained cyclic systems. It also reacts with dipolar species and with a large number of nucleophiles.

Tetrahalogenated benzynes have been the primary source of study within these laboratories. It has been reasoned[4] that the effect of the four electron withdrawing halogens will cause a significant increase in the electrophilicity of the intermediate over that of benzyne and hence affect the reactivity.

Tetrahalogenobenzynes have been generated in a variety of ways the more important of which are discussed below.

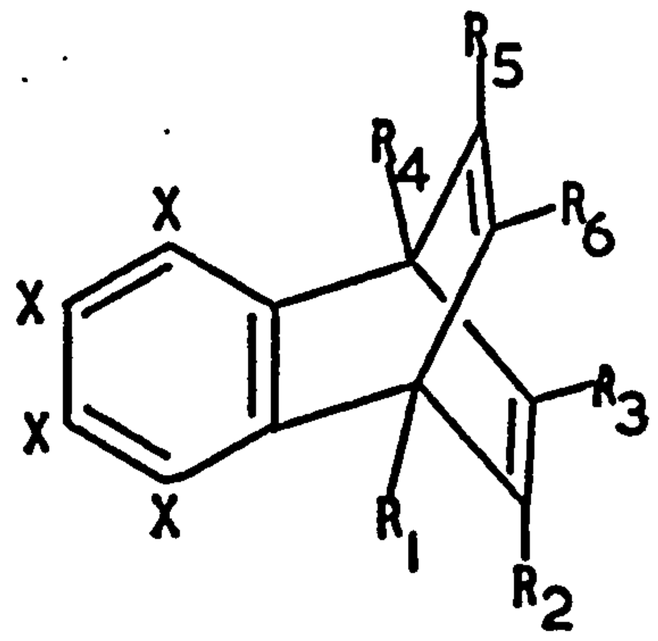
Pentafluorophenyl lithium[5] has been prepared and eliminates lithium fluoride at about 0^{o} to generate tetrafluorobenzyne. Similarly pentachlorophenyl lithium[6] acts as a precursor for tetrachlorobenzyne.

Pentafluorophenyl magnesium halides[7] and pentachlorophenyl magnesium

chloride[8] have been prepared and decompose in analogous manner to the o-halophenyl magnesium halides to give tetrafluorobenzyne and tetrachlorobenzyne respectively.

Tetrahaloanthranilic acids yield the corresponding tetrahalogenobenzynes by aprotic diazotisation with butyl nitrite, (F^{9}, Cl^{10a}, Br^{10b}, I^{10b}).

Although benzyne will cyclo-add to a simple arene[11,12] the yield of the 1,4-adduct is low. Tetrahalobenzynes undergo 1,4-cycloaddition reactions with arenes readily and in good yield.[10,13-15] The products of these reactions are the tetrahalobenzobarrelene derivatives.



X =Halogen

The majority of the reactions so far investigated are those in which the R-groups are alkyl.

More recently the reactions of tetrahalobenzynes with methoxyarenes[16] and with tertiary aminoarenes[17] have been studied. The major products isolated from these reactions are the 1-substituted tetrahalobenzobarrelenes.

Two objects of the research reported in this thesis were, to investigate further the chemistry of the reactions of tetrahalogenobenzynes with tertiary arylamines, and also to investigate potential reactions of benzobarrelenes which have bridgehead functions capable of taking part in rearrangements.

CHAPTER 1

The Reactions of Tetrahalobenzynes with

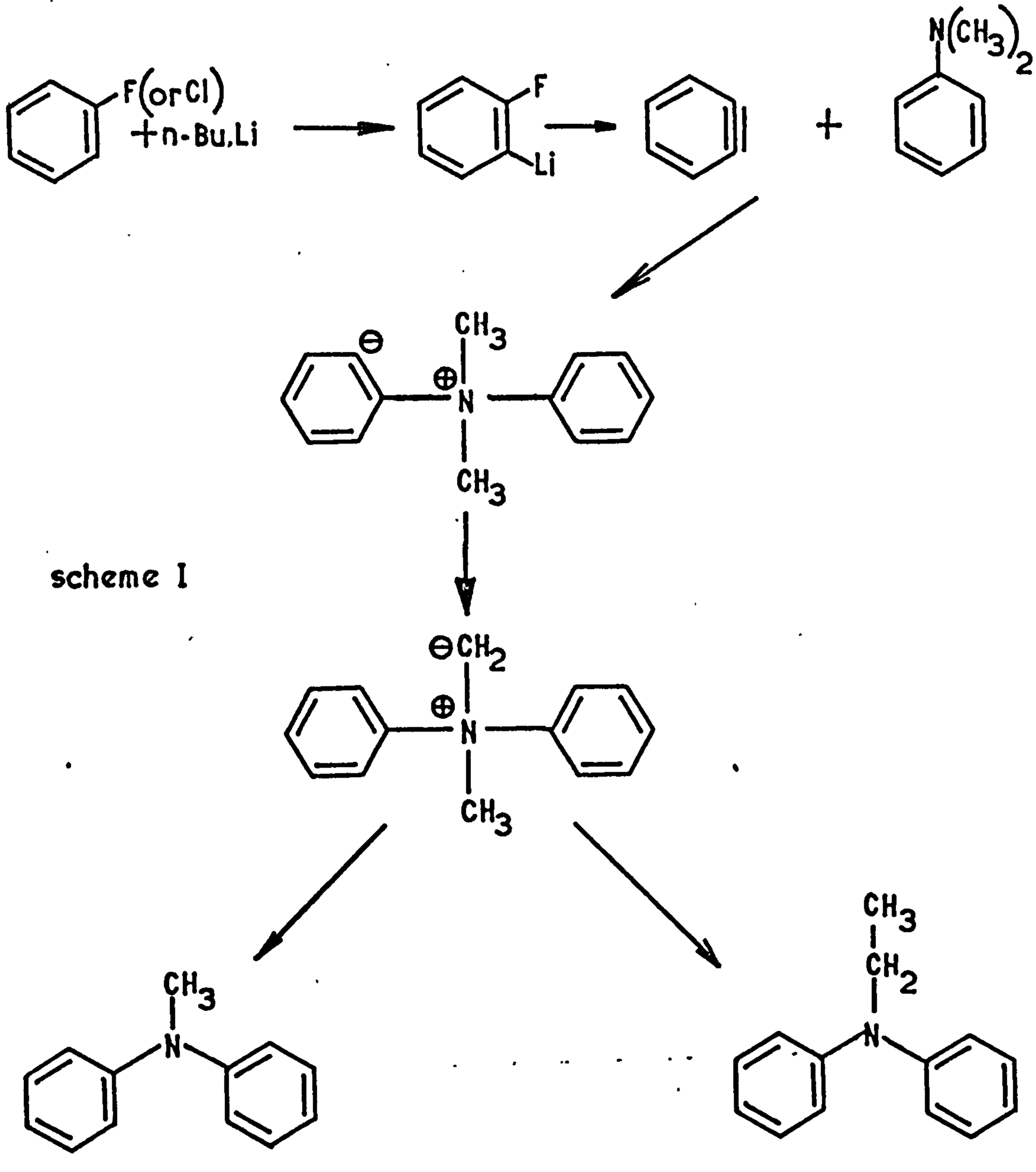
Tertiary Aryl Amines

Introduction

Benzyne has been reacted with tertiary amines[1] including N,N-dimethylaniline.[18,19]

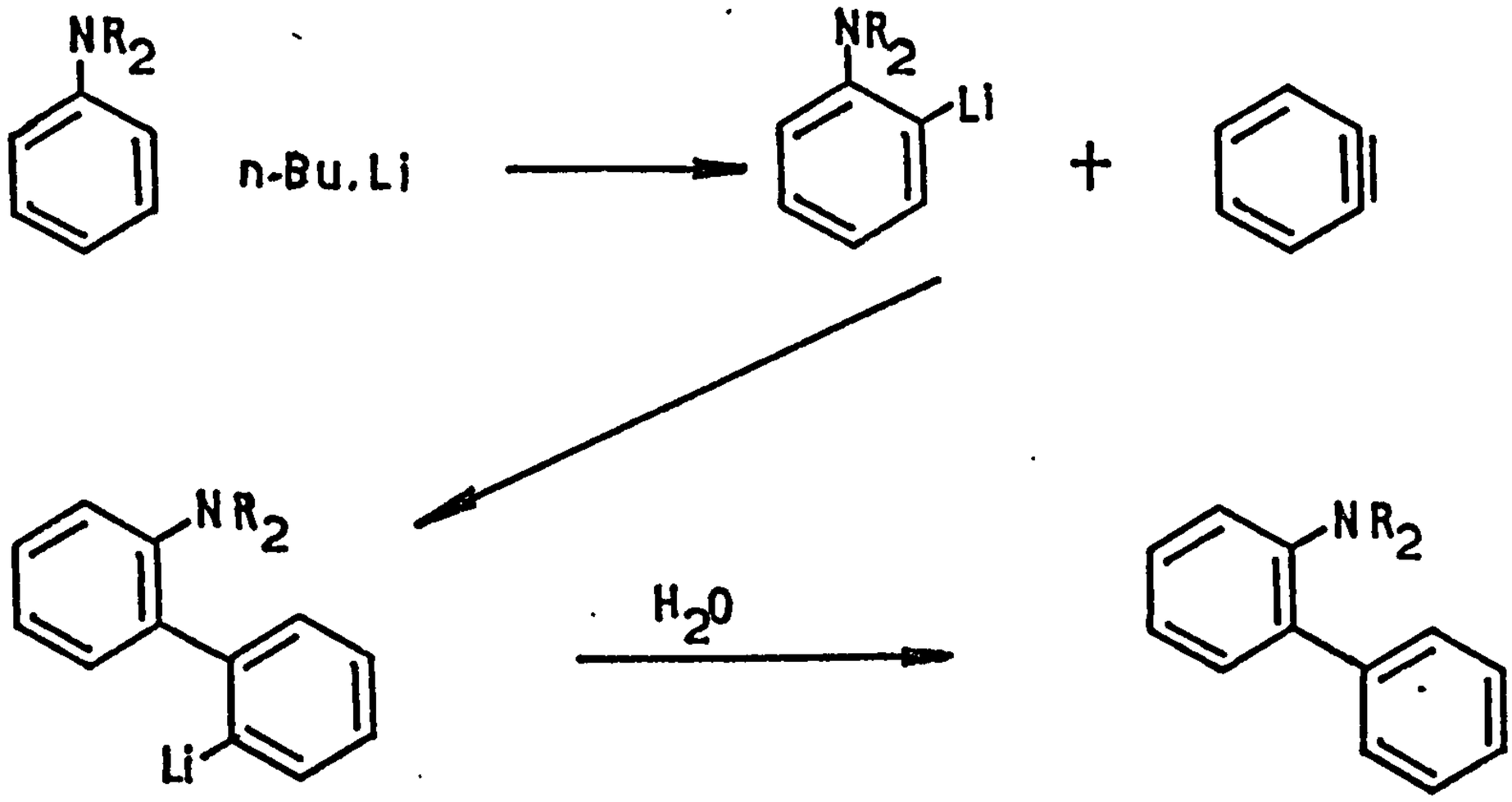
In the reaction with N,N-dimethylaniline, benzyne was generated from fluorobenzene and n-butyl lithium. The products of the reaction were shown to be N-ethyldiphenylamine isolated in 1.4% yield and N-methyldiphenylamine isolated in 12% yield.

The formation of these products has been rationalised in terms of the reaction pathway shown in scheme I.



scheme I

At higher temperatures and if the less reactive chlorobenzene was used as the benzyne precursor, N,N-dialkylbiphenyls were isolated.[18,19] These are thought to arise by ortho metallation of N,N-dimethylaniline followed by the addition of benzyne, scheme II.



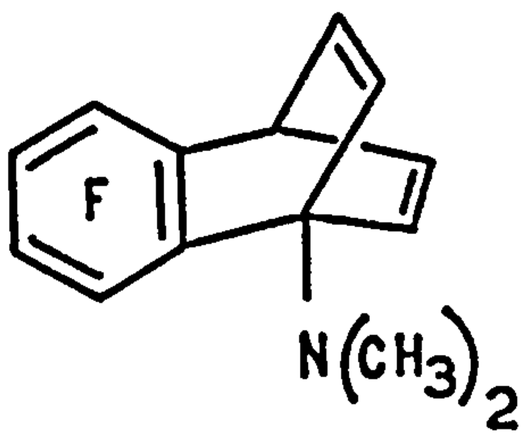
scheme II

Owing to the low yields in this reaction further mechanistic studies were not carried out.

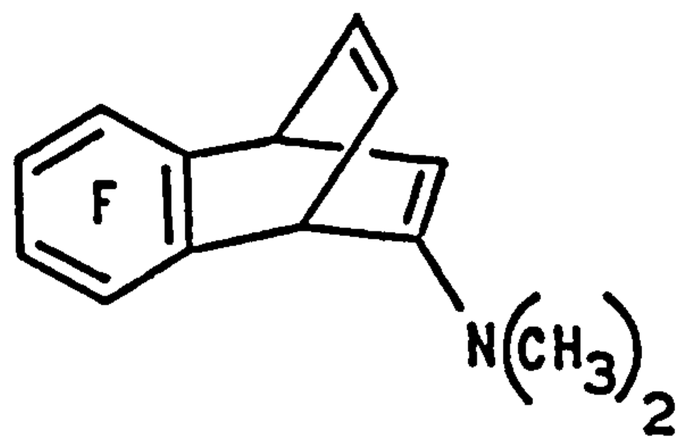
Early results[20] showed that the reaction products derived from the addition of tetrafluorobenzyne to N,N-dimethylaniline were significantly different from those obtained in the benzyne reaction. Indeed further work[17] showed that the products varied considerably depending on the reaction conditions.

When tetrafluorobenzyne was generated by decomposition of pentafluorophenyl magnesium bromide at 80° in N,N-dimethylaniline the three products were all derived from attack on the aromatic portion of the aryl amine. The major product was the expected 1,4-cyclo-adduct *(1) isolated in 10% yield. A minor product, in 0.75% yield, was shown to be the benzobarrelenone (2), evidently derived from hydrolysis of the other possible 1,4-cyclo-adduct, in this case an enamine (3).

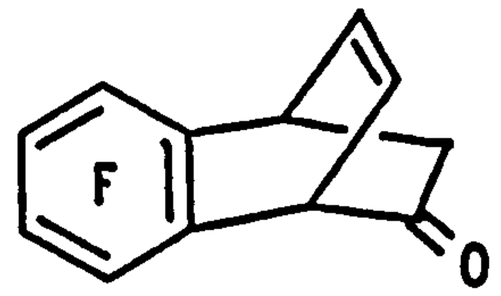
*F in this formula (or F or X in others) represents all available aryl-ring positions substituted by F (or by X).



(1)

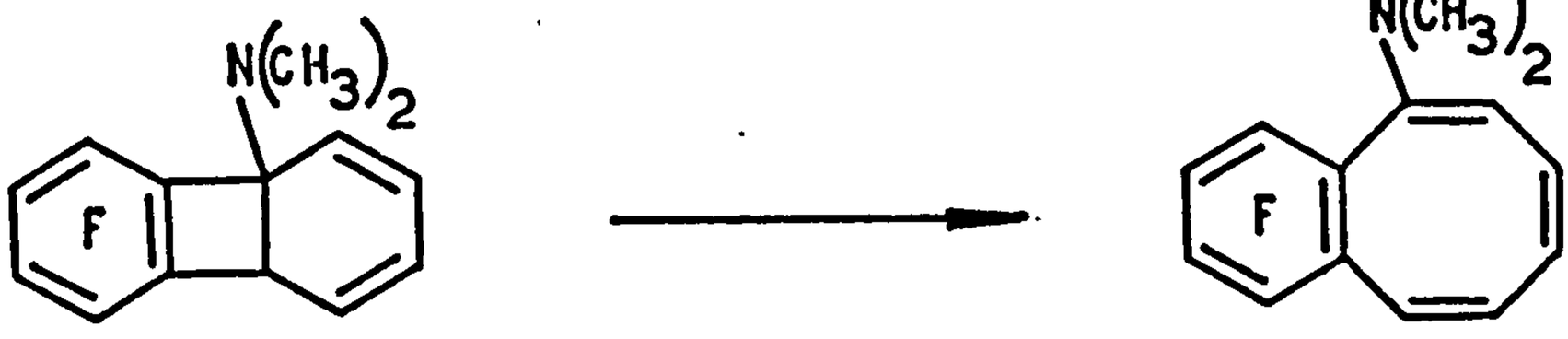


(3)



(2)

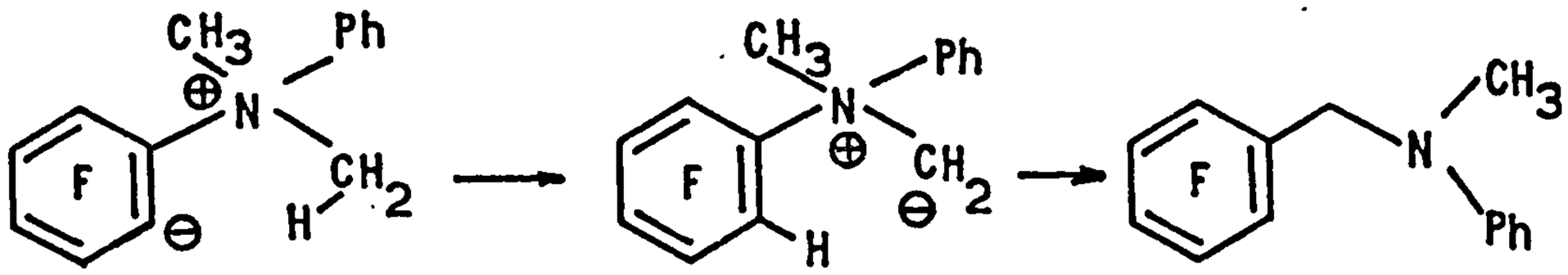
The remaining product, isolated in 1.5% yield, was stable to brief treatment with dilute acid and was not reduced with sodium borohydride in methanol. It was reduced with 2 moles of hydrogen over a palladium catalyst to give a tetrahydro derivative which also did not show typical properties of an enamine. This and its spectroscopic data led the authors to assign the structure as the 4a,8b-dihydrobiphenylene (4). They were surprised that the compound apparently did not convert by valence bond isomerisation to the benzocyclooctatetraenamine (5).



(4) (5)

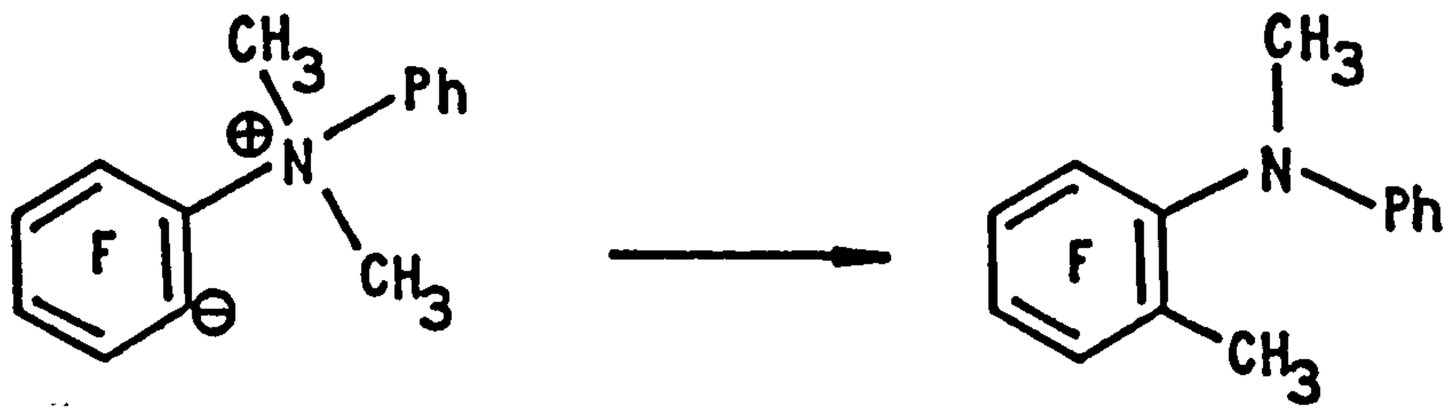
When tetrafluorobenzyne was generated at room temperature from pentafluorophenyl lithium in ether containing N,N-dimethylaniline, apart

from the three products (1), (2), and (4) they obtained a fourth product which was shown to be the tetrafluorobenzyl methylaniline (6). This product was derived by an unusual Stevens rearrangement of the ylide (7) in which the tetrafluoroaryl group migrates.



(8) (7) (6)

A fifth product was obtained when pentafluorophenyl lithium was decomposed at room temperature in light petroleum containing excess of N,N-dimethylaniline and was shown to be N-methyl-N-phenyl-tetrafluoro-o-toluidine (9). This product was derived by charge neutralisation in the initial betaine (8) although whether the reaction proceeds intramolecularly is not established.



(8) (9)

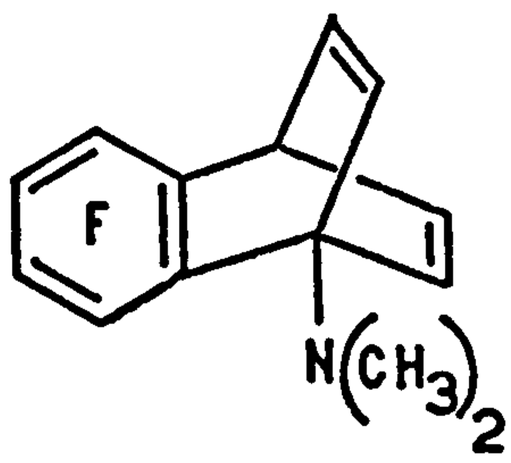
The differences in the reactions of tetrahalobenzynes with N,N-dimethylaniline obviously merit further investigation.

Discussion

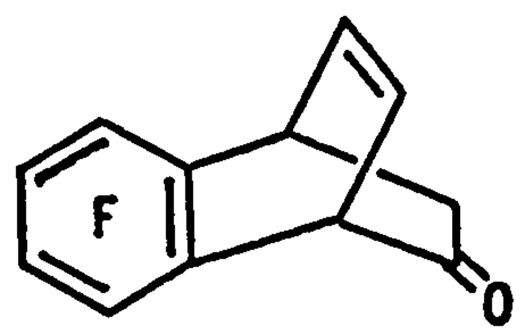
Initially it was decided to re-investigate the reaction of tetrafluorobenzyne with N,N-dimethylaniline in an attempt to fully characterise the products formed.

In the reactions of benzynes with tertiary amines there are usually a number of products formed and consequently a number of reaction mechanisms operate.[21] The products may often be interrelated by many different pathways and mechanistic investigations are therefore complicated. In many cases they can only be regarded as speculative.[1]

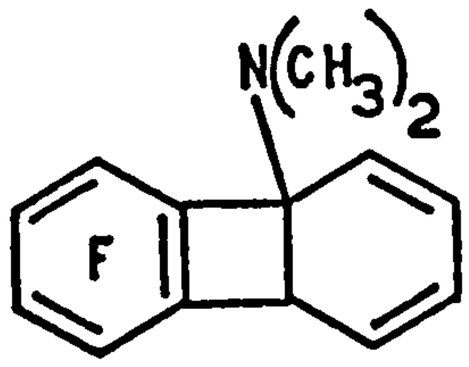
When pentafluorophenyl lithium is decomposed at room temperature in ether containing an excess of N,N-dimethylaniline, four products are formed and have been assigned the structures[17] (1), (2), (4) and (6).



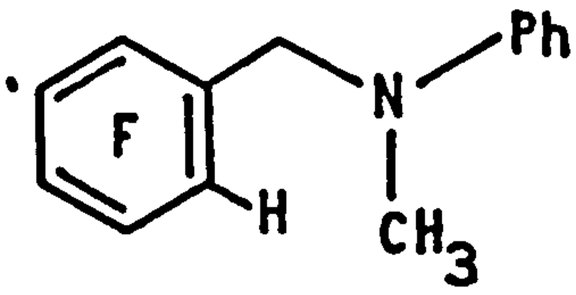
(1) 5.5 %



(2) 0.5 %



(4) 12.5 %

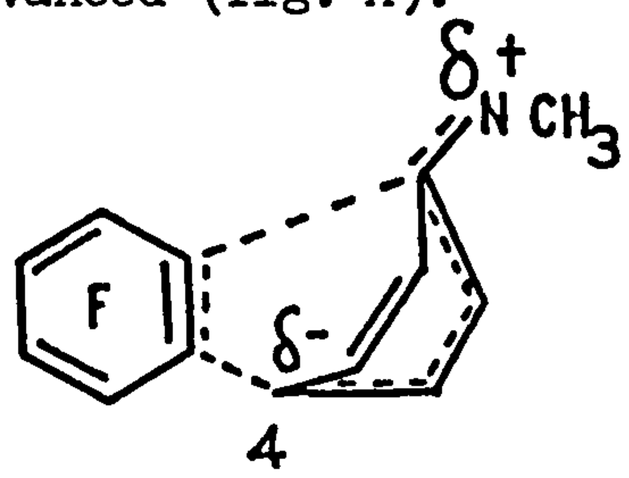


(6) 9.5 %

This reaction was repeated and the isolated product ratio was found to be (1) 18%; (2) 7%; (4) 10%; and (6) 13%. These results are in better agreement with the ratios obtained by g.l.c. on the crude reaction products namely (1) 12: (2) 3: (4) 7: (6) 8.

The 1-N,N-dimethylaminobenzobarrelene (1) was easily characterised by comparison of its spectral data with similar compounds prepared previously in these laboratories.[20] This compound has also been studied owing to the N-methyl groups showing long range ^{19}F-H coupling.[22] Its formation as the major product suggests the participation of the electron-releasing N,N-dimethyl group. In the transition state leading to (1) the bonds are not necessarily being formed synchronously and attack by the electrophile at position 4 is likely to be more advanced (fig. A).

fig.A



The benzobarrelenone (2) was undoubtedly derived by hydrolysis of the alternative 1,4-cycloadduct (3). The structure of the benzobarrelenone (2) has been well established by previous workers.[20, 23]

Product (4) which is the 1,2-cycloadduct of tetrafluorobenzyne and N,N-dimethylaniline is a 4a,8b-dihydrobiphenylene.

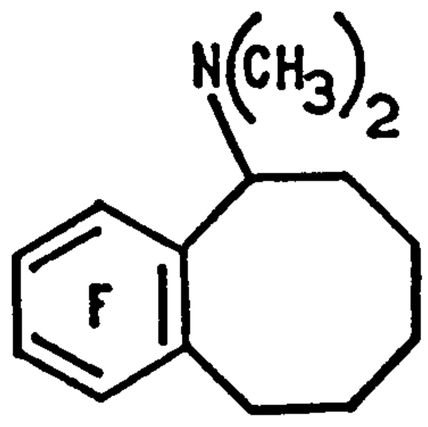
This is an interesting product as no stable examples of this system appear to be known.[24,25] These systems are usually postulated as intermediates which rapidly undergo valence bond isomerisation to the thermally more stable benzocyclo-octatetraenes.[26,27] By analogy

one would expect the product (4) to undergo valence bond isomerisation to the aminobenzocyclo-octatetraene (5). In the reaction of benzyne with benzene one of the products obtained is benzocyclo-octatetraene, but the presumed primary product, 4a,8b-dihydrobiphenylene, was not detected.[11]

(4) (5)

The evidence which favoured the published[17] structure (4) rather than the ring opened form structure (5) was the u.v. spectrum showed a cyclohexadiene chromophore, $\lambda_{max.}$ 263 nm., (ϵ 7000.). The ^{1}H n.m.r. spectrum showed resonances at τ 3.38 - 4.5 (4H), τ 5.15 (1H), and τ 7.42 (6H), and structurally significant ions were observed in the mass spectrum at m/e 269, 254, 240, 225, and 224.

Catalytic hydrogenation over palladium on carbon gave a tetrahydro derivative which could be further reduced using Adams catalyst and acetic acid to give a cyclic amine (9).



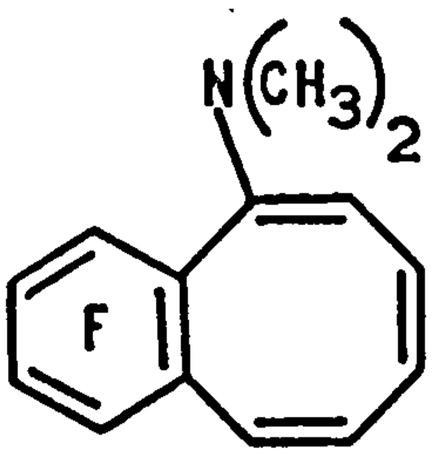
(9)

Neither the unreduced nor the tetrahydro derivative was affected by brief heating in mineral acid. Also the tetrahydro derivative was not reduced with sodium borohydride in methanol.

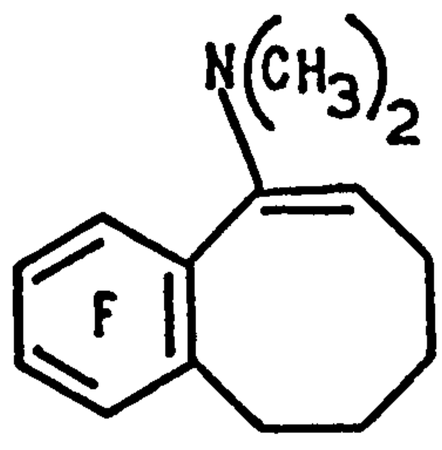
These results suggested that the compound had the structure (4) and that the tetrahydro derivative had the structure (10).

(4) (10)

The alternative structures namely (5) for the unreduced species and (11) for the tetrahydro derivative were expected to be hydrolysed in aqueous acid as they were enamines. Also they would be expected to be reduced with sodium borohydride.



(5)



(11)

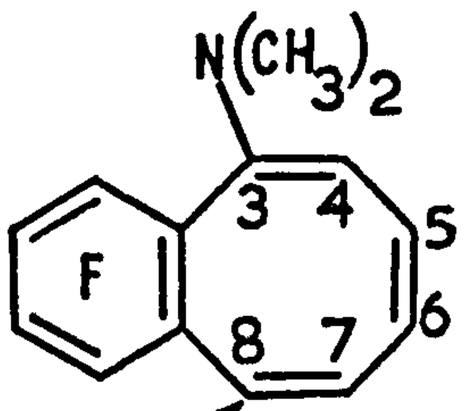
The evidence outlined so far is inconclusive, particularly since Diels-Alder adducts were not obtained with typical dienophiles nor could N-oxides or quaternary salts be formed. A re-examination was clearly necessary to solve this structural problem.

The u.v. spectrum, although it agrees with a cyclohexadiene chromophore, could equally be due to a substituted benzocyclo-octatetraene.[26] The i.r. spectra of both the unreduced and the tetrahydroderivative show a strong absorption at 1640 cm.$^{-1}$ characteristic of enamines.[28] The ^{1}H n.m.r. spectrum shows a resonance for one vinyl proton at fairly low field as a quartet centred at τ 3.53 with coupling constants of 12 Hz. and 1.5 Hz..

The chemical shift of this proton compares well with the vinyl proton resonances in some model systems. Bicyclo[4.2.0]octa-2,4,7-triene[29] shows a multiplet at τ4.37 and an annelated bicyclo[4.2.0]-octatriene[30] shows an A_2B_2 pattern centred at τ4.47 both of which are at considerably higher field than in the adduct. However, the chemical shift is better compared with the vinyl proton resonances in benzocyclo-octatetraene.[31] The protons adjacent to the benzo-ring resonate at τ3.49 and further show coupling of 12 Hz. to the next vinyl proton.

The other coupling constant of 1.5 Hz. may be attributed to ^{19}F-H coupling. In support of this the tetrachloro-analogue (12) shows only a doublet at τ3.49 (J = 12 Hz.).

(5)

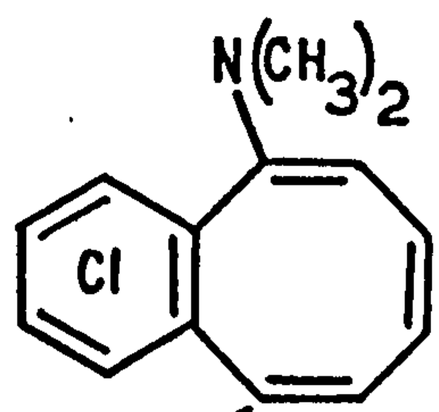


τ 3.53

$J_{8,7}$ = 12 Hz.

$J_{8,F}$ = 1.5 Hz.

(12)



τ 3.49

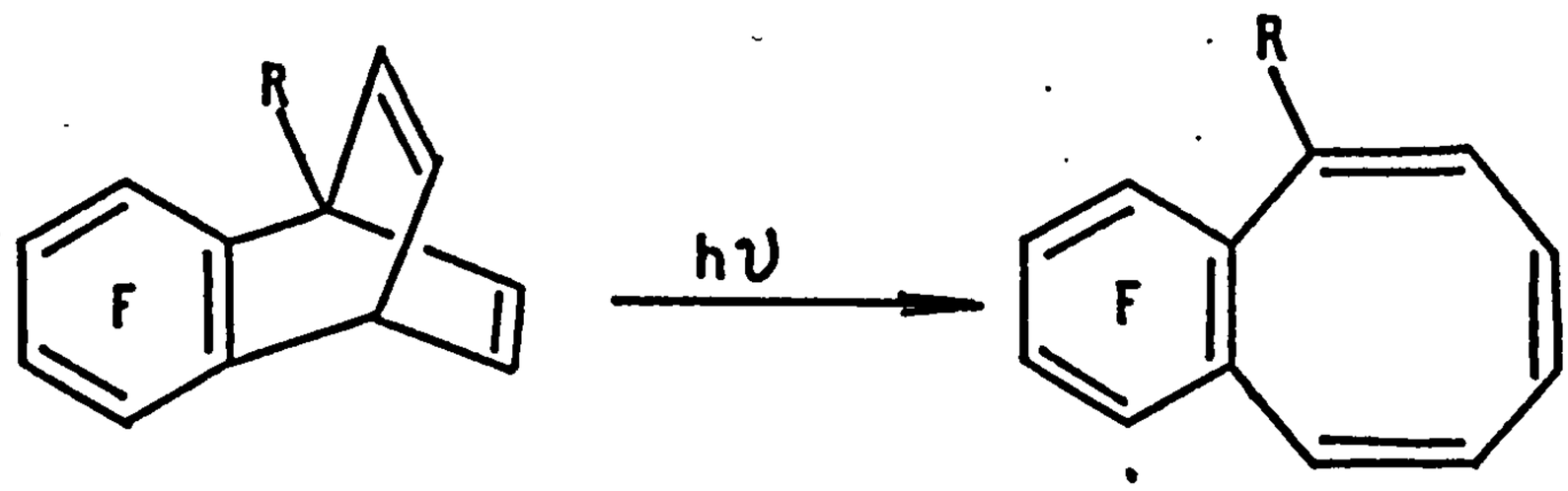
$J_{8,7}$ = 12 Hz.

The ^{1}H n.m.r. spectra of compounds (5) and (12) also show broadened doublets at ca. τ 5.21, J = 3 Hz.. These τ values are rather low for a bridgehead methine proton as in structure (4) but are in good agreement for the chemical shift of an enamine vinylic proton.[28] The 3 Hz. coupling constant is a little high for a benzocyclo-octatetraene where the normal $J_{4,5}$ coupling constant is 2 Hz.,[31] but this may be due to a distortion effect in these particular systems.

Brief heating to 150° in an inert atmosphere caused no change in the structure of the compound as shown by ^{1}H n.m.r. spectroscopy.

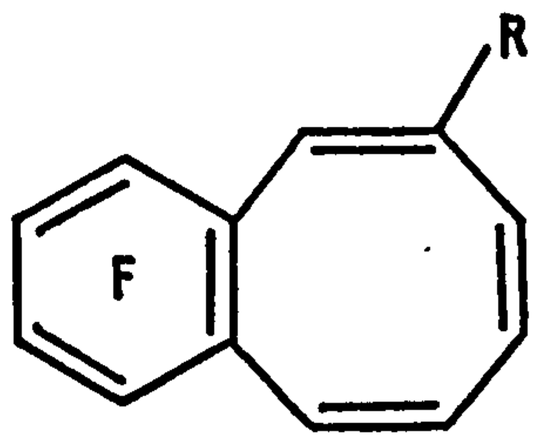
It was beginning to appear therefore that the bicyclic structure (4) for this product was incorrect and that the monocyclic structure (5) was the more reasonable one.

Independent synthesis of the monocyclic structure (5), R = NMe_2 was attempted by irradiation of compound (1) R = NMe_2. This method of preparation has been used for the conversion of tetrafluorobenzobarrelene (1) R = H to tetrafluorobenzocyclo-octatetraene (5) R = H.[32]



(1) (5)

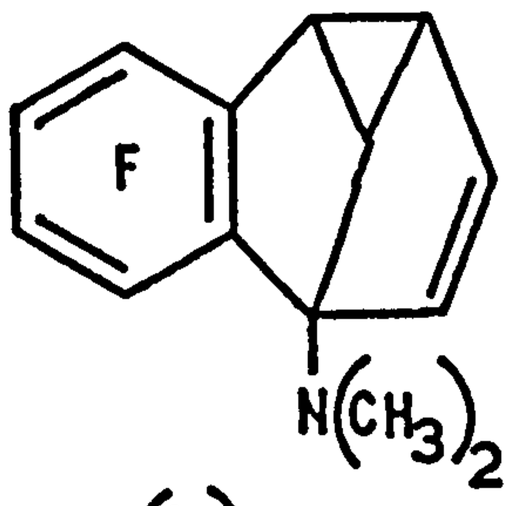
Other mechanistic studies[33] on a related system indicate that the benzocyclo-octatetraene formed would be an isomer having the structure (13).



(13)

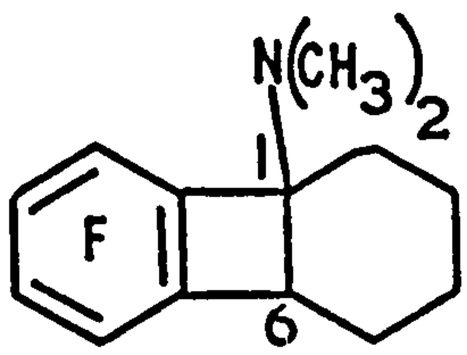
However when the reaction was carried out with (1) R = NMe_2, apart from a considerable amount of polymeric material, three products were isolated. The first was recovered starting material, 30%. The second product, in 6% yield, was identical by its spectroscopic properties to the previously isolated compound to which structure (5) R = NMe_2 was now assigned.

The third product isolated, in 2% yield was tentatively assigned the benzosemibullvalene structure (14) on the basis of its ^1H n.m.r. spectrum and by comparison with a similar compound prepared in these laboratories.[20]

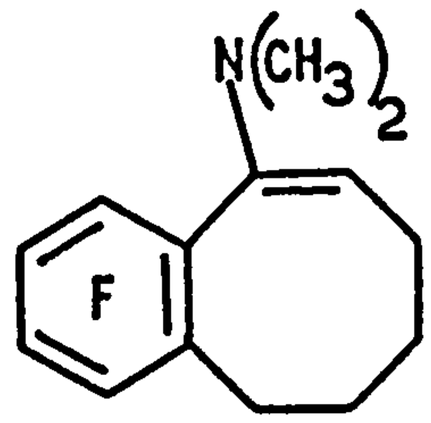


(14)

Difficulties in characterising the product, derived from 1,2-addition of tetrafluorobenzyne and N,N-dimethylaniline, were undoubtedly due to its ease of polymerisation. The tetrahydro derivative however was considerably more stable and an analysis for $C_{14}H_{15}F_4N$ could be obtained. It was thought therefore that it would be more profitable to examine its structure in more detail rather than the unreduced compound. To distinguish between the possible structures (10) and (11), for the tetrahydro derivative, should be fairly easy.



(10)



(11)

The aminobenzocyclobutene (10) was prepared by the reaction of tetrafluorobenzyne with N,N-dimethylaminocyclohexene (see chapter 2), and a comparison with the tetrahydro compound showed that they were not the same. It is just possible that the two compounds were <u>cis</u> and <u>trans</u> isomers about the 1,6-bond and are therefore different. However by ^1H n.m.r. spectroscopy it was thought that the differences in the two spectra were more than would be expected for merely a difference of <u>cis</u> or <u>trans</u> isomers. The tetrahydro derivative by ^1H n.m.r. spectroscopy shows a triplet at τ 5.24, J = 8 Hz.; a singlet at τ 7.47, (6H)-N,N-dimethyl, and a multiplet at τ 6.8-9.0 (8H), as compared with the aminobenzocyclobutene which shows a

multiplet at τ 6.25 - 6.5 (1H); a singlet at τ 7.69 (6H); a multiplet at τ 7.7 - 8.2 (4H) and a multiplet at τ 8.2 - 8.9 (4H).

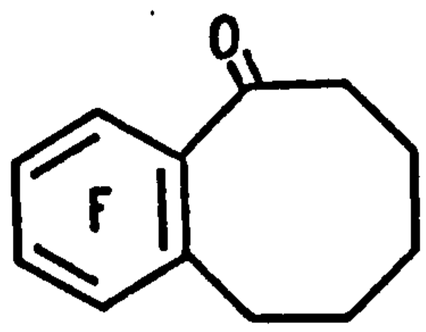
The i.r. spectra show a strong band at 1640 cm.$^{-1}$ for the tetrahydro derivative but no such band for the aminobenzocyclobutene. The u.v. spectra were also significantly different.

This information supports the structure (11).

The tetrahydro derivative was reported[17] to be stable to brief heating with dilute mineral acid. However, when heated for 6 hr. in aqueous ethanol, containing a small amount of hydrochloric acid, a quantitative yield of a ketone $C_{12}H_{10}F_4O$ was obtained.

^{1}H N.m.r. spectroscopy showed presence of methylene groups adjacent to carbonyl or aryl with resonance absorptions at τ 7.1 - 7.5 (4H) and saturated methylene groups at τ 8.0 - 8.5 (6H).

The i.r. spectrum contains a carbonyl absorption at 1710 cm.$^{-1}$., and the u.v. spectrum has a maximum at $\lambda_{max.}$ 264 (ϵ 660) nm.. The (1,2)tetrafluorobenzocyclooctan-3-one (15) would have these spectral properties.



(15)

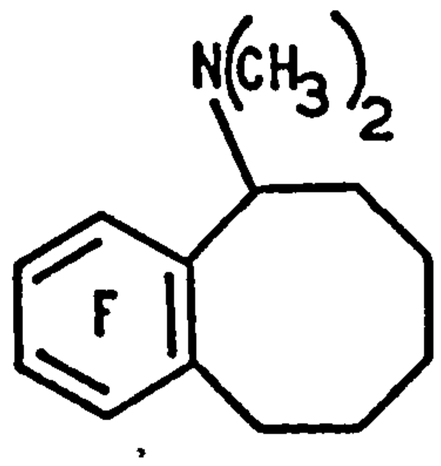
The i.r. carbonyl absorption of 1710 cm.$^{-1}$ is high for an aryl ketone;[34] however this is not unusual in polyfluoro aryl carbonyl compounds.[35,36]

In accord with structure (15), the compound undergoes base catalysed hydrogen exchange, in dioxan containing deuterium oxide,[37] to give a ketone containing 11.5% d_1 and 88.5% d_2.

The ^1H n.m.r. spectrum shows a multiplet at τ 7.1 - 7.5 (2H) and a multiplet at τ 8.0 - 8.5 (6H).

The tetrahydro derivative does not appear to be an enamine as it was not reduced with sodium borohydride.[17] It may be that this compound is a particularly stable enamine owing to participation of the electrophilic tetrafluoroaryl group, since this group could undoubtedly reduce the nucleophilicity by an inductive effect. The mechanism for the reduction of enamines is dependent on the formation of the corresponding immonium species which is then reduced. It is usual to bring this about with an acid.[28]

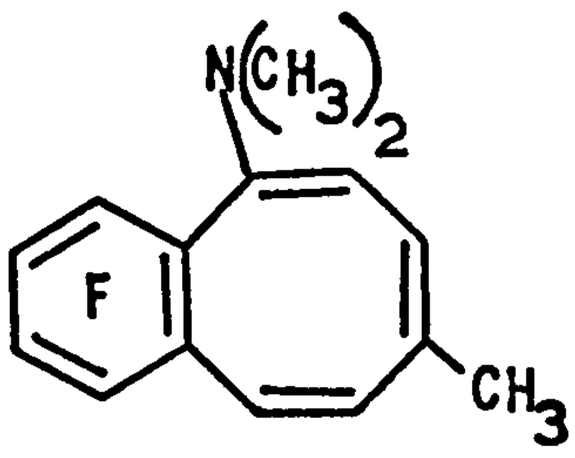
The tetrahydro compound was smoothly converted to the amine (9) in 98% yield, using sodium borohydride in tetrahydrofuran containing glacial acetic acid.



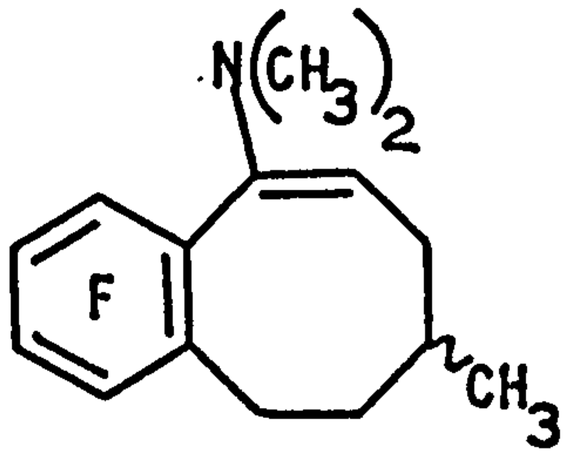
(9)

An attempt to convert the ketone (15) back to the original enamine (5) using Weingarten's[38] method failed, and the experiment was not repeated using different conditions.

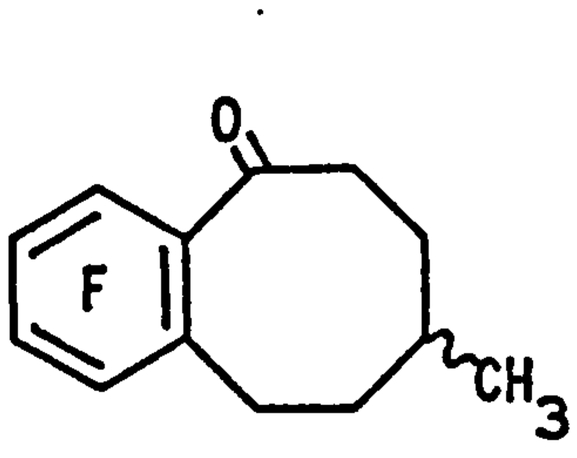
Tetrafluorobenzyne was also allowed to react with N,N-dimethyl-p-toluidine and gave a benzocyclo-octatetraene (16) which could be reduced to a tetrahydro derivative (17) and then hydrolysed to the ketone (18).



(16)



(17)



(18)

^{13}C N.m.r. spectroscopy is becoming increasingly useful in structure determination particularly since the introduction of Pulse Fourier Transform techniques.[39]

The subject has recently been reviewed.[40]

The ^{13}C n.m.r. spectrum of compound (15) has been obtained at 25.2 M.Hz. using the P.F.T. method, fig. B. The proton decoupled spectrum shows a very low field resonance at 4878 Hz. downfield from T.M.S. which is consistent with a carbonyl group conjugated to an unsaturated system. Also the spectrum shows resonances at 1183 Hz., attributed to a benzylic methylene, and at 693, 610, 583 Hz., corresponding to three methylene groups. The non-proton decoupled spectrum shows a triplet, $J_{^{13}C-H}$ = 135 Hz., for the resonance at 1183 Hz., which is consistent for a $-CH_2-$ group. The unsaturated carbon atoms are missing in the spectrum, fig. B, as a result of coupling to fluorine which was not easily removed.

200 Hz.

^{13}C SPECTRUM

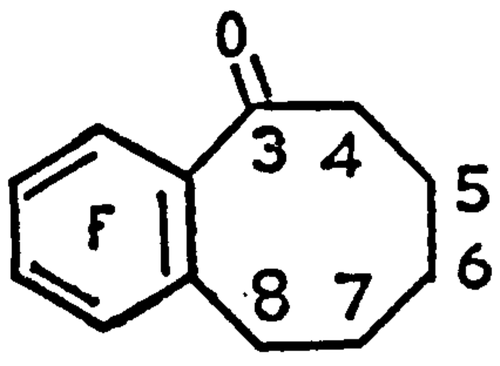
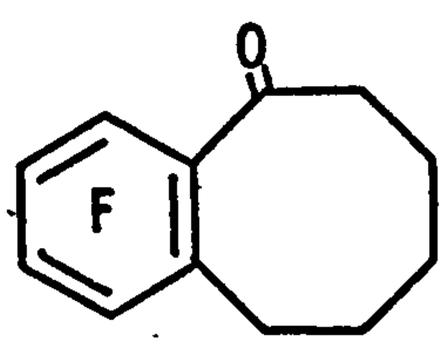


fig. B

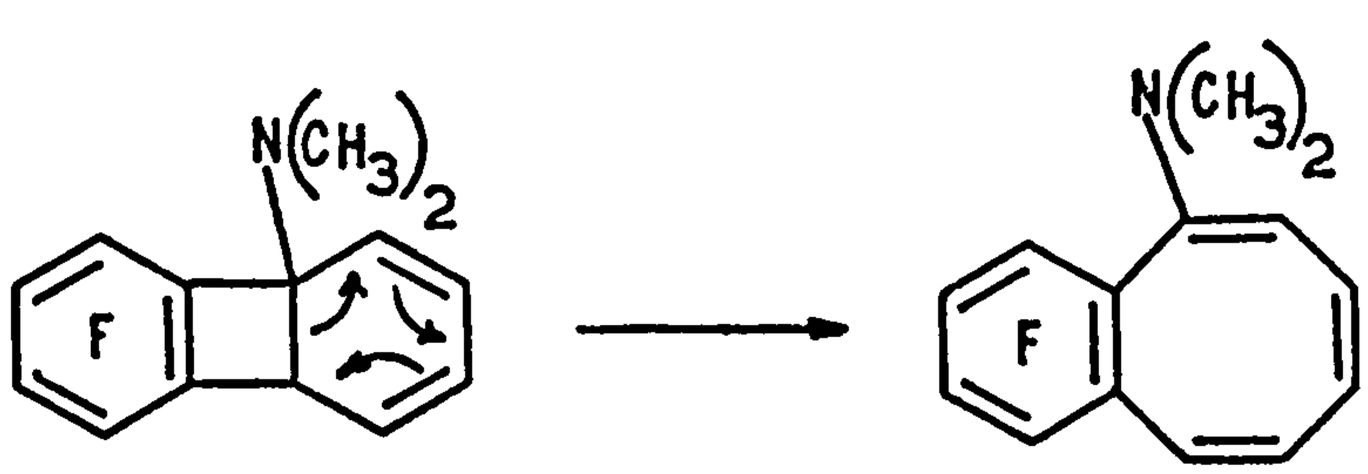
The chemical shift values are in agreement with available chemical shift data.[41]

These results agree with the proposed structure of ketone (15).



(15)

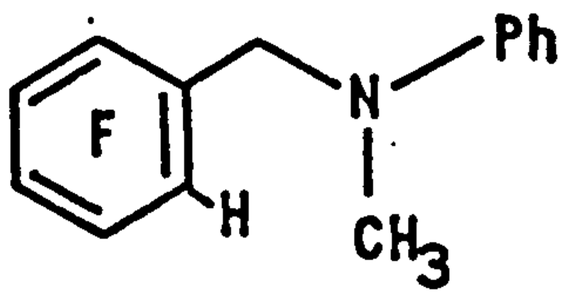
It is reasonable to assume that the product derived from the 1,2-addition of tetrafluorobenzyne to N,N-dimethylaniline is in fact 3-N,N-dimethylamino-(1,2)-tetrafluorobenzocyclo-octatetraene (5), and that it is derived from valence bond isomerisation in the primary product (4).



(4) (5)

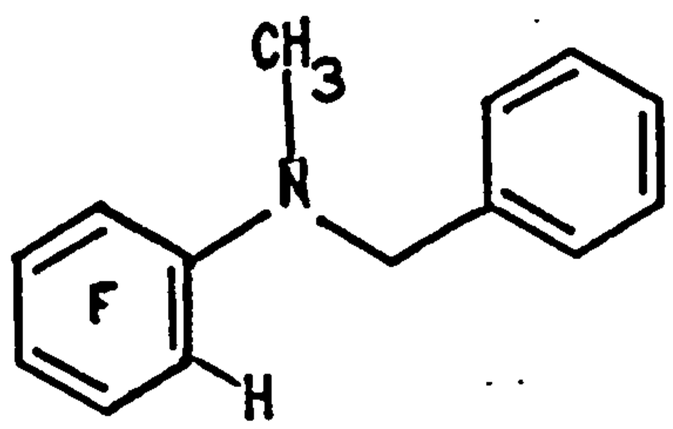
The remaining product in the reaction of tetrafluorobenzyne with N,N-dimethylaniline in ether will now be discussed.

This product has been assigned the structure (6).[17]



(6)

^{1}H N.m.r. spectroscopy shows a multiplet τ 2.65 - 3.5 (6H), aromatic hydrogens; a broad singlet at τ 5.55, (2H), -N-CH_2-; and a singlet at τ 7.05, (3H), -N-CH_3. I.r. spectroscopy shows significant absorptions at 3080 cm.$^{-1}$ (w), aromatic C-H; 2920, 2850 cm.$^{-1}$(w), aliphatic C-H; 1515, 1490 cm.$^{-1}$ (s), aromatic C-F; and 753, 695 cm.$^{-1}$, mono substituted aromatic ring. At this point the isomeric structure (19) could be considered as an alternative to the N-methyl-N-1,2,3,4-tetrafluorobenzylaniline (6).



(19)

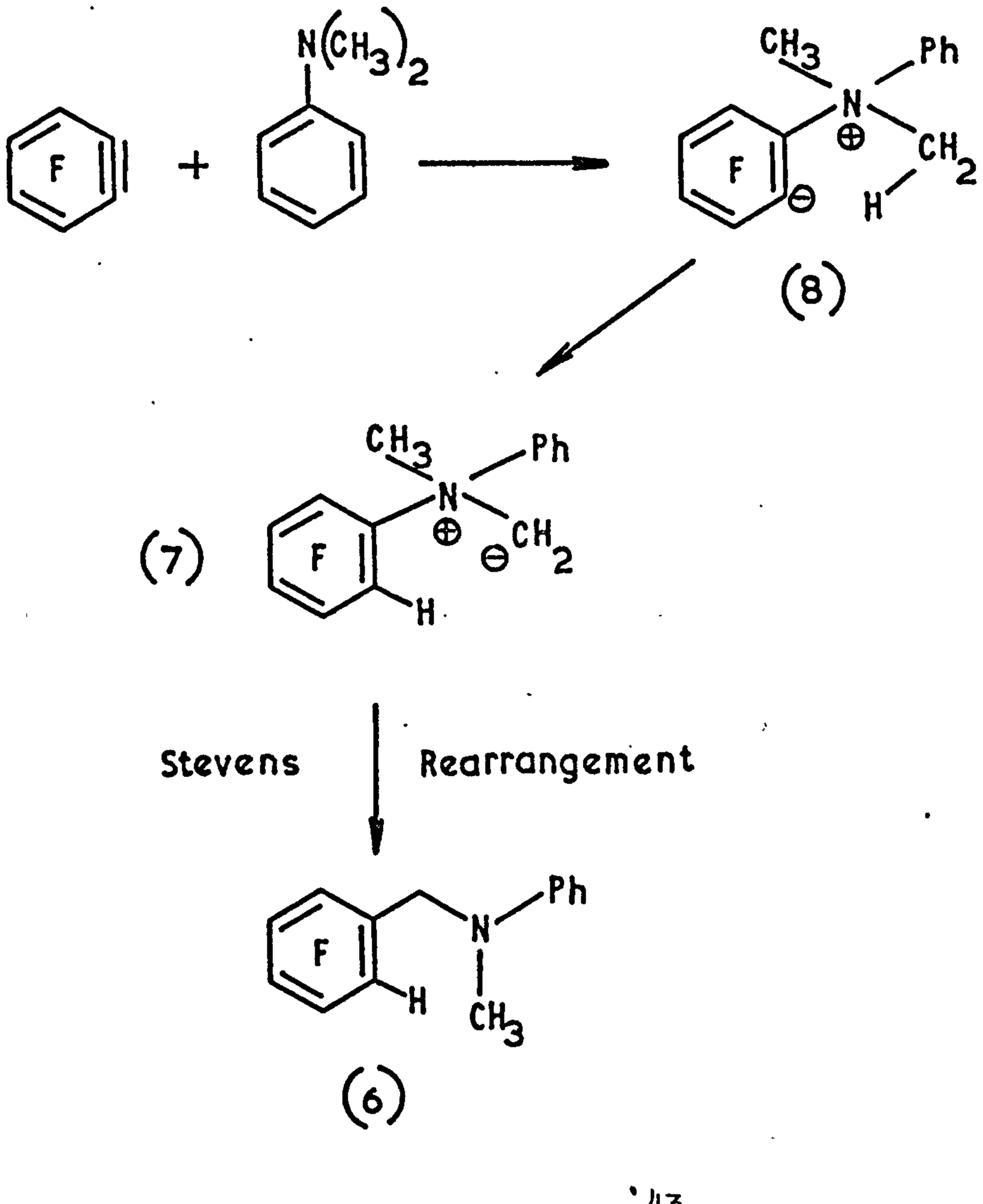
However the mass spectral data, table I, shows fragmentations consistent with structure (6) rather than (19).

Table I

m/e	Relative Abundance	Possible fragmentation
269	100%	Molecular ion
163	55%	$[C_7H_3F_4]^+$
120	86%	$[C_8H_{10}N]^+$
106	63%	$[C_7H_8N]^+$
77	77%	Ph^+

If structure (19) was correct a fragment ion corresponding to $[C_7H_7]^+$ (tropylium ion) would be expected for α cleavage of a benzyl derivative.[42] This ion was not observed.

The formation of the tetrafluorobenzyl aniline (6) is interesting as it would appear the tetrafluoroaryl group has migrated by a Stevens rearrangement of the ylide (7).

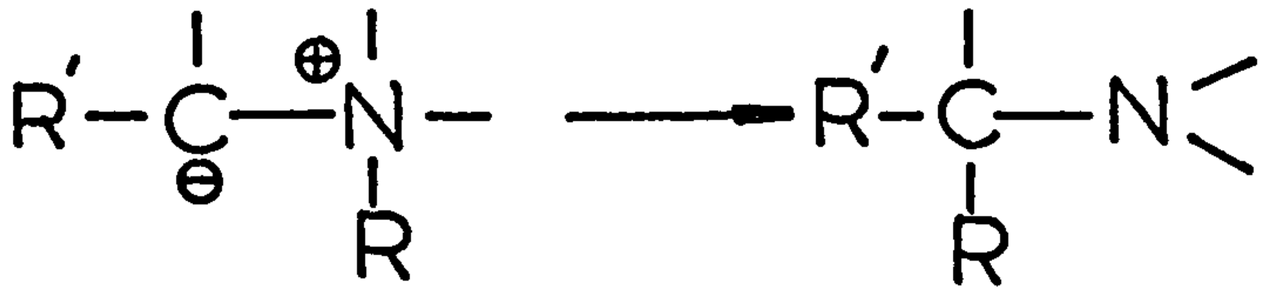


No verified examples of Stevens rearrangements[43] involving migration of an aryl group were reported prior to the preliminary publication of this work.[17] Migration involving a naphthyl group in a Stevens

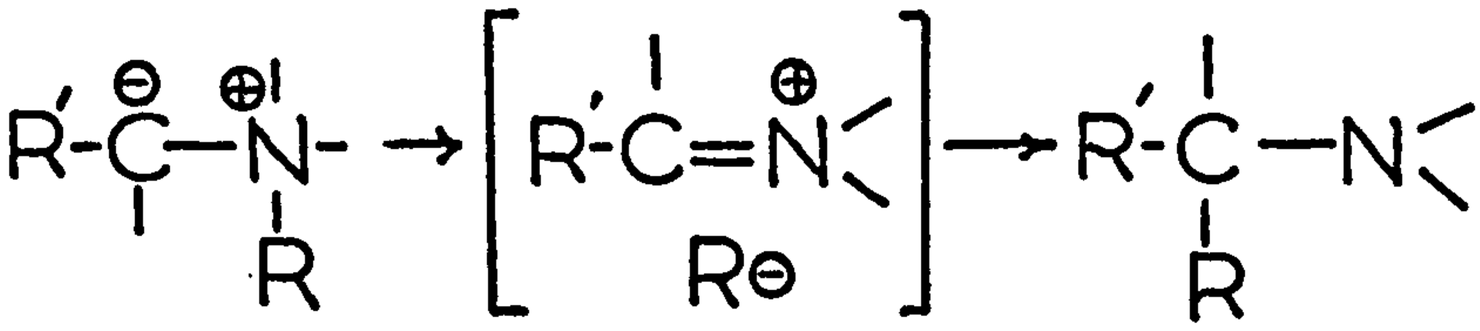
rearrangement has since been reported.[44]

Although the Stevens rearrangement[45] has been known for many years, and is regarded as an intramolecular process,[46] its mechanism is the subject of considerable argument.[47] Concerted, ion pair, and diradical mechanisms have been suggested.

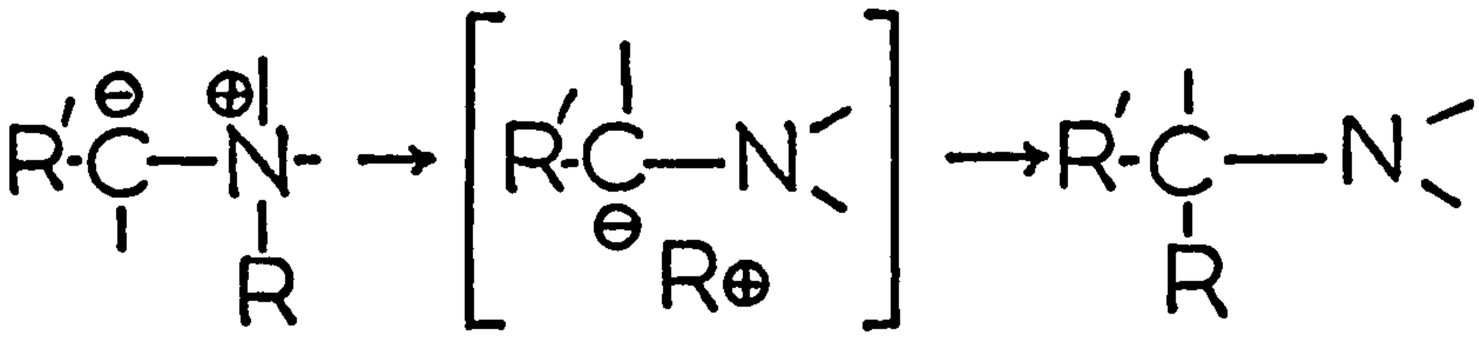
Concerted



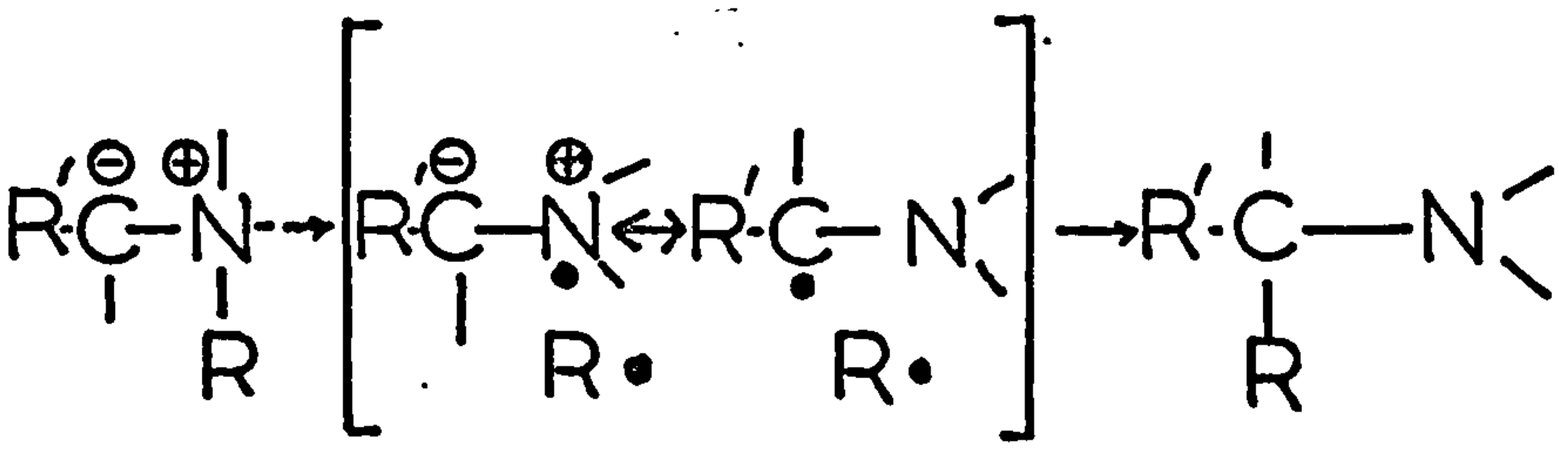
Ion pair a)



b)



Diradical



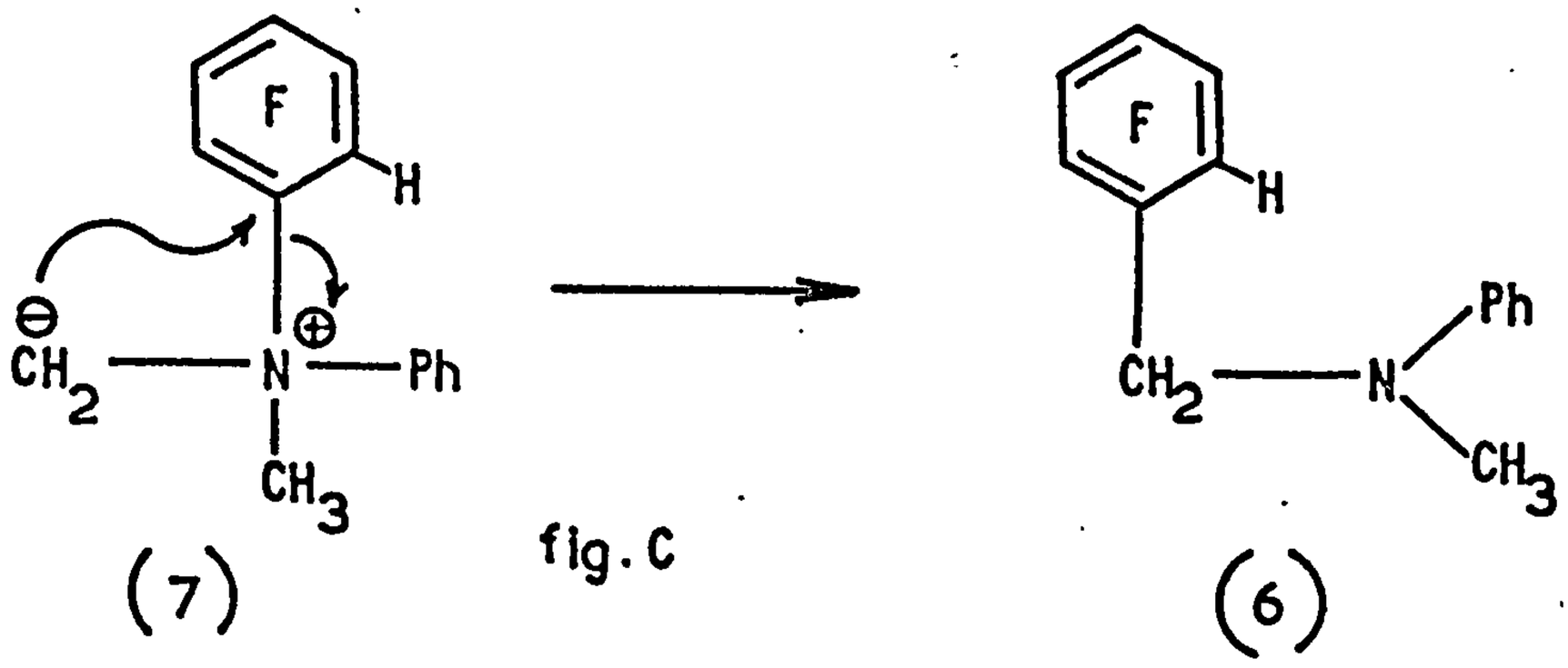
Use has been made of chemically-induced dynamic nuclear polarization techniques[47e - i], (C.I.D.N.P.) in order to establish the intermediacy of particular caged radicals.

Both in the ion pair and diradical mechanisms reaction must take place rapidly in order that conditions of intramolecular transfer are met.

In the diradical case this is compatible with the lifetimes of between 10^{-5} and 10^{-9} sec. as these are the suggested limits on the nuclear polarization process.[48]

No C.I.D.N.P. signals could be observed in the reaction of benzyne with N,N-dimethylaniline[19] although this may have been due to very low concentrations of any of the possible intermediates.

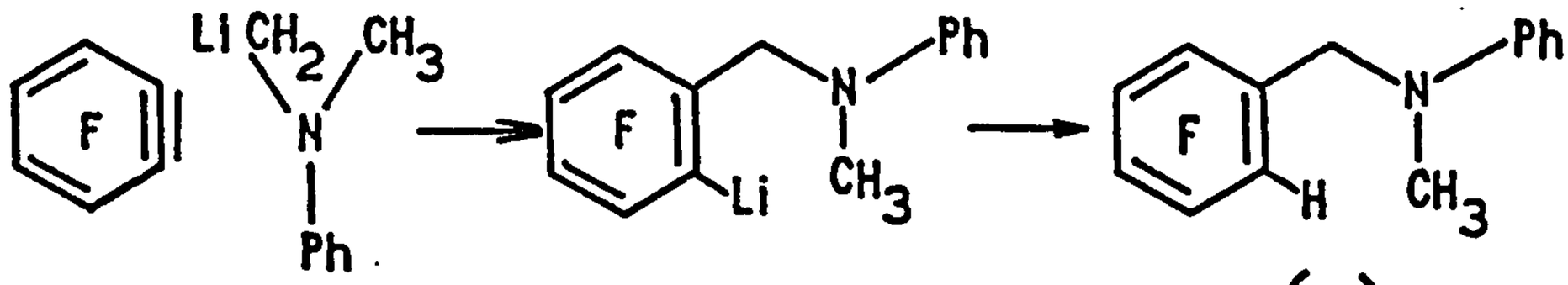
The mechanism for the rearrangement of the ylide (7) to the aniline (6) may be an ion pair or a diradical process. A possible alternative which is very reasonable, particularly in the light of the known ease of nucleophilic substitution of the tetrafluoroaryl system,[49] is the concerted reaction, fig. C.



(7) fig. C (6)

A similar concerted mechanism has been proposed[50] for the Stevens rearrangement in which a symmetry allowed reaction occurs.

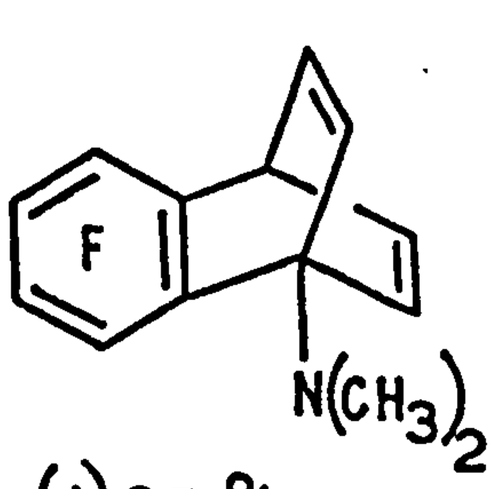
The aniline (6) could arise by reaction of tetrafluorobenzyne to metallated N,N-dimethylaniline thus :-



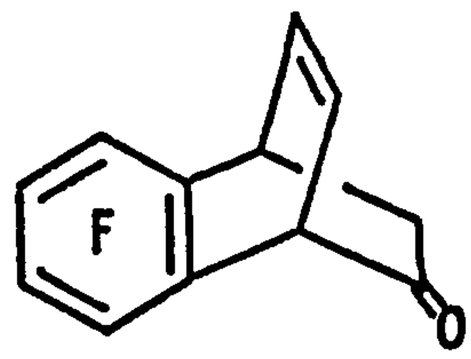
(6)

When the reaction mixture was quenched with deuterium oxide no incorporation of deuterium was detected in the compound (6), thus the reaction appears to be a genuine example of a Stevens rearrangement in which the aryl group migrates.

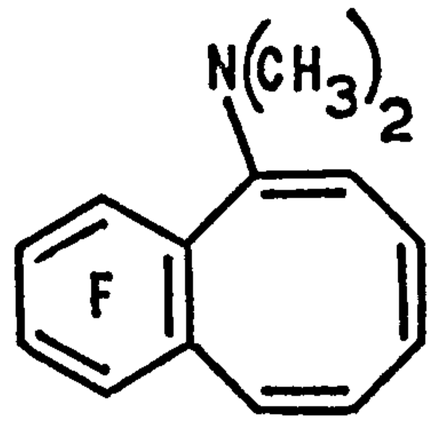
When pentafluorophenyl lithium was decomposed in N,N-dimethylaniline using light petroleum as the solvent, five products were obtained.[17] Four of them (1) (2) (5) and (6) have been previously discussed, and the fifth was shown to be N-methyl-N-phenyl tetrafluoro-o-toluidine (9).[17,20]



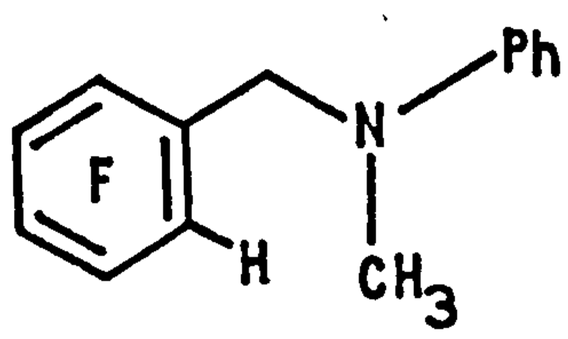
(1) 9.5 %



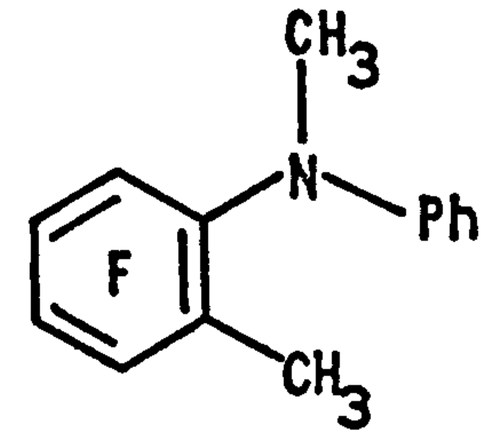
(2) 10 %



(5) 2 %

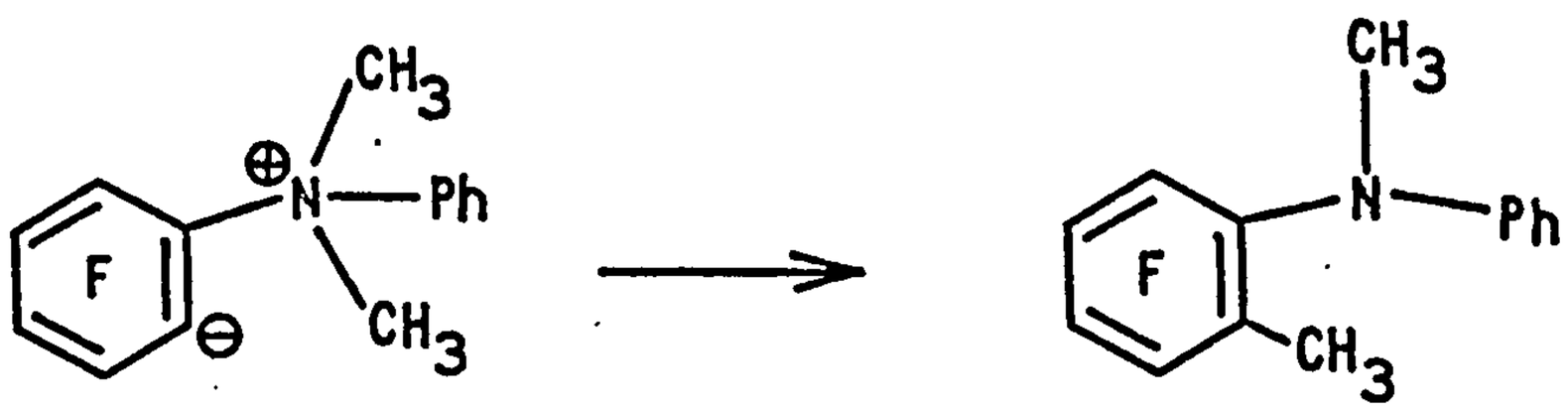


(6) 0.5 %



(9) 19 %

The formation of (9) was thought[17] to be derived by charge neutralisation in the betaine (8).



(8) (9)

This type of orthoanilide displacement is unusual as similar betaines derived from the reaction of benzyne with either N,N-dimethylaniline or N,N-dimethylbenzylamine do not undergo these displacements.[19] It is not known whether this rearrangement proceeds by an intra- or intermolecular mechanism. However, inspection of scale molecular models suggest that an intramolecular mechanism would require a front-side displacement of the methyl group which is therefore unlikely.

The reaction of tetrafluorobenzyne with N,N-dimethylaniline in light petroleum giving (9) as the major product suggests that the dipolar betaine (8) is hardly stabilised by solvation and therefore it tends to react rapidly to form a neutral species rather than the ylide (7). In ether as a solvent however, more solvation of the dipolar species results in a product derived from the ylide (7). When tetrafluorobenzyne was generated from the Grignard reagent, products derived from the betaine, or the ylide were not observed. This is most probably due to the magnesium salts complexing with the betaine thus eliminating further reaction. Similar complexing of betaines with magnesium salts has been observed.[21b, 51] Also when

tetrafluorobenzyne, generated from pentafluorophenyl lithium, was reacted with N,N-dimethylaniline in ether containing magnesium bromide, no products derived from the betaine were observed.

Experimental

All reactions involving organolithium or Grignard reagents, were carried out in glassware dried overnight at 120°, and under an atmosphere of dry, "white spot" nitrogen. All solvents were distilled and dried by conventional methods prior to usage. Organic solutions of products were dried over anhydrous magnesium sulphate.

Analytical thin layer chromatography was carried out using silica gel (GF_{254} according to Stahl), for layers 0.25 mm. thick. Preparative thin layer chromatography was carried out using silica gel (PF_{254} according to Stahl) for layers 0.75 mm. thick.

Analytical gas chromatography was carried out using a Pye 104 series gas chromatograph with hydrogenation flame ionisation detection. The 5 ft. columns used were :

A 10% S.E. 30 on firebrick.

B 20% S.E. 30 on chromosorb w.

C 10% S.E. 52 on chromosorb w.

D 10% Carbowax on chromosorb w.

E 10% Apiezon on chromosorb w.

F 10% Diethylene Glycol Succinate on chromosorb w.

Infra-red spectra were determined for potassium bromide discs in the case of solids, or thin films in the case of liquids, unless otherwise stated, with a Perkin-Elmer 257 spectrophotometer. Ultra-violet spectra were determined for solutions on Pye SP 800 and SP 8000 spectrophotometers. ^{1}H Nuclear magnetic resonance spectra were determined at 60 M. Hz. for approximately 20% w/v solutions using tetramethyl-

silane as an internal standard. ^{19}F n.m.r. spectra were determined at 56.46 M.Hz., for solutions in trichlorofluoromethane and were recorded as δ values in p.p.m. from trichlorofluoromethane.

The n.m.r. spectra were recorded with a Perkin-Elmer R 10 spectrometer. ^{1}H n.m.r. spectra at 220 M.Hz. and 100 M.Hz. were recorded by the courtesy of the S.R.C..

Mass spectra were determined on an A.E.I. M.S. 12 mass spectrometer. High resolution mass spectrometry was carried out on an A.E.I. M.S. 9 at P.C.M.U. by the courtesy of the S.R.C. Melting points were determined on a Kofler block, and are uncorrected. All compounds were colourless unless stated otherwise.

Experiment 2 was performed by Mr. T.J. Ward, S.R.C. Research Assistant, Loughborough University, 1969.

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^{13}C nuclear magnetic resonance spectra were obtained at 25.2 M.Hz. by the courtesy of I.C.I. Ltd., Plastics Division.

1. Reaction of tetrafluorobenzyne with N,N-dimethylaniline.

n-Butyl lithium (50 ml., 2.35 molar hexane solution) was added to bromopentafluorobenzene (24.7 g., 0.1 mole) in ether (150 ml.) at -50°. The mixture was stirred at this temperature for 15 min. then N,N-dimethylaniline (70 ml.) was added. The external cooling source was removed, the reaction mixture was allowed to warm to room temperature and stirred for 18 hr.. Water was added, and the organic phase separated and then distilled to remove ether and excess N,N-dimethylaniline.

The residual oil was dissolved in ether (100 ml.) and extracted with a) 1N hydrochloric acid (3 x 25 ml.) to give fraction 1

b) 2N hydrochloric acid (4 x 25 ml.) to give fraction 2

c) 30% hydrochloric acid (5 x 25 ml.) to give fraction 3.

The acid fractions were neutralised with solid sodium carbonate and extracted with ether. Removal of the ether gave from fraction 1 1-N,N-dimethylamino(7,8)tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene, (1), (4.91 g., 18%); m.p. 83° (from ethanol) (lit.[20] 82° from methanol); ^{1}H n.m.r. τ (CCl_4) 2.9 - 3.4 (m., 4H); 4.75 - 5.05 (m., 1H); and 7.31 (d., 6H, J = 5 Hz.),

ν_{max}^{KBr} 2980, 2900, 2870, 2830, 1640, 1490, 1345, 1305, 1270, 1260, 1105, 1050, 1000, 960, 840, 785, 730, 710, and 680 cm.$^{-1}$,

$\lambda_{max}^{Methanol}$ 211 (ϵ 4570); 219 sh. (3880); and 265 sh. (510) nm..

Removal of ether and elution through a short column of alumina gave from fraction 2, 3-N,N-dimethylamino(1,2)tetrafluorobenzocyclo-octa-tetraene, (5), (2.68 g., 10%), b.p. 118° at 3mm. (yellow).

An analysis could not be obtained as the compound was unstable and tended to polymerise very easily.

^{1}H N.m.r. τ (CCl_4) 3.4 - 4.6 (m., 4H); 5.21 (d., 1H, J = 3.0 Hz.), and 7.47 (s., 6H);

υ_{max} 3020, 2960, 2890, 2850, 2810, 1650, 1630, 1520, 1470, 1415, 1380, 1355, 1155, 1140, 1120, 1080, 1037, 985, 875, 745, 685, and 665 cm.$^{-1}$;

$\lambda_{max}^{cyclohexane}$ 217 (ϵ 11,870); 250 sh. (6400) nm.

Mass spectrometry M^+ 269.

Removal of ether gave from fraction 3, N-2,3,4,5-tetrafluorobenzyl-N-methylaniline,(b), (3.4 g., 13%), b.p. 115° at 2 mm..

(Found: C, 62.45; H, 4.25; N, 5.1%; M [Mass spectrometry] 269, $C_{14}H_{11}F_4N$ requires C, 62.5; H, 4.1; N, 5.2%, M. 269);

^{1}H n.m.r. τ ($CDCl_3$) 2.65 - 3.5 (m., 6H); 5.55 (broad s., 2H); and 7.05 (s., 3H);

υ_{max} 3080, 2920, 2850, 1610, 1530, 1515, 1490, 1350, 1260,1220, 1195, 1110, 1045, 1000, 945, 920, 860, 753, and 695 cm.$^{-1}$.

Removal of ether from the basic fraction gave (7,8)tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (2), (1.7 g., 7%), m.p. 72-73° (after sublimation) (lit.[52] 72.5 - 73.5°).

υ_{max} 3080, 2940, 1738, 1500, 1421, 1386, 1334, 1310, 1130, 1115, 1090, 1080, 1070, 1030, 917, 870, 750 and 717 cm.$^{-1}$.

Ratio of these four products in the crude reaction mixture was shown by g.l.c. (column A) to be

Compound (1)	(5)	(6)	(2)
Ratio 12	: 7	: 8	: 2

2. Reaction of tetrafluorobenzyne with N,N-dimethylaniline .

a) Ether solution of pentafluorophenyl lithium was added to a boiling solution of N,N-dimethylaniline in hexane, the product ratio was determined by g.l.c. (column A).

Compound	(1)	(5)	(6)	(2)
Ratio	12	15	8	4

b) Repeat of experiment 1 with magnesium bromide present in the reaction mixture gave the product ratio g.l.c. (column A).

Compound	(1)	(5)	(6)	(2)
Ratio	24	5	0	6

c) Repeat of experiment 1 using light petroleum b.p. 60/80 as the solvent rather than ether, gave as isolated products :

Compound (1) 9.5%

Compound (5) 2%

Compound (6) 0.5%

Compound (2) 10% and N-methyl-N-phenyl-2,3,4,5-tetrafluoro-o-toluidine, (9), 19% (identical to a sample prepared previously in these laboratories[20]).

d) By decomposition of pentafluorophenylmagnesium chloride in N,N-dimethylaniline at 80° gave as isolated products :

		g.l.c. ratio
Compound (1)	10%	15
Compound (5)	1.5%	3
Compound (2)	0.75%	4

3. Reaction of tetrafluorobenzyne and N,N-dimethyl-p-toluidine .

Bromopentafluorobenzene (37.2 g.,0.15 mole) in ether (100 ml.) was added to magnesium (4.35 g.) in ether (10 ml.) at such a rate

so as to maintain boiling of the solvent. The mixture was heated under reflux for 45 min., N,N-dimethyl-p.toluidine (68 g.) added, and ether was distilled until the internal temperature was raised to 80°. Heating was maintained at this temperature for 5 hr.. Work up by the acid extraction procedure (experiment 1) gave :-

a) From 1N hydrychloric acid, a mixture of two products, i and ii which were separated by preparative t.l.c. using ether/light petroleum b.p. 60/80 (1:4)as eluant.

i. 1-N,N-dimethyl-4-methyl(7, 8)tetrafluorobenzobicyclo[2.2.2]-octa-2,5,7-triene (1.5 g., 4%); m.p. 49-50° (from light petroleum b.p. 60-80°),(Found: C, 64.0; H, 4.85; N, 4.9% M [mass spectrometry] 283, $C_{15}H_{13}F_4N$ requires C, 63.6; H, 4.6; N, 4.95%; M. 283);

^{1}H n.m.r. τ (CCl_4) 3.1 (d., 2H, $J_{23} = J_{65} = 7$ Hz.);
3.58 (d., 2H $J_{32} = J_{56} = 7$ Hz.);
7.38 (d., 6H, $J_{HF} = 4.5$ Hz.);
and 7.97 (d., 3H, $J_{HF} = 6$ Hz.);

υ_{max}^{KBr} 3000, 2950, 2890, 2840, 2800, 1648, 1618, 1583, 1480, 1342, 1270, 1156, 1140, 1105, 1040, 980, 890, 850, and 700 cm.$^{-1}$,

and ii. This product was not characterised fully. (350 mg.)

b) 3-N,N-dimethylamino-6-methyl(1,2)tetrafluorobenzocyclo-octatetraene, (16), (1.4 g., 3%).

This product was unstable and an analysis was not obtained.

^{1}H N.m.r. τ ($CDCl_3$) 3.4 - 4.6 (m., 3H); 5.1 (m., 1H);
7.47 (s., 6H); and 8.3 (broad s., 3H);

υ_{max} 3000, 2950, 2880, 2840, 2800, 1630, 1520, 1499, 1465, 1405, 1315, 1135, 1117, 1077, 1057, 990, 980, and 810 cm.$^{-1}$

c) 5-methyl(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (1.6 g., 4%) m.p. 80-82° (from methanol) (lit.[23] 76-80°);

^{1}H n.m.r. τ (CCl_4) 3.81 (m., 1H); 5.45 (dd., $J_{1,6}$ = 6 Hz., J_{HF} = 2 Hz.), 5.73 (m., 1H); 8.0 (d., 3H, $J_{5,6}$ = 1.5 Hz.) and 7.6 - 8.2 (ABX octet 2H);

υ_{max} 3070, 2990, 2920, 1735, 1500, 1445, 1390, 1320, 1310, 1120, 1085, 1040, 1015, 920, 880, 830, 790, and 700 cm^{-1}..

4. Reaction of tetrachlorobenzyne with N,N-dimethylaniline.

By lithio route as in experiment 1 gave after work up by the acid extraction procedure (experiment 1), 1-N,N-dimethylamino(7,8)-tetrachlorobenzobicyclo[2.2.2]octa-2,5,7-triene (10.3 g., 31%); m.p. 110° (from ethanol).

(Found: C, 50.2; H, 3.3; N, 4.25%; M [mass spectrometry] 335

$C_{14}H_{11}Cl_4N$ requires C, 50.3; H, 3.3; N, 4.2%; M. 335),

^{1}H n.m.r. τ (CCl_4) 2.9 - 3.3 (m., 4H $J_{2,3} = J_{6,5}$ = 7 Hz.; $J_{2,4} = J_{6,4}$ = 2 Hz.; $J_{3,4} = J_{5,4}$ = 5.5 Hz.);

4.55 - 4.85 (m., 1H, $J_{4,2} = J_{4,6}$ = 2 Hz., $J_{4,3} = J_{4,5}$ = 5.5 Hz.); and 7.36 (s., 6H),

υ_{max} 2960, 2840, 2800, 1632, 1587, 1460, 1375, 1360, 1341, 1328, 1151, 1110, 942, and 695 $cm.^{-1}$,

$\lambda_{max}^{methanol}$ 223 (ϵ 26700) nm..

and 3-N,N-dimethyl(1,2)tetrachlorobenzocyclo-octatetraene, (12), (1.3 g., 4%), yellow oil.

An analysis could not be obtained for this compound owing to its instability and ease of polymerisation;

^{1}H n.m.r. τ (CCl_4) 3.3 - 4.5 (m., 4H);

5.32 (d., 1H, J = 3.2 Hz.); and 7.48 (s., 6H);

υ_{max} 3000, 2960, 2880, 2800, 1625, 1410, 1360, 1340, 1320, 1172, 1098, 785, 712, 695, and 655 cm.$^{-1}$.

Other products were present but were not isolated.

5. Photolysis of 1-N,N-dimethylamino(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-2,5,7-triene (1).

The compound (1) (2 g.) in light petroleum b.p. 60-80° (200 ml.) was photolysed with a medium pressure Hanovia lamp in a dry nitrogen atmosphere for 100 hr.. Solvent was removed, the remaining black oil was eluted through a short column of alumina and gave a mixture (765 mg.) which was separated by preparative t.l.c. using ether/light petroleum b.p. 40-60° (1:1) as eluant and gave three major products:

a) recovered starting material (592 mg., 30%)

b) 3-N,N-dimethylamino(1,2)tetrafluorobenzocyclo-octatetraene (5) (120 mg., 6%) identical (by t.l.c. and spectral data) to previously prepared material; experiment 1,

c) 5-N,N-dimethylamino(3,4)-tetrafluorobenzotricyclo[3.3.0.$0^{2,8}$]-octa-3,6-diene, (14), (40 mg., 2%);

^{1}H n.m.r. τ (CCl_4) 4.25 (d., 1H, $J_{6,7}$ = 5.0 Hz.);

4.85 (dd., 1H, $J_{7,6}$ = 5.0 Hz.; $J_{7,8}$ = 2.0 Hz.);

6.65 (d., 2H, $J_{1,8}$ = 6.5 Hz., $J_{2,8}$ = 6.5 Hz.);

7.05 (dt., 1H; $J_{8,7}$ = 2 Hz.; $J_{8,2}$ = 6.5 Hz;

$J_{8,1}$ = 6.5 Hz.); and 7.75 (s., 6H);

υ_{max} 3060, 2990, 2960, 2880, 2840, 2800, 1500, 1392, 1350, 1328, 1230, 1025, 950, 925, 830, and 800 cm.$^{-1}$.

6. Hydrogenation of 3-N,N-dimethylamino-(1,2)-tetrafluorobenzocyclo-octatetraene (5).

The benzocyclo-octatetraene (5) (700 mg.) in ethanol (40 ml.) was reduced slowly with hydrogen in the presence of pre-reduced palladium

on charcoal catalyst (70 mg., 10% Pd/C).

Removal of the solvent and catalyst left the impure product which gave, after preparative t.l.c. (1:9 ether/light petroleum b.p. 40-60°), 3-N,N-dimethylamine-(1,2)-tetrafluorobenzocyclo-octa-1,3-diene; (11), (428 mg. 61%); m.p. 62 - 63° (from Hexane).

(Found: C, 61.55; H, 5.5; N, 5.25% M. [mass spectrometry] 273, $C_{14}H_{15}F_4N$ requires C, 61.55; H, 5.55; N, 5.15% M. 273).

^{1}H n.m.r. τ (CCl_4) 5.24 (t., J = 8 Hz. 1H); 7.47 (s., 6H);

and 6.8 - 9.0 (m., 8H);

υ_{max}^{KBr} 3000, 2940, 2862, 2800, 1633, 1512, 1470, 1400, 1353, 1310, 1216, 1177, 1128, 1050, 1012, 943, 821 cm.$^{-1}$.,

$\lambda_{max}^{cyclohexane}$ 212 (ϵ 17700); 275 sh. (2200) nm..

7. Hydrogenation of 3-N,N-dimethylamino-6-methyl-(1,2)-tetrafluorobenzocyclo-octatetraene (16).

The compound (16) (632 mg.) was hydrogenated as in experiment 6 and gave after elution (light petroleum b.p. 60-80°) through a short alumina column 3-N,N-dimethylamino-6-methyl-(1,2)-tetrafluorobenzocyclo-octa-1,3-diene (17), (490 mg. 77%);

b.p. 94° at 0.25 mm..

(Found: C, 62.6; H, 6.25; N, 4.65% M [mass spectroscopy] 287

$C_{15}H_{17}F_4N$ requires C, 62.7; H, 6.0; N, 4.9% M. 287);

^{1}H n.m.r. τ (CCl_4) 5.25 (t., J = 8.5 Hz. 1H); 7.49 (s., 6H);

6.7 - 9.0 (m., 7H), and 9.16 (d., J = 5 Hz. 3H);

υ_{max} 2960, 2925, 2880, 2800, 1635, 1515, 1475, 1405, 1360, 1325, 1133, 1120, 1070, 1060, 1050, 1020, 980, 920, and 820 cm.$^{-1}$.

8. Hydrogenation of 3-N,N-dimethylamino-9,10,11,12-tetrachloro-(1,2)-benzocyclo-octatetraene (12).

The compound (12) (100 mg.) was hydrogenated as in experiment 6 and gave, after elution (light petroleum b.p. 60-80°) through a short alumina column, 3-N,N-dimethylamino-(1,2)-tetrachlorobenzocyclo-octa-1,3-diene, (70 mg., 70%), m.p. 81 - 82° (from ethanol).

(Found: C, 49.65; H, 4.45; N, 4.1; $C_{14}H_{15}N\,Cl_4$ requires C, 49.6; H, 4.45; N, 4.15%);

^{1}H n.m.r. τ (CCl_4) 5.3 (t., J = 7 Hz. 1H);

7.44 (s., 6H), and 6.8 - 9.0 (m., 8H).

9. Hydrolysis of 3-N,N-dimethylamino-9,10,11,12-tetrafluoro-(1,2)-benzocyclo-octa-1,3-diene (11).

The compound (11) (100 mg.) in aqueous ethanol (5 ml., 10%) and concentrated hydrochloric acid (2 drops) was heated under reflux for 6 hr. (The reaction course was monitored by g.l.c. (column A). If the hydrochloric acid was omitted from the reaction mixture hydrolysis did not occur). Evaporation of the solvents under reduced pressure gave (1,2)-tetrafluorobenzocyclo-octen-3-one (15), (90 mg. 100%); b.p. 72° at 0.3 mm..

(Found: C, 58.4; H, 4.15% M [mass spectrometry] 246;

$C_{12}H_{10}F_4O$ requires C, 58.55; H, 4.1% M. 246);

^{1}H n.m.r. τ ($CDCl_3$) 7.1 - 7.5 (m., 4H), 8.0 - 8.5 (m., 6H);

ν_{max} 2940, 2875, 1710, 1645, 1515, 1480, 1385, 1297, 1201, 1125, 1050, 935, and 875 cm.$^{-1}$,

$\lambda_{max}^{cyclohexane}$ 264 (ϵ 660) nm..

10. Deuteriation of (1,2)-tetrafluorobenzocyclo-octen-3-one (15).

The ketone (15) (68 mg.) in dioxan (2 ml.), deuterium oxide (1 ml.),

and sodium methoxide (5 mg.) was heated under reflux for 50 hr. The mixture was cooled, solvents partially removed and the product extracted with ether. The oil, which was obtained after removal of the ether, was subjected to preparative t.l.c. and gave 4,4-[$^2H_2$](1,2)-tetrafluorobenzocycloecten-3-one (58 mg., 85%);

^{1}H n.m.r. τ ($CDCl_3$) 7.1 - 7.5 (m., 2H); 8.0 - 8.5 (m., 6H).

Mass spectrometry: M.$^+$ 248 11.5% d_1; 88.5% d_2.

11. Hydrolysis of 3-N,N-dimethylamino-6-methyl-(1,2)-tetrafluorobenzo-cyclo-octa-1,3-diene, (16).

The compound (16) (200 mg.) in aqueous ethanol (6.5 ml. 25%) was treated under reflux for 48 hr. The mixture was cooled and concentrated by partial removal of the solvents under reduced pressure. Water (10 ml.) was added and the mixture extracted with ether (3 x 5 ml.). The ether extracts were combined, dried over magnesium sulphate, and after removal of the drying agent and solvent gave 6-methyl-(1,2)-tetrafluorobenzocyclo-octen-3-one (18), (160 mg., 88%), an oil.

(Found: C, 60.1; H, 4.6%; M. [mass spectrometry] 260;

$C_{13}H_{12}F_4O$ requires C, 60.0; H, 4.65%; M. 260);

^{1}H n.m.r. τ (CCl_4) 7.0 - 7.5 (m., 4H); 7.8 - 8.9 (m., 5H); and

9.0 (d., 3H, J = 6 Hz.);

ν_{max} 2958, 2952, 2878, 1713, 1645, 1514, 1478, 1459, 1383, 1293, 1126, 1113, 1065, 971, 868, 858, and 818 cm.$^{-1}$.

12. Reduction of 3-N,N-dimethylamino-(1,2)-tetrafluorobenzocyclo-octa-1,3-diene, (11).

Sodium borohydride[53] (500 mg.) was added to a solution of compound (11), (200 mg.) in tetrahydrofuran (10 ml.) under a nitrogen atmosphere. Glacial acetic acid (6 ml.) was added dropwise to the

stirred solution over a period of 25 min.. The mixture was heated under reflux for 60 min., cooled, sodium hydroxide (20 ml., 20%) was added and the mixture extracted with ether (4 x 10 ml.). Each of the ether extracts was washed with saturated sodium chloride solution, then combined, dried and after removal of the solvent gave 3-N,N-dimethylamino-(1,2)-tetrafluorobenzocyclo-oct-1-ene, (9), (197 mg., 98%); m.p. 38.5° (after sublimation).

(Found: C, 62.4; H, 6.25; N, 5.15; $C_{14}H_{17}F_4N$ requires C, 62.55; H, 6.2; N, 5.1%);

^1H n.m.r. τ ($CDCl_3$) 5.9 - 6.4 (m., 2H); 7.0 - 7.4 (m., 1H); 7.83 (s., 6H); and 7.8 - 8.8 (m., 8H);

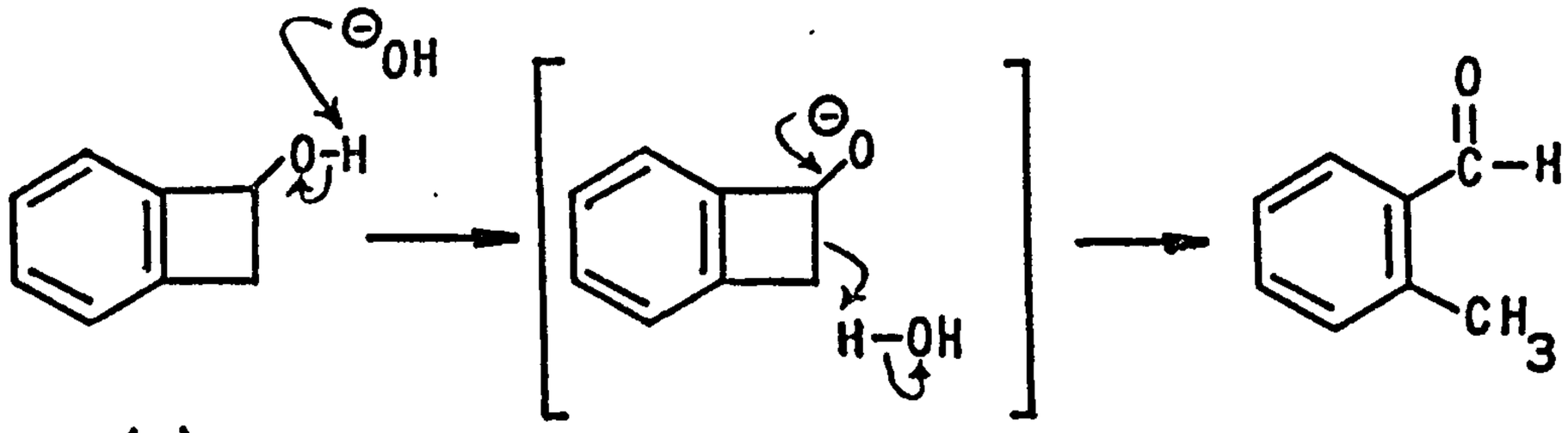
υ_{max} 2940, 2870, 2815, 2780, 1650, 1515, 1480, 1380, 1095, 1035, 940, and 880 $cm.^{-1}$.

CHAPTER 2

The Hydrolysis Reactions of some Amino-benzobicyclo Compounds

Introduction

Benzocyclobutenols are reported to be easily hydrolysed under basic conditions.[54] The benzocyclobutenol (1) readily gives o-tolualdehyde (2) in dilute sodium hydroxide.

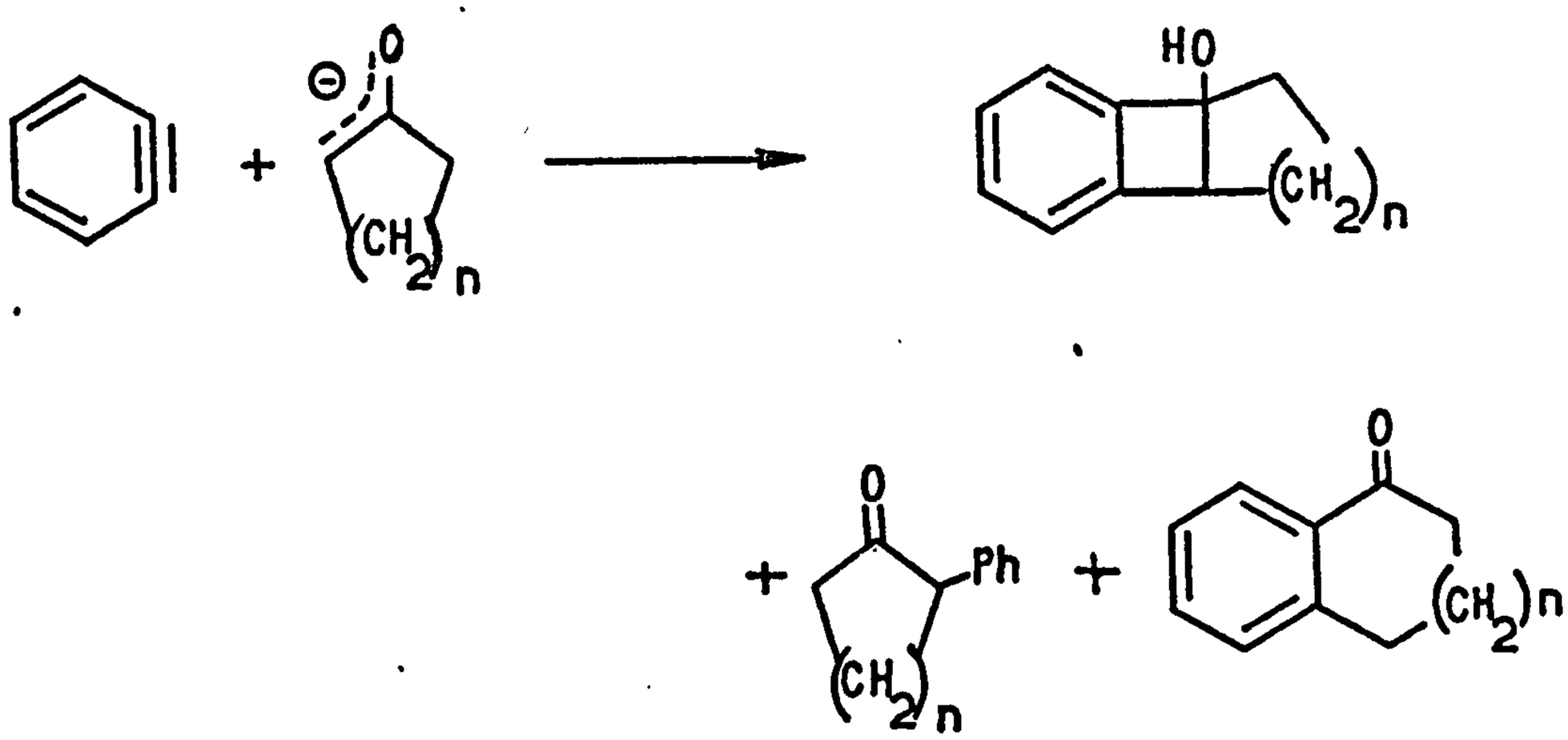


(1) (2)

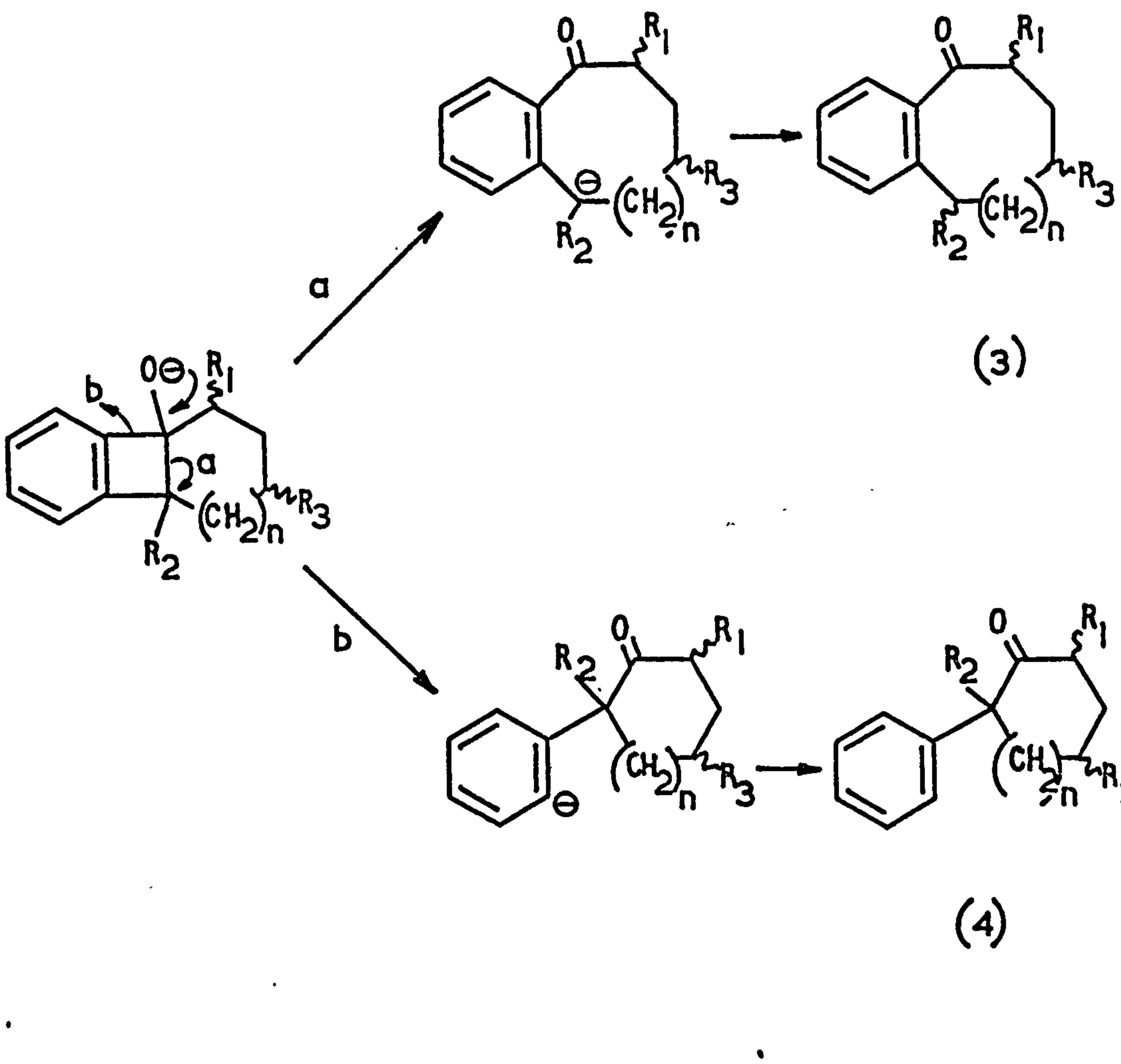
The driving force for this type of cleavage is the relief of strain present in the cyclobutene system.

The compounds are however stable in dilute mineral acids, thus suggesting the intermediacy of an anionic species in the base rearrangement.

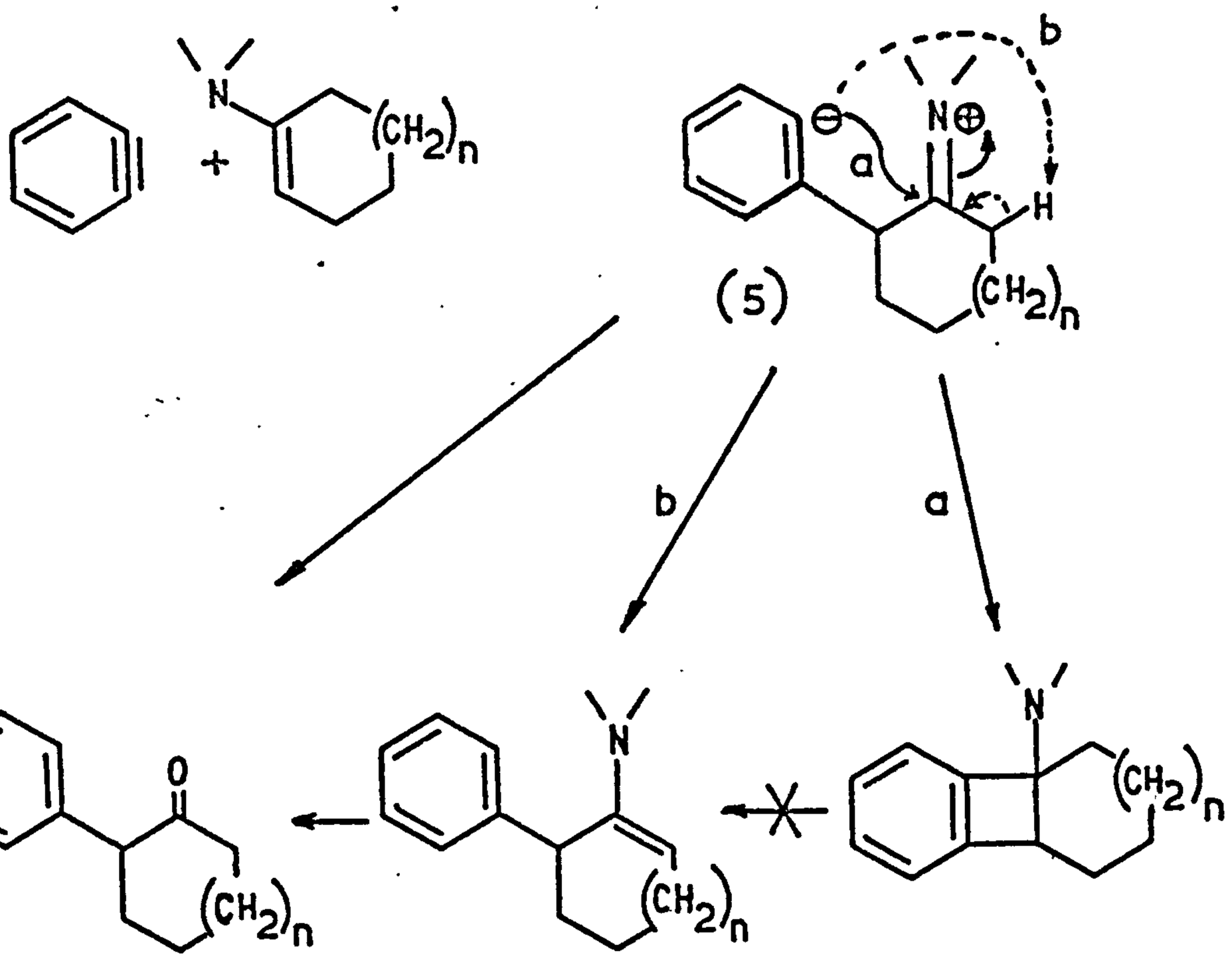
Similar benzocyclobutenols have been prepared by Caubere by the reaction of benzyne with certain ketone enolates.[55]



These reactions are always accompanied by ketonic products. In previous studies by the same workers[56] the benzocyclobutenes were not isolated as they readily gave ketones under the reaction conditions. A more recent study[55,57] of the decomposition of these benzocyclobutenols shows that the cyclobutene ring can be cleaved in one of two ways leading to two types of ketone, (3) and (4).



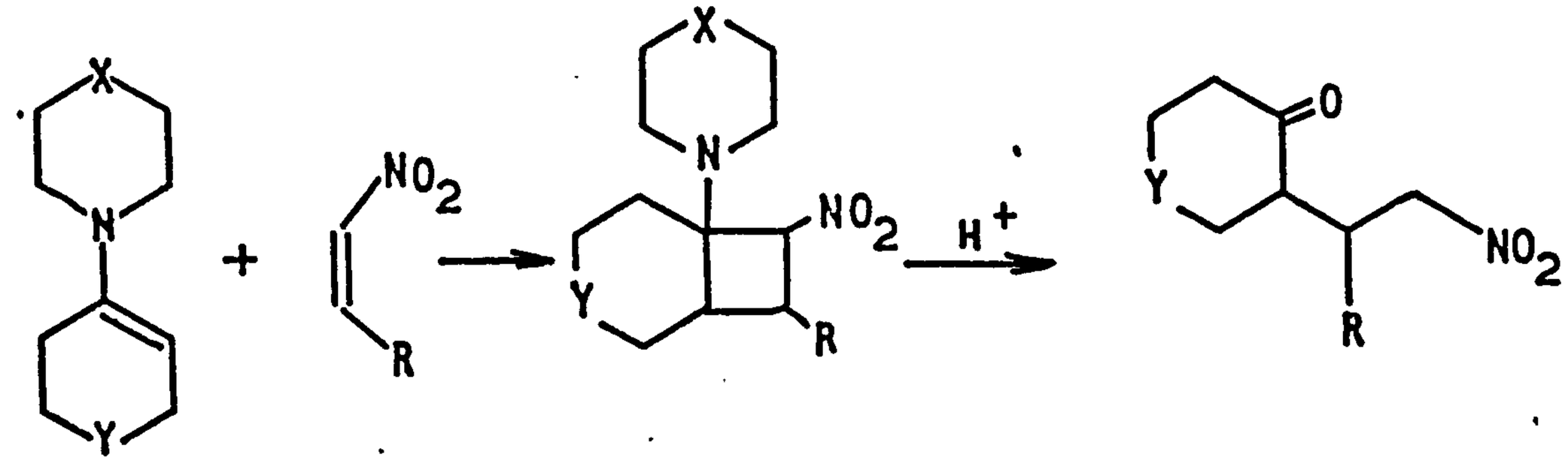
The reactions of benzyne with enamines give similar benzocyclobutenes.[58] These products are also often accompanied by ketones which are thought to arise by the hydrolysis of an intermediate zwitterion (5), or of an enamine (6) which is derived by intramolecular proton transfer.



(5)

(6)

There are no reported examples of these amino-benzocyclobutenes being hydrolysed to the ketones either on work up or under the reaction conditions. Certain enamines have been reacted with nitroethylenes to form aminocyclobutanes which do however hydrolyse in dilute mineral acid to give 2-substituted ketones.[59]

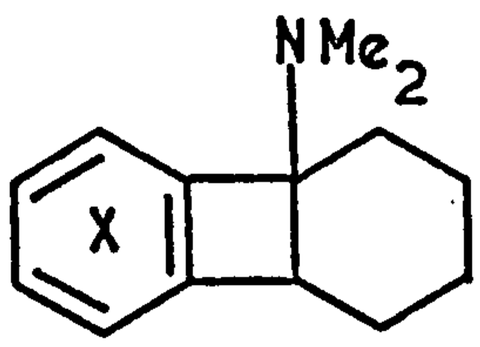


We noticed that the behaviour of the amino-tetrahalo-benzocyclobutenes towards hydrolysis was markedly different from the unhalogenated species. We wished to investigate the effect of the tetrahaloaryl function and what other structural features were necessary to bring about these hydrolysis reactions.

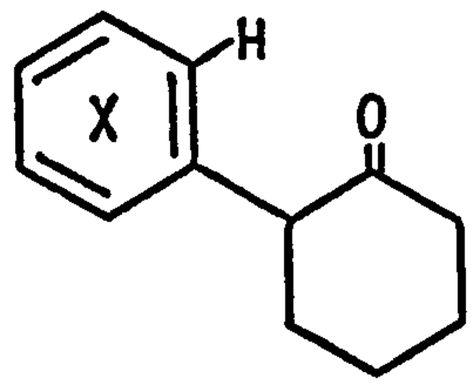
Discussion

(2 + 2) Cycloaddition reactions of benzynes with olefins have been the subjects of considerable discussion over the past few years.[62-71] It is generally accepted the reactions proceed by a two step mechanism involving either diradicals or dipolar species. The (2 + 2) cycloadditions of benzyne to enamines most probably involve a dipolar species.[58a]

In the present work we found that the reaction of tetrafluorobenzyne with 1-N,N-dimethylaminocyclohexene gave two products; compound (7) X = F isolated in 46% yield and compound (8) X = F isolated in 6%.



(7)



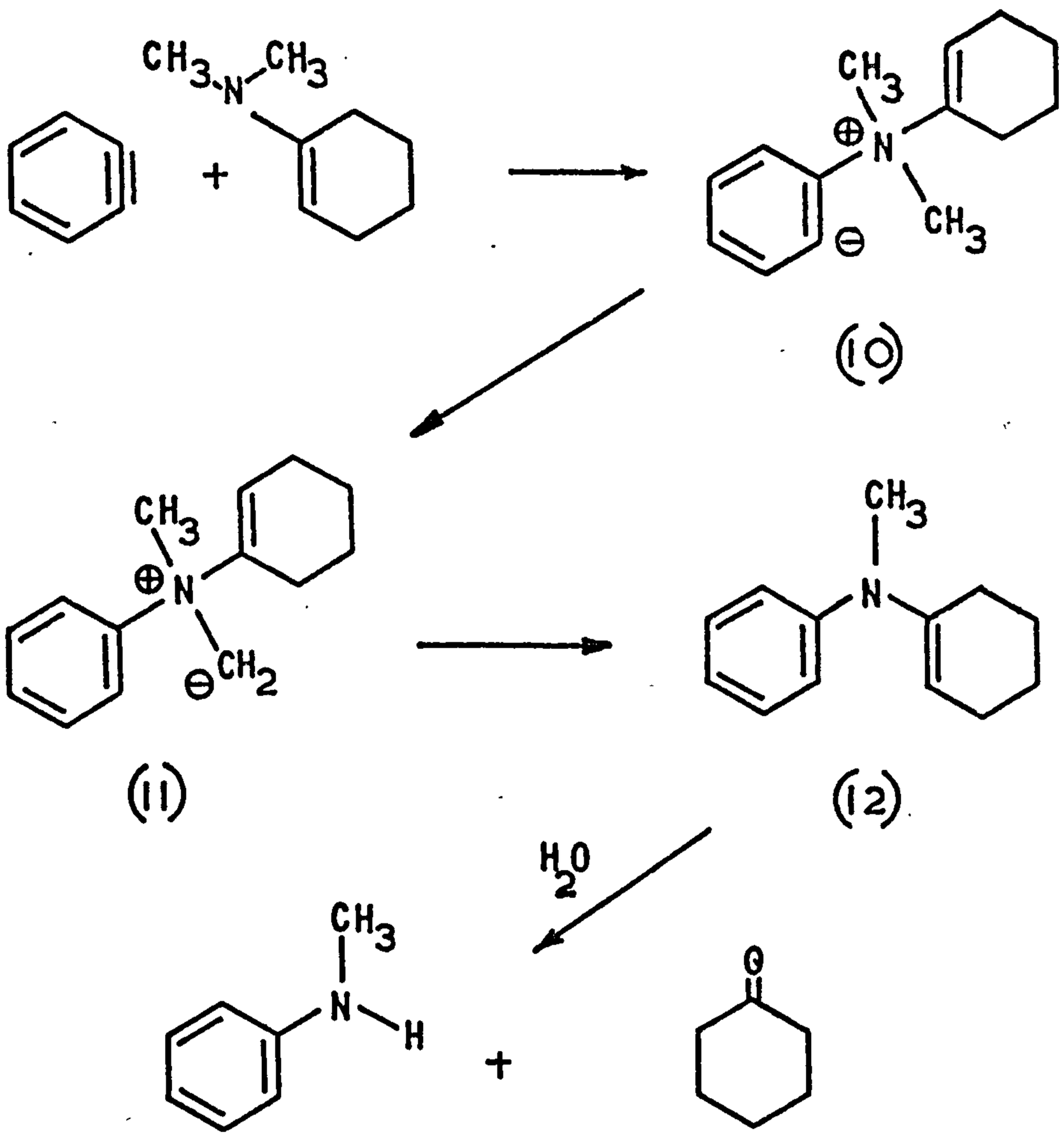
(8)

The structure of compound (7) X = F was readily assigned from its ^{1}H n.m.r. spectrum (table 1), which compared well with similar compounds.[58b] Likewise the structure of the compound (8) X = F was evident from the spectral data.

The ^{1}H n.m.r. spectrum (table 2) showed a resonance at τ 3.0 - 3.5 as a multiplet characteristically spin-spin coupled to fluorine, which was assigned to the proton on the tetrafluoroaryl ring. The i.r. spectrum showed a carbonyl absorption at υ_{max} 1710 cm.$^{-1}$ which was expected for a 2-arylcyclohexanone.

The reaction of tetrachlorobenzyne with 1-N,N-dimethylaminocyclohexene gave the adduct, (7) X = Cl in 37% yield.

When however benzyne was reacted with 1-N,N-dimethylamino cyclohexene three products were obtained; 2-phenylcyclohexanone (8) X = H formed in 7% yield; compound (7) X = H in 18% yield, and N-methylaniline (9) which was isolated in 3% yield. The N-methylaniline most probably arises by a sequence of reactions, the first of which involves attack of benzyne on the nitrogen atom to form a betaine (10). This betaine could rearrange by intramolecular proton transfer to give an ylide (11) which by loss of carbene would give the enamine derivative (12).The enamine would undoubtedly be hydrolysed during work up to give N-methyl aniline.



This type of reaction involving benzynes and tertiary amines was discussed in chapter 1 of this thesis. It is, however, unusual for the nitrogen of enamines to act as the nucleophilic centre. Both the 2-phenylcyclohexanone, (8) X = H and the N-methylaniline were compared with authentic samples.

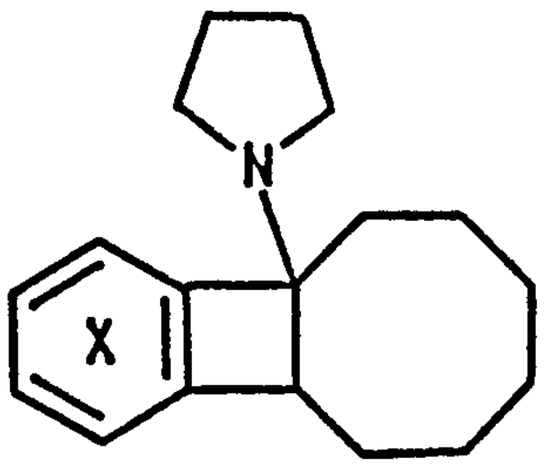
Table 1

Compound	Aromatic protons	Bridgehead methine	-N(Me)(Me)	-N(CH2)(CH2)	Methylene protons
(7)X=F		6.25-6.5 (m)	7.69(s)		7.7-8.2(m) and 8.2-8.9(m)
(7)X=Cl		6.37(t) J=4.5Hz.	7.68(s)		7.7-9.0(m)
(7)X=H	2.9(m)	6.45(t) J=4 Hz.	7.72(s)		8.0-8.4(m) 8.4-9.0(m)
(13)X=F		6.4-6.7(m)		7.0-7.7(m)	7.9-8.7(m)
(13)X=H	3.03(m)	6.52(t) J=6.5Hz.		7.1-7.6(m)	8.0-9.0(m)

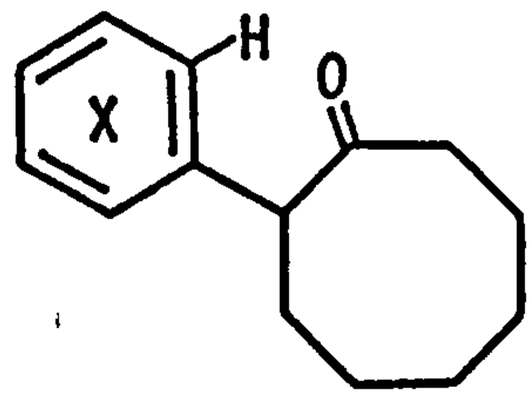
Table 2

Compound	Aromatic protons	Methine proton	Methylene protons
(8) X=F	3.0-3.5 (m)	6.0-6.5(m)	7.4-8.5(m)
(8) X=Cl	2.79 (s)	5.73-6.1 (m)	7.3-8.4 (m)
(8) X=H	2.7-3.2 (m)	6.4-6.8 (m)	7.5-8.8 (m)
(14) X=F	2.58-3.08 (m)	5.64 (t) J= 7.5 Hz.	7.3-7.65 (m) 7.65-9.0 (m)

Tetrafluorobenzyne and benzyne were reacted with 1-pyrrolidino-cyclo-octene and gave the expected adducts, (13) X=F or H respectively.



(13)



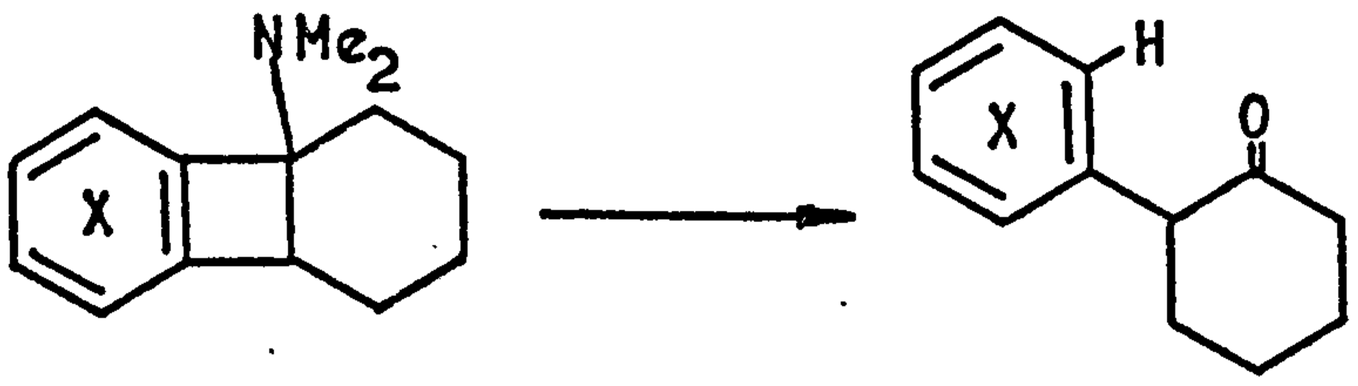
(14)

These two adducts were formed in good yield (13) X=F 50% and (13) X=H, 60%. Products corresponding to the 2-aryl ketone, compound (14), were not observed in the reaction products.

The structures (13) were assigned on the basis of their ^1H n.m.r. spectra (table 1.)

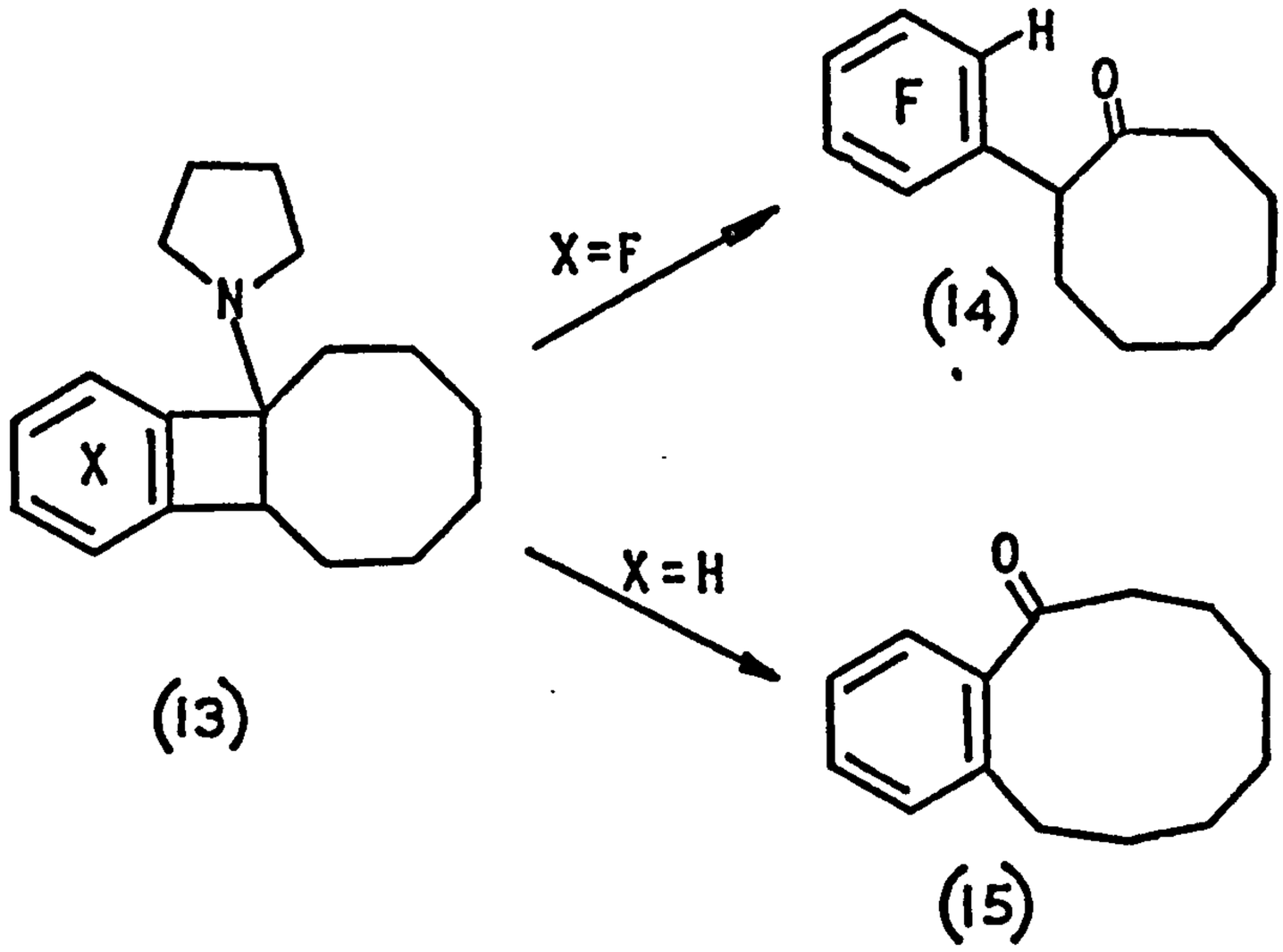
Although correct C, H and N analyses have been obtained for all the adducts, the tetrafluorinated compounds were particularly unstable and tended to hydrolyse rapidly in a moist atmosphere.

When the adducts (7) X=F or X=Cl were heated in aqueous ethanol containing acid, they were hydrolysed to the 2-arylcyclohexanones (8) X=F and (8) X=Cl in good yield.



(7) (8)

The adduct (7) X=H was, however, stable under similar conditions, a result which has also been observed in a related system.[58a] When the compound (13) X=F was hydrolysed in acidic aqueous ethanol a 76% yield of the 2-aryl cyclo-octanone, compound (14) X=F, was obtained.

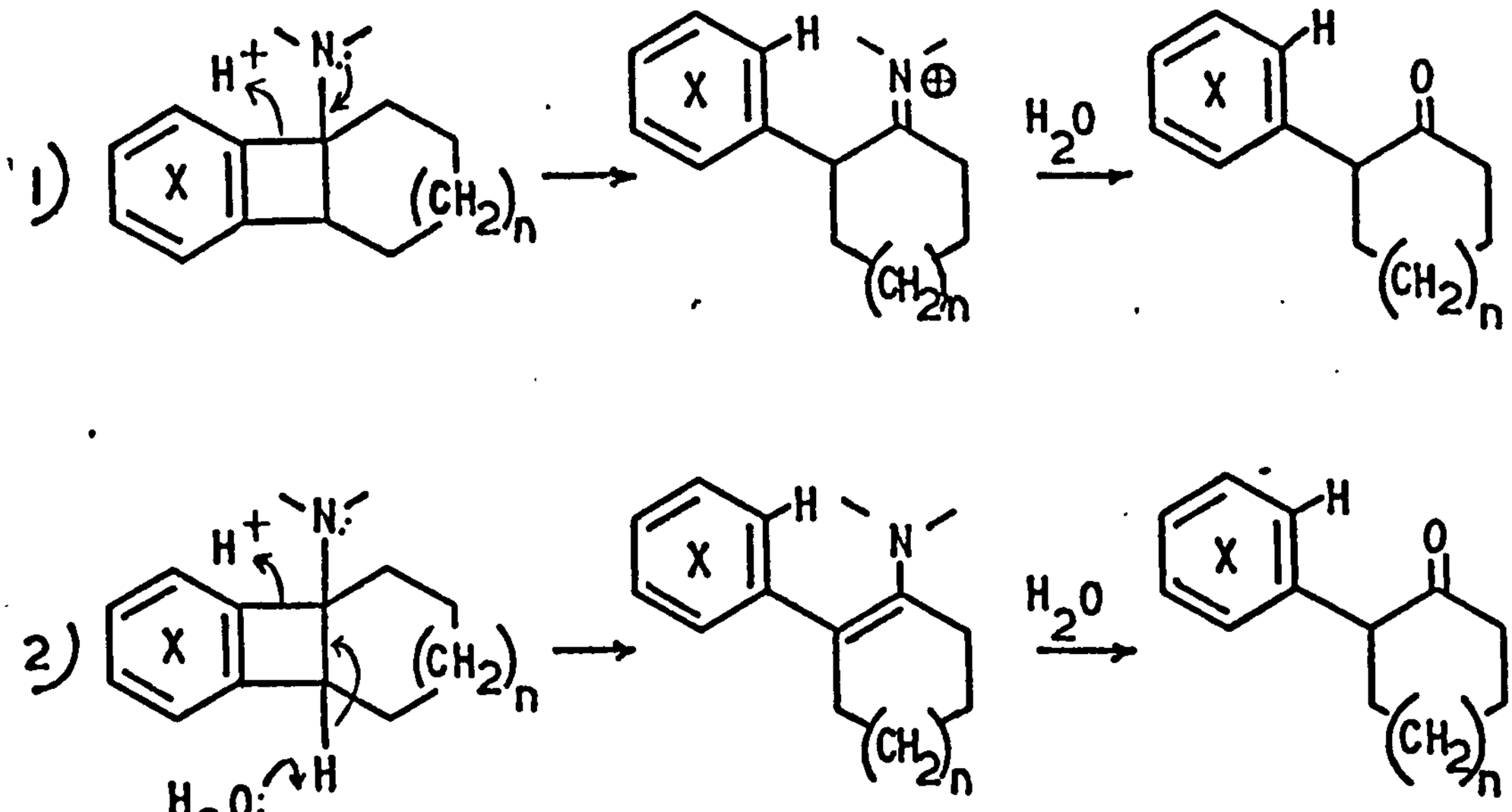


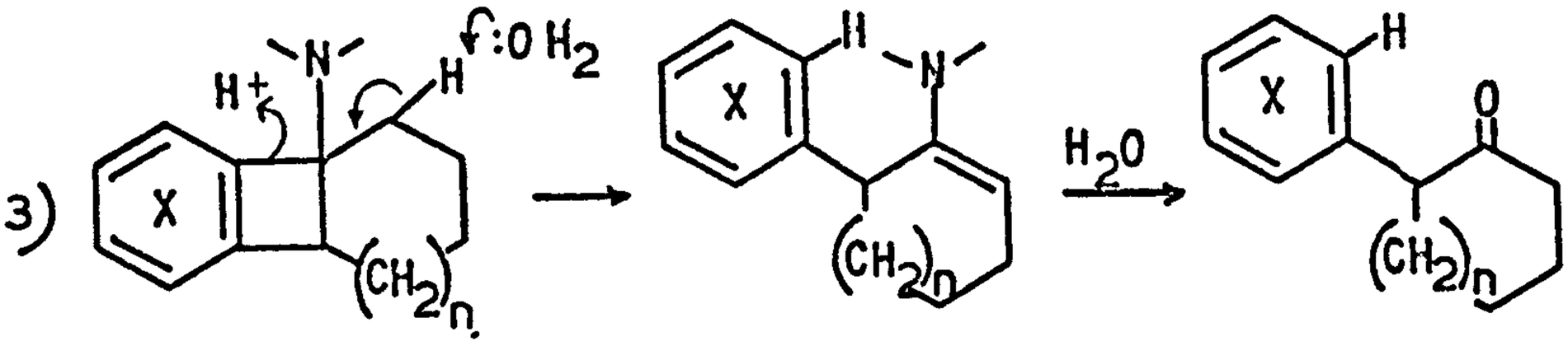
(13) (14) (15)

However, the corresponding compound (14) X=H underwent hydrolysis more slowly and gave a totally different ketone (15) in 99% yield.

The structure of the compound (14) followed from its ^{1}H n.m.r. spectrum (table 2) and its other spectral properties. ^{1}H N.m.r. spectroscopy of compound (15) showed resonances at τ 2.81 (broad singlet) due to the aromatic protons; at 7.0-7.4 (multiplet 4H) which was assigned to the methylene protons adjacent to the carbonyl group and aryl ring; and at τ 8.8-9.4 (multiplet 10H) due to the remaining saturated methylene groups. I.r. spectroscopy indicates a carbonyl adjacent to an aryl ring υ_{max} 1683 cm.$^{-1}$. The u.v. spectrum showed absorption maxima at λ 211 (ϵ 18,000); 239 (6,710); and 277 (1,050) nm., again consistent with a carbonyl group adjacent to an aryl ring.

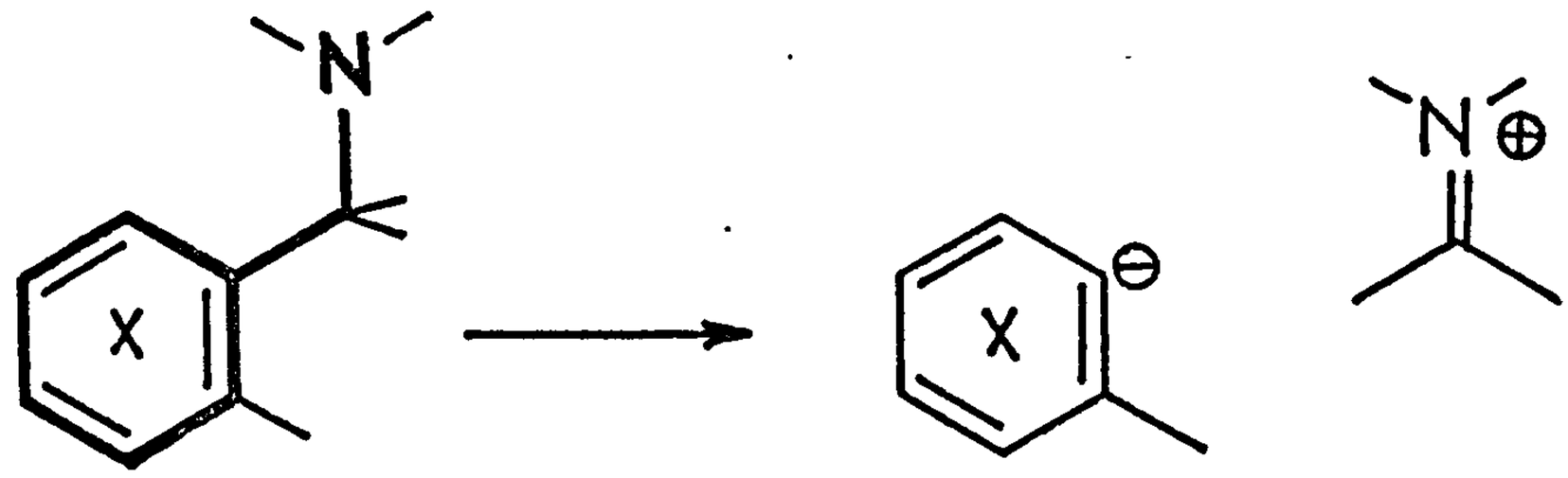
These few hydrolysis reactions clearly demonstrate a pronounced difference between amino-benzocyclobutenes and their corresponding tetrahalo-analogues. It appeared that the tetrahaloaryl function directs the cleavage of the cyclobutene ring in one particular direction; possible mechanisms are shown below.



3) 

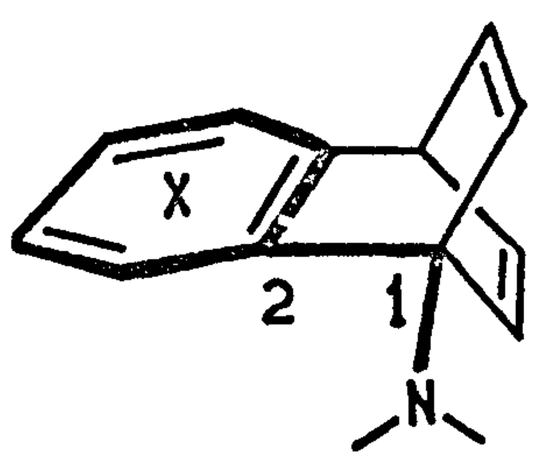
Mechanistic studies in deuterated solvents led to multiply deuterated ketones, due to proton exchange via the enol form of the ketone; the results were therefore not meaningful. The mechanism 1) was thought to be the most likely although the others cannot be excluded.

It was of interest to know if this type of cleavage reaction was general for compounds which contain the carbon fragment A.

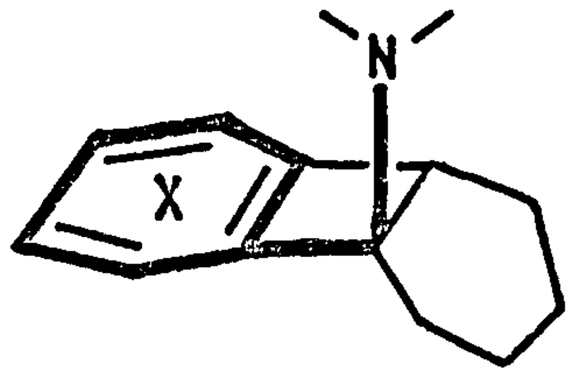


fragment A.

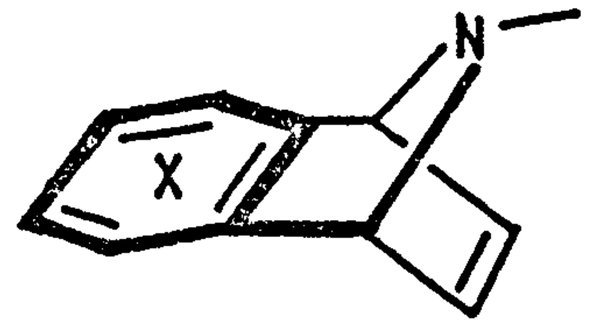
Compounds which contain this fragment are readily available. The reaction of tetrahalobenzynes with anilines (chapter 1 of this thesis) produces one such compound (16) and the reaction of tetrahalobenzynes with N-methyl-pyrrole another,[15] compound (17).



(16)



(7)

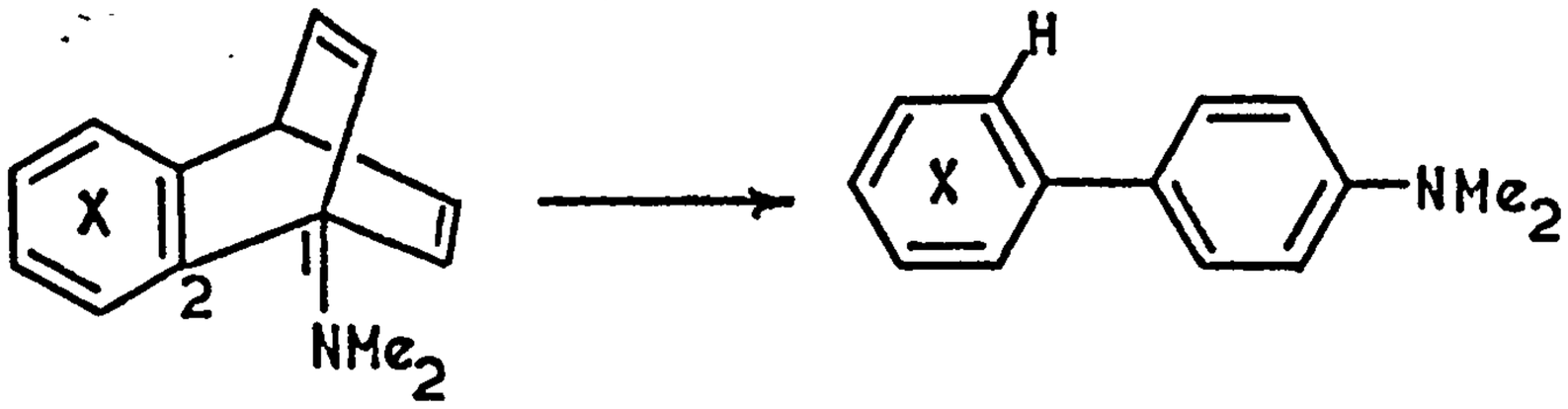


(17)

There are, however, differences in the geometry of the $N\text{-}C_1\text{-}C_2$ fragments and also in the strain energies associated with each of these compounds.

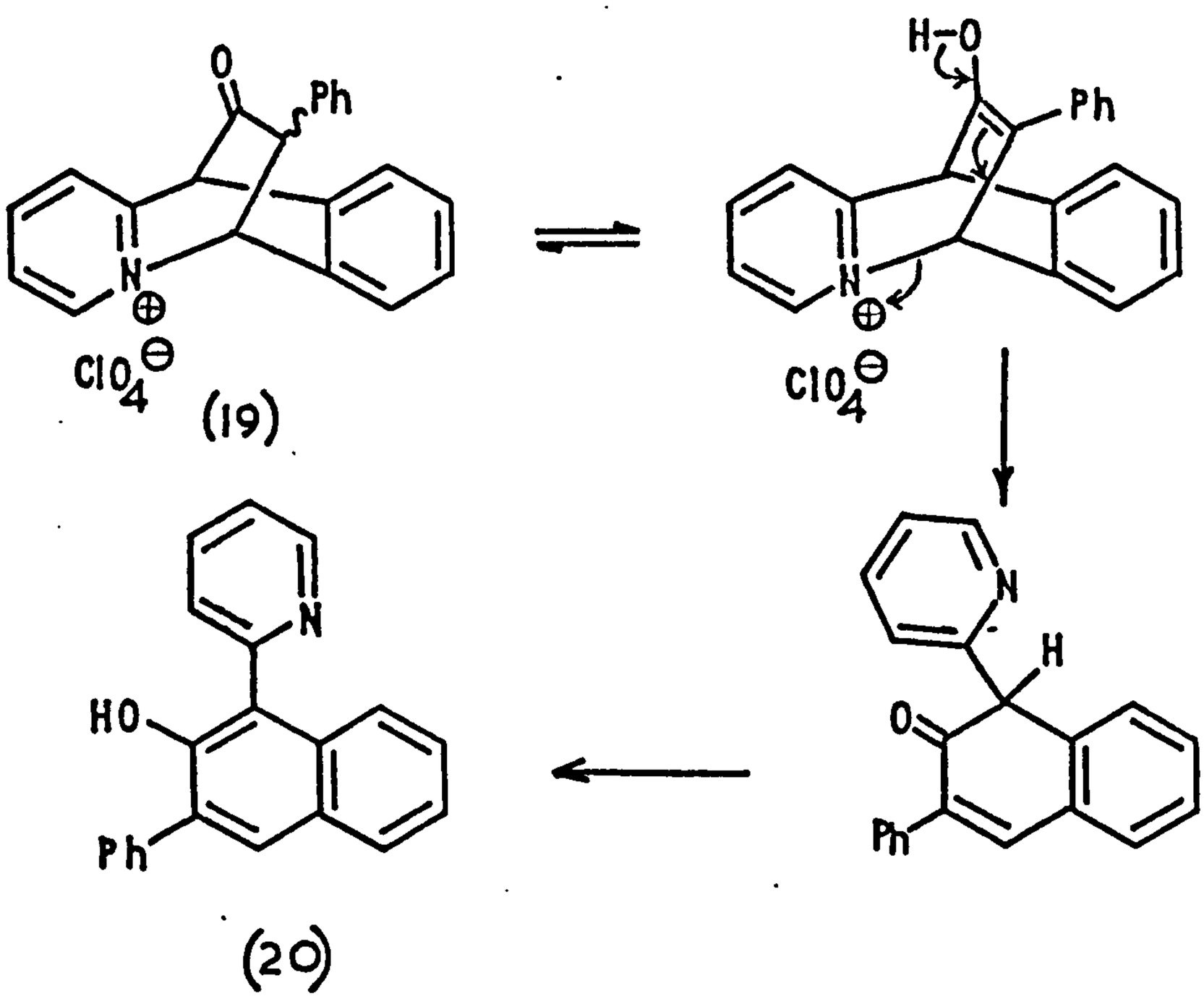
1-N,N-dimethylaminobenzobarrelenes

When the compounds (16; X=F or Cl) were heated in aqueous ethanol biaryl derivatives (18; X=F or Cl) were obtained in essentially quantitative yield.



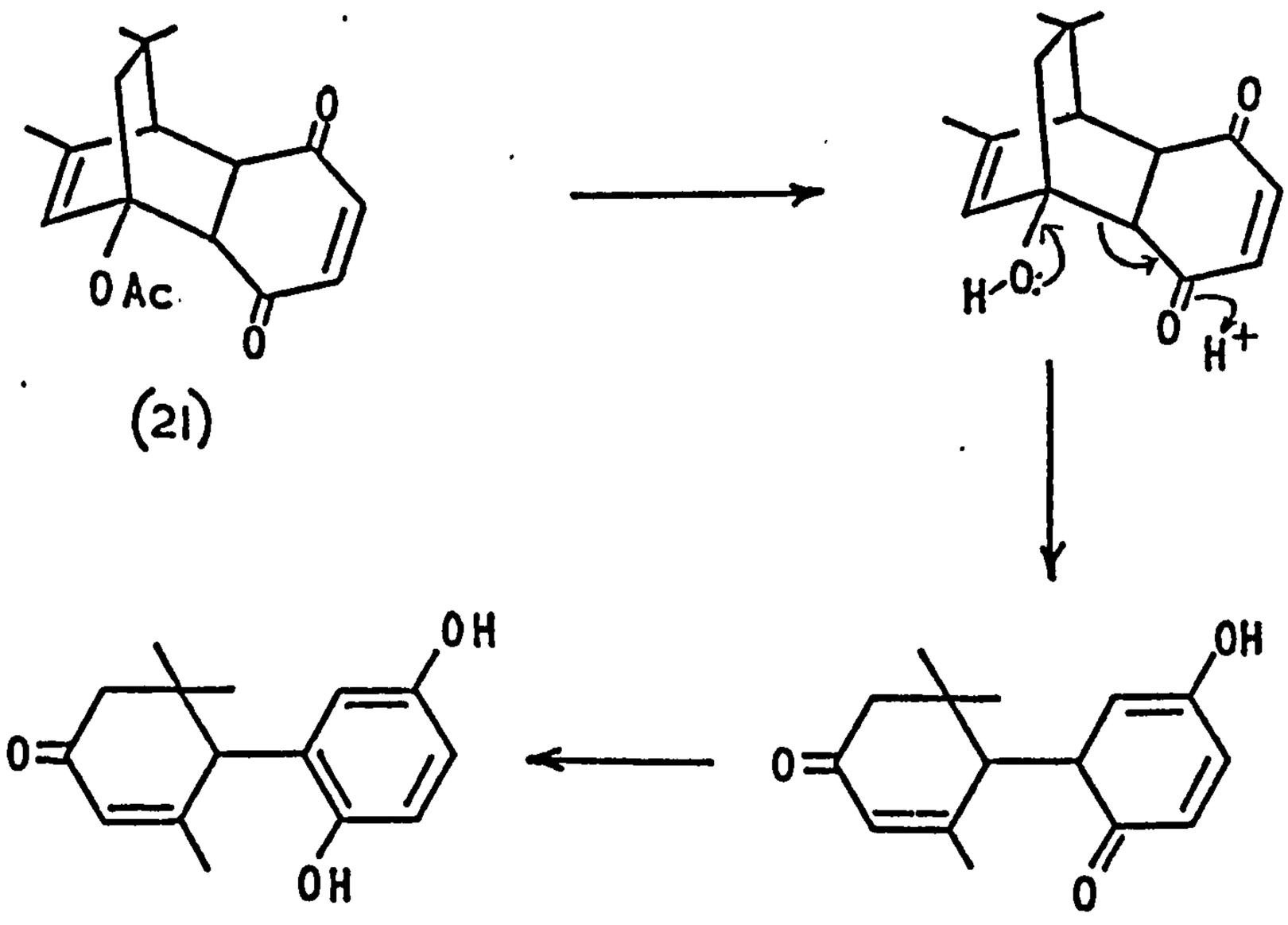
(16) (18)

The formation of biaryl derivatives from the benzobarrelene system involving C_1-C_2 carbon atom cleavage has few precedents. One example[72] involves the conversion of the azonia-ethanoanthracene perchlorate (19) to a naphthol (20).



(19) (20)

Another related cleavage reaction[73] involves a Grob fragmentation[74] of the quinone adduct (21) to give compound (22).



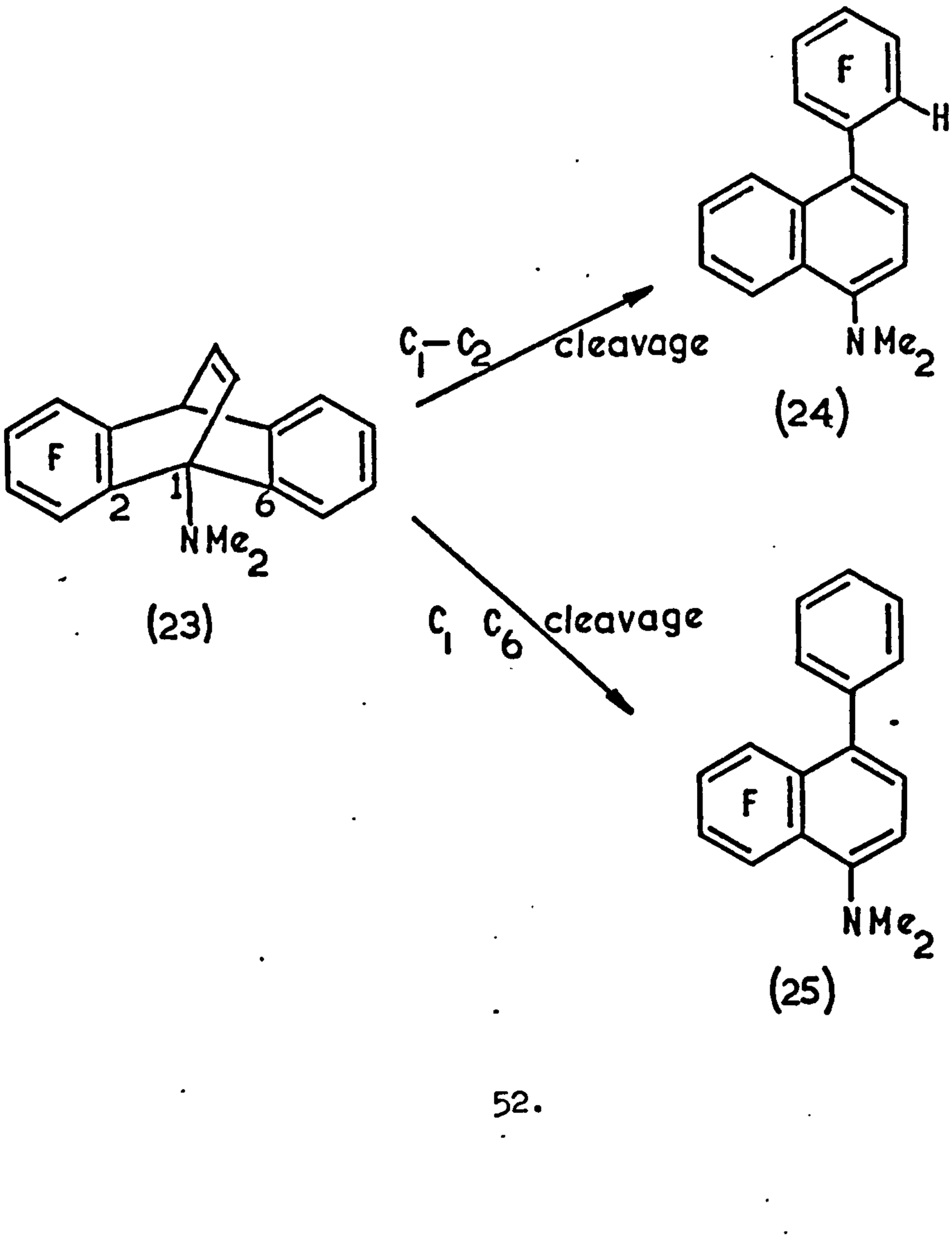
(21)

(22)

The structures of the biaryl compounds (18;X=F, or X=Cl) followed from their spectroscopic data. For example the ^1H n.m.r. spectrum of (18) X=F shows a quartet centred at τ 2.75 (2H), which is the (AA') part of AA'BB' spectrum with J_{AB} = 9 Hz., with further spin-spin coupling to fluorine of 1 Hz., a multiplet at τ 2.8-3.3 (1H), aromatic proton coupled to fluorine; a doublet at τ 3.39 (2H) (BB') (J_{BA} = 9 Hz.), and a singlet at τ 7.02 (6H) due to the N,N-dimethyl protons. The u.v. spectrum shows absorption maxima at λ 220 (ϵ 13,500) and 310 (24,050) nm., typical of a 4-amino-biphenyl derivative.

In an attempt to investigate the mechanism of the reaction the compound (16) X=F, was rearranged in dimethoxyethane containing deuterium oxide, and gave 4'-N,N-dimethylamino-2[^{2}H]-3,4,5,6-tetrafluorobiphenyl. Mass spectrometry showed the incorporation of deuterium to be better than 99% d_1. The position of deuteration followed from the ^{1}H n.m.r. spectrum which showed the disappearance of the multiplet at 2.8 - 3.3. In a control reaction deuterium was not incorporated into the compound (18) X=F under identical reaction conditions. This implies that the mechanism must involve an intermolecular process.

In order to demonstrate the directing ability of the tetrafluoroaryl ring the compound (23) was prepared by the reaction of tetrafluorobenzyne with 1-N,N-dimethylamino-naphthalene.

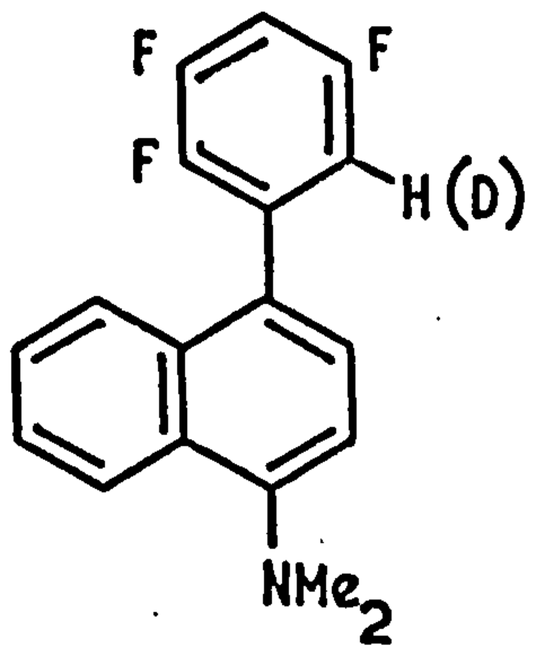


The compound (23) could, in theory, give two products. Cleavage of the C_1-C_2 bond would give compound (24) or C_1-C_6 bond cleavage would give compound (25).

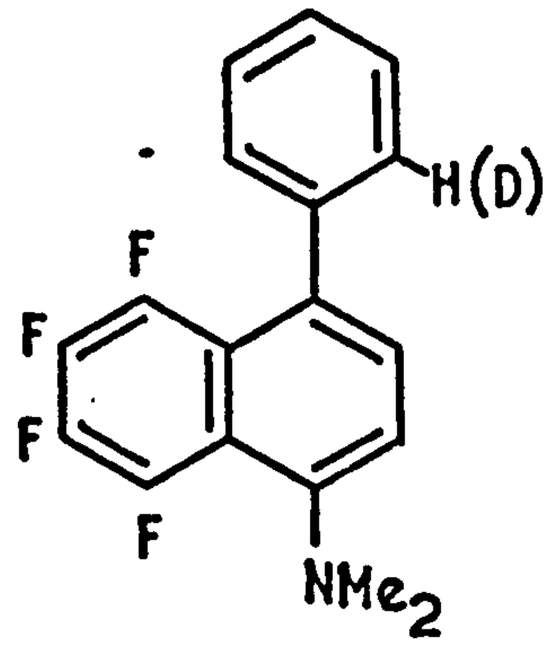
When the compound (23) was heated in aqueous diglyme at 140° in a sealed tube, only one product was formed. ^{1}H N.m.r. spectroscopy of this product showed resonances at τ 1.7-1.95 (1H) typical of a naphthalene peri proton, a multiplet at τ 2.5-3.3 (6H) due to aromatic protons, and a singlet at τ 7.13 (6H) which was assigned to the N,N-dimethyl group. On the basis of this data alone it was impossible to say whether the compound formed in the rearrangement was (24) or (25). Compound (24) seemed the most reasonable, as there appeared to be one naphthalene peri proton and also the N,N-dimethyl group was a singlet; a doublet would be expected for compound (25) due to spin-spin coupling with fluorine.

The mass spectrum was uninformative as fragment ions corresponding to either the loss of a phenyl group, m/e 77, for compound (25), or the loss of a tetrafluoroaryl group, m/e 149, for compound (24), were both less than 4% of the molecular ion peak.

The most convincing evidence in favour of the structure (24) was obtained from a comparison of ^{19}F n.m.r. spectra of the undeuterated and the monodeuterated species.



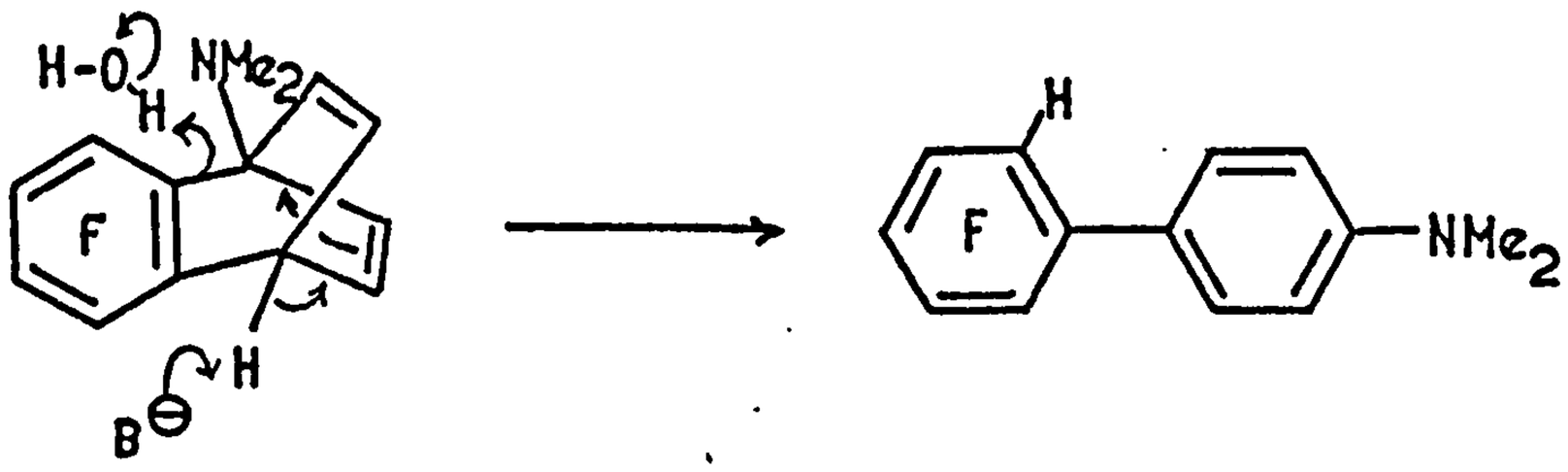
(24)



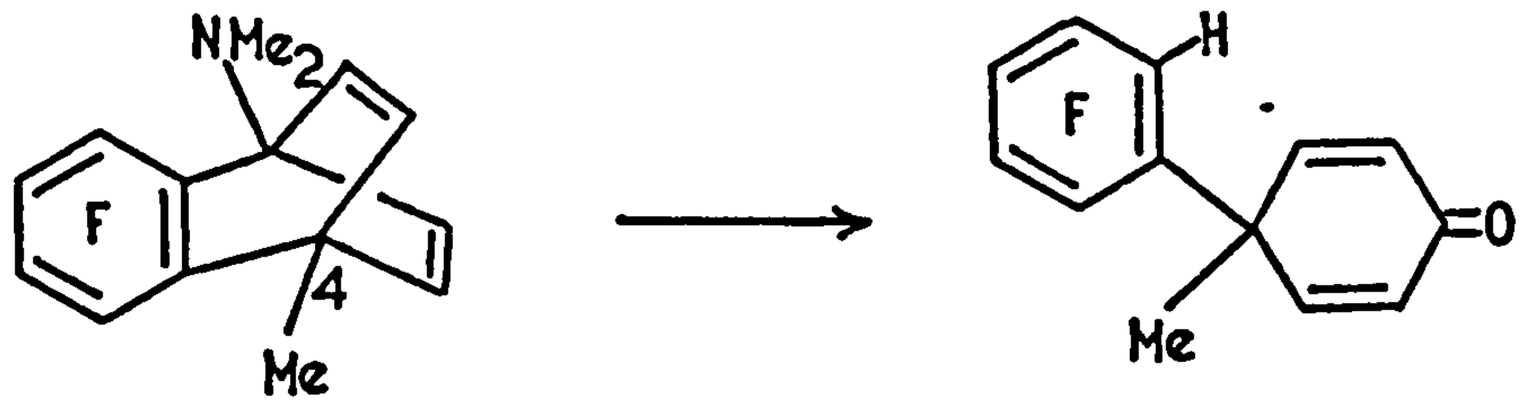
(25)

The ^{19}F n.m.r. spectra of the compounds showed ^{19}F-H coupling in the undeuterated case; however the spectrum of the monodeuterated compound was considerably simplified owing to smaller ^{19}F-D coupling. If the structure (25) was correct the ^{19}F n.m.r.spectra would show little change on deuteration. (The ^{19}F spectra of these and other compounds will be discussed in more detail at a later stage).

It was necessary to show whether aromatisation was the driving force in these rearrangements.

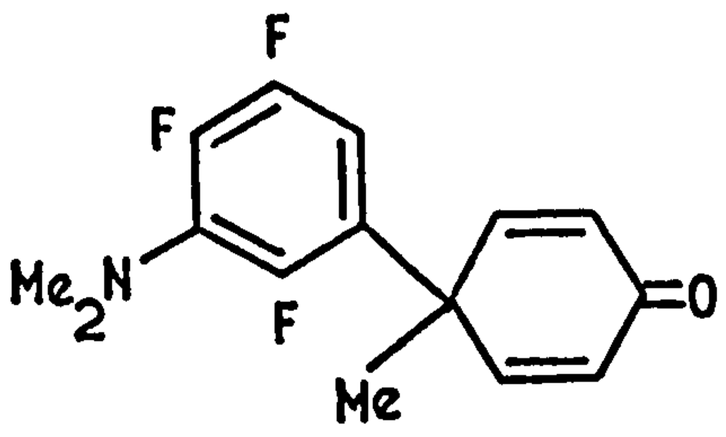


To this end the compound (26) was prepared (Chapter 1) and its rearrangement was studied. If aromatisation was the driving force the compound (26) should not rearrange, as removal of a proton from position 4 is effectively blocked by the alkyl group. However in aqueous diglyme at 140°, the compound rearranged to the dienone (27) which was isolated in 25% yield.

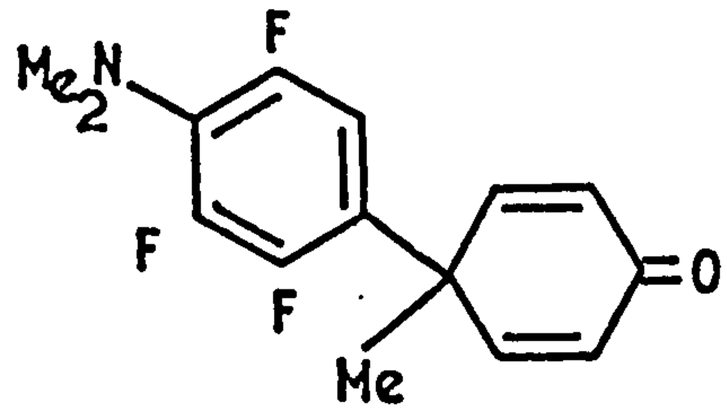


(26) (27)

The spectral properties of the dienone (27) compare well with the unhalogenated analogue prepared by Zimmerman.[75] ^{1}H N.m.r. shows a doublet centred at τ 3.12 (2H) ($J_{32} = J_{56}$ = 10 Hz.) which was due to the C_3,C_5 vinyl protons; at τ 2.85-3.3 there was a multiplet (1H) assigned to the hydrogen on the tetrafluoroaryl ring; at τ 3.8 there was a doublet (2H) ($J_{23} = J_{65}$ = 10 Hz.), which was due to the vinyl protons at C_2,C_6; and at τ 8.31 a doublet (J = 1 Hz.) (3H) which was assigned to the 4-methyl group. I.r. spectroscopy showed absorptions at υ_{max} 2980 and 2940 cm.$^{-1}$ due to C-H stretching modes; 1675 cm.$^{-1}$ due to the cyclohexadienone carbonyl group; 1635 cm.$^{-1}$, due to the olefin C-C stretching mode; and 1520 and 1480 cm.$^{-1}$, due to fluorinated aromatic ring. U.v. spectroscopy showed absorption maxima at λ 238 (ϵ 16,400) and 265 sh. (3090) nm. An inseparable mixture of cyclohexadienones, compounds (28) and (29), was also isolated in 39% yield, (ratio 1:1.5), from the rearrangement of the compound (26).



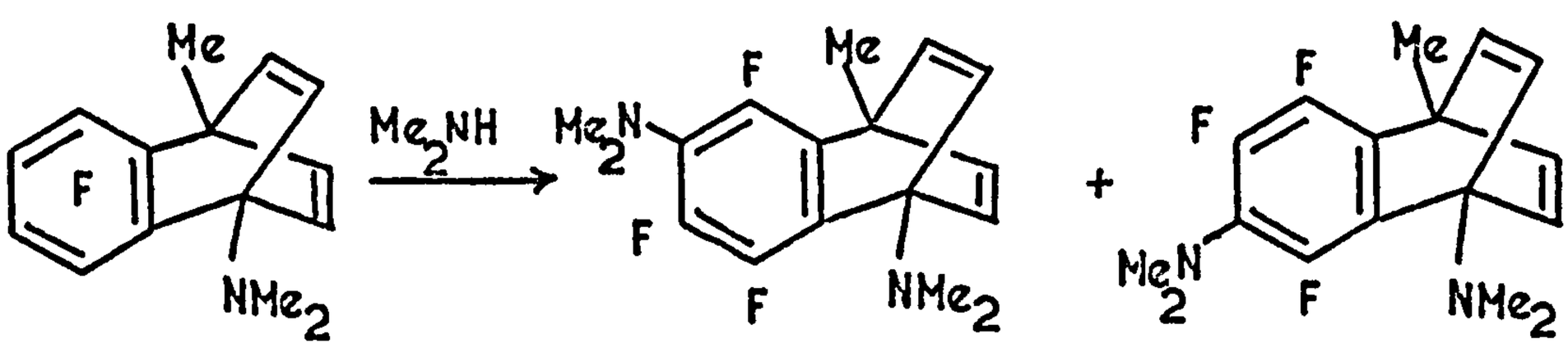
(28)



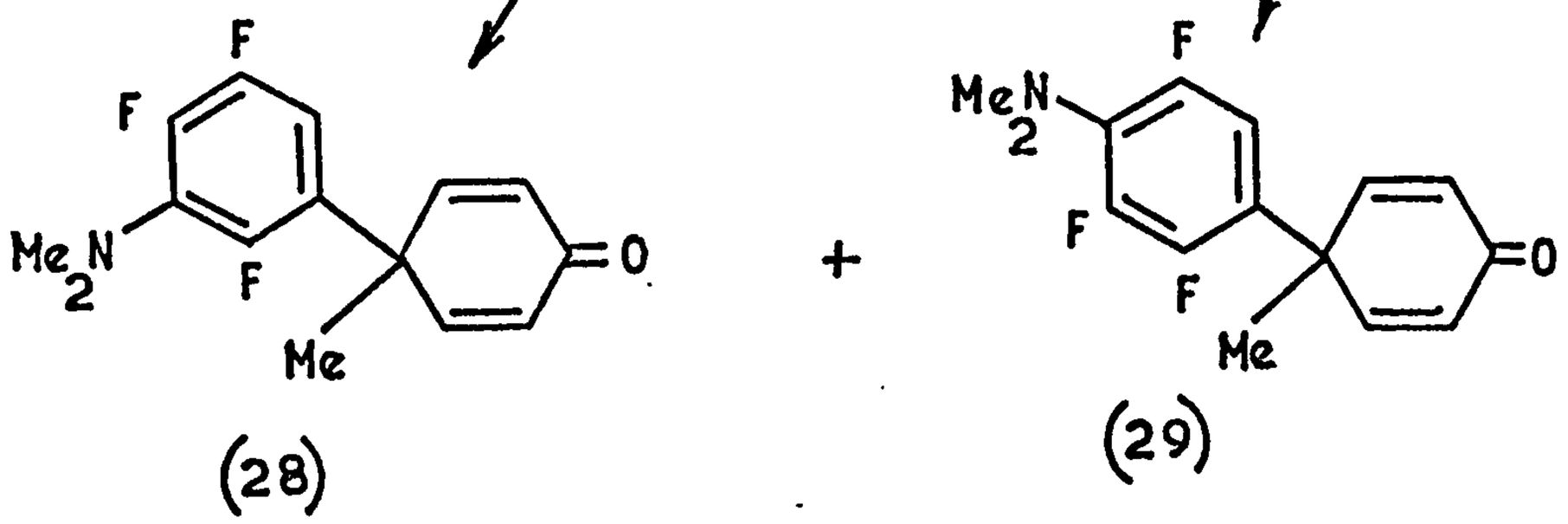
(29)

The structure assignment was based on the spectral properties of the mixture. ^{1}H N.m.r. showed the N,N-dimethyl resonance at τ 7.11, as a triplet (J = 1.5 Hz.) which was to be expected for long-range coupling to two adjacent fluorine atoms. ^{19}F N.m.r. spectroscopy showed multiplets at δ 128.7 (0.8F), δ133.4 (1.2 F), δ 150.2 (2F),

δ 153.8 (1.2 F), and δ 154.9 (0.8F). Mass spectrometry showed a molecular ion at M^+ 281. As the two dienones are formed in the ratio 1:1.5 it suggests that they are formed from substitution of fluorine in the initial adduct (26). Since dimethylamine is produced in the formation of (27) from compound (26), and the reaction is performed in a sealed tube, it is reasonable that the dimethylamine will displace a fluorine atom[49] to give a mixture of two compounds (30) and (31).



(30) (31)



(28) (29)

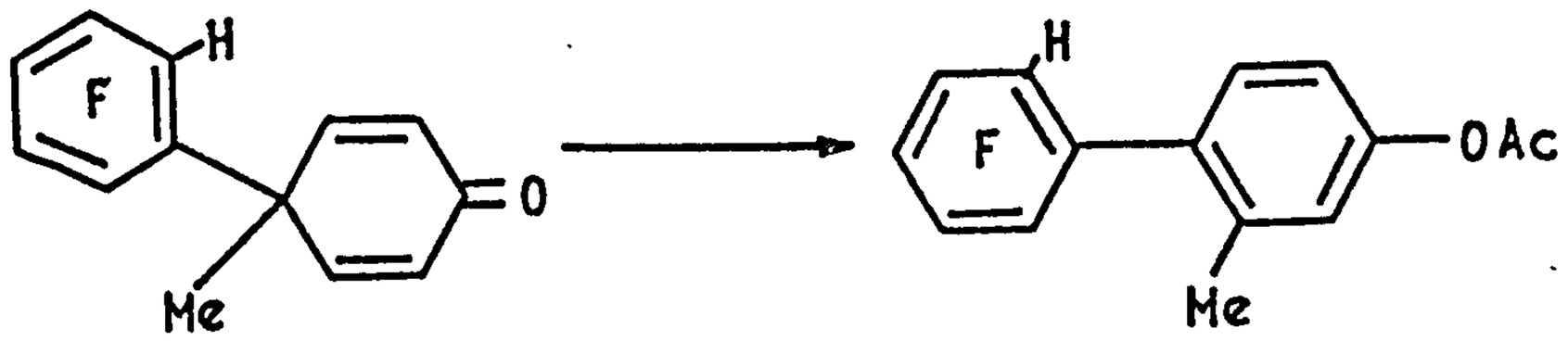
ratio 1:1

Dimethylamine produced in the reaction of (30) and (31) to (28) and (29) would be expected to substitute a fluorine atom in the cyclohexadienone (27) para to the cyclohexadienone group preferentially, thus

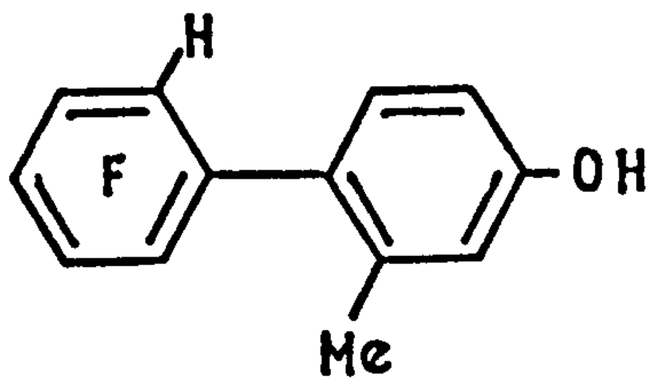
leading to an increase in the amount of compound (29) formed.

In order to confirm this series of reactions,control experiments should be performed to determine the position of substitution in both the dienone, compound (27), and the adduct, compound (26). These experiments have not been carried out so the above mechanism is only speculative.

The cyclohexadienone, compound (27) has been rearranged, in perchloric acid containing acetic anhydride, to the biphenyl acetate compound (32). Removal of the acetyl group with base gives the biphenol (33).



(27) (32)

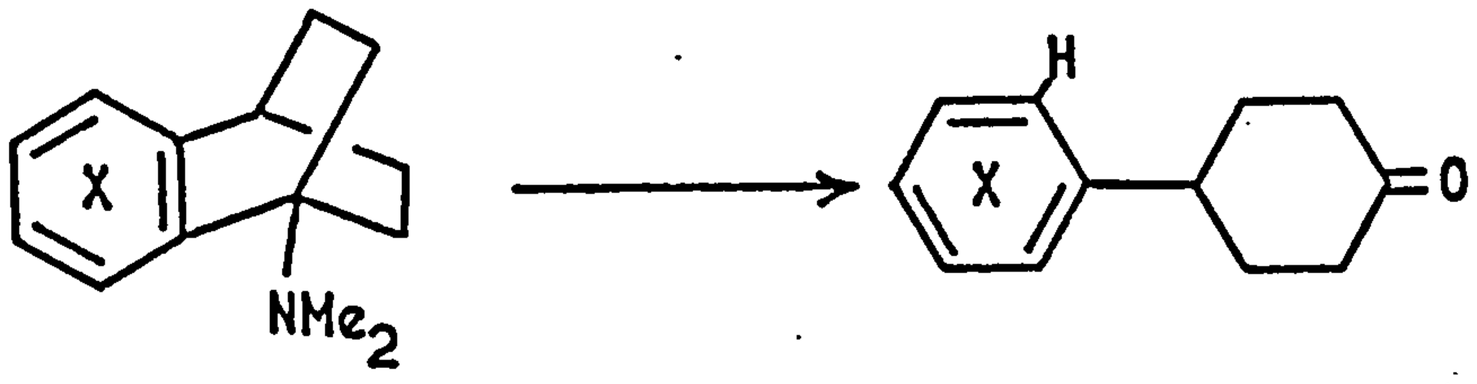


(33)

The structural assignments of the products (32) and (33) were based on their spectral data. ^{1}H N.m.r. spectroscopy of compound (33) shows

a resonance at τ 7.85 (3H, width $\frac{1}{2}$ height = 3 Hz. aromatic methyl group); τ 5.44 (broad singlet, 1H phenolic hydroxy group); τ 3.2-3.5 as a multiplet (3H) due to protons at C-3', C-5' and C-2; and τ 3.04 (doublet, J = 8 Hz., with some fine coupling, 1H) due to proton C-6'. An alternative structure is possible where the tetrafluoroaryl group has migrated in preference to the methyl group in the dienone rearrangement, however this was thought to be unlikely owing to the highly electrophilic character of the tetrafluoroaryl group.

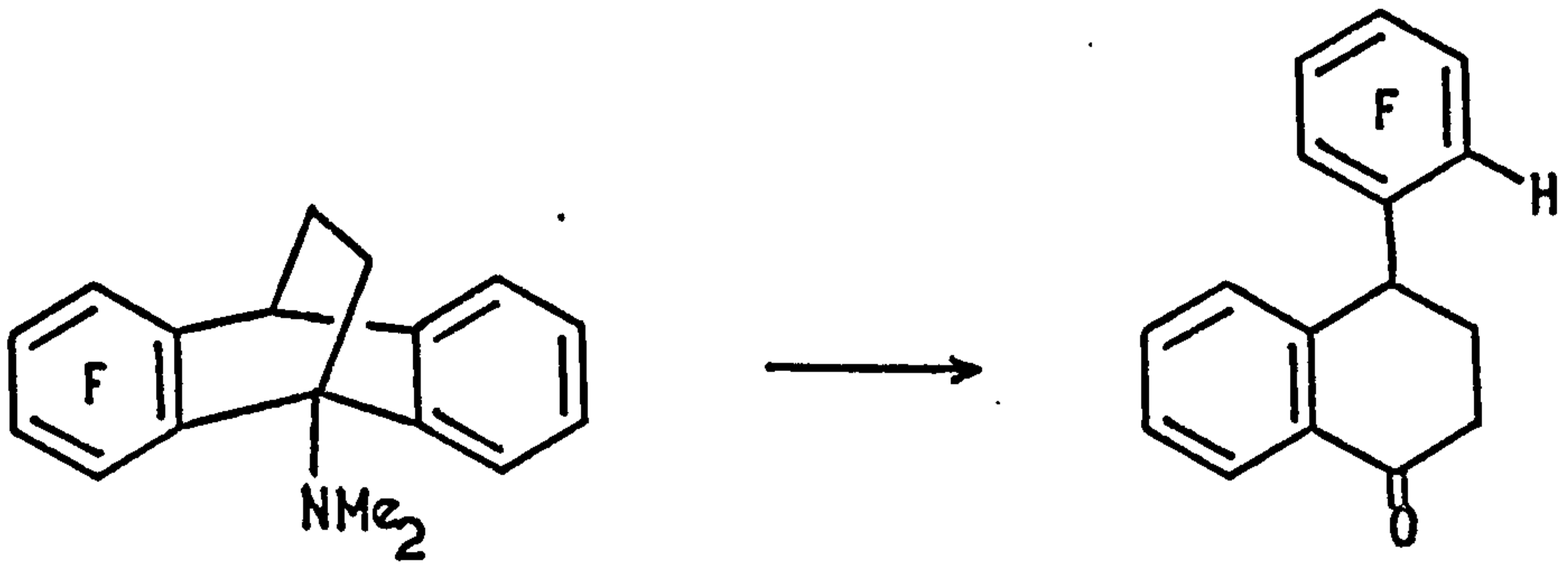
If the rearrangements of the amino-tetrahalobenzobarrelenes to the biaryl derivatives, or cyclohexadienone derivatives were governed solely by the electron withdrawing capacity of the tetrahaloaryl ring, and the electron availability on the nitrogen atom, one would anticipate that the tetrahydro derivative, compound (34), would rearrange, giving after hydrolysis the 4-aryl cyclohexanone, compound (35),



(34) (35)

Attempts to bring about this conversion have failed. .

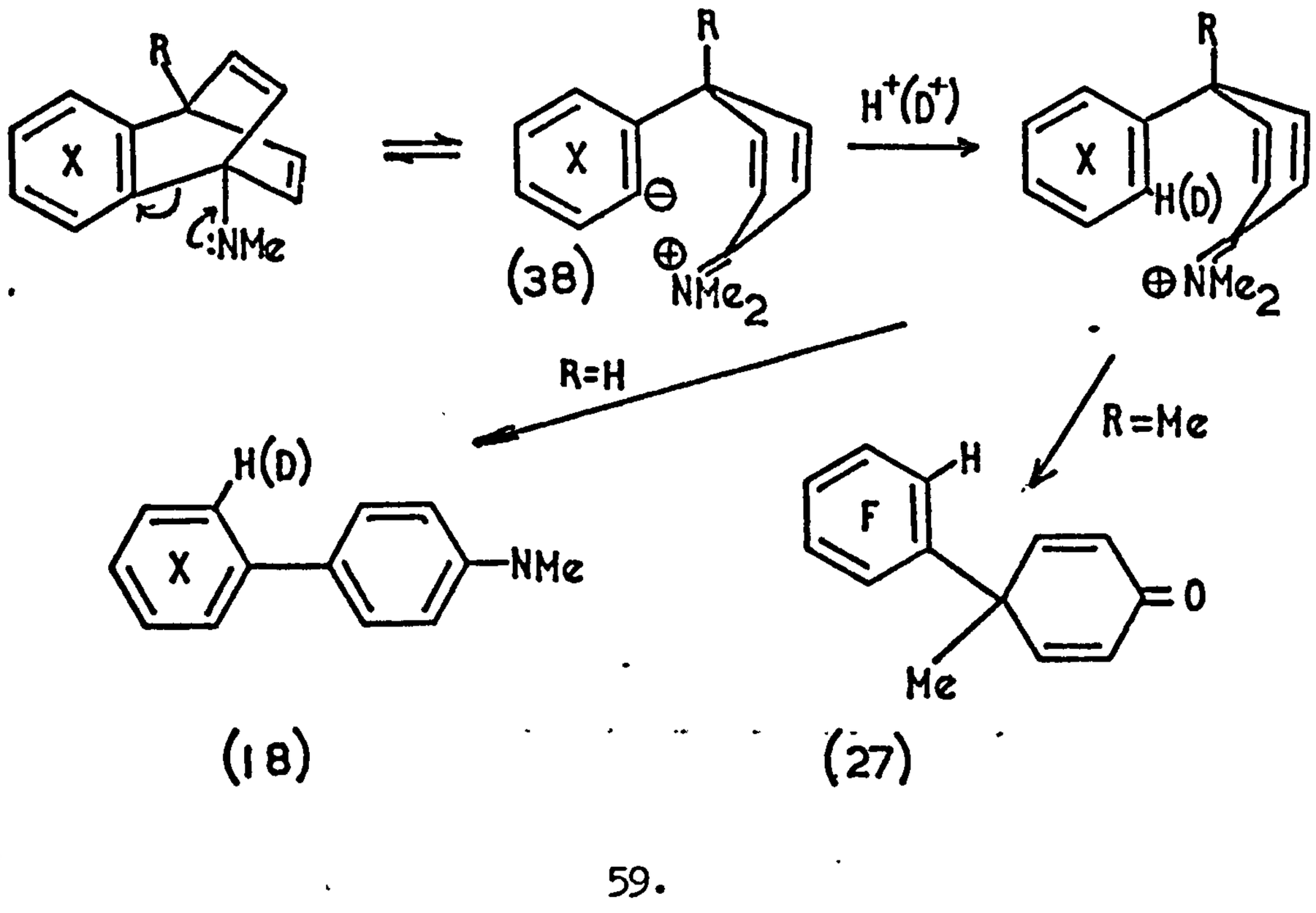
However the reduced dibenzobarrelene compound (36) was rearranged in aqueous glycerol at 190° for 127 hours and gave the α-tetralone (37).



(36) (37)

The i.r. spectrum of compound (37) showed an absorption at ν 1690 cm.$^{-1}$ which was to be expected for an α-tetralone.[76] The chemical shifts of the protons in (37) compare well with those of α-tetralone itself.[77] The ^{1}H n.m.r. spectrum showed resonances at τ 1.85 - 2.15 a multiplet (1H), which was assigned to the aromatic proton nearest the carbonyl group; a multiplet at τ 2.4 - 2.8, two aromatic protons; at τ 2.9 - 3.2 a multiplet (1H), assigned to the aromatic proton nearest the tetrafluoroaryl group; a multiplet at τ 3.3 - 3.8 (1H) due to the proton on the tetrafluoroaryl ring; a triplet (J = 6 Hz. 1H) which was assigned to the methine proton, and at τ 7.2 - 7.9 was a multiplet (4H) due to the remaining methylene protons.

A mechanism which accounts for the rearrangements of the 1-N,N-dimethylaminotetrahalobenzobarrelene derivatives in protic media is shown below.



(18) (27)

These results have been presented in a preliminary communication.[78]

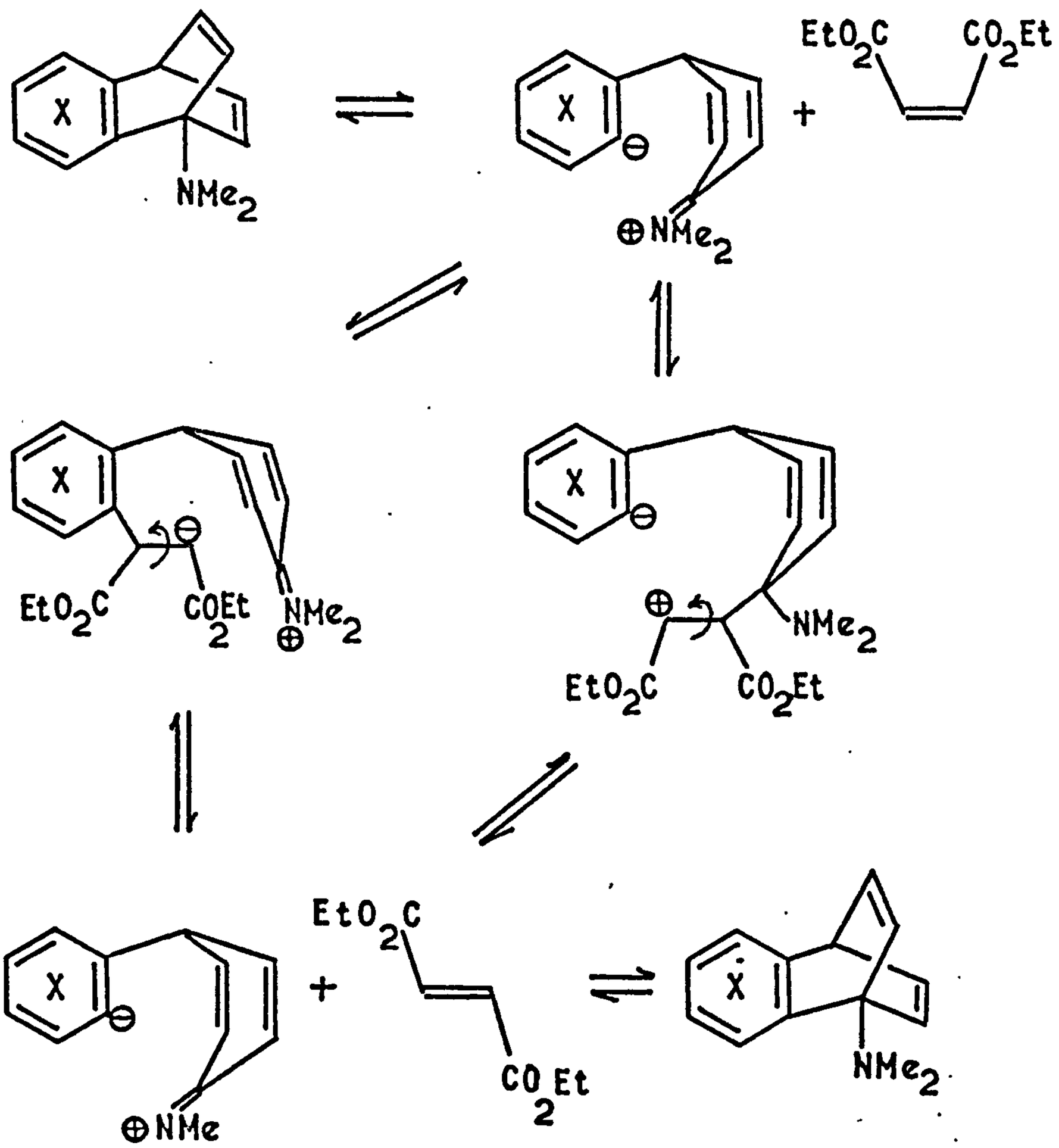
The mechanism in protic media leads to the reversible formation of a zwitterionic species (38). This zwitterion (38) is stabilised to some to some extent by cross conjugation with the two double bonds of the barrelene system. Protonation of the zwitterion would be an irreversible process and the remaining course of the reaction will be determined by the R-group. If R=H,aromatisation occurs fairly rapidly to form the biaryl derivatives. If R=Me,the aromatisation pathway is blocked and reaction occurs by hydrolysis of the immonium species to give the ketone. The mechanism could be presented as a diradical process. However, as there appears to be a strong solvent dependence in this reaction, for example no reaction occurs in wet benzene even after heating under reflux for 100 hr., it is reasonable to assume the reaction is more likely to be ionic in character.

Also if a diradical process was involved, one might anticipate that the deuteration level, when the reaction is carried out in a mixture of dimethoxyethane and deuterium oxide, would be less than the observed value of 99% d_1 due to some hydrogen atom abstraction from the glyme.

When the compound (16) X=F was heated in dimethoxyethane in the presence of trichlorobromomethane, which is a known radical trap,[79] no reaction occurs.

In an attempt to trap the zwitterionic species (38),the amino-benzobarrelene, compound (16) X = F, was heated in a mixture of dimethoxyethane and diethyl maleate. No adduct was obtained. However, we were surprised to observe that the diethyl maleate was isomerised to diethyl fumarate. Tertiary amines do not cause isomerisation

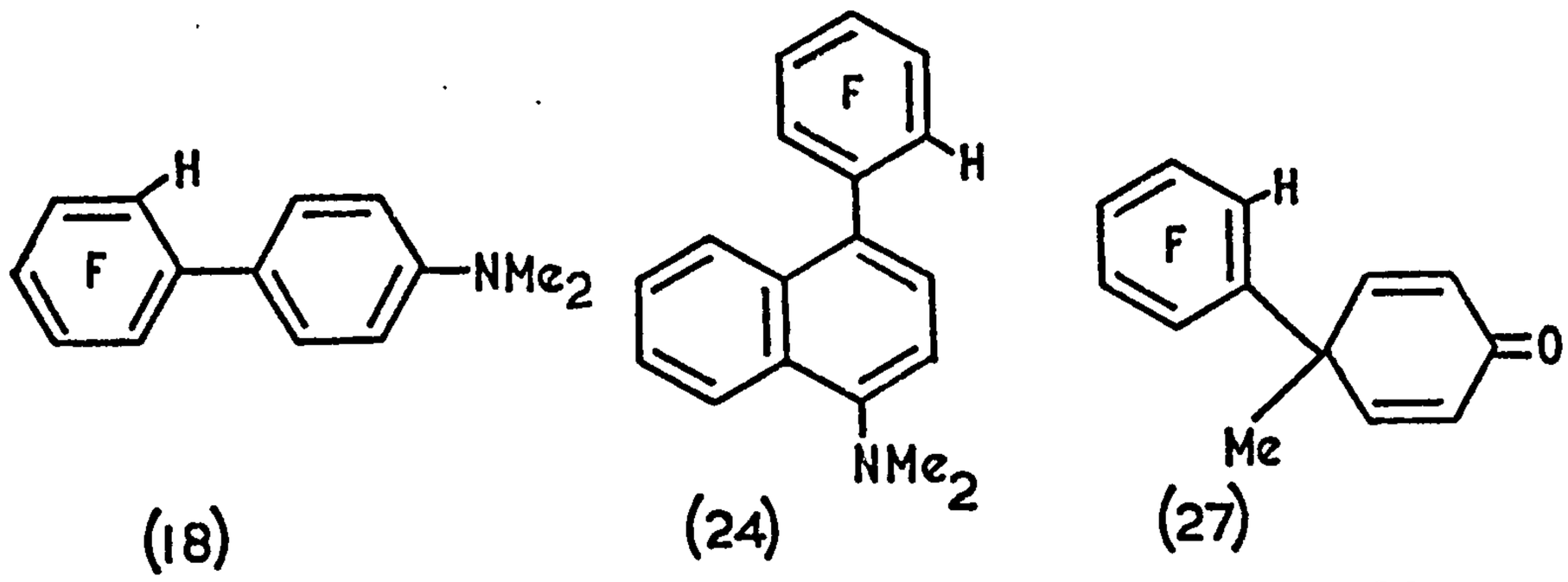
of maleate to fumarate,[80] although secondary amine will. This was checked in our system by heating the fully reduced aminobenzobarrelene, compound (34 X=F), in a mixture of dimethoxyethane and diethyl maleate. No isomerisation had occurred. The result can possibly be rationalised in terms of addition of the diethyl maleate to the zwitterion, followed by a bond rotation, then elimination of the more stable fumarate regenerating the zwitterion.



The isomerisation of maleate to fumarate in this system is some evidence in support of a reversible formation of the zwitterion species from the aminobenzobarrelene.

^{19}F Spectra

In the majority of compounds reported in this thesis ^{19}F n.m.r. spectra would be uninteresting. In some compounds that contain an aromatic proton in the same ring as the four fluorine atoms, the ^{1}H n.m.r. spectrum shows a characteristic coupling pattern which can be used as a structural aid. However, in some examples, the aromatic proton is obscured in the ^{1}H n.m.r. spectrum by other protons resonating at similar chemical shifts. ^{19}F N.m.r. spectra can then be used to determine the presence of a proton in a tetrafluoroaryl ring. Examples where the aromatic proton was obscured by other protons of similar chemical shift include the compounds (18),(24),and (27).



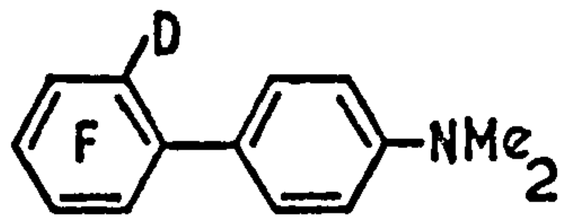
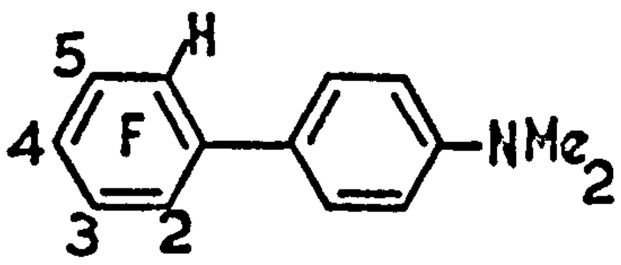
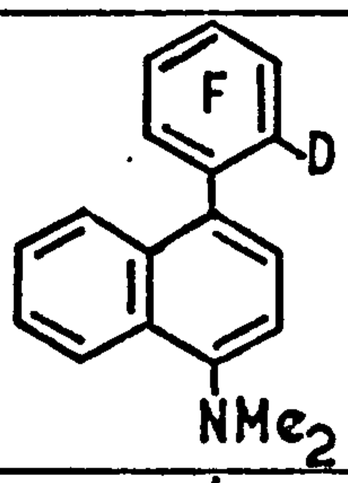
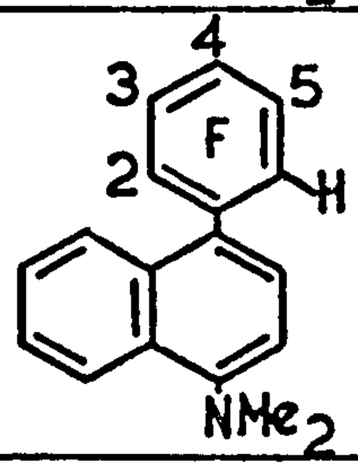
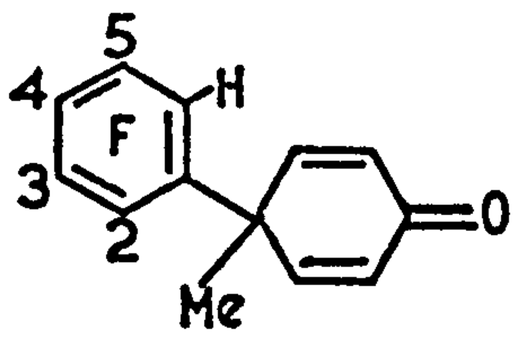
(18) (24) (27)

The size of the spin-spin coupling constants in the ^{19}F n.m.r. spectra of polyfluoroaryl compounds are usually in the order $J_o^{FF} > J_p^{FF} > J_m^{FF}$ [81] and the proton coupling usually follows the pattern $J_o^{HF} > J_m^{HF} > J_p^{HF}$. This treatment should be approached with some caution.[82] Fortunately, compounds where the proton was replaced by a deuterium atom were available in two cases (18) and (24). Examination of the ^{19}F n.m.r. spectra of these compounds showed simplified spectra by removal of the ^{19}F-H spin-spin coupling and replacing it with the much smaller ^{19}F-D coupling. The ortho and para ^{19}F-^{19}F spin-spin coupling constants were measured

from the spectra of the deuterated compounds (fig. 1 and fig. 3) and the remaining ^{19}F-H coupling constants were obtained from the spectra of the non-deuterated compounds (fig. 2 and fig. 4 respectively.) The results are shown in the table 3.

The ^{19}F n.m.r. spectrum of the dienone, compound (27), has also been analysed and the results compare favourably with the compounds (18) and (24), (table 3).

Table 3

Compound	δ p.p.m.	o-coupled Hz.	m-coupled Hz.	p-coupled Hz.
		J_{23}=22.6 J_{34}= 22 J_{45}= 22.5		J_{25}=12
	F_2=155.1 F_3=167.2 F_4=171.5 F_5=150.8	J_{23}=22.6 J_{34}=22 J_{45}=22.5 J_{5H} =12	J_{4H}=7.8 J_{2H}=8 J_{35}=2 J_{24}=2	J_{25}=12 J_{3H}=2.2
		J_{23}=22.2 J_{34}=21.5 J_{45}=22.0		J_{25}=12
	F_2=149.3 F_3=166.1 F_4=168 F_5=150	J_{23}=22.2 J_{34}=21.5 J_{45}=220 J_{5H}=11.5	J_{4H}=8 J_{2H}=7 J_{35}=2	J_{25}=12 J_{3H}=2.0
	F_2=145.2 F_3=166.8 F_4=177.6 F_5=146.3	J_{23}=21.3 J_{34}=21.5 J_{45}=22 J_{5H}=11	J_{4H}=7.5 J_{2H}= - J_{35}=2 J_{24}=3.5	J_{25}=12 J_{3H}=2

By the comparison of the spectra of the mono deutero and undeuterated compounds, it was also possible to assign the chemical shifts of the fluorine atoms without recourse to published chemical shift data.

For example the monodeuterated compound (18) shows (fig. 1) two triplets and two quartets at lower field. The two triplets must be due to a fluorine atom with two adjacent fluorines i.e. F_3 or F_4. The spectrum of the undeuterated compound (fig. 2) shows that the lower field triplet was essentially unchanged and was therefore assigned as F_3. The other triplet shows additional spin-spin coupling and was assigned as F_4. The two quartets in the spectrum of the monodeuterated compound were due to the F_2 and F_4 fluorine atoms.

In the spectrum of the undeuterated compound the higher field quartet was now coupled to a meta hydrogen and also shows some fine splitting due to coupling to the other aromatic protons; this was assigned as F_2. The other quartet was now coupled to an ortho hydrogen and was assigned as F_5.

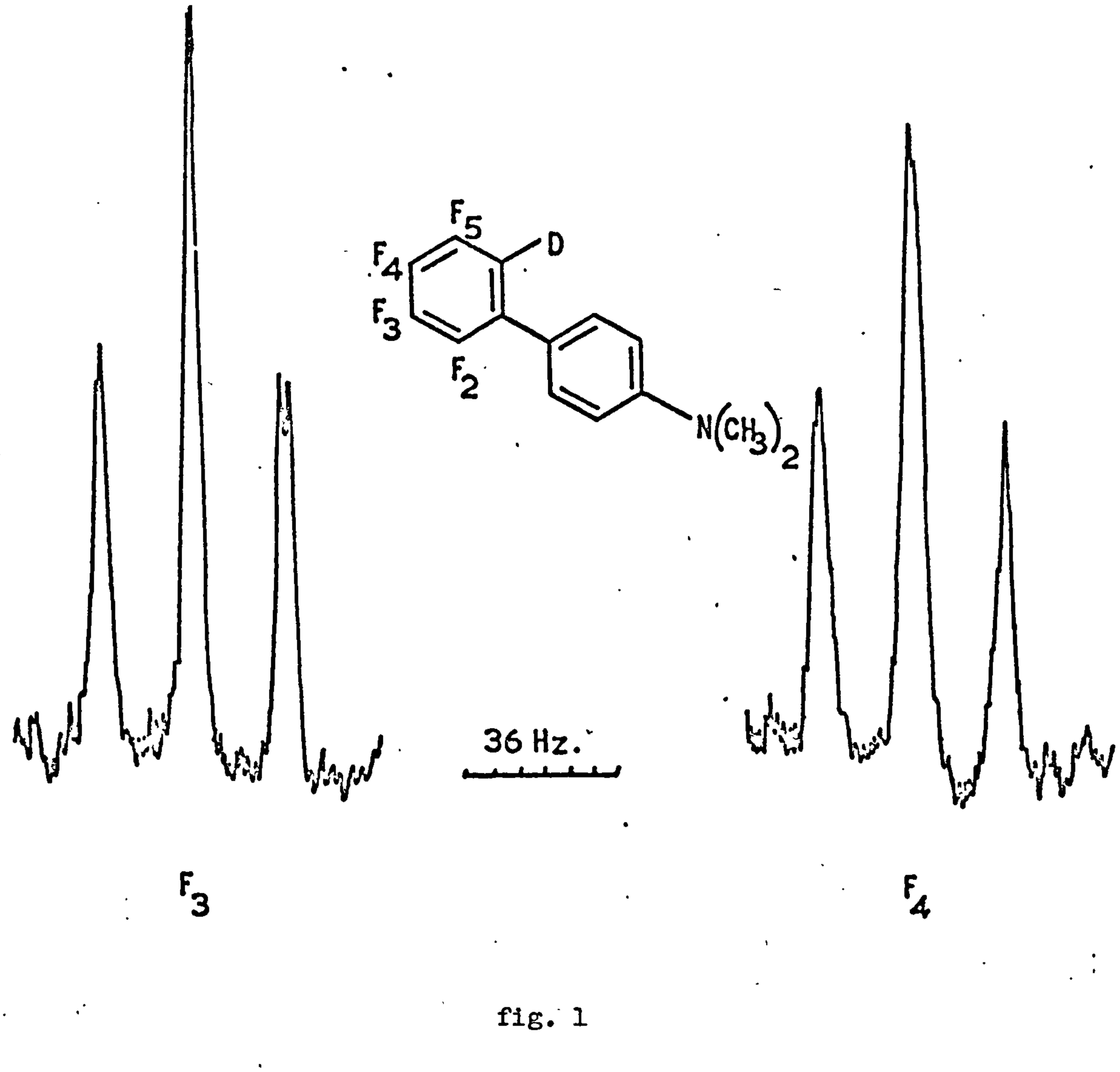


fig. 1

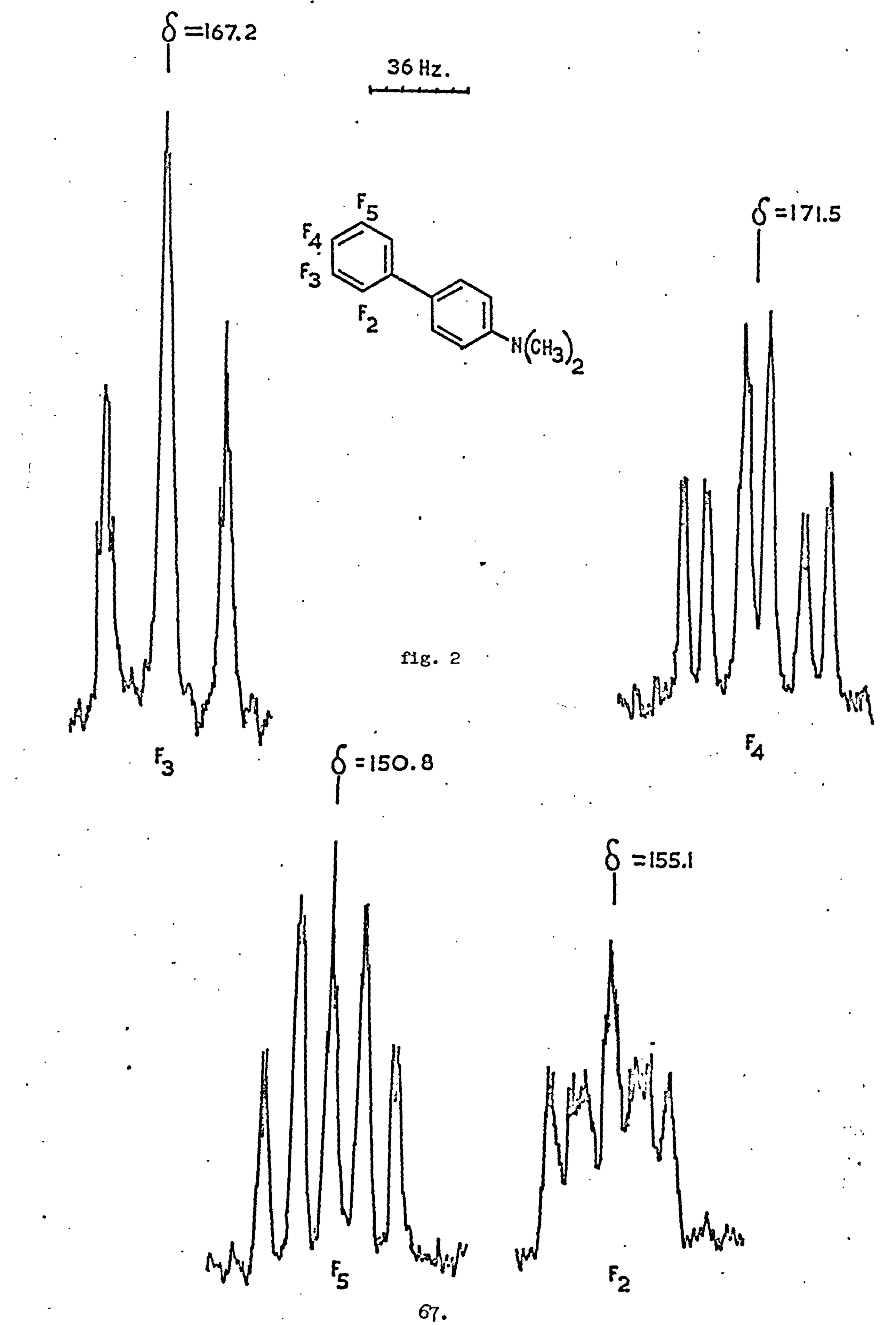


fig. 2

fig. 4

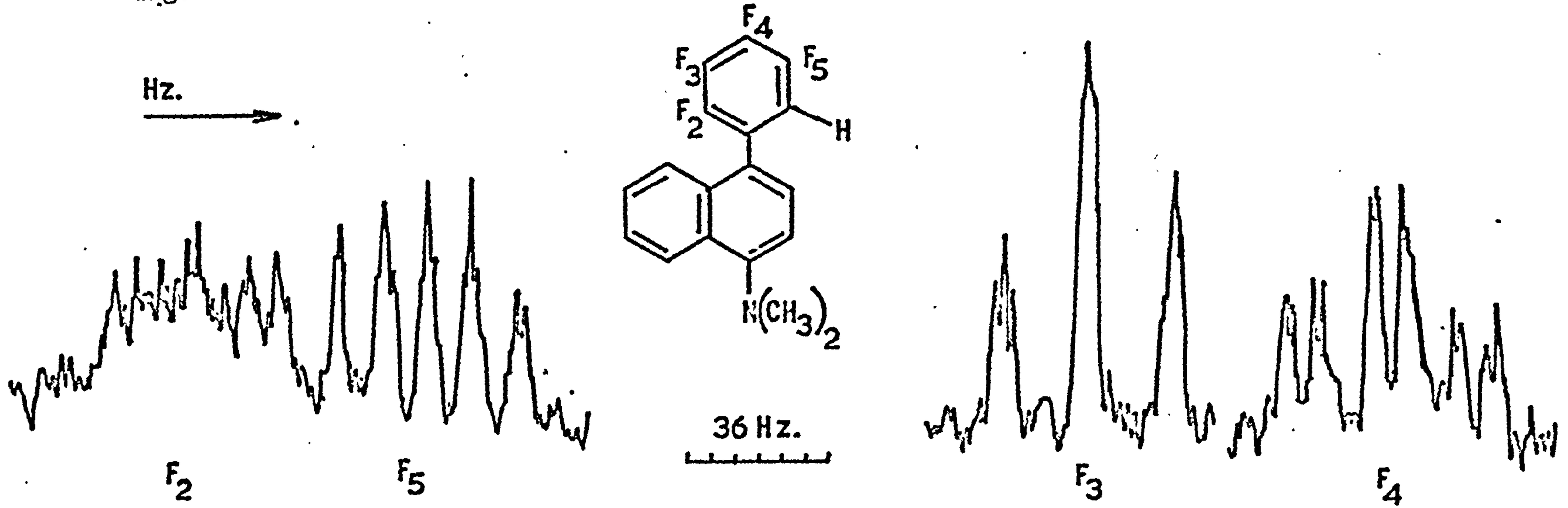
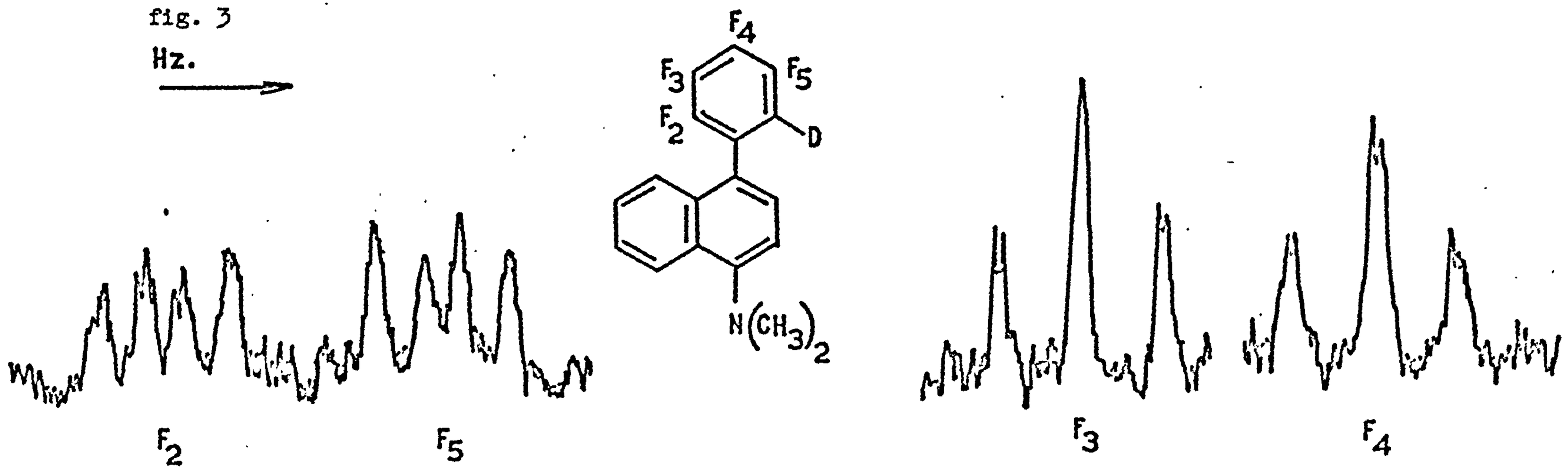
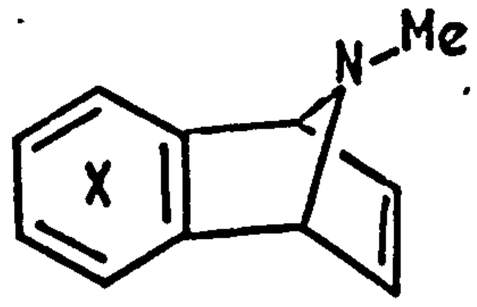

Hz.
F4
F3
F5
F2
H
N(CH3)2
36 Hz.
F2
F5
F3
F4

fig. 3


Hz.
F4
F3
F5
F2
D
N(CH3)2
F2
F5
F3
F4

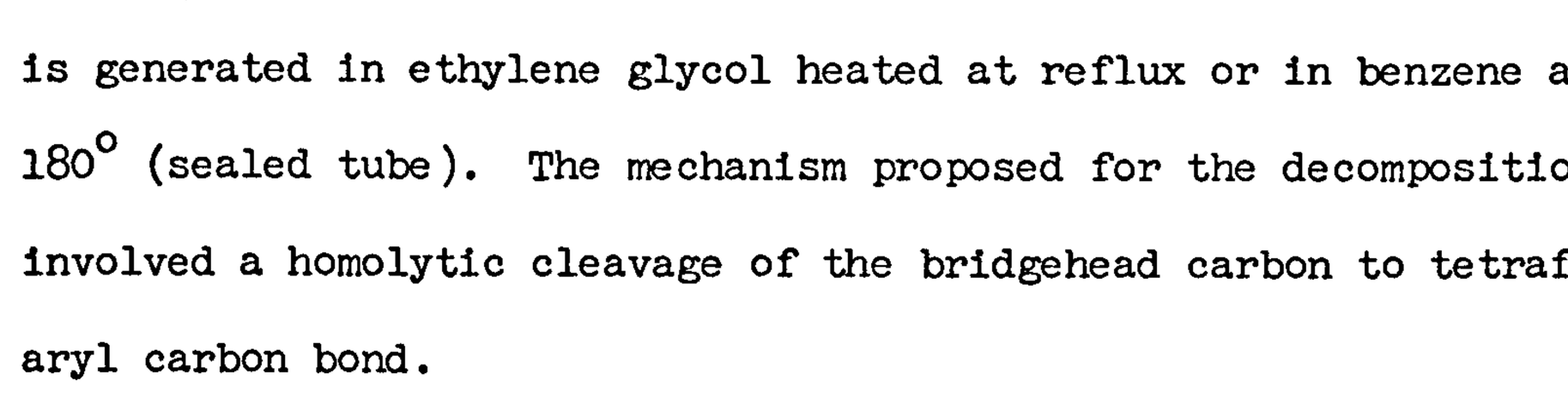
N-methyimino-dihydronaphthalenes

Benzyne has been allowed to react with a large number of pyrrole derivatives; the usual product that is obtained is an imino-dihydronaphthalene derivative. Tetrahalobenzynes react with N-methylpyrrole to give the imino dihydronaphthalenes, compounds (17) X=F[15] or Cl[83].



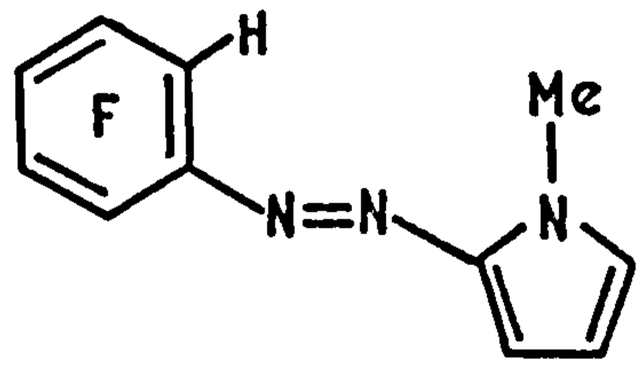
(17)

Recent studies[84] of the thermal decomposition reactions of compound (17) show that 2'-(2,3,4,5-tetrafluorophenyl)-N¹-methyl-pyrrole (38) is generated in ethylene glycol heated at reflux or in benzene at 180° (sealed tube). The mechanism proposed for the decomposition involved a homolytic cleavage of the bridgehead carbon to tetrafluoroaryl carbon bond.



(17) (38)

As part of our studies on the rearrangements of compounds containing the carbon fragment, N - C - tetrafluoroaryl, we have also investigated reactions of this compound. In aqueous ethanol heated under reflux the compound (17) rearranges to give the compound (38) in 80% yield. The structure of the compound (38) was based on its spectral properties and by an independent preparation. The preparation involved the decomposition of a tetrafluorophenyl diazonium salt in N-methyl pyrrole, (a similar method has been used to form 2-phenyl furans,[85] and 2-tetrahalophenylfurans).[86] The products of the reaction were the expected 2'-(2,3,4,5-tetrafluorophenyl)-N'-methyl-pyrrole (38) in 14% yield, and the azo compound (39) isolated in 40% yield.



(39)

Other methods of preparing the compound (38) had failed.[84]

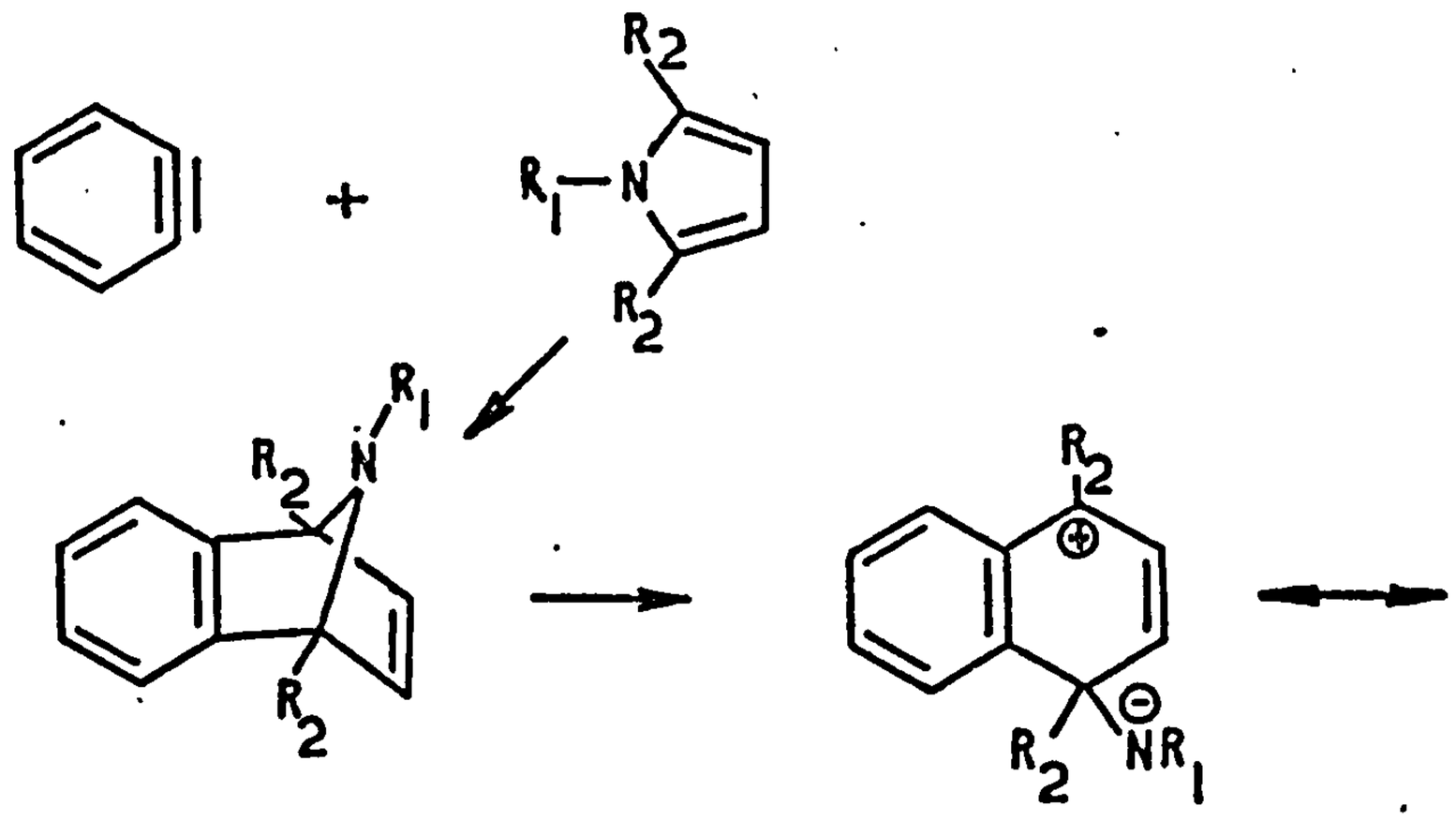
When the compound (17) was heated in glyme, containing deuterium oxide, 2'(2-[^{2}H]-3,4,5,6-tetrafluorophenyl)-N'-methyl-pyrrole was formed, which was shown by mass spectrometry to contain greater than 99% d_1.

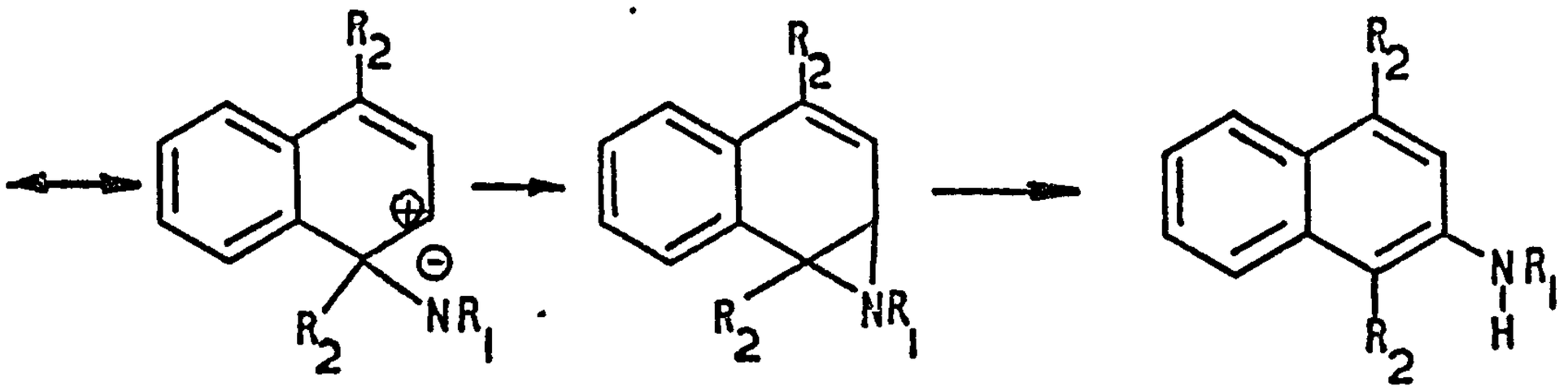
The position of deuteration was shown by ^{1}H n.m.r. from the absence of the resonance signal at τ 2.8 - 3.3. A control reaction showed that no deuterium was incorporated into compound (38) under similar reaction conditions. These results suggest that the mechanism is intermolecular in protic media. Also, since the reaction proceeds

fairly readily in aqueous ethanol and in ethylene glycol when heated under reflux, but is considerably slower in benzene (not at all at 80°), it seems reasonable to suggest that the mechanism is ionic in character. When the compound (17) was heated in d_6 benzene at 160° the product, compound (37) was shown by mass spectrometry to contain no deuterium. It was thought that at 160°, if a radical mechanism was operating, there might be some radical abstraction of deuterium from the d_6 benzene. It would have been more reasonable, however, to use d_8-toluene.

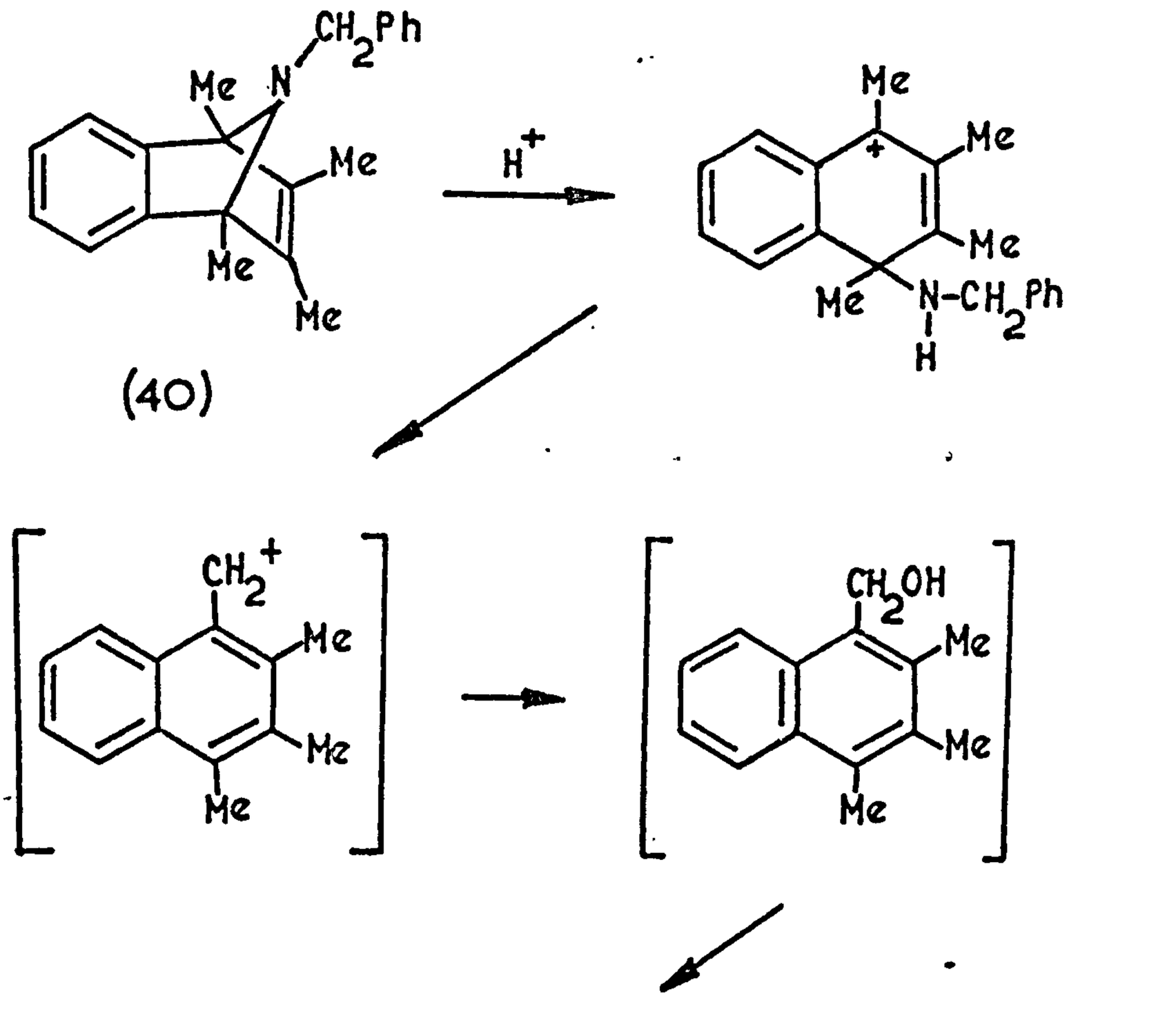
The division between a dipolar or a diradical mechanism is usually small and therefore arguments for or against should be approached with caution.[87]

The last step in the formation of the compound (37) involves a loss of a proton (or hydrogen atom). If this process was blocked with a methyl group at the bridgehead positions the rearrangement would undoubtedly follow a different course. It has been reported that the reaction of benzyne with 1,2,5-trisubstituted pyrroles does not lead to the expected adduct but to a 2-amino-naphthalene derivative.[88] The amino-naphthalene was thought to be derived from the unstable initial adduct.

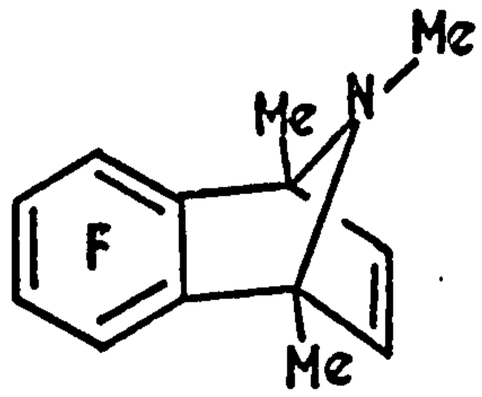




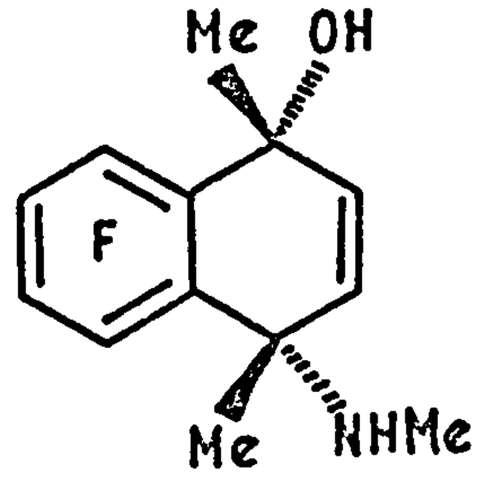
A stable dibridgehead-substituted adduct with a penta-substituted pyrrole has been obtained.[89] This adduct (40) in dilute mineral acid gives a bis[2,3,4-trimethyl naphthyl-(1)-methyl]ether (41).



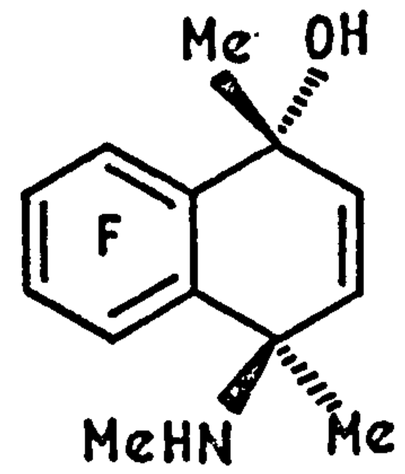
However, when we reacted·tetrafluorobenzyne with 1,2,5-trimethylpyrrole three products were isolated from the reaction mixture, the adduct (42) and an epimeric mixture of amino-alcohols (43) and (44).



(42)



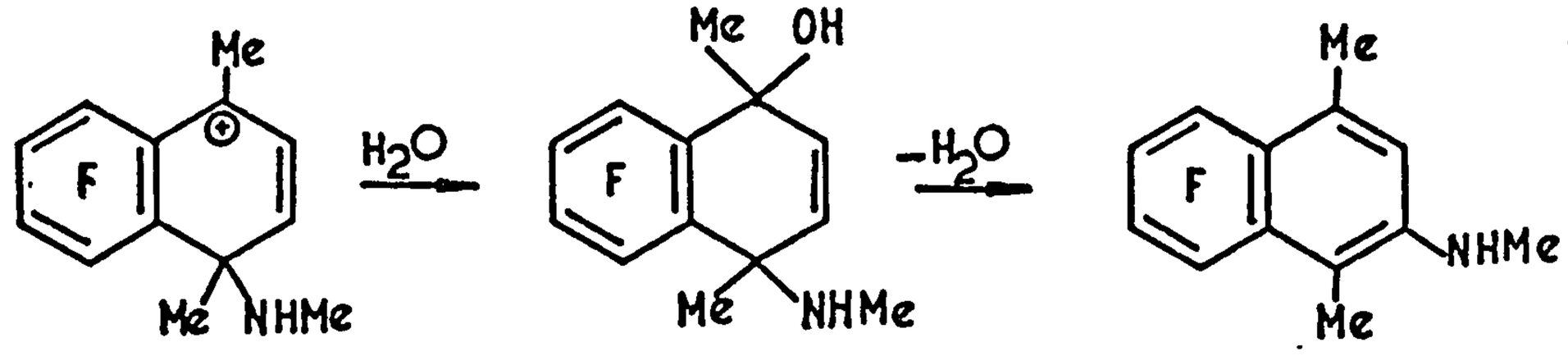
(43)



(44)

The adduct (42) was, as expected, very unstable and attempts to study its hydrolysis reactions led to black tars.

The formation of (43) and (45) arise by the attack of water on the intermediate (45). The trapping of this intermediate is some evidence in support of the previously proposed mechanism[88] for the decomposition of the benzyne——1,2,5-trisubstituted pyrrole adduct. Attempts to convert the compounds (43) and (45) to the 2-amino naphthalene (46) have failed.



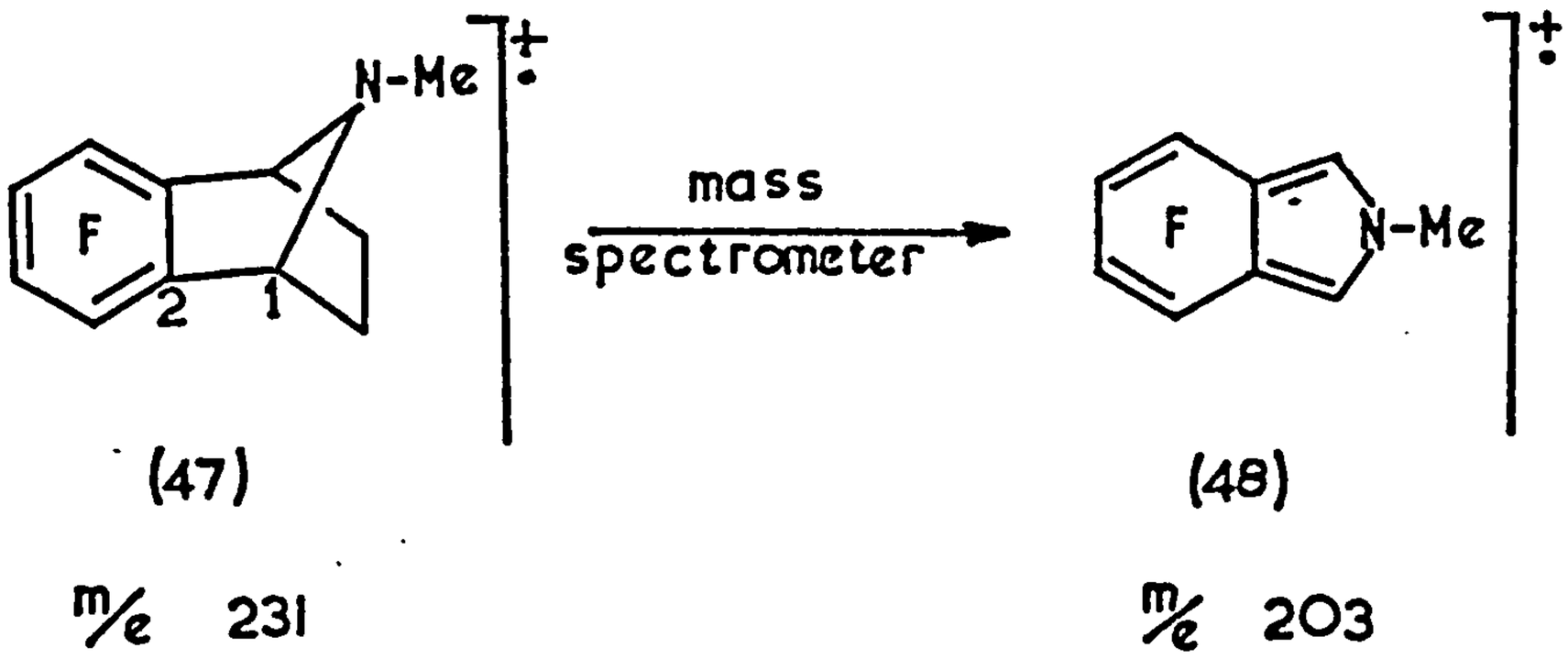
(45)

(46)

The method used to prepare 1,2,3-trimethylpyrrole and 1-methyl-pyrrole involved methylation of the free amine with methyl iodide in dimethyl sulphoxide and potassium hydroxide. This procedure was similar to that used by Gillis for the methylation of phenols.[90] The yields were high, > 86% after distillation, and the method was very convenient to use.

The literature methods of methylating pyrroles usually involve the alkali metal[91] or more recently thallium salts.[92] These methods although they work well, are less convenient to use than the Gillis procedure.

In the rearrangement of the 1-N,N-dimethylaminotetrahalobenzobarrelenes, it appeared that the double bonds were required for the rearrangement to proceed. It was therefore of interest to examine the possible reactions of the reduced N-methyl-pyrrole tetrafluorobenzyne adduct, compound (47), in aqueous solvents. When this compound was prepared the mass spectrum showed that the molecular ion was of low relative abundance, the base peak was at m/e 203, this corresponds to the loss of m/e 28 (ethylene). This compound apparently undergoes an easy retro-Diels-Alder reaction in the mass spectrometer to form an ion which could correspond to N-methyl tetrafluoroisoindole (48).



(47) m/e 231

(48) m/e 203

The unreduced compound (17) has also been shown to break down on thermolysis,[84] possibly to the isoindole which was not isolated but which gave N-methyl-tetrafluoro phthalimide.

When the compound (47) was heated under reflux in aqueous ethanol for 80 hours, no reaction occurred. However when the compound was heated in a sealed tube in degassed aqueous ethanol at 120° the compound underwent the retro-Diels-Alder reaction. There was no evidence for the alternative breakdown, namely cleavage of the C_1-C_2 bond. The retro-Diels-Alder reaction was investigated in more detail and is reported in the following chapter.

Experimental

The general methods are as described in Chapter 1.

The enamines in the following experiments were prepared by Weingarten's method.[38]

N,N-dimethylaminocyclohexene.....59%

1-pyrrolidinocyclo-octene.....67%.

1. Reaction of tetrafluorobenzyne with N,N-dimethylaminocyclohexene.

n-Butyl lithium in hexane (10 ml., 0.02 mole) was added to a solution of bromopentafluorobenzene (5g., 0.02 mole) in ether (30 ml.) at -70° and the mixture was stirred for 30 min.. 1-N,N-Dimethylaminocyclohexene (0.5 g., 0.06 mole) was added, the external cooling source was removed, and the reaction mixture allowed to warm to room temperature. The mixture was heated under reflux (40-45°) for 5 hr., cooled, and diluted with ether (50 ml.) Water (100 ml.) was then added and the ethereal layer was extracted with portions of 2N-hydrochloric acid (4 x 25 ml.). The acid extracts were combined and neutralised immediately by the addition of solid sodium carbonate. The product was extracted with ether and the solution dried. The removal of the solvent and drying agent gave an oil (2.9 g.). This oil was eluted through a short column of alumina and gave 1-N,N-dimethylaminotetrafluoro-(7,8)-benzobicyclo[4.2.0]octa-7-ene,(7) X=F, (2.5 g. 46%);

b.p. 112° 3 mm.,

(Found: C, 61.35; N,55; N, 4.85% M. [mass spectrometry] 273;

$C_{14}H_{15}F_4N$ requires C,61.55; H,5.55; N,5.15% M.273);

^1H n.m.r.τ (CCl_4) 6.25 - 6.5 (m., 1H); 7.69 (s., 6H);

7.7 - 8.2 (m., 4H); and 8.2 - 8.9 (m., 4H);

υ_{max} 2938, 2880, 2849, 2800, 1635, 1500, 1400, 1387, 1349, 1280,

1031, and 897 $cm.^{-1}$.

Removal of the ether and cyclohexanone left an oil which was purified by elution through a short column of alumina and gave 2-(2',3',4',5'-tetrafluorophenyl)cyclohexanone, (8) X=F, (300 mg. 6%);

m.p. 95° (from ethanol);

(Found: C,59.05; H,4.1% M [mass spectrometry] 246;

$C_{12}H_{10}F_4O$ requires C,58.5; H,4.1% M. 246);

^1H n.m.r. τ (CCl_4) 3.0 - 3.5 (m., 1H); 6.0 - 6.5 (m., 1H);

7.4 - 8.5 (m., 8H);

ν_{max}^{KBr} 2954, 2865, 1710, 1631, 1524, 1490, 1346, 1314, 1215, 1192,

1118, 1069, 1052, 974, 947, 903, 874, 726, and 686 cm.$^{-1}$

$\lambda_{max}^{ethanol}$ 209 (ϵ 5740), 261 (960) nm..

2. Reaction of tetrachlorobenzyne with N,N-dimethylaminocyclohexene.

n-Butyl lithium in hexane (7.2 ml. 0.02 mole) was added to a stirred suspension of hexachlorobenzene (5.7 g. 0.02 mole) in ether (30 ml.) at -70°. The mixture was stirred at this temperature for 1 hr. then N,N-dimethylaminocyclohexene (5 g. 0.04 mole) was added. The external cooling source was removed and the reaction mixture was allowed to warm to room temperature. The reaction mixture was heated under reflux (45°) for 4 hr. Work up as in the previous experiment gave 1-N,N-dimethylaminotetrachloro-(7,8)-benzobicyclo[4.2.0]octa-7-ene, (7) X=Cl (2.5 g., 37%), m.p. 79-79.5°, (from light petroleum b.p.60-80°C);

(Found: C,49.9; H, 4.5; N,4.0; $C_{14}H_{15}Cl_4N$ requires C,49.6; H,4.5; N,4.15%);

^1H n.m.r. τ ($CDCl_3$) 6.37 (t., J = 4.5 Hz. 1H);

7.68 (s., 6H); and 7.7 - 9.0 (m., 8H);

ν_{max}^{KBr} 2965, 2930, 2860, 2775, 1456, 1445, 1360, 1330, 1270, 1144,

1067, 900, and 800 cm.$^{-1}$.

3. Reaction of benzyne with N,N-dimethylaminocyclohexene.

o-Fluorobromobenzene (3.5 g., 0.02 mole) in tetrahydrofuran (30 ml.) was added dropwise to magnesium turnings (0.5 g.) in tetrahydrofuran (5 ml.) and N,N-dimethylaminocyclohexene (7.5 g., 0.06 mole) at such a rate so as to maintain boiling of the solvent. The mixture was heated under reflux for 2 hr., cooled and the solvent removed to leave an oil. Ether was added and the solution was washed with water and then extracted with 2N hydrochloric acid (4 x 25 ml.). The organic phase gave, after the removal of ether and cyclohexanone, 2-phenylcyclohexanone, (8) X=H, (240 mg., 7%), m.p. 54-56° (from aqueous alcohol) (lit.[93] m.p. 50-53°);

^{1}H n.m.r. τ (CCl_4) 2.7 - 3.2 (m., 5H); 6.4 - 6.8 (m., 1H);
and 7.5 - 8.8 (m., 8H);

ν_{max}^{KBr} 3080, 3042, 2940, 2870, 1710, 1610, 1510, 1455, 1440, 1315, 1132, 1067, 765, and 705 cm.$^{-1}$.

The combined acid extracts were neutralised by the addition of solid sodium carbonate and the basic products were extracted with ether. The ethereal solution was dried and removal of the solvent gave an oil (1.1 g.), which was separated by preparative t.l.c. and gave :

a) N-methylaniline (123 mg. 3%);

^{1}H n.m.r. τ (CCl_4) 2.8 - 3.8 (m., 5H); 6.55 (broad s., 1H);
7.34 (s., 3H);

ν_{max} 3430, 3060, 3030, 3000, 2920, 2900, 2830, 1612, 1515, 1480, 1455, 1428, 1325, 1270, 1183, 1157, 1077, 870, 750, and 698 cm.$^{-1}$,

and b) 1-N,N-dimethylamino-(7,8)-benzobicyclo[4.2.0.]octa-7-ene,(7) X=H, (750 mg., 18%); b.p. 120° 3 mm.;

(Found: C, 83.0; H, 9.6; N, 6.9% M [mass spectrometry] 201;
$C_{14}H_{19}N$ requires C, 83.55; H, 9.5; N, 6.95%;M. 201).

4. Reaction of tetrafluorobenzyne with 1-pyrrolidinocyclo-octene.

As in experiment 1, using 0.09 mole of 1-pyrrolidinocyclo-octene gave 1-pyrrolidinotetrafluoro-(9,10)-benzobicyclo[6.2.0]dec-9-ene (13) X=F, (7.4 g., 50%); m.p. 52-54°;

(Found: C, 66.05; H, 6.5; N, 4.2%; M. [mass spectrometry] 327;

$C_{18}H_{21}F_4N$ requires C, 66.1; H, 6.45; N, 4.3%; M. 327)

^1H n.m.r. τ (CCl_4) 6.4 - 6.7 (m., 1H); 7.0 - 7.7 (m., 4H);

and 7.9 - 8.7 (m., 16H);

ν_{max} 2930, 2860, 1615, 1515, 1470, 1395, 1353, 1200, 1052, 1010,

980, 925, and 715 cm.$^{-1}$.

2-(2',3',4',5',-Tetrafluorophenyl)cyclo-octanone was not detected by g.l.c. (column A) in the neutral fraction.

5. Reaction of benzyne with 1-pyrrolidinocyclo-octene.

As in experiment 3, using 0.09 mole of the enamine gave 1-pyrrolidino-(9,10)-benzobicyclo[6.2.0]dec-9-ene, (13) X=F, (6.8 g. 60%) m.p. 68.5 - 69° (from hexane);

(Found: C, 84.75; H, 9.95; N, 5.35% M. [mass spectrometry] 255;

$C_{18}H_{25}N$ requires C, 84.65; H, 9.85; N, 5.5%; M. 255);

^1H n.m.r. τ(CCl_4) 3.03 (m., 4H); 6.52 (t., 1H);

7.1 - 7.6 (m., 4H); and 8.0 - 9.0 (m., 17H);

ν_{max} 3085, 2950, 2860, 2813, 1598, 1468, 1458, 1402, 1353, 1344, 1320, 1264,

1196, 1126, 1041, 913, and 733 cm.$^{-1}$.

2-Phenylcyclo-octanone was not detected by g.l.c. (column A) in the neutral fraction.

6. Preparation and pyrolysis of 1-pyrrolidino-(9,10)-benzobicyclo[6.2.0]-deca-9-ene-N-oxide.

The compound (13) X=H, (400 mg.) was dissolved in methanol (10 ml.) and after the addition of hydrogen peroxide (7 ml., 100 vol.) the mixture was stirred for 3 days at room temperature. Sodium bisulphite (excess) was added and the mixture warmed on a water bath at 50° for 2 hr.. The solvents were partially removed under reduced pressure, water (5 ml.) was added, and the mixture was extracted with chloroform.

The chloroform extracts were dried, and after the removal of the solvent gave an oil (500 mg.) which was pyrolysed at 200° and 1.5 m.m. to give the crude product.

Preparative thin layer chromatography gave (9,10)-benzobicyclo-[6.2.0]deca-1,9-diene, (60 mg., 21%) M. [mass spectrometry] 184;

$C_{14}H_{16}$ requires M. 184;

^{1}H n.m.r. τ ($CDCl_3$) 2.85 (s., 4H); 4.2 (t., J = 5 Hz.);

5.8 - 6.2 (m., 1H); and 7.5 - 9.3 (m., 10H);

u.v. $\lambda_{max}^{cyclohexane}$ 300 (ϵ 6575); 292 (6980); 289 sh. (5350);

282 sh. (4025); 256 (13,500); 247 (14,400); 225 (7790); and

216 (10,200) n.m..

7. Hydrolysis of 1-N,N-dimethylaminotetrachloro-(7,8)-benzobicyclo-[4.2.0]octa-7-ene.

The compound (7) X=Cl, (100 mg.) was dissolved in ethanol (7.5 ml.); water (2.5 ml.) and concentrated hydrochloric acid [2 drops]. The mixture was heated under reflux for 6 hr.. Removal of the solvents gave 2-(2',3',4',5'-tetrachlorophenyl)-cyclohexanone (8) X = Cl (98 mg., 98%); m.p. 118° - 118.5° (from hexane);

(Found: C, 46.15; H, 3.35; $C_{12}H_{10}Cl_4O$ requires C, 46.15; H, 3.2%);

^{1}H n.m.r. τ ($CDCl_3$) 2.79 (s., 1H); 5.73 - 6.1 (m., 1H), and
7.3 - 8.4 (m., 8H);

υ_{max}^{KBr} 2950, 2895, 1715, 1423, 1358, 1195, 1123, 890, 827, 763, and 710 cm.$^{-1}$.

8. Hydrolysis of 1-N,N-dimethylaminotetrafluoro-(7,8)-benzobicyclo-[4.2.0]octa-7-ene (7) X=F.

By a similar method (exp. 7) for 1 hr. gave 2-(2',3',4',5'-tetrafluorophenyl)-cyclohexanone (8) X=F, (99%);

m.p. 95° (from ethanol).

Identical to an authentic sample (exp. 1.)

9. Attempted hydrolysis of 1-N,N-dimethylamino-(7,8)-benzobicyclo-[4.2.0]octa-7-ene (7) X=H

By a similar method (exp. 7) gave only recovered starting material as identified by t.l.c., g.l.c., and infra-red spectroscopy.

10. Hydrolysis of 1-pyrrolidinotetrafluoro-(9,10)-benzobicyclo[6.2.0]-deca-9-ene (13) X=F.

The compound (13) X=F (1 g.) was dissolved in ethanol (22.5 ml.) and water (2.5 ml.). Concentrated hydrochloric acid (4 drops) was added and the mixture was heated under reflux until g.l.c. analysis (column A) showed that starting material was completely absent (2 hr.). The reaction mixture was cooled and the solvents removed by evaporation under reduced pressure. The residual oil was dissolved in ether (20 ml.) and this solution was washed with water. Drying and removal of the solvent gave 2-(2',3',4',5'-tetrafluorophenyl)cyclo-octanone, (14) X=F, (640 mg. 76%); m.p. 51.5 - 52°;

(Found: C,61.5; H, 5.15% M. [mass spectrometry] 274;

$C_{14}H_{14}F_4O$ requires C, 61.3; H, 5.15%;M. 274);

^{1}H n.m.r. τ (CCl_4) 2.58 - 3.08 (m., 1H); 5.64 (t., 1H);

7.3 - 7.65 (m., 2H); and 7.65 - 9.0 (m., 10 H).

ν_{max} 3060, 2935, 2850, 1711, 1628, 1530, 1488, 1370, 1218, 1109, 1038, 992. 980, 937, 862, 731, and 700 cm.$^{-1}$,

U.v. $\lambda_{max}^{ethanol}$ 212 (ϵ 5150); 262 (935); and 288 (284) n.m..

11. Hydrolysis of 1-pyrrolidino-(9,10)-benzobicyclo[6.2.0]deca-9-ene.

The compound (13) X=H (1 g.) was dissolved in aqueous ethanol (25 ml. 10% water). Concentrated hydrochloric acid (4 drops) was added and the mixture was heated under reflux for 8 hr., (the reaction course was analysed by g.l.c. (column A)). The mixture was cooled and the solvents removed by evaporation under reduced pressure to give an oil. Ether was added and the solution was extracted with 2N-hydrochloric acid (3 x 15 ml.) to remove the remaining starting material (50 mg. after work up). The ethereal layer was dried over magnesium sulphate and after the removal of solvent and drying agent gave (1,2)-benzocyclo-dec-3-one, (15) (748 mg. 99% based on converted starting material)

m.p. 52-53°; (lit.[94] b.p.156-160° at 11 torr.)

(Found: C, 83.3; H, 9.0% M. [mass spectrometry] 202, $C_{14}H_{18}O$ C,83.15; H,9.0%);

^{1}H n.m.r. τ (CCl_4) 2.81 (broad s., 4H); 7.0 - 7.4 (m., 4H);

and 8.0 - 9.4 (m., 10 H);

ν_{max} 3080, 2950, 2813, 2853, 1683, 1600, 1573, 1483, 1470, 1443, 1262, 1223, 1010, and 758 cm.$^{-1}$,

U.v. $\lambda_{max}^{cyclohexane}$ 214 (ϵ 16,150); 235 (7570); and 276 (1040) n.m.,

$\lambda_{max}^{ethanol}$ 211 (ϵ 18,000); 239 (6710); and 277 (1050) n.m..

12. Isomerisation of 1-N,N-dimethylamino-(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-2,5,7-triene.

The compound (16) X=F, (400 mg.) was heated under reflux in aqueous ethanol (10 ml., 1:3) for 20 hr., and gave on cooling a crystalline

product (342 mg.). Removal of the solvent from the filtrate gave unconverted starting material (32 mg.) and a further quantity of product (15 mg.) which was shown to be 4'-N,N-dimethylamino-2,3,4,5-tetrafluorobiphenyl, (18) X=F, (total 339 mg., 85%);

m.p. 122-123° (from aqueous ethanol);

(Found: C, 62.35; H, 4.2; N, 5.3%; M.[mass spectrometry] 269;

$C_{14}H_{11}F_4N$ requires C, 62.45; H, 4.15; N, 5.2%; M. 269);

^1H n.m.r. τ (CCl_4) 2.75 (m., 2H (AA'), J_{AB} = 9 Hz., J_{A-F} = 1 Hz.); 2.8 - 3.3 (m., 1H); 3.39 (m., 2H) (BB'), J_{BA} = 9 Hz.); and 7.02 (s., 6H);

ν_{max} 2910, 2810, 1615, 1515, 1480, 1365, 1235, 1200, 1075, 1012, 990, 855, 812, and 710 cm.$^{-1}$,

$\lambda_{max}^{ethanol}$ 220 (ϵ13,500); 310 (24,050) n.m.,

^{19}F n.m.r. δ 150.8 p.p.m. (m., 1F); 155.1 p.p.m. (m., 1F); 167.2 p.p.m. (m., 1F); and 171.5 p.p.m. (m., 1F).

13. Isomerisation of compound (16) X=F in the presence of sodium hydroxide.

The compound (16) X=F (1 g.) was heated under reflux in aqueous ethanol (20 ml., 1:3) containing sodium hydroxide (100 mg.) for 18 hr.. Water (5 ml.) was added and the mixture,on cooling,gave white crystals of 4'-N,N-dimethylamino-2,3,4,5-tetrafluorobiphenyl, (18) X=F, (.95g., 95%).

14. Isomerisation of compound (16) X=F in the presence of deuterium oxide.

The compound (16) X=F (250 mg.) was heated under reflux in 1,2-dimethoxyethane (10 ml., anhydrous) and deuterium oxide (5 ml.) for 48 hr.. The crystals which formed on cooling were separated by filtration and gave 4'-N,N-dimethylamino-2[^2H]-3,4,5,6-tetrafluoro biphenyl (190 mg., 76%);

^{1}H n.m.r. τ(CCl_4) 2.74 (m., 2H (AA'), J_{AB} = 9 Hz., J_{A-F} = 1 Hz.); 3.39 (m., 2H (BB') J_{BA} = 9 Hz); and 7.02 (s., 6H).

Mass spectrometry: M^+ 270, 99% d_1.

4'-N,N-Dimethylamino-2,3,4,5-tetrafluorobiphenyl (75 mg.) was heated under reflux in 1,2-dimethoxyethane (3 ml.) and deuterium oxide (1 ml.) for 48 hr.. The crystals, on cooling, were shown to be unchanged starting material by ^{1}H n.m.r. and mass spectrometry.

15. Isomerisation of 1-N,N-dimethylamino-(7,8)-tetrachlorobenzobicyclo-[2.2.2.]octa-2,5,7-triene, (16) X=Cl.

The compound (16) X=Cl (1 g.) was heated under reflux in aqueous ethanol (20 ml. 1:3) for 24 hr., and gave, on cooling, 4'-N,N-dimethamino-2,3,4,5-tetrachlorobiphenyl (18) X=Cl (0.93 g., 93%); m.p. 112° (from ethanol);

(Found: C, 50.0; H, 3.25; N, 4.1%; M. [mass spectrometry] 335; $C_{14}H_{11}Cl_4N$ requires C, 50.3; H, 3.3; N, 4.2%; M. 335);

^{1}H n.m.r. τ(CCl_4) 2.7 (s., 1H); 2.83 (m., 2H (AA'), J_{AB} = 9 Hz.,); 3.38 (m., 2H (BB'), J_{BA} = 9 Hz.) and 7.03 (s., 6H);

υ_{max} 2805, 1612, 1521, 1408, 1360, 1345, and 811 cm.$^{-1}$,

$\lambda^{ethanol}_{max}$ 218 (ϵ 32,600); 235 sh. (19,400); and 323 (18,400) n.m..

16. Preparation of 1-N,N-dimethylamino-(2,3)-tetrafluorobenzo-(5,6)-benzobicyclo-[2.2.2]octa-2,5,7-triene (23).

n-Butyl lithium (30 ml. 2.1 mole hexane solution) was added to a solution of bromopentafluorobenzene (14.8 g., 0.06 mole) in ether (75 ml.) at -70° and the mixture was stirred for 30 min.. 1-N,N-dimethylaminonaphthalene[95] (20 g., 0.12 mole) was added, the external cooling source was removed, and the reaction mixture allowed to warm to room

temperature. The solution, after stirring for 18 hr., was diluted with ether (150 ml.) and washed with water (4 x 100 ml.). The ethereal solution was dried over sodium sulphate and gave a dark brown oil after removal of ether and excess 1-N,N-dimethylaminonaphthalene. The oil was dissolved in ether (150 ml.) and extracted with 1N-hydrochloric acid (3 x 25 ml.). The combined acid extracts were neutralised, extracted with ether, and dried. Removal of the solvent gave an oil (8.26 g.). The major component was isolated by column chromatography and gave 1-N,N-dimethylamino-(2,3)-tetrafluorobenzo-(5,6)-benzobicyclo-[2.2.2.]octa-2,5,7-triene, (23), (5.68 g., 30%); m.p. 94 - 96° (from light petroleum b.p. 60-80°);

(Found: C, 67.9; H, 4.0; N, 4.5%; M. [mass spectrometry] 319;

$C_{18}H_{13}F_4N$ requires C, 67.7; H, 4.1; N, 4.4%; M. 319);

^{1}H n.m.r. τ (CCl_4) 2.3 - 2.6 (m., 1H); 2.7 - 3.2 (m., 5H);

4.5 - 4.8 (m., 1H); and 7.1 (d., 6H J_{HF} = 5 Hz.);

ν_{max}^{KBr} 3080, 3030, 2980, 2850, 2810, 1630, 1500, 1338, 1300, 1160,

1108, 1070, 950, 911, 800, 756, 710, and 681 cm.$^{-1}$.

17. Reduction of 1-N,N-dimethylamino-(2,3)-tetrafluorobenzo-(5,6)-benzobicyclo[2.2.2.]octa-2,5,7-triene.

The compound (23) (500 mg.) in ethanol (25 ml.) was reduced with hydrogen in the presence of pre-reduced palladium on charcoal catalyst (40 mg., 10%). Removal of the solvent and catalyst gave 1-N,N-dimethyl-amino-(2,3)-tetrafluorobenzo-(5,6)-benzobicyclo[2.2.2.]octa-2,5-diene (36), (500 mg., 99%); m.p. 100-101° (from ethanol);

(Found: C, 67.2; H, 4.85; N, 4.35%; M. [mass spectrometry] 321;

$C_{18}H_{15}F_4N$ requires C, 67.3; H, 4.7; N, 4.35%; M. 321);

^{1}H n.m.r. τ (CCl_4) 2.3 - 2.6 (m., 1H); 2.6 - 3.1 (m., 3H);

5.38 - 5.55 (m., 1H); 7.25 (d, 6H J_{HF} = 7 Hz.); and 8.0-8.6 (m.,4H);

υ_{max}^{KBr} 2960, 2880, 2815,. 1500, 1483, 1470, 1365, 1315, 1110, 1086, 1035, 970, 820, and 770 cm.$^{-1}$.

18. Isomerisation of 1-N,N-dimethylamino-(2,3)-tetrafluorobenzo-(5,6)-benzobicyclo[2.2.2.]octa-2,5,7-triene (23).

The compound (23) (200 mg.) in diglyme (7.5 ml.) and water (2.5 ml.) was heated in a sealed tube at 140° for 36 hr.. Water (10 ml.) was added to the cooled reaction mixture and the products were extracted with ether. The ethereal solution was dried and gave an oil after the removal of the solvent. Preparative t.l.c. gave recovered starting material (32 mg.) and 4'-N,N-dimethylamino-1'-(2,3,4,5-tetrafluorophenyl)-naphthalene, (24), (101 mg., 60%);m.p. 85-86° (from ethanol);
(Found: C, 67.65; H,4.2; N, 4.45%; M. [mass spectrometry] 319;
$C_{18}H_{13}F_4N$ requires C, 67.7; H, 4.1; N, 4.4%; M. 319);
^{1}H n.m.r. τ (CCl_4) 1.7 - 1.95 (m., 1H); 2.5 - 3.3 (m., 6H); and 7.13 (s., 6H);
υ_{max}^{KBr} 3080, 2950, 2880, 2840, 2800, 1635, 1577, 1520, 1475, 1395, 1325, 1195, 1143, 1090, 1045, 1015, 965, 905, 860, 825, 800, and 766 cm.$^{-1}$,
$\lambda_{max}^{methanol}$ 219 (ϵ 36,500); 240 sh. (13,700); and 323 (8200)n.m.,
^{19}F n.m.r. δ 149.3 p.p.m. (m., 1F); 150 p.p.m. (m, 1F); 166.1 p.p.m. (m., 1F); and 168 p.p.m. (m., 1F)..

19. Isomerisation of 1-N,N-dimethylamino-(2,3)-tetrafluorobenzo-(5,6)-benzobicyclo[2.2.2.]octa-2,5,7-triene (23) in the presence of deuterium oxide.

The compound (23) (200 mg.) in diglyme (7.5 ml.) and deuterium oxide (2.5 ml.) was heated at 140° for 48 hr.. Work up as before (experiment 18), gave 4'-N,N-dimethylamino-1'-(6[^{2}H]-2,3,4,5-tetrafluorophenyl)naphthalene (24) (120 mg., 60%)

^{1}H n.m.r. τ (CCl_4) 1.7 - 2.0 (m., 1H); 2.5 - 3.1 (m., 5H); and
7.13 (s., 6H)..

Mass spectrometry: M^+ 320 , 99% d_1.

20. Isomerisation of 1-N,N-dimethylamino-(2,3)-tetrafluoro-(5,6)-benzobicyclo[2.2.2.]octa-2,5-diene (36).

The compound (36) (237 mg.) in glycerol (7.5 ml.) and water (2.5 ml.) was heated in a sealed tube at 190° for 127 hr.. Water (10 ml.) was added to the cooled reaction mixture, which was then extracted with carbon tetrachloride. The combined extracts were dried, removal of the solvent gave an oil which was separated by preparative t.l.c. and gave unchanged starting material (99 mg.) and 4-(2',3',4',5'-tetrafluorophenyl)-α-tetralone, (37), (16 mg., 13%); m.p. 95-96° (from ethanol); (Found: C, 65.5; H, 3.5%; M. [mass spectrometry] 294; $C_{16}H_{10}F_4O$ requires C, 65.3; H, 3.45%; M. 294)

^{1}H n.m.r. τ(CCl_4) 1.85 - 2.15 (m., 1H); 2.4 - 2.8 (m., 2H);
2.9 - 3.2 (m., 1H); 3.3 - 3.8 (m., 1H);
5.38 (t., 1H J = 6 Hz.); and 7.2 - 7.9 (m., 4H);

υ_{max} 2960, 2881, 1690, 1601, 1525, 1485, 1453, 1370, 1331, 1290, 1105, 1040, 1010, 952, and 857 cm.$^{-1}$,

$\lambda_{max}^{methanol}$ 218 (ϵ 15,200); 246 (6, 850); and 291 (1,230) n.m..

21. Isomerisation of 1-N,N-dimethylamino-4-methyl-(7,8)-tetrafluoro-benzobicyclo[2.2.2]octa-2,5,7-triene (26).

The compound (26) (900 mg.) in diglyme (15 ml.) water (5 ml.) and sodium hydroxide (10 mg.) was heated in a sealed tube at 140° for 60 hr.. The mixture was cooled, poured into water (100 ml.) and extracted with ether. The extracts were dried; removal of the solvent gave an oil which was separated by preparative t.l.c. and gave a) 4'-methyl-4'-(2,3,4,5-tetrafluorophenyl)-cyclohexadienone (27), (201 mg., 25%);

m.p. 92 - 93°; (from hexane);

(Found: C, 61.05; H, 3.05%; M. [mass spectrometry] 256;

$C_{13}H_8F_4O$ requires C, 60.95; H, 3.15%; M. 256);

^{1}H n.m.r. τ (CCl_4) 3.12 (d., 2H (AA'), J_{AB} = 10 Hz.);

3.8 (d., 2H (BB'), J_{BA} = 10 Hz.); 2.85 - 3.3 (m., 1H);

and 8.31 (d., 3H, J = 1 Hz.);

$\nu_{max}^{CHCl_3}$ 2980, 2940, 1675, 1635, 1520, 1480, 1401, 1352, 1147, 1090,

1020, 950, 912, and 860 cm.$^{-1}$,

$\lambda_{max}^{ethanol}$ 238 (ϵ 16,400); 265 sh. (3090) n.m.,

^{19}F n.m.r. δ 145.2 (1F); 146.3 (1F); 166.8 (1F); and 177.6(1F)..

b) An inseparable mixture of dienones (0.344 g.)

4'-methyl-4'-(4-N,N-dimethylamino-2,3,5-trifluorophenyl)-cyclohexadienone

(29) and 4'-methyl-4'-(3-N,N-dimethylamino-2,4,5-trifluorophenyl)-cyclo-

hexadienone (28) in the ratio 1.5:1;

^{1}H n.m.r. τ ($CDCl_3$) 3.1 (d., 2H (AA') J_{AB} = 10 Hz.);

3.0 - 3.5 (m., 1H); 3.83 (d., 2H (BB'), J_{BA} = 10 Hz.);

7.11 (t., 6H, J_{HF} = 1.5 Hz.); and 8.33 (d., 3H,

J_{HF} = 1 Hz.).

ν_{max} 2990, 2950, 2900, 2820, 1673, 1630, 1512, 1465, 1400, 1250,

1200, 1068, 1017, and 860 cm.$^{-1}$.

Mass spectrometry M.$^+$ 281.

^{19}F n.m.r. δ 128.7 (0.8F); 133.4 (1.2F); 150.2 (2F)

153.8 (1.2F) and 154.9 (0.8F

22. <u>Rearrangement of 4-methyl-4'-(2,3,4,5-tetrafluorophenyl)-cyclo-</u>

<u>hexadienone</u> (27).

The dienone (27) (50 mg.) was dissolved in carbon tetrachloride (25 ml.) at 0° and perchloric acid (4 drops 60%) in acetic anhydride

(1 ml.) was added dropwise.

The mixture was stirred at 0° for 15 min. then poured into water (50 ml.). The organic phase was washed with water, sodium bicarbonate solution (5 ml., 5%), water, and finally dried over magnesium sulphate.

Removal of the drying agent and solvent gave,after preparative t.l.c.

a) unreacted starting material (10 mg.) (by t.l.c., and ^{1}H n.m.r. spectroscopy).

b) 4'-Acetyl-2'-methyl-2,3,4,5-tetrafluorobiphenyl (32),

(39 mg., 93% based on converted starting material);

m.p. 71 - 73° (from ethanol);

(Found: C, 60.65; H, 3.55%; M. [mass spectrometry] 298;

$C_{15}H_{10}F_4O_2$ requires C, 60.4; H, 3.4%; M. 298).

^{1}H n.m.r. τ (CCl_4) 2.7 - 3.4 (m., 4H); 7.76 (s., 3H);

and 7.77 (m., 3H);

ν_{max} 3015, 1760, 1630, 1530, 1495, 1482, 1372, 1192, 1177, 1078,

1004, 990, 957, 907, and 835 cm.$^{-1}$;

$\lambda_{max}^{methanol}$ 214 (ϵ 17,250); 236 (10,800); and 260 sh. (2,820) n.m..

23. Hydrolysis of 4'-acetyl-2'-methyl-2,3,4,5-tetrafluorobiphenyl (32)

The acetate (32) (20 mg.) in aqueous ethanol (1 ml., 5%) and sodium carbonate (5 mg.) was stirred at room temperature for 3 hr.. Solvents were removed by evaporation under reduced pressure and ether added. The ethereal layer was washed with dilute sulphuric acid, water, then dried. Removal of the solvent and drying agent gave 4'-hydroxy-2'-methyl-2,3,4,5-tetrafluorobiphenyl (33), (14 mg., 82%); 105°-106° (from ethanol);

(Found: C, 61.25; H, 3.35; $C_{13}H_8F_4O$ requires C, 61.15; H, 3.15%);

^{1}H n.m.r. τ (CCl_4) 2.9 - 3.4 (m., 4H); 5.44 (broad s., 1H); and

7.89 (broad s., 3H);

$\nu_{max}^{CHCl_3}$ 3580, 3300, 2920, 1620, 1525, 1500, 1480, 1371, 1295, 1184, 1077, 1002, 990, 951, 865, and 836 cm.$^{-1}$.

24. Reduction of 1-N,N-dimethylamino-(7,8)-tetrafluorobenzobicyclo-[2.2.2.]octa-2,5,7-triene. (16) X=F.

The compound (16) X=F (2 g.) was hydrogenated in the usual manner (experiment 17) and gave 1-N,N-dimethylamino-(7,8)-tetrafluorobenzo-bicyclo[2.2.2.]oct-7-ene (34), (1.8 g., 89%); m.p. 76 - 78° (from ethanol) (lit.[20] m.p. 78° from methanol);

^{1}H n.m.r. τ (CCl_4) 6.5 - 6.7 (m., 1H); 7.58 (d., 6H; J_{HF} = 5 Hz.), and 8.0 - 8.9 (m., 8H).

25. Attempted isomerisation of compound (34).

Gave unchanged starting material after reaction in diglyme/water (3:1) in a sealed tube at 140° for 89 hr..

26. Attempted trapping of intermediate in the isomerisation reaction.

1-N,N-dimethylamino-(7,8)-tetrafluorobenzobicyclo[2.2.2.]octa-2,5,7-triene (16) X=F (540 mg.) in glyme (15 ml.) and diethyl maleate (700 mg.) was heated under reflux for 106 hr.. G.l.c. analysis (column B) showed the presence of starting material, diethyl maleate, and diethyl fumarate. Separation by preparative t.l.c. gave unchanged starting material, (480 mg.); and diethyl fumarate (270 mg.). The products were identified from their spectroscopic data.

When diethyl maleate was heated under reflux in glyme no isomerisation occurred.

When the fully reduced compound (34) was heated under reflux in glyme containing diethyl maleate no isomerisation occurred.

27. Attempted isomerisation of 1-N,N-dimethylamino-(7,8)-tetrafluoro-benzobicyclo[2.2.2.]octa-2,5,7-triene (16) X=F in benzene

The compound (16) X=F (100 mg.) in benzene (15 ml.) was heated under reflux for 100 hrs.. G.l.c. analysis (column C) showed only starting material to be present.

Water (1 ml.) was added and the mixture heated under reflux for a further 30 hr.. G.l.c. analysis (column B) only showed the presence of unconverted starting material.

28. Preparation of N-methylpyrrole

Pyrrole (13.4 g., 0.2 mole) was added to a stirred suspension of potassium hydroxide (44.8 g., 0.8 mole) in dimethyl sulphoxide (400 ml.) and the mixture stirred for 40 min.. Methyl iodide (56.8 g., 0.4 mole) was added and stirring continued for a further 30 min. to form a pale yellow solution.

Water (400 ml.) was added and the mixture extracted with ether (3 x 100 ml.). The ether extracts was washed with water (2 x 50 ml.), combined and dried over calcium chloride in a nitrogen atmosphere. Ether was removed using a heated Vigreux column (2 ft.), N-methylpyrrole distilled at 112-115° (13.9 g., 86%).

29. Preparation of 1,2,5-trimethylpyrrole

1,2,5-Trimethylpyrrole was prepared from 2,5-dimethylpyrrole[96] by a similar method (exp. 28) and gave, after distillation at 60° 11 mm., an 86% yield.

30. Reaction of tetrafluorobenzyne with N-methylpyrrole

By an identical method to that used by Coe[15] gave 1,2,3,4-tetra-fluoro-5,8-dihydro-5,8-(N-methylimino)-naphthalene (17), (72%); m.p. 75 - 80° (after sublimation) (lit.[15] m.p. 76°); ^{1}H n.m.r. τ ($CDCl_3$) 2.95 - 3.2 (m., 2H); 5.05 - 5.2 (m., 2H); and 7.45 (s., 3H).

31. Reaction of tetrachlorobenzyne with N-methylpyrrole

n-Butyl lithium (24 ml., 2:1 molar hexane solution) was added dropwise to a suspension of hexachlorobenzene (10.7 g., 0.038 mole) in ether (70 ml.) at -60°. The mixture was stirred for 45 min., N-methylpyrrole (7.5 g., 0.093 mole) added and the reaction allowed to warm to room temperature. The mixture was heated under reflux for 60 min., cooled, and ether (70 ml.) added. The solution was extracted with 2N-hydrochloric acid. The acid extracts were washed with ether, neutralised, and extracted with ether. The ethereal solution was dried and after removal of the solvent gave a dark brown solid (6.5 g.). Elution with ether -light petroleum, b.p. 40-60° (1:1) through a column of silica gave 1,2,3,4-tetrachloro-5,8-dihydro-5,8-(N-methylimino)-naphthalene[83] (2.35 g., 21%); m.p. 157 - 158°;

^{1}H n.m.r. τ (CCl_4) 2.9 - 3.2 (m., 2H); 5.1 - 5.3 (m., 2H); and 7.8 (s., 3H);

ν_{max}^{KBr} 3110, 2955, 2880, 2800, 1450, 1353, 1300, 1200, 1115, 920, 850, 800, 760, and 695 cm.$^{-1}$.

32. Isomerisation of 1,2,3,4-tetrafluoro-5,8-dihydro-5,8-(N-methylimino)-naphthalene, (17) X=F.

The compound (17) X=F (150 mg.) was heated under reflux in ethylene glycol (2 ml.) for 4 hr..

Water (10 ml.) was added to the cooled reaction mixture and the product was extracted with ether.

The ether extract was washed with water, dried, and removal of the solvent gave an oil which crystallised at -20°, and was shown to be 2'-(2,3,4,5-tetrafluorophenyl)-N-methylpyrrole (38), (110 mg., 73%); m.p. 25 - 26° (lit.[84] m.p. 28 - 29°).

^{1}H n.m.r. τ ($CDCl_3$), 2.8 - 3.3 (m., 1H), 3.26 (t., 1H J = 2.5 Hz.), 3.82 (d., J = 2.5 Hz.) and 6.45 (d., 3H, J = 1.5 Hz.);

ν_{max} 3106, 2956, 1626, 1557, 1516, 1492, 1460, 1350, 1290, 1200, 1182, 1085, 893, 818, and 718 cm.$^{-1}$.

33. Isomerisation of 1,2,3,4-tetrachloro-5,8-dihydro-5,8-(N-methylamino)-naphthalene (17) X=Cl

A similar method to that used in experiment 32 gave 2'-(2,3,4,5-tetrachlorophenyl)-N-methylpyrrole (81%); m.p. 99 - 101° (after sublimation).

^{1}H n.m.r. τ ($CDCl_3$) 2.58 (s., 1H); 3.25 (t., 1H, J = 2.8), 4.7 - 4.9 (m., 2H), and 6.54 (s., 3H);

ν_{max}^{KBr} 3085, 2940, 1484, 1400, 1340, 1305, 1250, 1185, 900, 810, 730, and 650 cm.$^{-1}$;

$\lambda_{max}^{Ethanol}$ 210 (ϵ 37,600) and 305 (6400) n.m..

Attempted isomerisation of compound (17) X=Cl in either boiling aqueous ethanol or benzene at 160° in a sealed tube gave only starting material.

34. Isomerisation of 1,2,3,4-tetrafluoro-5,8-dihydro-5,8-(N-methylimino)-naphthalene in aqueous ethanol.

The compound (17) X=F (150 mg.) in ethanol (6.5 ml.) and water (1 ml.) was heated under reflux for 48 hr.. Evaporation under reduced pressure gave 2'-(2,3,4,5-tetrafluorophenyl)-N-methylpyrrole (38), (160 mg., 80%) having identical spectroscopic data to the previously prepared material (experiment 32).

35. Isomerisation of compound (17) X=F in the presence of deuterium oxide.

The compound (17) X=F (200 mg.) in dry diglyme (10 ml.) and deuterium oxide (1 ml.) was heated under reflux for 18 hr.. Removal

of the solvents followed by preparative t.l.c. gave 2'-(2-[^{2}H]-3,4,5,6-tetrafluorophenyl)-N-methylpyrrole (110 mg., 55%).

^{1}H n.m.r. τ (CCl_4) 3.3 - 3.4 (m., 1H), 3.8 - 4.0 (m., 2H) and 6.45 (d., 3H, J = 1.5 Hz.).

Mass spectrometry: M^+ 230, 99% d_1.

2'-(2,3,4,5-tetrafluorophenyl)-N-methylpyrrole (43 mg.) in glyme (3 ml.) /deuterium oxide (0.3 ml.) was heated under reflux for 20 hr.. Work up gave undeuterated starting material as shown by ^{1}H n.m.r. and mass spectrometry.

36. Isomerisation of compound (17) X=F in d_6 benzene.

The compound (60 mg.) in degassed benzene (0.5 ml., 99.5% d_6) was heated in a sealed tube at 160° for 18 hr..

The reaction mixture was cooled, solvent removed and the remaining dark brown oil subjected to preparative t.l.c. and gave 2'-(2,3,4,5-tetrafluorophenyl)-N-methylpyrrole (38) (36 mg., 58%), ^{1}H n.m.r. and mass spectrometry showed no incorporation of deuterium.

37. Reaction of N-methylpyrrole with tetrafluoroaniline in the presence of amyl nitrite.

Tetrafluoroaniline (830 mg., 0.005 mole) was dissolved in carbon tetrachloride (50 ml.) and to this solution was added N-methylpyrrole (6.5 g., 0.08 mole), isoamyl nitrite (1 ml., 0.0075 mole) and acetic anhydrode (1.55 g., 0.015 mole). The mixture was heated under reflux for 1 hr., cooled, then stirred at room temperature for 3 hr.. The solvent and the excess starting materials were removed by distillation under reduced pressure and gave an oil which was eluted (light petroleum b.p. 60-80°) through a column of alumina. The products in order of elution were a) 2'-(2,3,4,5-tetrafluorophenyl)-N-methylpyrrole (38) (155 mg., 14%), which was identical to the previously prepared material by

^{1}H n.m.r., i.r. spectroscopy and t.l.c., b) 2'-(2,3,4,5-tetrafluorobenzeneazo)-N^1-methylpyrrole (39), (480 mg., 40%);

m.p. 95 - 96° (yellow needles from hexane);

(Found: C, 51.15; H, 2.9; N, 16.35%; M. [mass spectrometry] 257;

$C_{11}H_7F_4N_3$ requires C, 51.35; H, 2.75; N, 16.35%; M. 257);

^{1}H n.m.r. τ (CCl_4), 2.4 - 2.9 (m., 1H), 3.0 - 3.15 (m., 1H), 3.23 (q., 1H, J_{23} = 4.5 Hz., J_{24} = 1 Hz.), 3.75 (q., 1H, J_{32} = 4.5 Hz., J_{34} = 3 Hz.), and 6.06 (s., 3H);

ν_{max}^{KBr} 3127, 3100, 2960, 2935, 2860, 1631, 1500, 1483, 1380, 1325, 1245, 1175, 1110, 1050, 1040, 960, 908, 862, 730, and 713 cm.$^{-1}$.

$\lambda_{max}^{Ethanol}$ 350 sh. (ϵ 9,000); 398 (17,000) n.m..

38. Reaction of tetrafluorobenzyne with 1,2,5-trimethylpyrrole.

By an identical method to that used by Coe[15] gave a black tarry product which was distilled and gave at 80-85° 1 m.m. 5,8-dimethyl-1,2,3,4-tetrafluoro-5,8-dihydro-5,8-(N-methylimino)naphthalene (42), (.8 g., 6%); m.p. 54° (from hexane);

^{1}H n.m.r. τ ($CDCl_3$) 3.25 (s., 2H); 7.96 (s., 3H); and 8.23 (broad s., 6H);

ν_{max}^{KBr} 2990, 2980, 2960, 2880, 2800, 1490, 1385, 1320, 1195, 1150, 1100, 1020, 880, 785, and 720 cm.$^{-1}$.

Mass Spectrometry: M^+ = 257.

The compound was unstable and showed signs of decomposition even at -20° in a nitrogen atmosphere. At 85 - 120° 1 m.m. gave a mixture of products which were separated by preparative t.l.c. using chloroform as eluant and gave a) 5α-hydroxy-8β-N-methylamino-5,8-dihydro-5,8-dimethyl-1,2,3,4-tetrafluoronaphthalene (44), (810 mg., 6%);

m.p. 156 - 158° (from methanol);

(Found: C, 56.55; H, 4.75; N, 5.15%, M. [mass spectrometry] 275,

$C_{13}H_{13}F_4NO$ C, 56.75; H, 4.75; N, 5.1%; M. 275);

^1H n.m.r. τ ($CDCl_3$) 4.1 (d., 1H, J = 4.5 H .);

4.75 (d., 1H, J = 4.5 Hz.); 7.5 (broad s., 2H); 8.11

(broad s., 6H); and 8.4 (d., 3H), J = 1 Hz.).

υ_{max} 3600, 3400, 2990, 2950, 2810, 1650, 1515, 1490, 1455, 1370,

1120, 1040, 1000, 985, and 860 $cm.^{-1}$.

b) 5α-hydroxy -8α-N-methylamino-5,8-dihydro-5,8-dimethyl-1,2,3,4-tetrafluoronaphthalene (43) (720 mg., 5%);

m.p. 123 - 127° (from hexane),

^1H n.m.r. τ ($CDCl_3$) 4.0 - 4.2 (m., 1H); 4.7 - 4.9 (m., 1H);

7.8 - 8.4 (m., 2H); 8.0 (s., 3H); 8.1 (m., 3H);

and 8.5 (d., 3H, J = 1.5 Hz.);

υ_{max} 3350 broad, 2950, 2800, 1650, 1515, 1490, 1460, 1450, 1370,

1290, 1120, 1045, 1000, 905, and 750 $cm.^{-1}$.

Mass Spectrometry: $M.^+$ 275.

CHAPTER 3

The preparation of some Isoindoles and

Isobenzofurans by a retro-Diels-Alder reaction

Introduction

Isoindoles[97,98] and isobenzofurans[99] have been the subjects of considerable interest both from their theoretical and synthetic points of view.

Although substituted isoindoles[100] and isobenzofurans[101] have been known for some time the parent isoindole[102] and isobenzofuran[103] have only been prepared recently. Isoindole[104] has been observed previously in the base catalysed decomposition of N-benzyloxyisoindoline and was characterised by trapping with dienophiles. Likewise, isobenzofuran[105-108] has been demonstrated to be a transient intermediate.

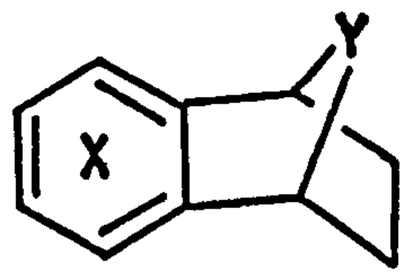
Many theoretical calculations have been performed on the unstable isoconjugate isomers of the stable indole and benzofuran species with considerable variation in the results. The most recent calculations[109] appear to give the best correlation with experimental observations. Dewar has calculated,[109] using a semiempirical SCF-MO π approximation method, that isoindole with a resonance energy of 11.6 K.cal./$_{mole}$ is much less stable than indole at 23.8 K.cal./$_{mole}$, and that isobenzofuran with a resonance energy of 2.4 K.cal./$_{mole}$ is practically devoid of aromatic character and resembles a polyene.

Both isoindoles and isobenzofurans are highly reactive species, particularly so when the 1,3-positions are unsubstituted. Fairly stable isoindoles where the 1,2,3-positions are unsubstituted are known, dibenz[e,g]isoindole[110] and benz[e]isoindole,[111] although these are the only two examples.

Many of the early methods of preparation of isoindoles and isobenzofurans suffered from the instabilities of the products as they tended to oxidise or polymerise. The use of flash vacuum pyrolysis eliminates many of the difficulties encountered in other pyrolytic or "wet chemical" methods.

Discussion

Interest has been shown recently in the apparent similarities between mass spectra, thermal, and photochemical processes.[112-114] We were encouraged therefore to investigate a group of compounds of the general structure (1) which showed a base peak in their mass spectra at $[M - 28]^+$.



(1)

High resolution mass spectrometry showed that the loss of 28 from the molecular ion was due to the loss of a molecule of ethylene (table 1).

Table 1

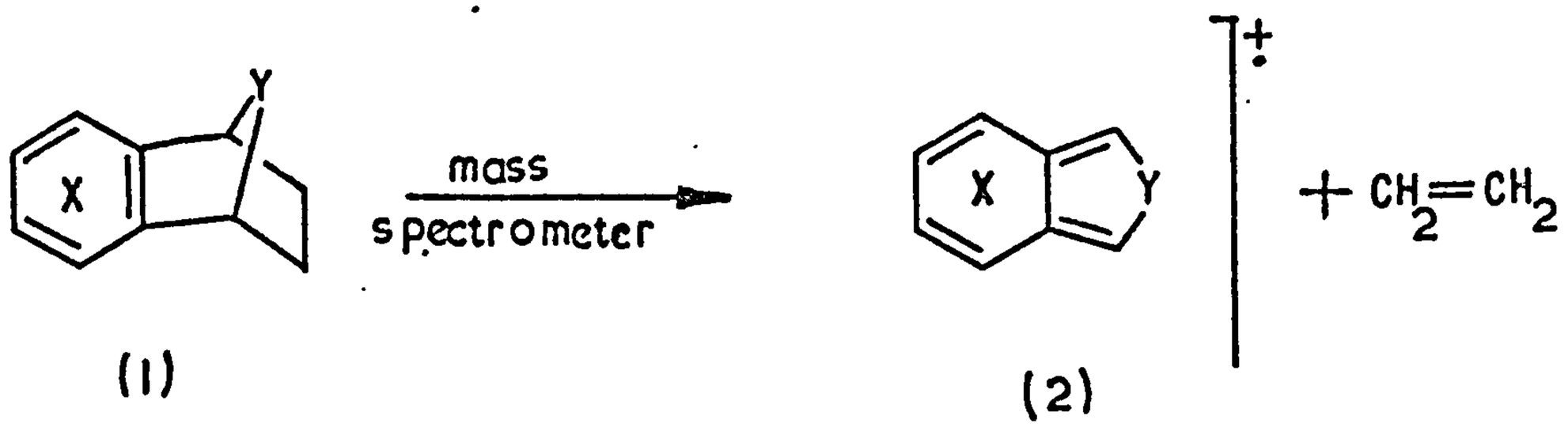
Precise mass measurement by high resolution mass spectrometry

Compound	Molecular ion M^+			M - 28		
	Formula	Calculated	Measured	Formula	Calculated	Measured
(1) X=F, Y=NMe_2	$C_{11}H_9F_4N$	231.0671	231.0667	$C_9H_5F_4N$	203.0358	203.0358
(1) X=F, Y=$>C=CMe_2$[115]	$C_{14}H_{12}F_4$	256.0876	256.0878	$C_{12}H_8F_4$	228.0562	228.0561
*(1) X=F, Y=$>C=O$[115]	No Molecular ion			$C_{10}H_6F_4$	202.0405	202.407
(1) X=F, Y=O	$C_{10}H_6F_4O$	218.0355	218.0356	$C_8H_2F_4O$	190.0042	190.0042
(1) X=Cl, Y=O	$C_{10}H_6Cl_4O$	281.9173	281.9181	$C_8H_2Cl_4O$	253.8860	253.8867

*Compound (1) X=F, Y=$>C=O$ M-28 corresponds to loss of CO.

◊ The measured masses of these ions are for ^{35}Cl.

This suggests that the molecular ions of the compounds (1), in the mass spectrometer, were undergoing a retro-Diels-Alder reaction to give ions corresponding to the isobenzo-derivatives (2).



(1) (2)

If this retro-Diels-Alder reaction could be imitated in the laboratory by pyrolytic techniques a source of interesting compounds would be available.

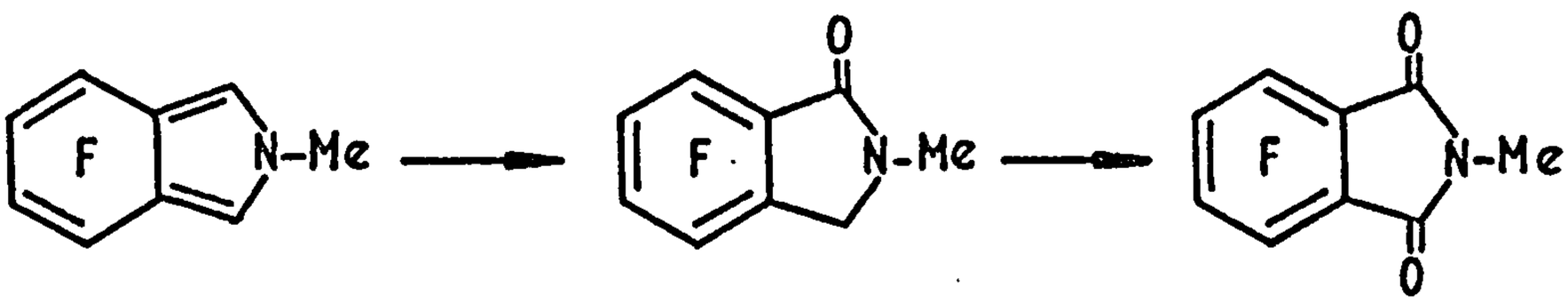
The compounds that were chosen for study initially, were those in which the X group was a halogen. The reason being that tetrahalo-compounds often show an increased stability compared with the non-halogenated species. For example tetrahalogeno-o-benzoquinones are much more stable than o-benzoquinone.[116]

When the compound (1) X=F, Y=N-Me, was heated in degassed aqueous ethanol, or benzene at 120° for 1 week a good yield of N-methyl-4,5,6-tetrafluoro isoindole, compound (2) X=F Y=N-Me, was obtained. This compound was remarkably stable and an analysis for $C_9H_5F_4N$ was obtained. The tetrachloro analogue also shows similar stability.[117] The stability may be due to a "push-pull" effect where the nitrogen at one end of the molecule has a tendency to donate electrons into the system which are withdrawn by fluorine atoms at the other end of the molecule.

The ^1H n.m.r. spectrum of compound (2) X=F,Y=NMe showed resonances

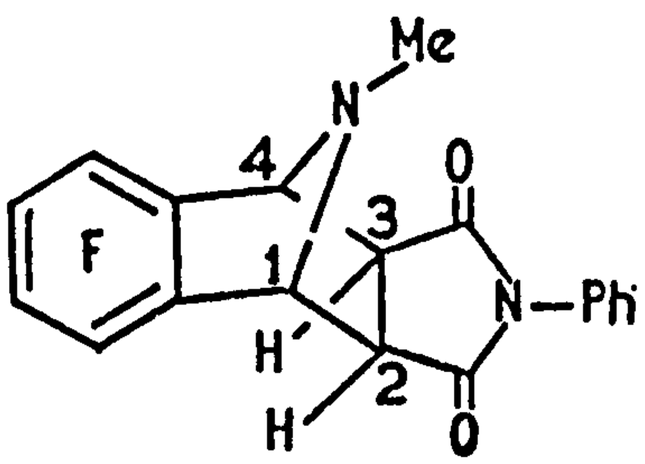
at τ 2.65 as a triplet, (2H, J_{HF} = 1 Hz.), which was assigned to the heterocyclic ring protons, and a singlet at τ 6.0 (3H), due to the N-methyl group. The i.r. spectrum showed absorptions at 3160 cm.$^{-1}$ (m), assigned to the isoindole C-H stretching mode; 1590 cm.$^{-1}$ due to olefinic double bond vibrations, and at 1510 and 1480 cm.$^{-1}$ are the absorptions due to fluorinated aromatic nucleus.

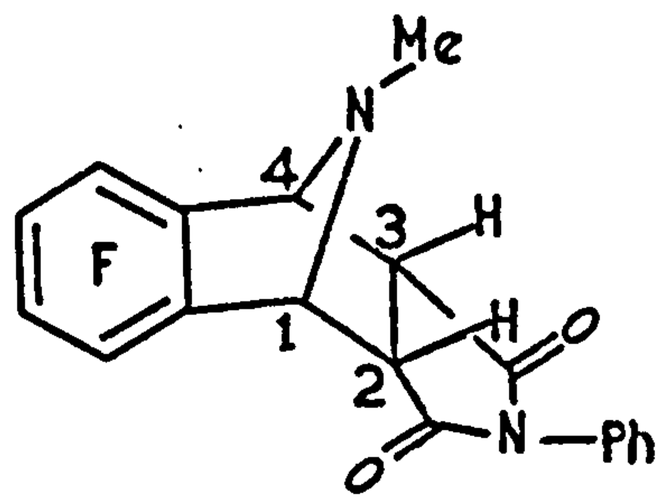
The isoindole (2), X=F, Y=NMe, was oxidised with potassium permanganate in acetone and gave the N-methyl-tetrafluorophthalimide (3). The phthalimide (3) was compared with an authentic sample prepared by the reaction of tetrafluorophthalic acid with methylamine. In oxygenated solution isoindole (2) X=F, Y=NMe, tends to be slowly oxidised to the phthalimide (3). This reaction can be catalysed by the addition of a trace of p-toluenesulphonic acid. The intermediate in the oxidation was the phthalimidine (3) but a sample of this could not be isolated in a pure form. Phthalimidines are expected as intermediates in the autoxidation of isoindoles.[118]



(3) (4)

The isoindole (2), X=F,Y=NMe, formed the expected adducts with N-phenyl maleimide reversibly at 120° in the ratio exo (5) : endo (6) of 1:1.





(5) (6)

The assignment of the stereochemistry of the 2 adducts follows from their ^{1}H n.m.r. spectra (table 2). The essential features of the ^{1}H n.m.r. spectra which led to the assignments are, firstly: spin-spin coupling between the two bridgehead protons on carbon atoms 1, (4) and 2, (3) for the exo case where the dihedral angle is $\simeq 90^{\circ}$ shows no coupling and the proton on C-2, (C-3) resonates as a singlet, the proton on C-1, (C-4) resonates as a broadened singlet owing to some fine coupling with the aromatic fluorine atoms. For the endo isomer, the dihedral angle is $\simeq 25^{\circ}$ and the protons on C-1, (C-4) and C-2,(C-3) resonate as multiplets. The protons on C-2, (C-3) in the exo isomer resonate at higher field than the protons in the endo isomer due to anisotropic shielding by the tetrafluoroaryl ring. Another characteristic feature of the endo isomer is the aromatic protons ortho to the nitrogen atom, resonate at higher field than do the remaining three aromatic protons. This can be attributed to anisotropic shielding by the tetrafluoroaryl group, fig. 1.

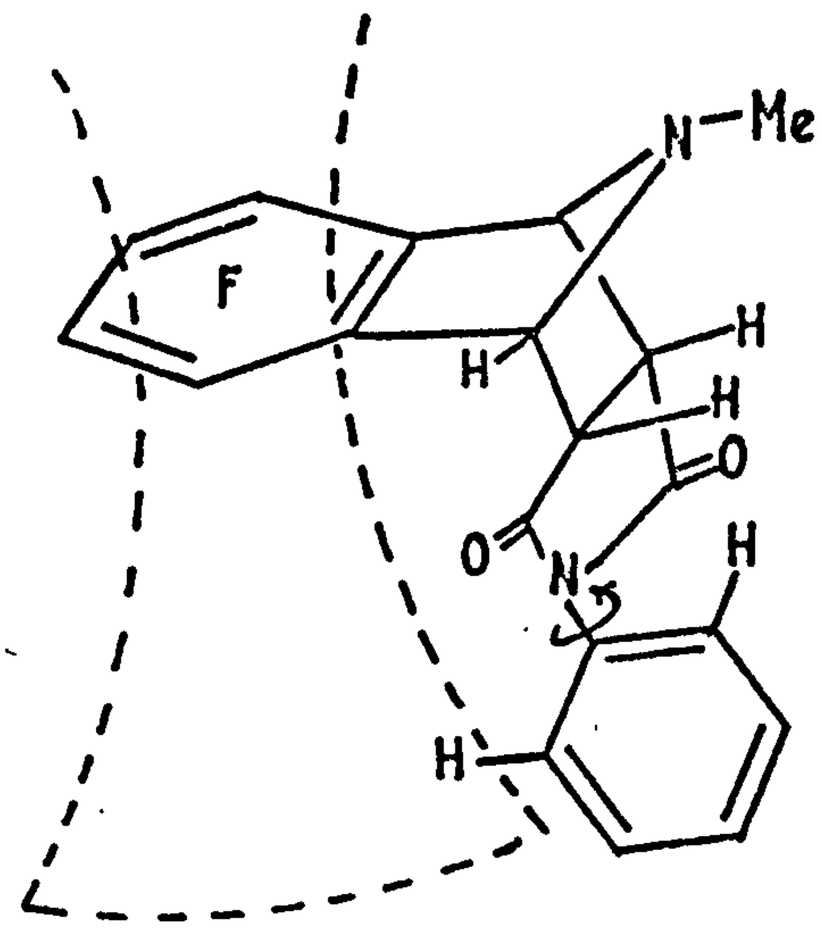


fig. I

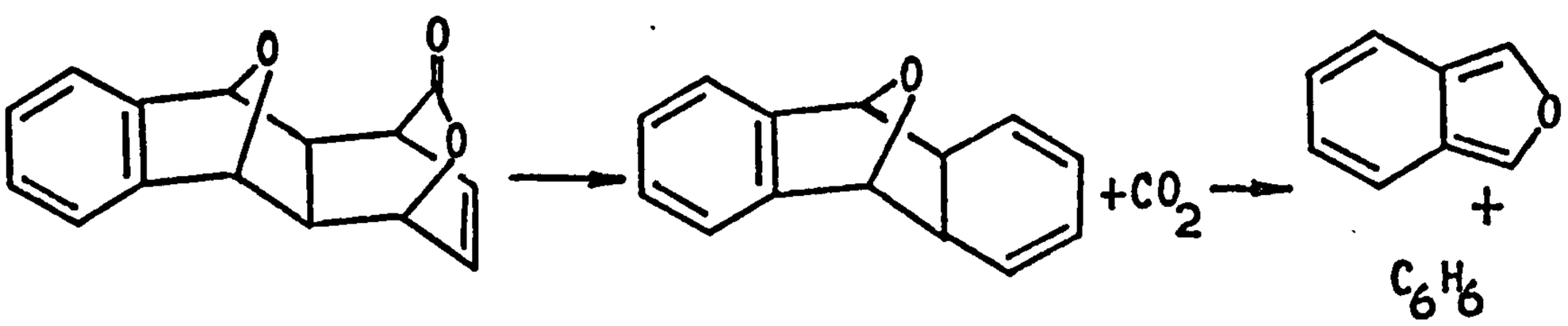
The high field shift of two aromatic protons in N-phenyl maleimide endo adducts has been observed in other examples.[119, 120] Although in one case[119] it was thought that these high field protons were due to two protons on the other aromatic ring; this cannot be the case in our example as there are only fluorine atoms in the other aromatic ring.

Table 2

Compound	Aromatic protons τ	C_1/C_4 methines τ	C_2/C_3 methines τ	N-Methyl τ
(5) exo	2.35-3.8; (5H)	5.16,(t),(2H) J_{HF}=1 Hz.	7.08(s) (2H)	7.94(s) (3H)
(6) endo	2.5-3.8;3.2-3.5; (3H) (2H)	5.0-5.2(m); (2H)	6.0-6.2(m); (2H)	7.85(s) (3H)
(10) exo	2.4-2.8; (5H)	3.9 broad (s) (2H)	6.79(s) (2H)	
(11) endo	2.5-2.8;3.25-3.45 (3H) (2H)	3.85-4.05(m) (2H)	6.0-6.15(m) (2H)	

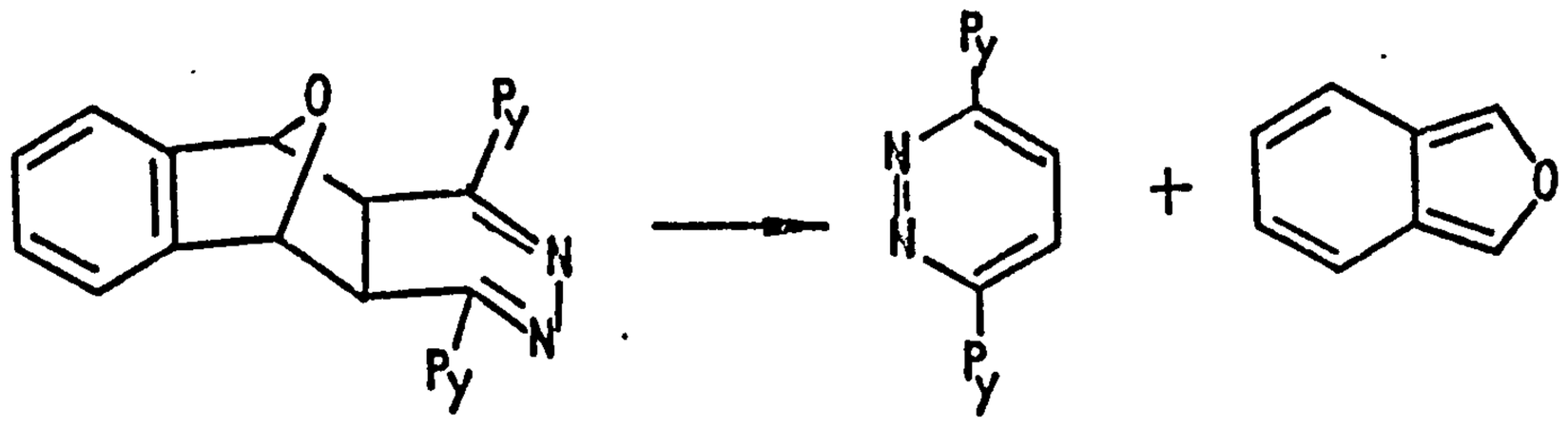
When the compound (1) X=F, Y=O, was heated at 120° in a solvent in a sealed tube no retro-Diels-Alder reaction occurred. The loss of ethylene from this compound was more difficult therefore than in the case where X=F, Y=NMe. However, when the compound was flash vacuum pyrolysed over a heated Nichrome wire at ca. 500° and 1.5 m.m. of mercury, an essentially quantitative yield of 4,5,6,7-tetrafluoroisobenzofuran was obtained. The ^{1}H n.m.r. spectrum showed a resonance at τ 1.85 as a triplet (J_{HF} = 1.5 Hz.). I.r. spectroscopy showed absorptions at 3170 cm.$^{-1}$ (s) due to the furanoid C-H vibrations, at 1600 cm.$^{-1}$ (s) due to the C=C stretching modes, and at 1515 cm.$^{-1}$ and 1500 cm.$^{-1}$ due to the fluorinated aromatic system.

Retro-Diels-Alder reactions are in common usage in chemical synthesis.[121] Most retro-Diels-Alder reactions involve pyrolytic techniques which can often cause some degradation of the products. The elegant work of both Wege and Warrener use very mild retro-Diels-Alder reactions and have successfully isolated the elusive parent isobenzofuran.[103] Wege's method[103a] involves pyrolysis of the compound (7) at 130°, the products of the reaction being carbon dioxide, benzene, and isobenzofuran.



(7)

Warrener[103b] decomposes the dihydropyridazine derivative (8) at 120° under reduced pressure to give the involatile pyridazine (9) and isobenzofuran.



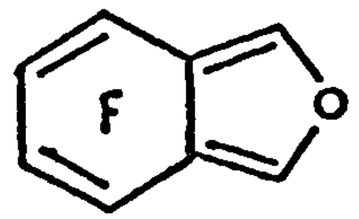
(8) (9)

The use of flash vacuum pyrolysis eliminates most of the problems of product decomposition associated with high temperature pyrolytic methods.

Simultaneously with our work on retro-Diels-Alder-reactions with elimination of ethylene, Wiersum has studied the loss of ethylene from the compound (1) X=H,Y=O to give isobenzofuran.[122] His results are essentially the same as our own.

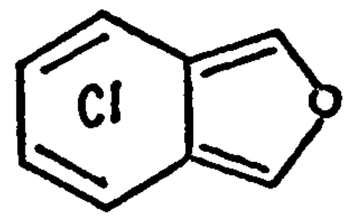
We have reacted the 4,5,6,7-tetrafluoroisobenzofuran with N-phenyl maleimide in benzene at room temperature which gives the exo (10) and endo (11) adducts in the ratio 1:2. The structures of these adducts were assigned on the basis of their ^{1}H n.m.r. spectra, table 2. In an attempt to study the stability of the tetrafluoroisobenzofuran,(2) X=F,Y=O other analogues have been prepared by flash vacuum pyrolysis. The decomposition of the compounds (2) X=F, Cl, H; Y=O was studied by ^{1}H n.m.r. spectroscopy by observing the reduction in area of the furanoid proton resonance absorptions. (X=F, Y=O graph 1; X =Cl, Y=O graph 2; X≐F, Y=O graph 3). A comparison of the compounds when the areas had reached half their original intensity,shows that the tetrafluorinated analogue was approximately 6 times as stable as the tetrachloro compound and had approximately 140 times the stability of isobenzofuran itself. These results together with related retro-Diels-Alder reactions have been presented in a preliminary communication.[123]

graph I (at room temperature)



100mg. in 0·5ml. $CDCl_3$
(internal STD. $CHCl_3$)

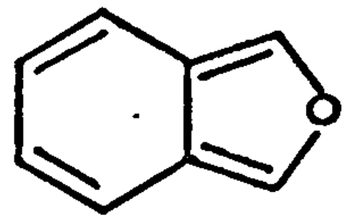
graph 2 (at room temperature)



25 mg. in 0·5 ml. $CDCl_3$

(internal STD. $CHCl_3$)

graph 3 (at Ca. 32°)



40 mg. in 0·5 ml. $CDCl_3$

(internal STD. CH_3CN)

Experimental

The general procedures are the same as those in chapter 1 p. 26.

1. Hydrogenation of 1,2,3,4-tetrafluoro-5,8-dihydro-5,8-(N-methylimino)-naphthalene.

Hydrogenation in the usual manner gave 1,2,3,4-tetrafluoro-5,6,7,8-tetrahydro-5,8-N-methyliminonaphthalene (1) X=F, Y=NMe, (100%); m.p. 81-80° (after sublimation);

^{1}H n.m.r. τ (CCl_4) 5.55 - 3.8 (m., 2H); 8.0 (s., 3H); 7.7 - 8.1 (m., 2H), and 8.6 - 9.0 (m., 2H);

$\nu_{max}^{CHCl_3}$ 2960, 2880, 2800, 1500, 1485, 1380, 1290, 1260, 1115, 1092, 1035, 950, 890, and 810 cm.$^{-1}$.

Molecular weight by high resolution mass spectrometry:

M.	$C_{11}H_9F_4N$	calculated	231.0671
		measured	231.0667
M-28	$C_9H_5F_4N$	calculated	203.358
		measured	203.358

Metastable for the transition 231→203

m^* = 174.4

2. Hydrogenation of 1,2,3,4-tetrafluoro-5,8-dihydro-5,8-epoxynaphthalene.

Hydrogenation in the usual manner gave 1,2,3,4-tetrafluoro-5,6,7,8-tetrahydro-5,8-epoxynaphthalene, (1) X=F, Y=O; m.p. 73 - 74°, (lit.[124] m.p. 74°),

^{1}H n.m.r. τ (CCl_4) 4.25 - 4.55 (m., 2H), and 7.7 - 8.8 (m., 4H);

ν_{max}^{KBr} 3020, 2975, 2890, 1500, 1400, 1390, 1305, 1270, 1140, 1080, 1040, 1010, 955, 920, and 810 cm.$^{-1}$.

Molecular weight by high resolution mass spectrometry:

M.	$C_{10}H_6F_4O$	calculated	218.0355
		measured	218.0356

M-28 $C_8H_2F_4O$ calculated 190.0042

measured 190.0044

Metastable for the transition 218 → 190

m^* = 165.5

3. Hydrogenation of 1,2,3,4-tetrachloro-5,8-dihydro-5,8-epoxy-naphthalene.

Hydrogenation in the usual manner gave 1,2,3,4-tetrachloro-tetrahydro-5,8-epoxy-naphthalene, (1) X=Cl, Y=O; m.p. 135 - 136° (from methanol),

^{1}H n.m.r. τ ($CDCl_3$) 4.25 - 4.6 (m., 2H); 7.6 - 8.8 (m., 4H).

ν_{max}^{KBr} 3020, 2970, 2880, 1465, 1450, 1370, 1315, 1285, 1210, 1150, 1000, 960, 910, 880, 815, 760, 720, and 690 cm.$^{-1}$.

4. Hydrogenation of 1,4-dihydro-1,4-epoxy-naphthalene.

Hydrogenation in the usual manner gave tetrahydro-1,4-epoxy-naphthalene, X=F, Y=O; oil, (lit.[125] b.p. 54° at 4 torr),

^{1}H n.m.r. τ ($CDCl_3$) 2.6 - 3.0 (m., 4H), 4.5 - 4.7 (m., 2H), and 7.7 - 8.9 (m., 4H).

5. Pyrolysis of compound (1) X=F, Y=NMe in aqueous ethanol.

The compound (1) X=F, Y=NMe (300 mg.) in degassed aqueous ethanol (5 ml., 25%) was heated in a sealed tube at 120° for 160 hr.. The mixture was cooled to 0° and gave N-methyltetrafluoroisoindole (2) X=F, Y=NMe (213 mg., 82%);

m.p. 152 - 154° (after sublimation).

(Found: C, 53.1; H, 2.7; N, 6.95%; M.[mass spectrometry] 203., $C_9H_5F_4N$ requires C, 53.2; H, 2.5; N, 6.9%; M. 203);

^{1}H n.m.r. τ (CCl_4) 2.65 (t., 2H, J_{HF} = 1 Hz.) and 6.0 (s., 3H).

ν_{max}^{KBr} 3160, 2975, 1590, 1570, 1510, 1480, 1390, 1355, 1205, 1015, 990, 795, and 740 cm.$^{-1}$,

λ_{max}^{EtOH} 255 (ϵ 1830); 300 sh. (4300); 311 (5200); and 322 sh. (4020) n.m..

The product gave a positiveEhrlich test.

6. Pyrolysis of compound (1) X=F, Y=NMe in in benzene.

The compound (1) X=F, Y=NMe, (50 mg.) in degassed benzene (1 ml.) was heated in a sealed tube at 120° for 1 week. Removal of the solvent gave N-methyltetrafluoroisoindole (43 mg., 99%) identical by its spectral data to the previously prepared compound.

The N-methyltetrafluorophthalimidine was detected by ^{1}H n.m.r. spectrometry τ ($CDCl_3$) 5.58 (broad s., 2H); 6.85 (s., 3H), and by i.r. spectroscopy ν_{max} 2930, 2860, 1718, 1515, 1500, 1400, 1315, 1150, 1145, 975, and 835 cm.$^{-1}$, but could not be obtained pure.

---

7. Pyrolysis of the compound (1) X=F, Y=NMe in benzene in the presence of N-phenyl maleimide.

The compound (1) X=F, Y=NMe, (100 mg.) in degassed benzene (1.5 ml.), N-phenyl maleimide (80 mg.) was heated in a sealed tube at 120° for 2 weeks, cooled and left at room temperature for 1 week. Removal of solvent gave a solid which was separated by preparative t.l.c. using chloroform as eluant and gave

1) exo-adduct (5), (103 mg., 67%) m.p. 220 - 222° (from methanol). (Found: C, 60.35; H, 3.35; N, 7.55, $C_{19}H_{12}F_4N_2O_2$ requires C,60.6; H, 3.2; N, 7.45%);

^{1}H n.m.r. τ ($CDCl_3$) 2.35 - 2.8 (m., 5H); 5.16 (m., 2H, J_{HF}= 1 Hz.); 7.08 (s., 2H), and 7.94 (s., 3H);

ν_{max}^{KBr} 3085, 2970, 2880, 2860, 2805, 1785, 1720, 1600, 1505, 1485, 1390, 1280, 1200, 1120, 1060, 980, 805, 755, 735, and 690 cm.$^{-1}$,

2) endo-adduct (6) (36 mg., 23%) m.p. 144 - 145° (from methanol). (Found: C, 60.5; H, 3.3; N, 7.35, $C_{19}H_{12}F_4N_2O_2$ requires C, 60.6; H, 3.25; N, 7.45%);

^{1}H n.m.r. τ ($CDCl_3$) 2.5 - 2.8 (m., 3H); 3.2 - 3.5 (m., 2H); 5.0 - 5.2 (m., 2H); 6.0 - 6.2 (m., 2H); and 7.85 (s., 3H); $\upsilon_{max}^{CHCl_3}$ 2960, 2930, 2880, 2865, 2805, 1790, 1725, 1605, 1500, 1380, 1300, 1180, 1130, 1070, 1020, 950, and 915 cm.$^{-1}$.

8. Reaction of N-methyltetrafluoroisoindole with N-phenyl maleimide.

The isoindole (2) X=F, Y=NMe, (10 mg.) in benzene (0.5 ml.) containing N-phenylmaleimide (8.5 mg.) was heated in a sealed tube at 120° for 1 week. The mixture was cooled, solvent removed, and the products separated by preparative t.l.c..

1) Exo-adduct, (5) (7.2 mg., 43%)
m.p. 222 - 223° mixed m.p. 222° identical by t.l.c., and i.r.spectroscopy to authentic material.

2) Endo-adduct, (6) (7.2 mg., 43%)
m.p. 142 - 144° mixed m.p. 141 - 145° identical by t.l.c., and i.r. spectroscopy to authentic material.

9. Isomerisation of N-phenyl maleimide/N-methyltetrafluoroisoindole exo adduct (5).

The adduct (5) (20 mg.) was heated in a sealed tube in degassed benzene (0.5 ml.) at 120° for 5 days. Isolation of the products gave ratio of exo to endo adducts 9 mg.: 8 mg.

10. Isomerisation of endo adduct (6).

By a similar experiment gave the ratio of exo to endo adducts as 1:1.

11. Preparation of N-methyltetrafluorophthalimide (4).

Tetrafluorophthalic acid (1.8 g.) was heated under reflux in aqueous methylamine (50 ml., 25%) for 3 hr.. Excess water and methylamine were removed by distillation and the temperature was raised to 240°. The yellow solid which formed on cooling was placed on a column of silica, eluted with benzene and gave N-methyltetrafluorophthalimide, (4) (520 mg., 32%); m.p. 154 - 156° (sealed tube) (lit.[84] m.p. 155°).

^{1}H n.m.r. τ ($CDCl_3$) 6.81 (s., 3H).

$\upsilon_{max}^{CHCl_3}$ 2935, 2860, 1790, 1770, 1730, 1500, 1440, 1395, 1375, 1315, 1160, 1005, and 940 cm.$^{-1}$.

12. Oxidation of N-methyltetrafluoroisoindole.

The isoindole (2) X=F, Y=NMe, (10 mg.) was dissolved in acetone (0.5 ml.) and acetone saturated with potassium permanganate was added dropwise until the pink colour remained for 1 hr.. The precipitated manganese dioxide was removed after 48 hr. at room temperature. Removal of the solvent gave, after recrystallisation from methanol, N-methyltetrafluorophthalimide (4), (6 mg., 53%), m.p. 152 - 154°, mixed m.p. 152 - 154°; i.r. spectrum and t.l.c. data were identical with authentic material.

13. Pyrolysis of 1,2,3,5-tetrafluorotetrahydro-5,8-epoxy-naphthalene.

The compound (1) X=F, Y=O (500 mg.) was passed over a heated nichrome wire (500°) under a vacuum of 1.5 mm. of mercury in a flow pyrolysis system.[30] The product was collected on a liquid nitrogen cold finger and gave 4,5,6,7-tetrafluoroisobenzofuran (430 mg., 99%); m.p. 40-42°;

^{1}H n.m.r. τ (CCl_4) 1.85 (t., J_{HF} = 1.5 Hz.),

υ_{max} 3170, 1710, 1600, 1530, 1515, 1500, 1430, 1415, 1370, 1050, 1010, and 870 cm.$^{-1}$,

$\lambda_{max}^{Ethanol}$ 236 sh. (ϵ 1100); 300 (3980); 313 (5010); and 325 sh. (3360) n.m..

14. Pyrolysis of 1,2,3,4-tetrachloro-5,6,7,8-tetrahydro-5,8-epoxy-naphthalene.

By a similar pyrolysis reaction to experiment 13 gave 4,5,6,7-tetrachloroisobenzofuran (77%) m.p. 115 - 120°

^{1}H n.m.r. τ ($CDCl_3$), 1.88 (s.,);

ν_{max} 3160, 2930, 1625, 1535, 1508, 1430, 1392, 1320, 1290, 1275, 1205, 1050, 985, 870, 795, 775, 750, and 650 cm.$^{-1}$,

$\lambda_{max}^{ethanol}$ 250 (ϵ 3680); 332 (4170); 344 (5550); and 355 (4220) n.m..

15. Pyrolysis of 1,4-epoxy-1,2,3,4-tetrahydronaphthalene.

Gave isobenzofuran (100%) m.p. 22 - 25° (lit.[103] m.p. ca. 20°)

^{1}H n.m.r. τ($CDCl_3$) 2.0 (s., 2H); 2.4 - 2.75 (m., 2H), and 3.0 - 3.3 (m., 2H).

$\nu_{max}^{CHCl_3}$ 3080, 3020, 2880, 1615, 1480, 1475, 1370, 1230, 1020, 887, and 700 cm.$^{-1}$.

16. Reaction of tetrafluoroisobenzofuran with N-phenyl maleimide.

The isobenzofuran (2) X=F, Y=O, (.25 g.) in benzene (3 ml.) was added to a solution of N-phenyl maleimide (.25 g.) in benzene (3 ml.). Crystals began to separate from the mixture after 1 min.. Removal of the solvent after 12 hr. gave a white solid which was separated by preparative t.l.c. and gave

1) Exo-adduct (10) (108 mg., 23%) m.p. 265 - 270°

(from chloroform),

^{1}H n.m.r. * τ($CDCl_3$) 2.4 - 2.8 (m., 5H); 3.9 (s., 2H); and 6.79 (s.,2H).

ν_{max}^{KBr} 3020, 1720, 1500, 1385, 1290, 1190, 1175, 1135, 1075, 965, 875, 800, 760, and 698 cm.$^{-1}$.

Molecular weight by high resolution mass spectrometry:-

	M^+	$M-173]^+$
Measured mass :	363.0535	190.0040
Expected formula:	$C_{18}H_9F_4NO_3$	$C_8H_2F_4O$
Calculated Mass:	363.0518	190.0042

* We thank P.C.M.U. for recording this spectrum at 100 M. Hz..

2) <u>Endo-adduct</u> (11), (220 mg., 47%),

m.p. 243 - 243.5° (from methanol);

(Found: C,59.25; H, 2.45; N,3.8; $C_{18}H_9F_4NO_3$ requires C, 59.3;

H, 2.15; N, 3.3%);

^{1}H n.m.r. τ($CDCl_3$) 2.5 - 2.8 (m., 3H); 3.25 - 3.45 (m., 2H);

3.85 - 4.05 (m., 2H); and 6.0 - 6.15 (m., 2H);

ν_{max}^{KBr} 3010, 1720, 1500, 1380, 1315, 1280, 1080, 970, 960, 920, 910,

900, 860, 815, 730, and 685 cm.$^{-1}$.

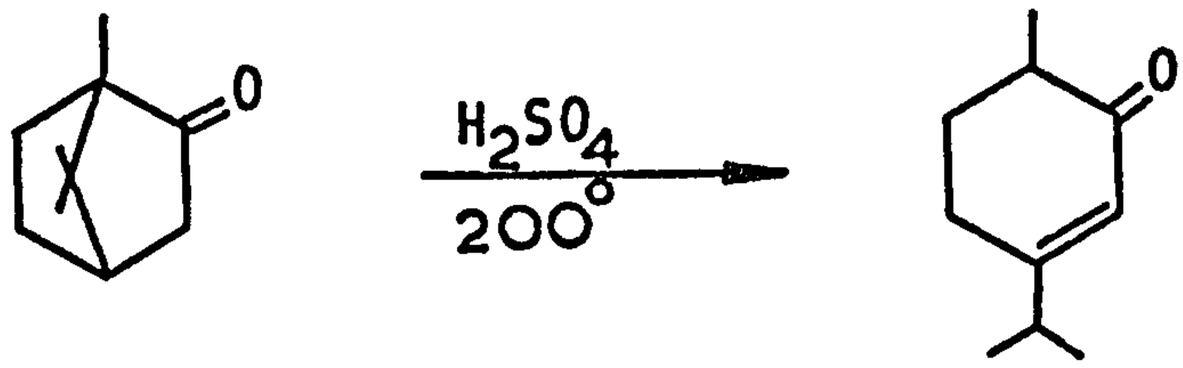
CHAPTER 4

Multiple Rearrangements of 1-Methoxybenzobarrelene

Derivatives

Introduction

The rearrangement of camphor to carvenone was initially studied about one hundred and thirty years ago,[127] although it was not until much later that it was fully understood.[128]

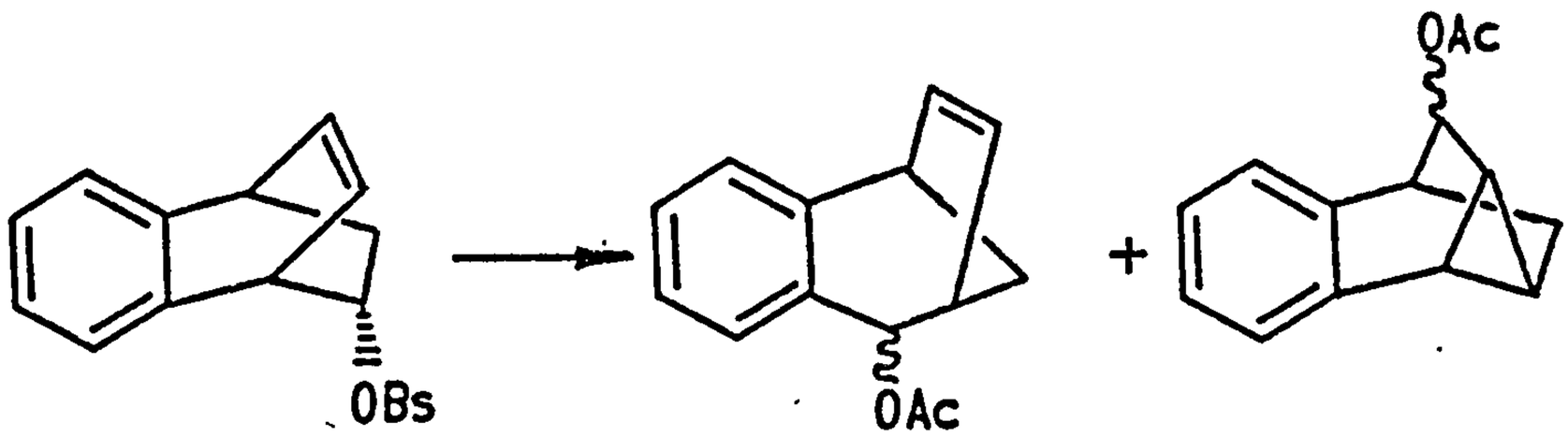


Since then the acid catalysed rearrangement of bicyclic molecules has become a very wide topic of research owing to the vast number of skeletal changes that are possible.[129]

Benzobicyclo[2.2.2]octadienyl and -trienyl derivatives are typical bicyclic molecules which can undergo rearrangement reactions. A limited number of examples will serve to illustrate the types of rearrangement in which these systems take part.

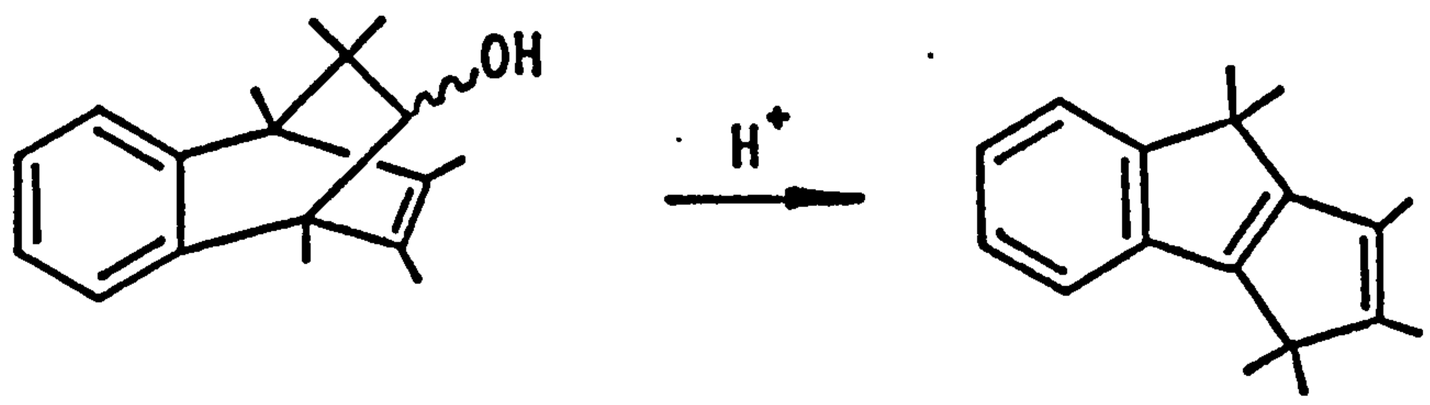
Wagner-Meerwein rearrangements have been observed in the solvolyses of benzo-bicyclo[2.2.2]octadienyl brosylates.[130] The products of the reactions depend on the stereochemistry of the initial brosylate, and in the main are benzo[3.2.1]octadienyl derivatives. Other products are obtained when the double bond is involved in the rearrangement reactions giving the benzo(3,4)tricyclo[3.2.1.$0^{2,7}$]octene system.

Exo-



Endo-

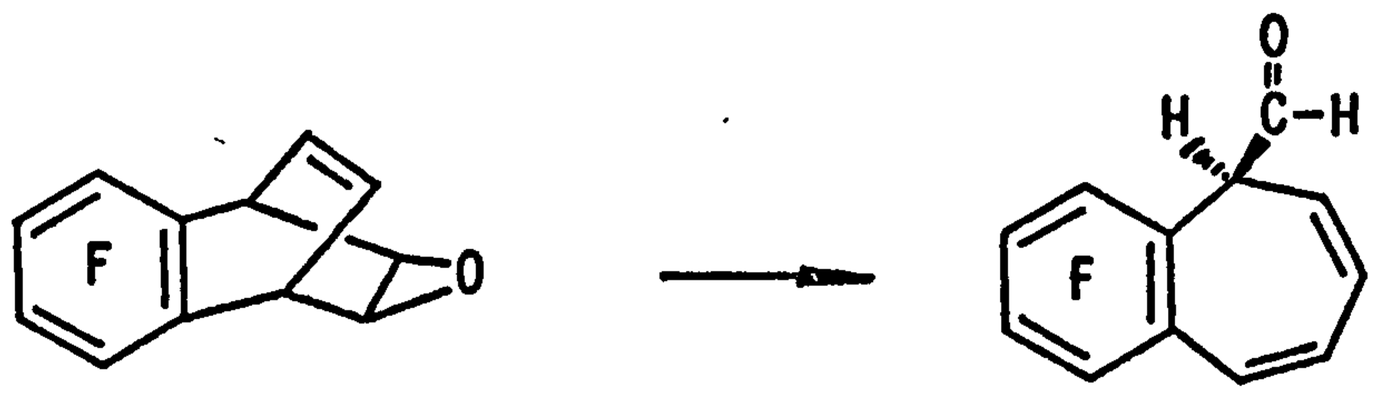
Conversion of certain dibenzobicyclo[3.2.1]octadienes back to the thermodynamically more stable dibenzobicyclo[2.2.2]octadienes occurs readily.[131] Similar conversions of a [3.2.1] system to the [2.2.2] system have been observed in the solvolysis reactions of benzobicyclo[3.2.1]octenyl formates.[132] Rearrangement of bicyclo-[2.2.2]octenyl derivatives under acid catalysis can also lead to the formation of [3.3.0] systems.[133] Thus for example the acid catalysed dehydration of a benzobicyclo[2.2.2]octadienol has been studied and after extensive rearrangement gives a cyclopentindene derivative.[134]



Rearrangement following the addition of electrophiles to benzobicyclo-[2.2.2]octatriene derivatives leads to products which are usually benzobicyclo[3.2.1] compounds.[135]

Fragmentation reactions leading to monocyclic compounds are also

known, as in the boron trifluoride etherate catalysed rearrangement of a benzobicyclo[2.2.2]octadienyl epoxide giving a benzocycloheptatriene aldehyde.[136]



We became interested in studying the chemistry of the major products derived from the reactions of tetrahalobenzynes with anisoles.

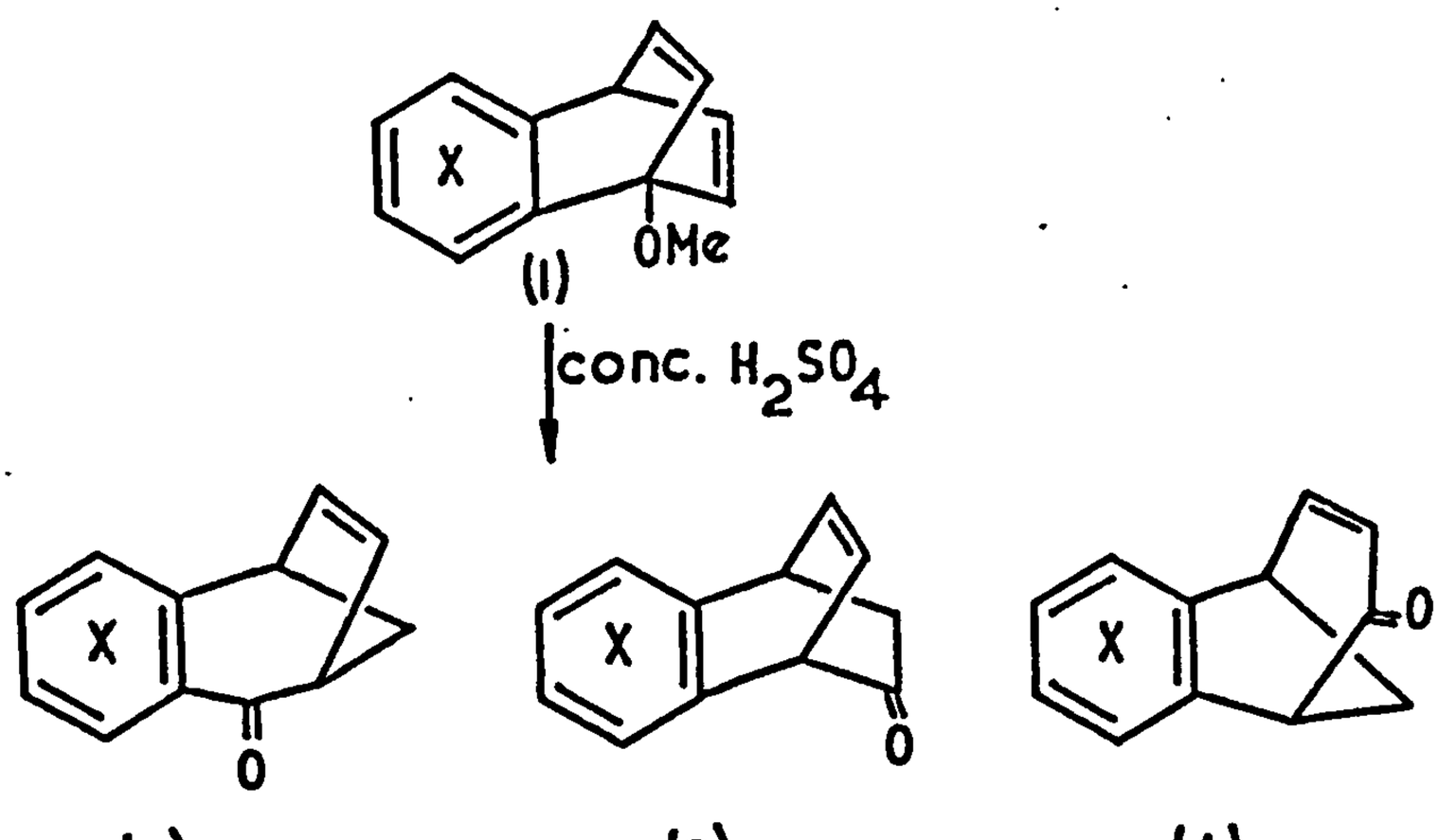
These products are 1-methoxytetrahalobenzobicyclo[2.2.2]octatrienes (1-methoxytetrahalobenzobarrelenes). This system contains the essential structural features which should make it reactive in acid catalysed rearrangements. It was thought that the methoxy group at the bridgehead position would have a considerable directing influence on the rearrangements, and further, that the reaction could be of synthetic value for the production of compounds which were difficult to obtain by other routes.

Discussion

The reactions of tetrahalobenzynes with methoxy-arenes to give 1-methoxytetrahalobenzobarrelenes have been studied in some detail. 10a, 13, 14, 16, 23, 137 However, the rearrangement of the products in acid had not been investigated.

Initially it was decided to concentrate our studies on one particular 1-methoxybenzobarrelene, (1) X=F, the reason being that this compound could be produced in good yield and a number of similar compounds were available in these laboratories for comparison purposes. We have, however, extended our studies to cover other such compounds (1) X=H and X=Cl.

The choice of rearranging media was determined by a few preliminary experiments which showed that strong mineral acids were required before any reaction occurred. In sulphuric acid the 1-methoxybenzobarrelenes gave three isomeric ketones (2), (3) and (4).

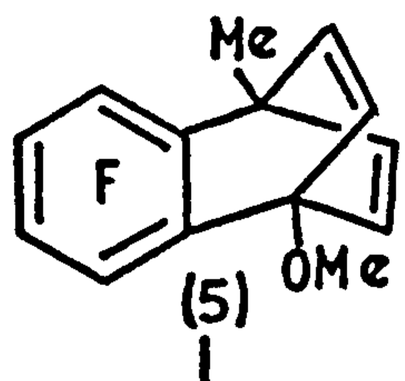


	(2)	(3)	(4)	
X=F	5	64	5	% Yield
X=Cl	3.2	76	4.5	
X=H	8	50	6.5	

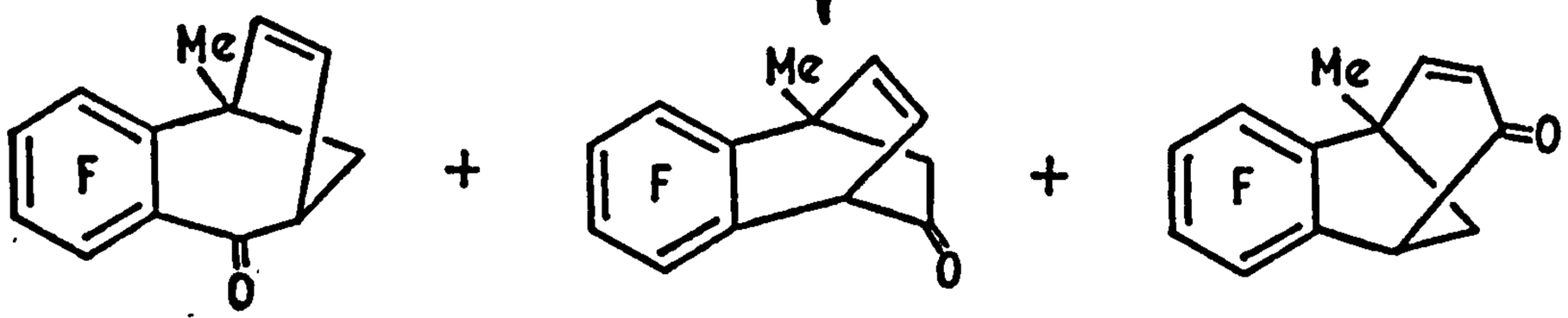
Possible mechanisms which account for the formation of these three ketones will be discussed in detail later, but by way of introduction a number of general comments can be made.

Firstly, the bulk of the reactions studied involve rearrangements of the 1-methoxybenzobarrelenes (1) in concentrated sulphuric acid at room temperature. The reactions are extremely rapid and a number of mechanistic pathways operate thus making any kinetic measurements difficult. The methods used to study the reaction mechanism have included the use of deuterium labelled 1-methoxybenzobarrelenes, deuterated solvents, specifically substituted methyl derivatives, and solvolytic reactions of certain tosylates.

Broadly speaking the three ketones (2), (3) and (4) are derived from different pathways and cannot be equilibrated under the reaction conditions. The use of specifically substituted methyl derivatives directs the initial protonation and hence affects the course of the rearrangements. For example, a methyl group at position-4 would be expected to have little effect on the rearrangement. This was found to be the case, and the rearrangement of (5) in sulphuric acid gave three isomeric ketones (6), (7), and (8).



(5)

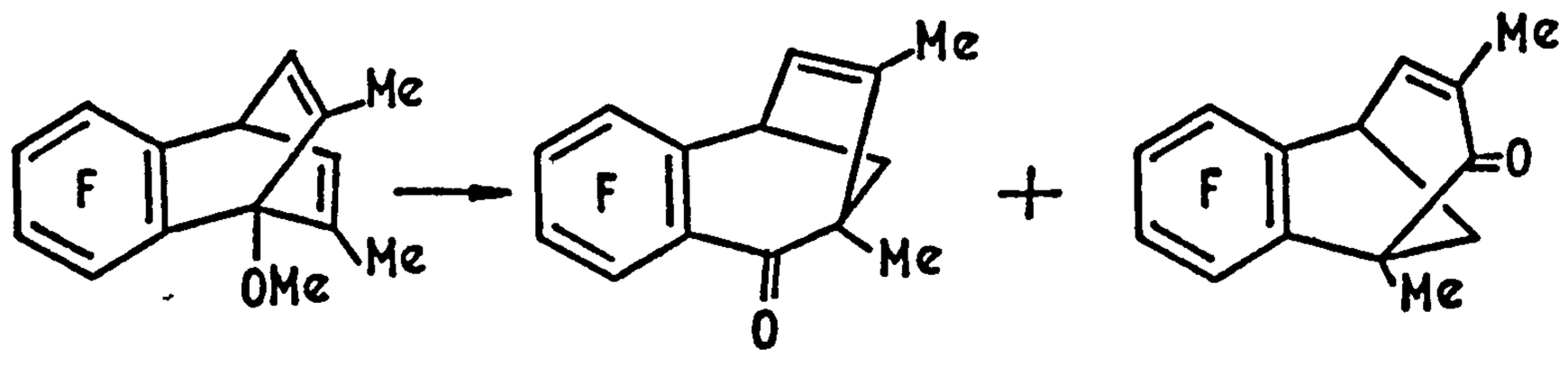


(6) (7) (8)

Methyl groups at positions-3 and -5, in the compound (9), direct the protonation, and in trifluoroacetic acid led to the formation of the benzobarrelenone derivative (10). Products corresponding to the other two ketone types were not observed.

(9) (10)

Likewise the compound (11) which has a methyl group at positions -2, and -6 gave, in trifluoroacetic acid, products (12) and (13), and in this case the corresponding benzobarrelenone was not detected.



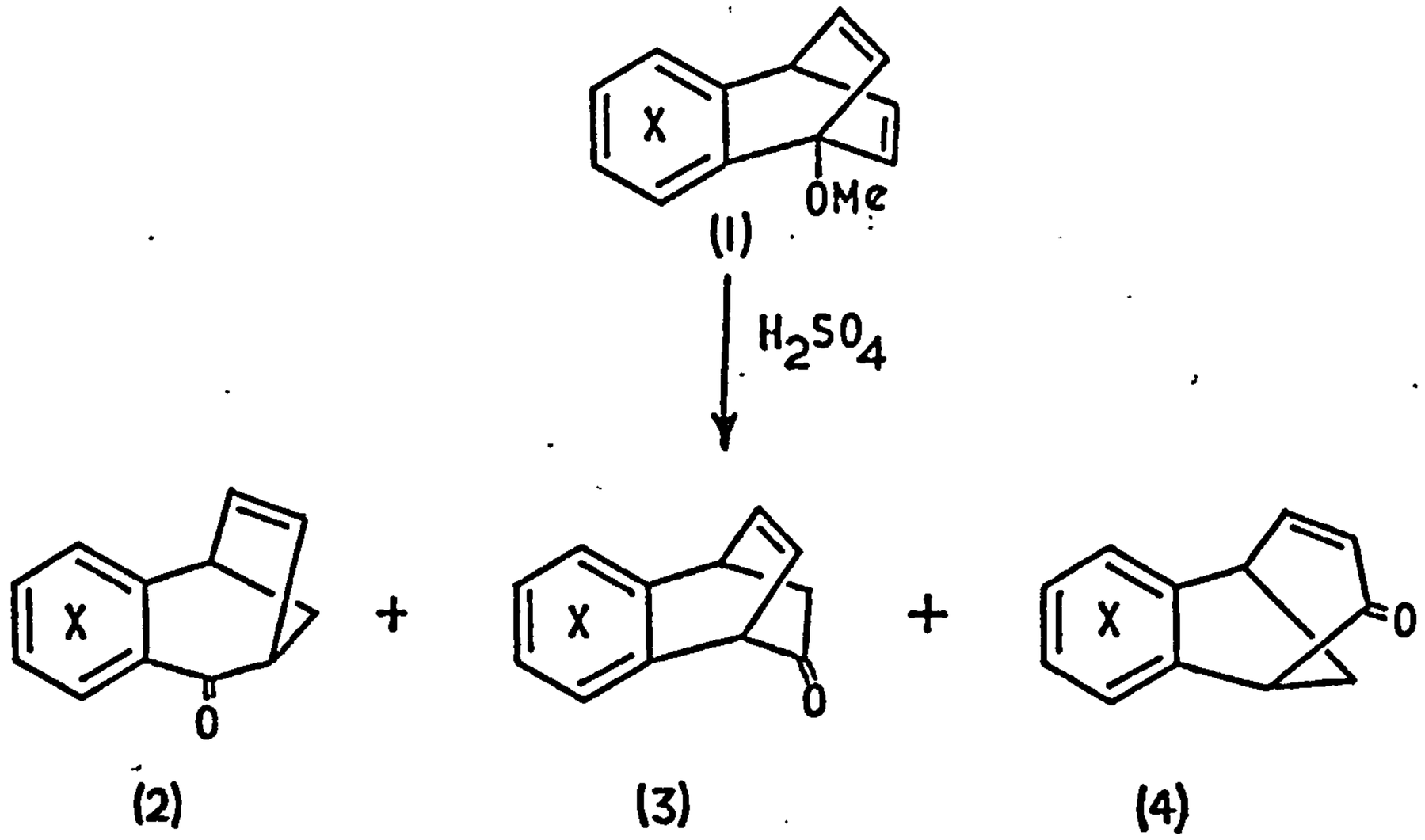
(11) (12) (13)

The mechanistic implications of these few reactions will be discussed under separate headings.

Unsubstituted 1-methoxybenzobarrelenes (1).

The 1-methoxybenzobarrelenes (1) X=F, Cl, or H, were obtained by the reaction of the appropriate benzyne with anisole. Both tetrafluoro- and tetrachlorobenzyne gave good yields of the benzobarrelenes. However, the reaction of benzyne, [generated from benzene diazonium 2-carboxylate] with anisole gave only a 2% yield of the 1-methoxybenzobarrelene, (1) X=H.

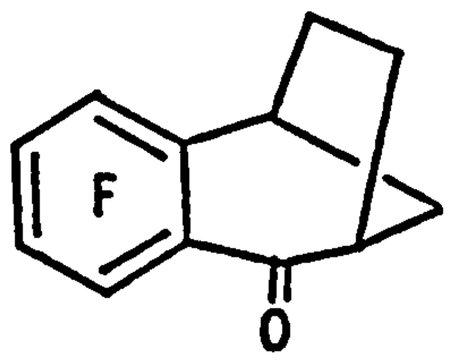
When the 1-methoxybenzobarrelene (1) X=F was dissolved in concentrated sulphuric acid and then immediately added to ice, three products were formed. These were isolated by preparative t.l.c. and gave (2) X=F in 5% yield; (3) X=F, 64%; and (4) X=F, obtained in 5% yield.



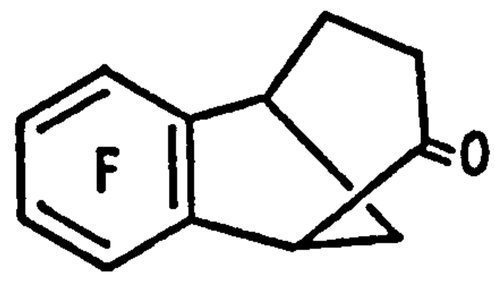
The major product, which was the benzobarrelenone (3) X=F, was readily characterised by comparison with authentic material.
The structure of the vinyl ketone (2) X=F, was determined from its spectral properties. I.r. spectroscopy showed a carbonyl absorption

at 1708 cm.$^{-1}$ which was typical for a tetrafluoroaryl carbonyl compound.[36] The compound was reduced with hydrogen to form a dihydro-derivative (14) whose carbonyl absorption in the i.r. spectrum was unchanged at 1708 cm.$^{-1}$. The ^{1}H n.m.r. spectrum of compound (2) X=F, (Table 1, p.177) was also in accord with the structure as the chemical shifts and spin-spin coupling data compare well with similar compounds.[130]

The structure of the αβ-unsaturated ketone (4) X=F, was also assigned on the basis of its spectral properties. I.r. spectroscopy showed a carbonyl absorption at 1690 cm.$^{-1}$, typical of an αβ-unsaturated ketone.[34] The compound was reduced to give a dihydroderivative (15), which by i.r. spectroscopy contained an absorption band at 1725 cm.$^{-1}$ due to a saturated carbonyl group. The ^{1}H n.m.r. spectrum (Table 2, p.178) showed the vinyl protons in characteristic positions for an αβ-unsaturated ketone at τ 2.6 and τ 4.55 with a coupling constant of 10.3 Hz..



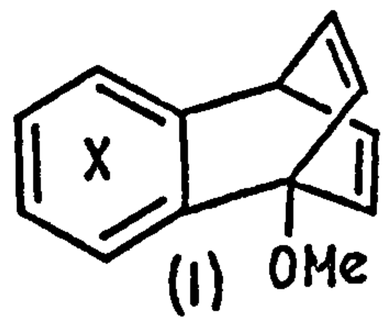
(14)



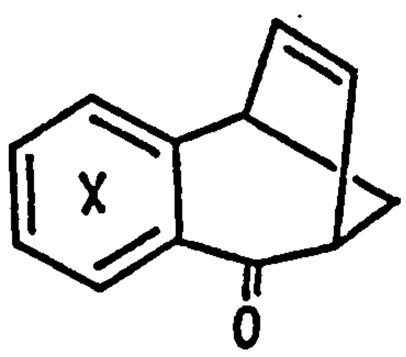
(15)

When the rearrangement of the compound (1) X=F, was studied in fluorosulphonic acid, the yield of the benzobarrelenone was 90%. The crude product from this rearrangement contained less than 4% of either of the other ketones (2) and (4) X=F. This reaction constitutes an excellent preparation of the benzobarrelenone which is otherwise difficult to obtain.

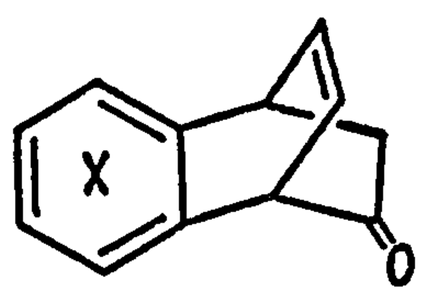
The 1-methoxybenzobarrelenes (1) X=Cl and X=H, have also been rearranged in concentrated sulphuric acid and gave the corresponding ketones (2),(3), and (4) in essentially the same ratios as the tetrafluorinated analogue.



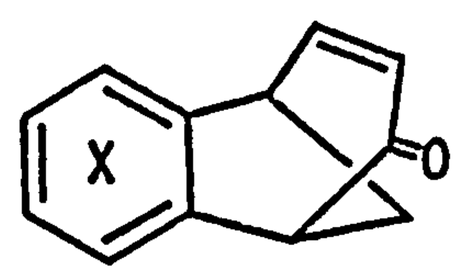
(1)



(2)



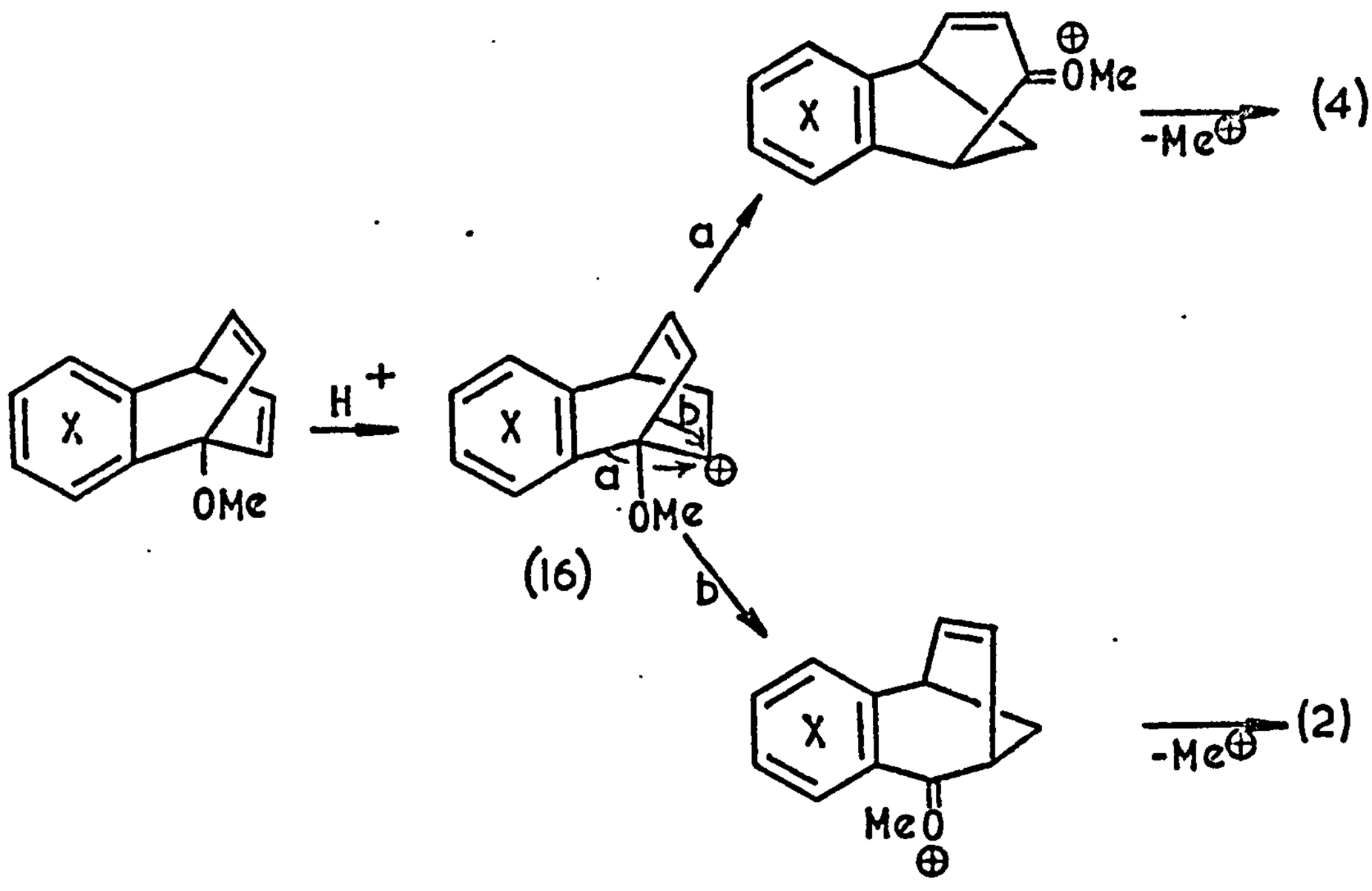
(3)



(4)

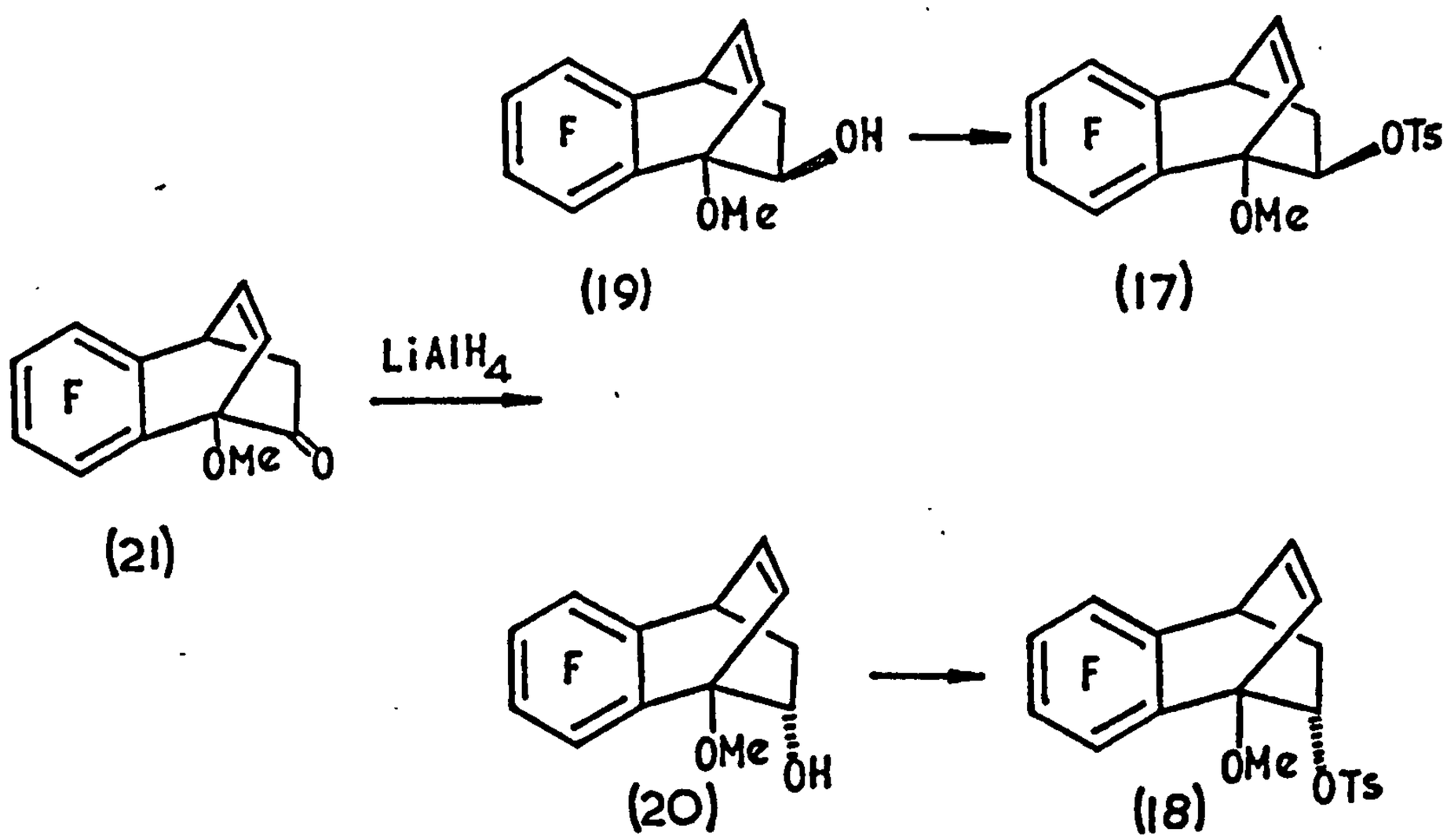
X=Cl	32	76	4·5	% Yield
X=H	8	50	6·5	

We were interested in finding a mechanism which could account for the formation of these three ketones (2), (3), and (4). It seemed reasonable that the sulphuric acid could protonate one of the double bonds of the benzobarrelene to form a carbonium ion intermediate (16). This could then rearrange in a manner most probably directed by the bridgehead methoxy group. Aryl migration (route a), after demethylation, would lead to the αβ-unsaturated ketone (4). A vinyl migration in the intermediate (route b) would give the vinyl ketone (2).

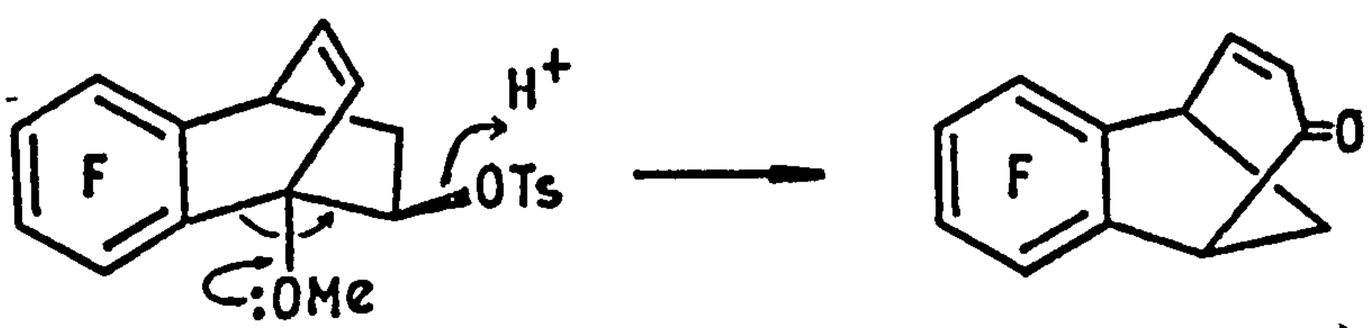


Rearrangements of this type are known in some simple systems.[138,139]

We proposed to test the mechanism by studying the solvolysis of the 2-exo-tosylate (17) and the 2-endo-tosylate (18). These tosylates were prepared in the usual manner from the corresponding alcohols (19) and (20), which were obtained by the lithium aluminium hydride reduction of the 1-methoxybenzobarrelen-2-one (21).

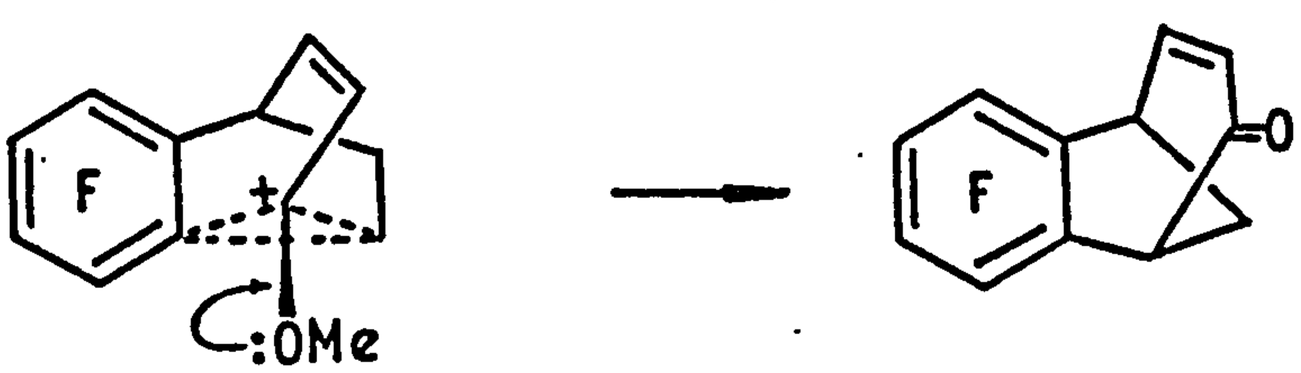


When the 2-exo-tosylate (17) was heated under reflux with trifluoroacetic acid a 98% yield of the αβ-unsaturated ketone (4) X=F, was formed. This high stereospecificity suggests that the reaction is concerted thus :-



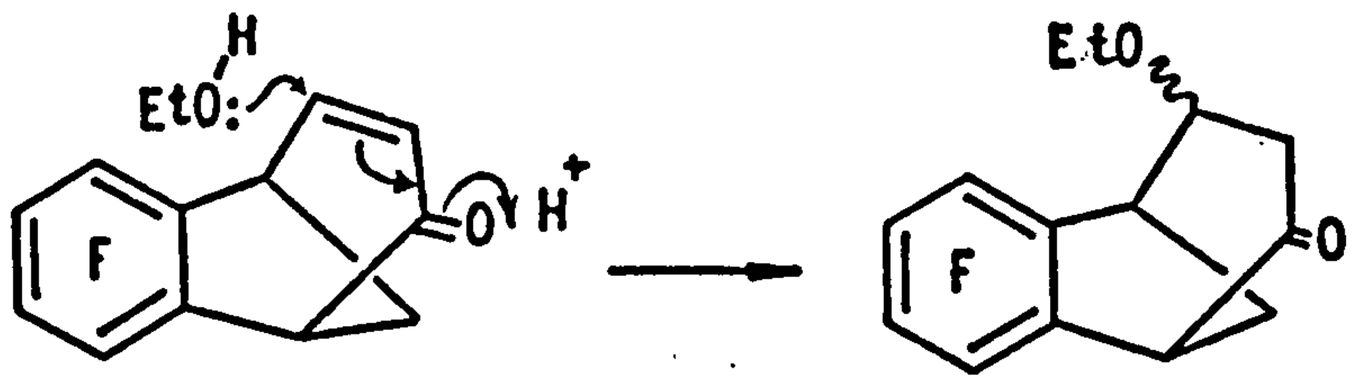
(2) (4)

or possibly involves a bridged ion (22) whose breakdown is governed by the methoxy group.



(22) (4)

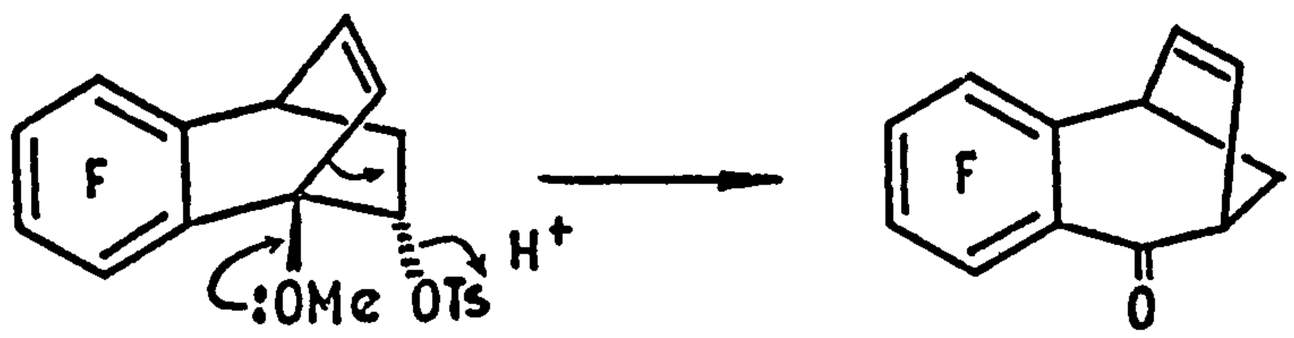
When the solvolysis of the 2-exo-tosylate (17) was studied in acidic ethanol the product was the compound (23). This was presumably formed from the αβ-unsaturated ketone by an acid catalysed Michael addition of ethanol.



(4) (23)

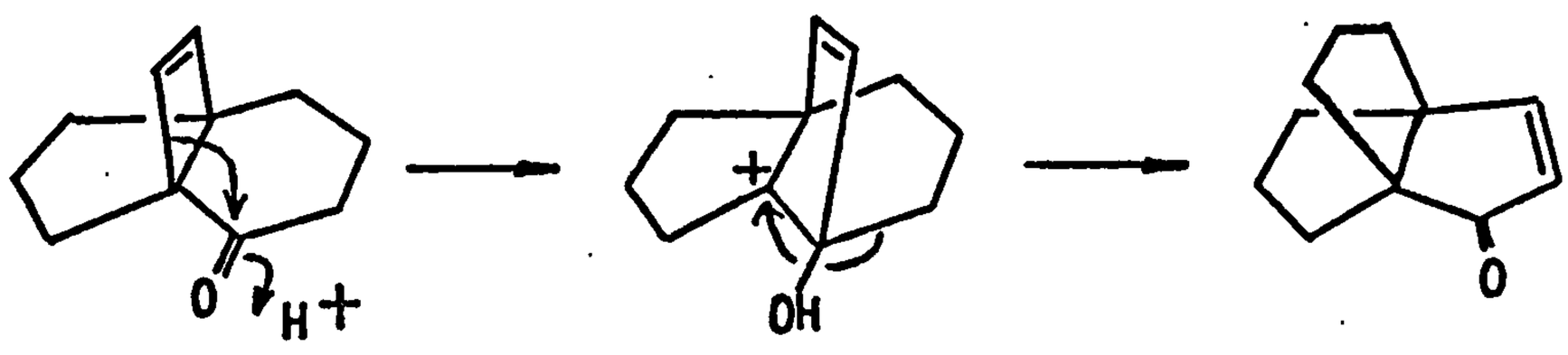
In concentrated sulphuric acid, the 2-exo-tosylate (17) gave the "αβ"-ketone (4) X=F, in 37% yield. Products corresponding to the vinyl ketone (2) X=F, or the benzobarrelenone (3) X=F, were not observed in these solvolysis reactions.

A study of the solvolysis of the 2-endo-tosylate (18) in glacial acetic acid containing acetic anhydride and sodium acetate led to the production of the vinyl ketone (2) X=F, in 92% yield. The high stereospecificity again suggests that the reaction could be concerted thus:-



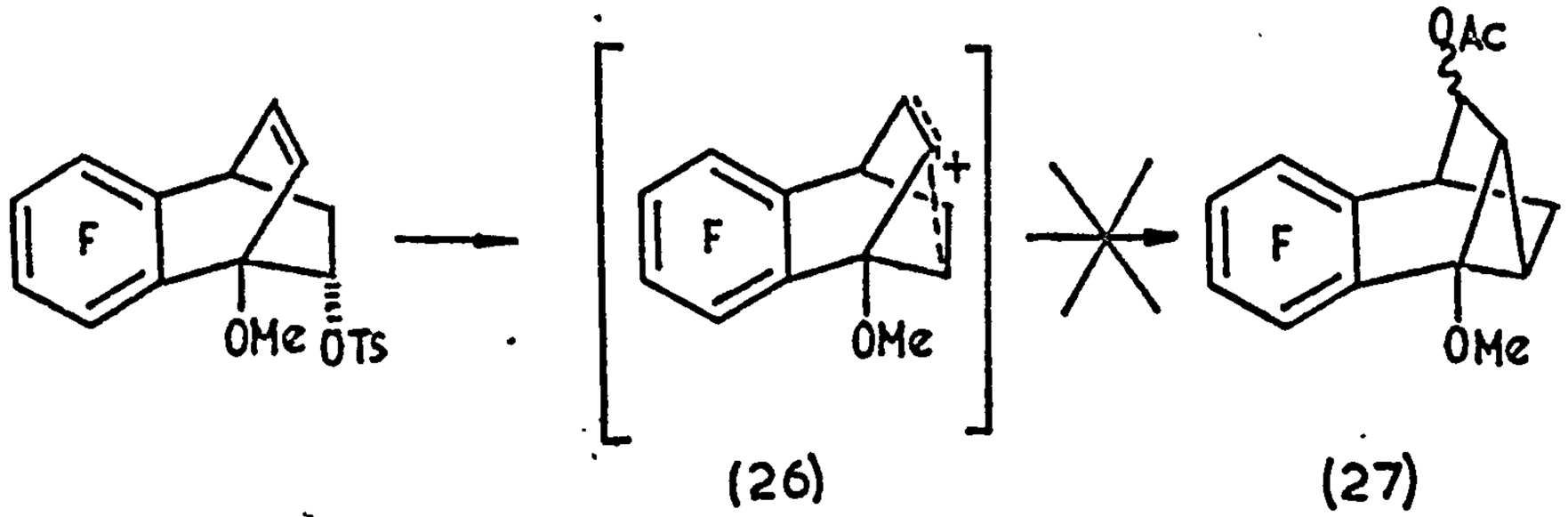
(18) (2)

1,2-Vinyl migrations of this type are known, for example the ketone (24) gives the ketone (25) in benzene using p-toluenesulphonic acid as a catalyst.[140]



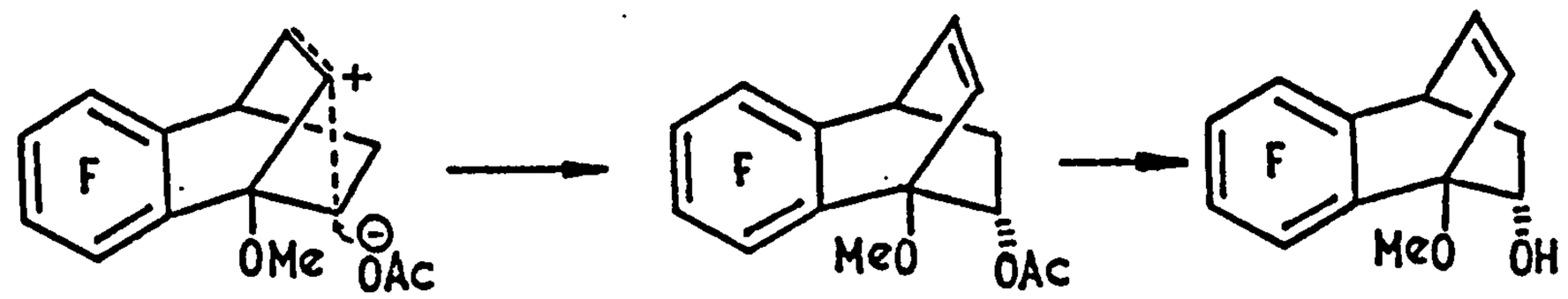
(24) (25)

In the solvolysis of the endo-tosylate (18) one might expect some anchimeric assistance from the other double bond to form a bridged ion (26), which by analogy to Tanida's work[130] could be solvolysed to give tricyclo derivatives (27). This was not observed in our system.



(26) (27)

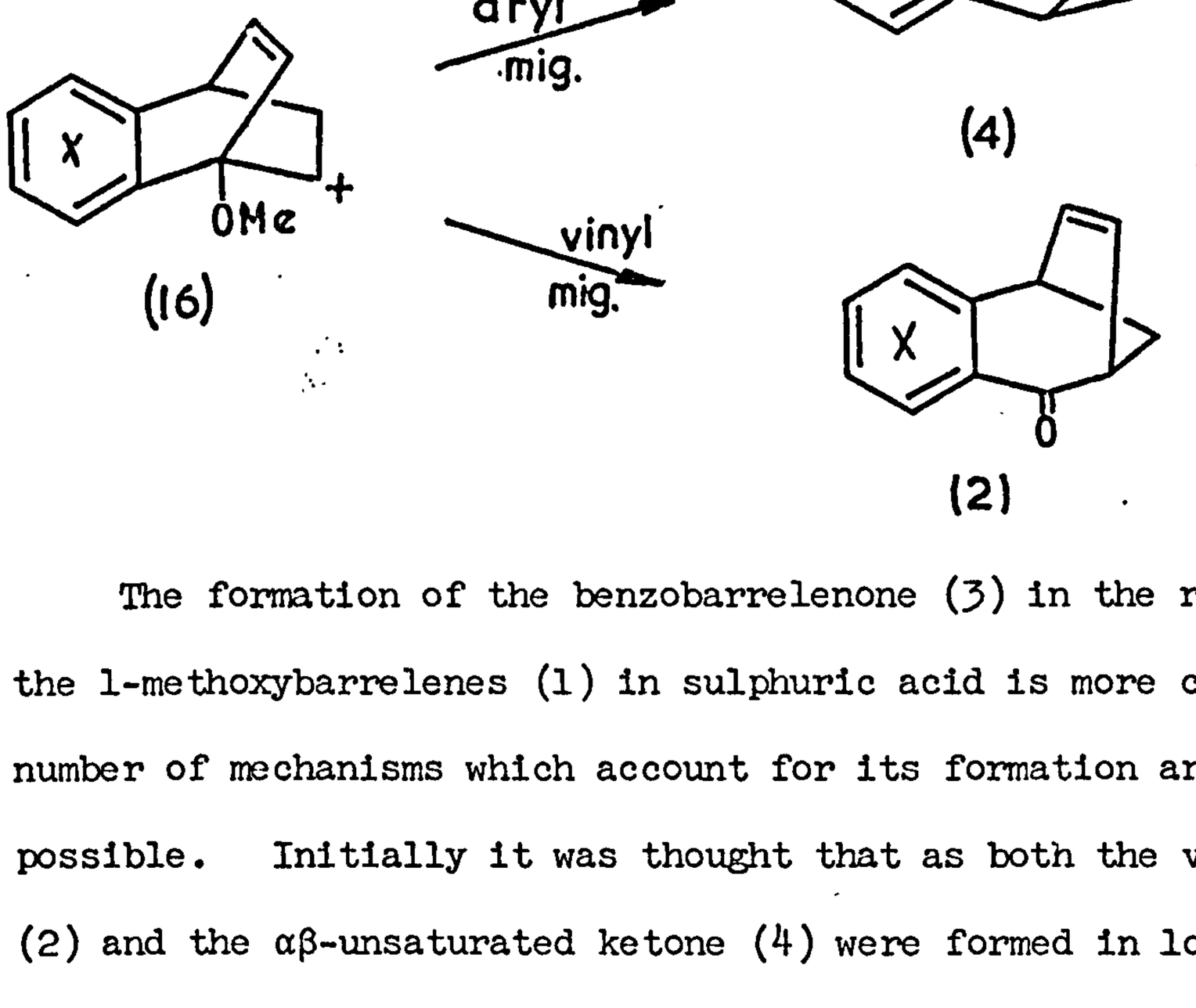
However some evidence for participation of the other double bond was found in one experiment where the reaction was worked up after a short time. A product corresponding to the 2-endo-acetate (28) was formed. This can possibly be rationalised in terms of solvolysis of the intermediate (26) in an alternative way to the formation of the tricyclo derivatives thus:-



(26) (28) (20)

The stereochemistry of the acetate (28) followed from its hydrolysis to the known endo-alcohol (20).

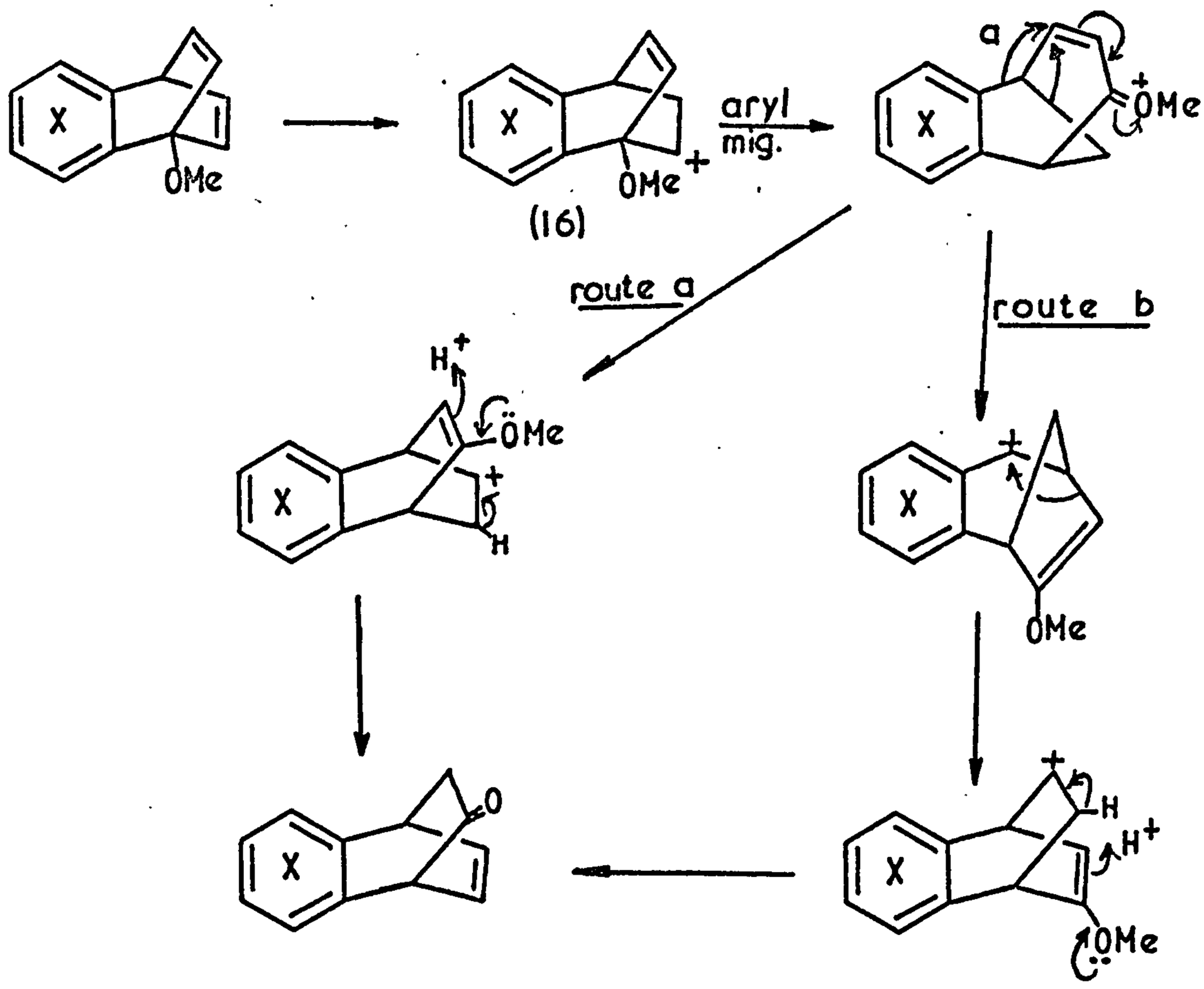
The formation of the vinyl ketone (2) and the αβ-unsaturated ketone (4) from a common carbonium ion intermediate (16) by either an aryl migration or a vinyl migration appeared to be mechanistically reasonable. Other alternatives will be discussed later.



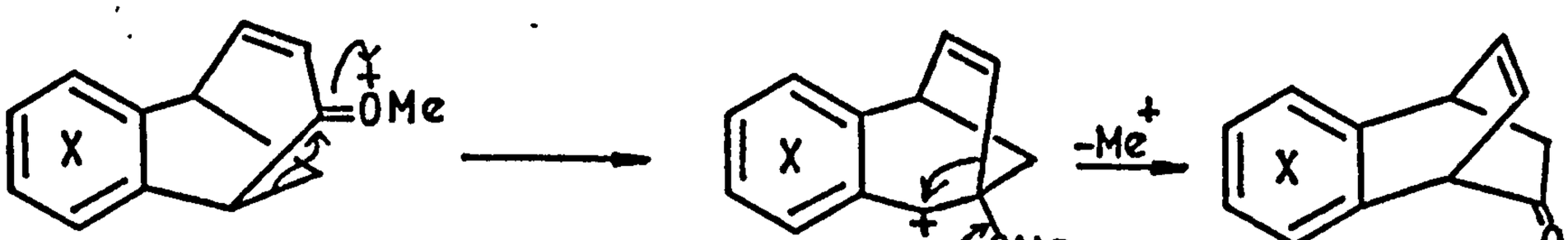
The formation of the benzobarrelenone (3) in the rearrangement of the 1-methoxybarrelenes (1) in sulphuric acid is more complex. A number of mechanisms which account for its formation are theoretically possible. Initially it was thought that as both the vinyl ketone (2) and the αβ-unsaturated ketone (4) were formed in low yield, they might be precursors of the benzobarrelenone (3). Some of the possible mechanisms are presented below. In these mechanisms the ions are represented as classical ions but may not necessarily be so. The steps in the mechanisms are also potentially reversible.

We proposed to test these various pathways by the use of deuterated solvents, equilibration studies, and by the use of specifically deuterated starting materials.

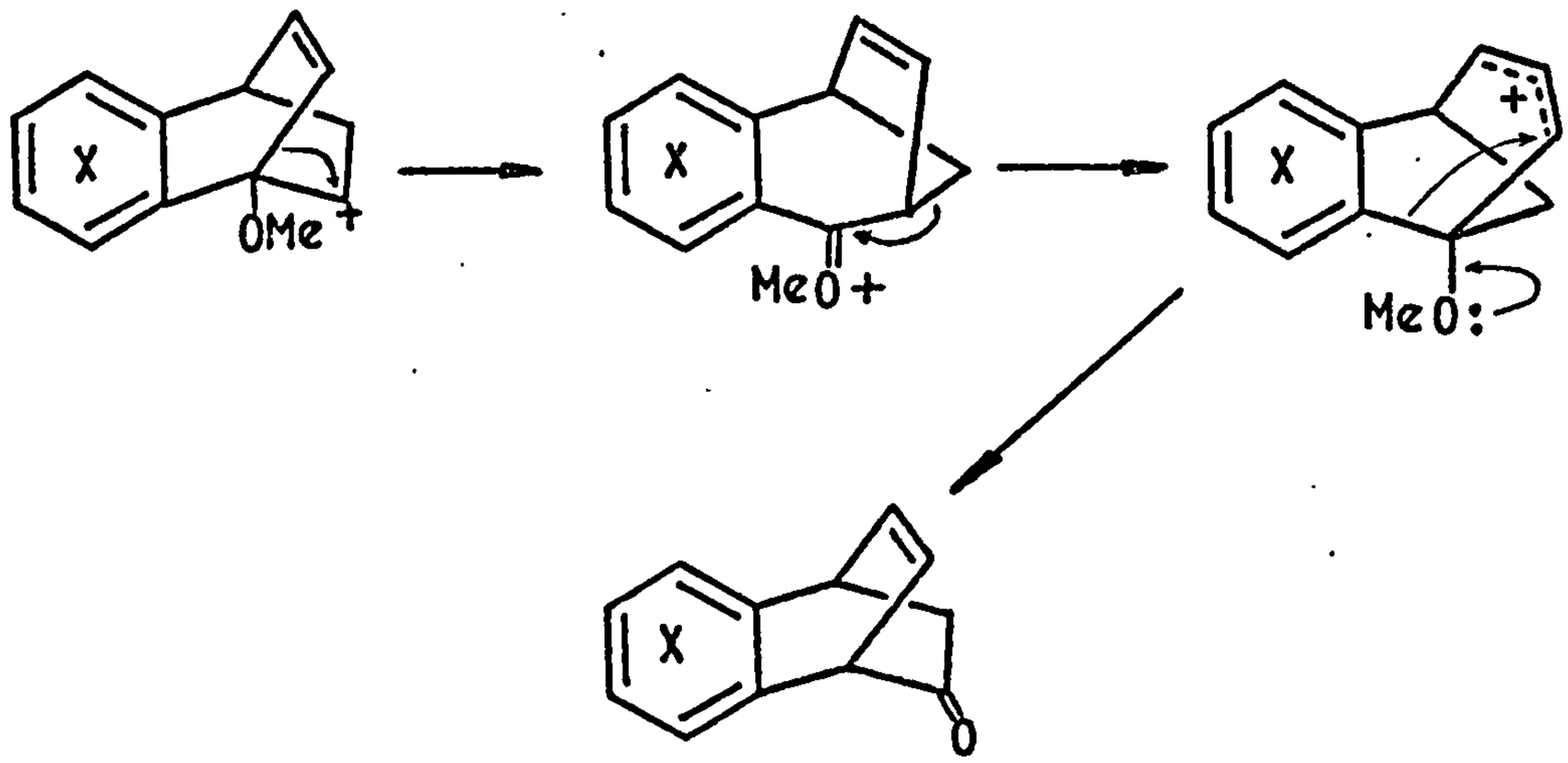
Mechanism I



Mechanism II



Mechanism III

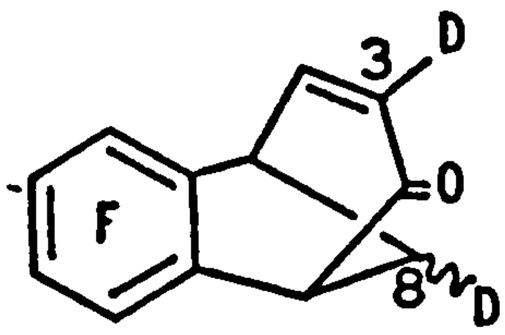


(3)

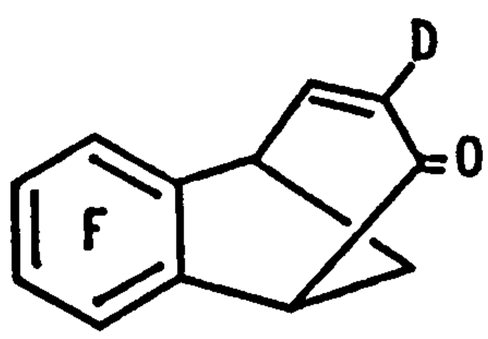
Deuterated solvents.

When the compound (1) X=F was dissolved in 80% D_2SO_4 at 80°, deuterated products corresponding to the αβ-unsaturated ketone and the benzobarrelenone were isolated.

Firstly the "αβ"-ketone (29) was shown by mass spectrometry to contain two deuterium atoms, the positions of which were shown by ^1H n.m.r. spectroscopy to be at C_3 and C_8.

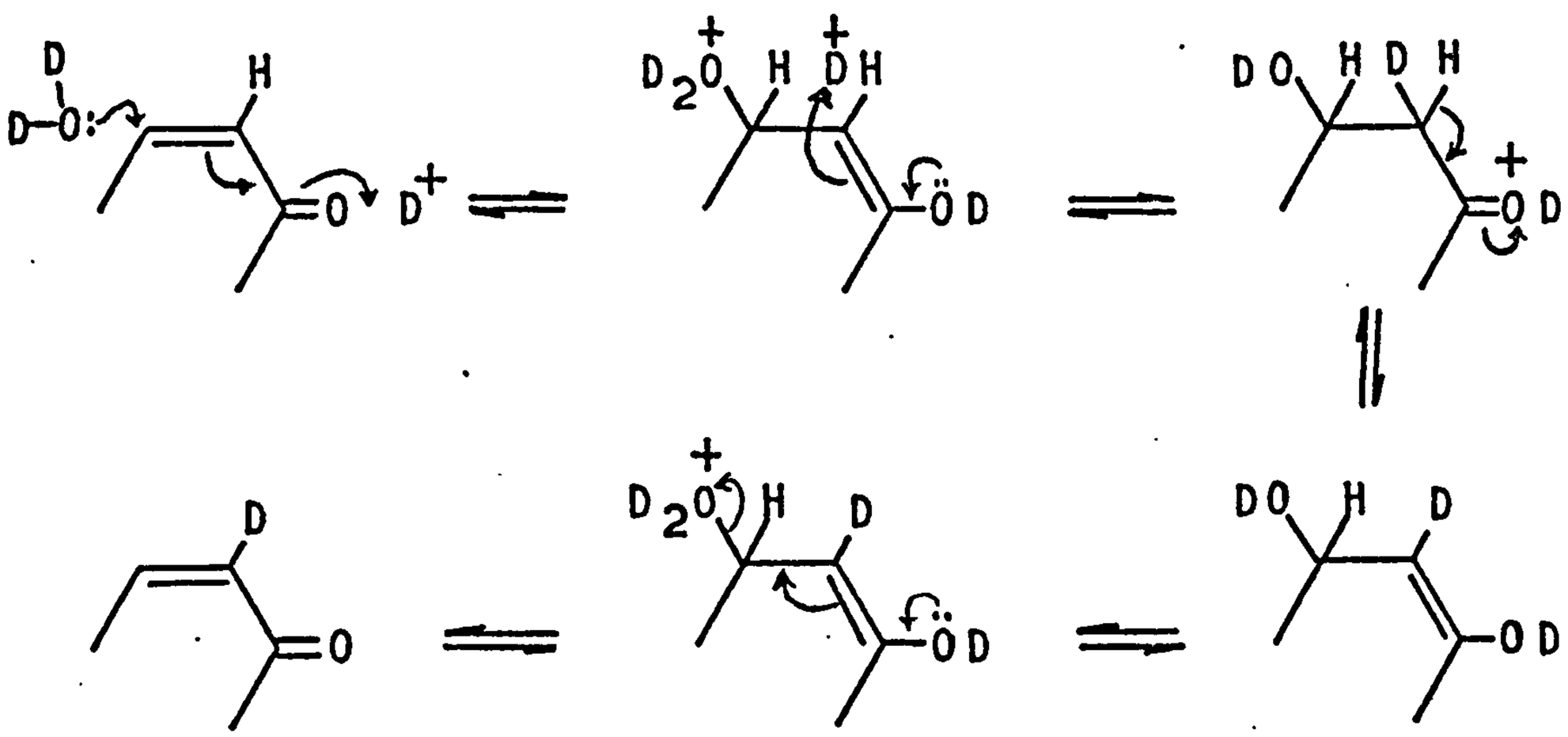


(29)



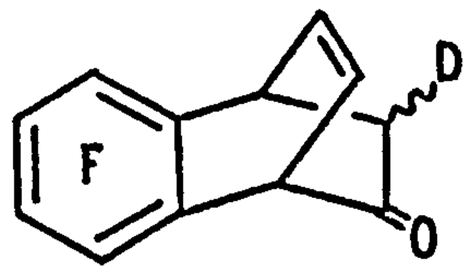
(30)

We had expected on the grounds of our proposed mechanisms, to find only one deuterium atom in the αβ-compound, at C_8. However, when the αβ-unsaturated ketone, (4) X=F, was treated under the same reaction conditions, the proton at C_3 was exchanged to give the mono-deutero αβ-unsaturated ketone (30). In concentrated acid no exchange occurs at this position. The exchange mechanism must involve an acid catalysed addition-elimination process thus:-



This pathway seemed reasonable particularly in the light of the addition of ethanol under acid catalysis during the solvolysis of the 2-exo-tosylate (17) to the compound (23). A similar α-hydrogen exchange in an αβ-unsaturated compound, phenalenone, has recently been reported.[141]

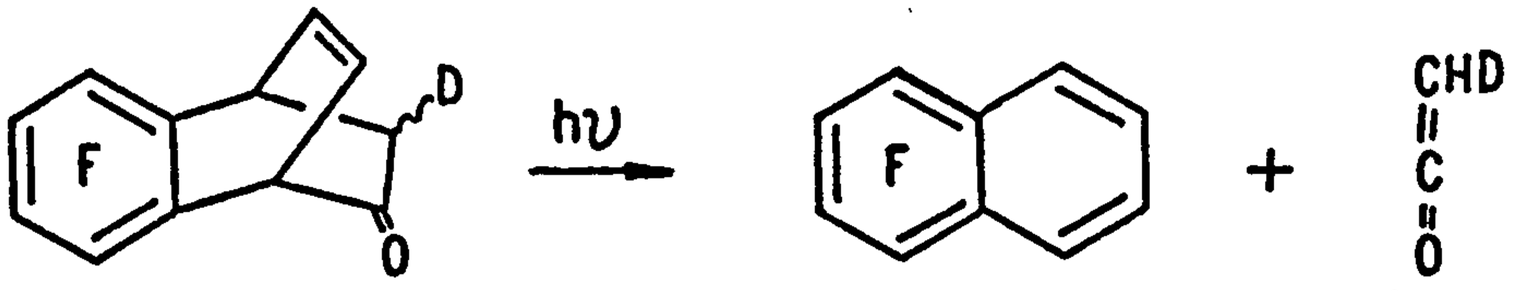
The benzobarrelenone (31) formed in the reaction of 1-methoxy-tetrafluorobenzobarrelene in 80% D_2SO_4 was shown by mass spectrometry and ^1H n.m.r. spectroscopy to have structure (31).



ratio exo D : endo D
10 : 7

(31)

When this result was compared with the proposed mechanisms, it was found that mechanism I could not be accommodated as one would expect to observe some deuterium in the vinyl positions. Also mechanism II might be expected to incorporate some deuterium into the vinyl position by α-hydrogen exchange in one of the intermediates. In order to be absolutely sure there was no deuterium in the vinyl positions the benzobarrelenone (31) was converted to the naphthalene (32) by photolysis. The naphthalene was shown, by mass spectrometry, to be completely undeuterated.



(31) (32)

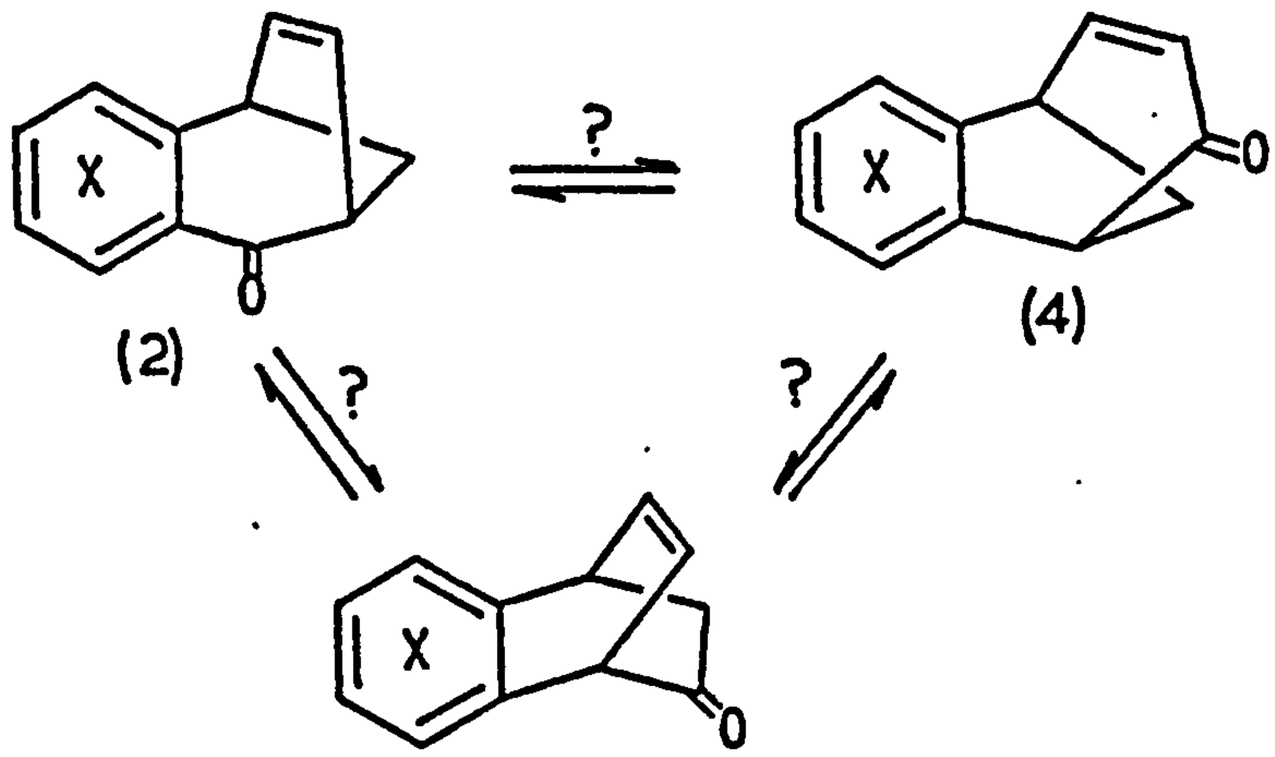
The photolysis of benzobarrelenones to naphthalenes has been studied previously.[142]

Concurrently with our studies on the rearrangement of 1-methoxybenzobarrelenes Barkhash has also investigated the rearrangement of (1) X=F to (3) X=F.[52] His studies with deuterated solvents gave results which were similar to our own. He has also shown that when

the benzobarrelenone (3) X=F was dissolved in D_2SO_4 then poured into deuterium oxide, or when the compound (31) was dissolved in H_2SO_4 then quenched with deuterium oxide no deuterium exchange occurs.

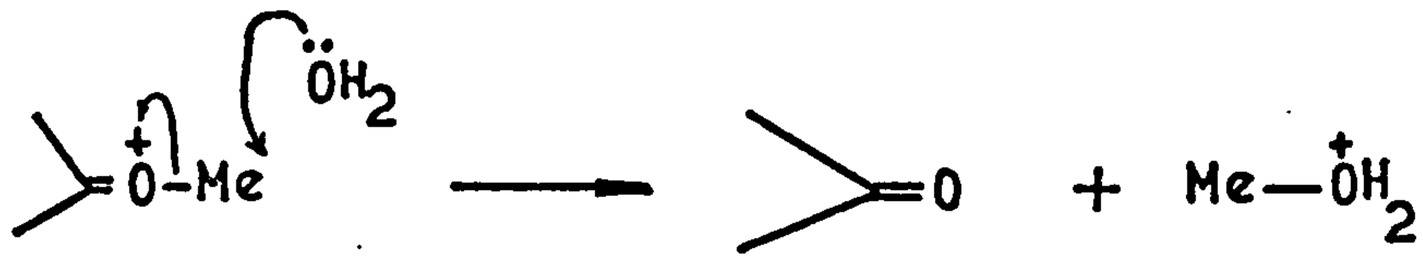
Equilibration Studies

We wished to investigate whether the benzobarrelenone (3) was formed from the vinyl ketone (2) or from the αβ-unsaturated ketone (4).

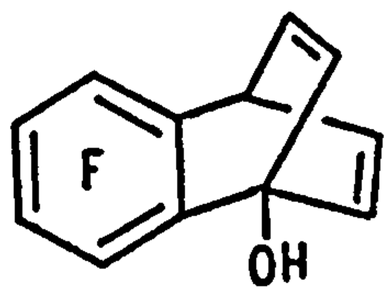


(3)

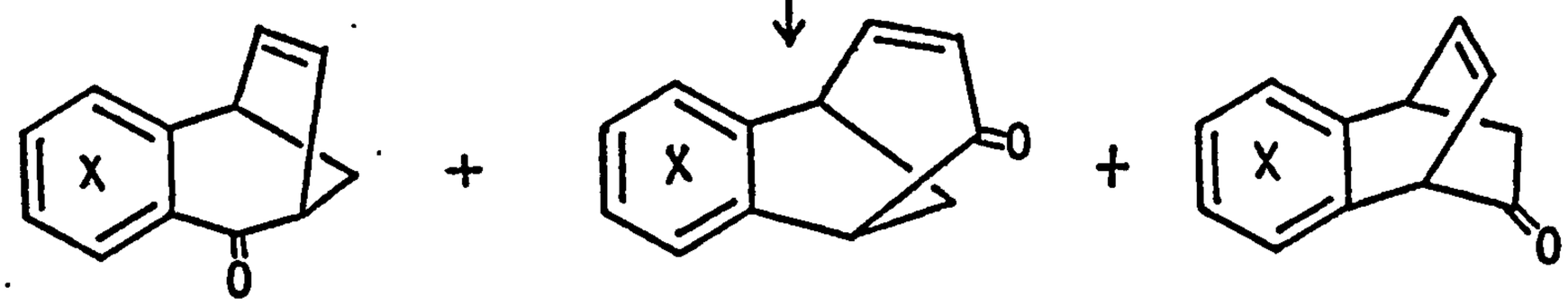
Before studying any possible equilibration processes, it was necessary to determine if the methoxyl methyl group in the methoxy rearrangements was an important structural feature. The methyl group was lost in the rearrangements presumably by demethylation of a methoxonium species:-



If, however, rearrangement was very fast compared with demethylation, a rapid equilibration of intermediate ions could result. The demethylation step would then occur when the reaction mixture was quenched with water (i.e. during its work up). If the rearrangement was slow versus demethylation then the resulting ketone, after protonation, could conceivably lead to a different ratio of equilibrating intermediate ions. However, when the 1-hydroxytetrafluorobenzobarrelene (33) was subjected to rearrangement in sulphuric acid, it gave essentially the same ratio of ketones (2) X=F, (3) X=F, and (4) X=F as we obtained from 1-methoxybenzobarrelene (1) X=F.



(33)



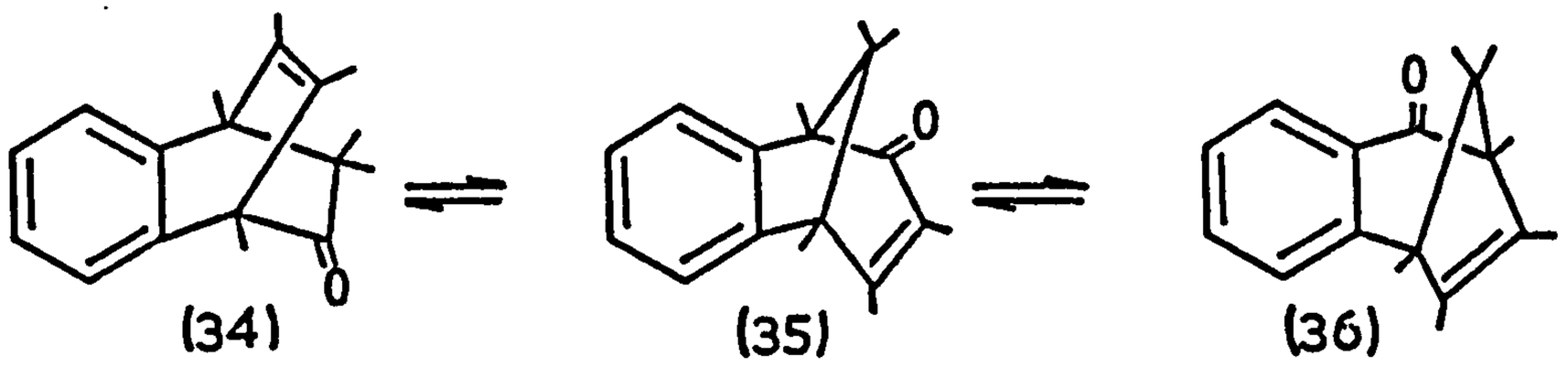
(2) (4) (3)

This suggests, either that the demethylation step is unimportant or that it occurs rapidly during the reaction. A number of attempts to interconvert the ketones (2) X=F, (3) X=F, and (4) have been investigated.

Firstly, the vinyl ketone (2), X=F was heated under reflux in trifluoroacetic acid and after 111 hours, g.l.c., t.l.c., and ^{1}H n.m.r.

spectroscopy all showed that no isomerisation to the other ketones had occurred. Similarly the benzobarrelenone (3) X=F, showed, after one month, no isomerisation. Also the αβ-unsaturated ketone (4) X=F, after 100 hours, showed no isomerisation to the other two ketones. In concentrated sulphuric acid the ketone (2) X=F was not isomerised after 1 hour. Similarly, the benzobarrelenone (3) X=F, and the αβ-unsaturated ketone (4) X=F, were unchanged after 3 hours in sulphuric acid.

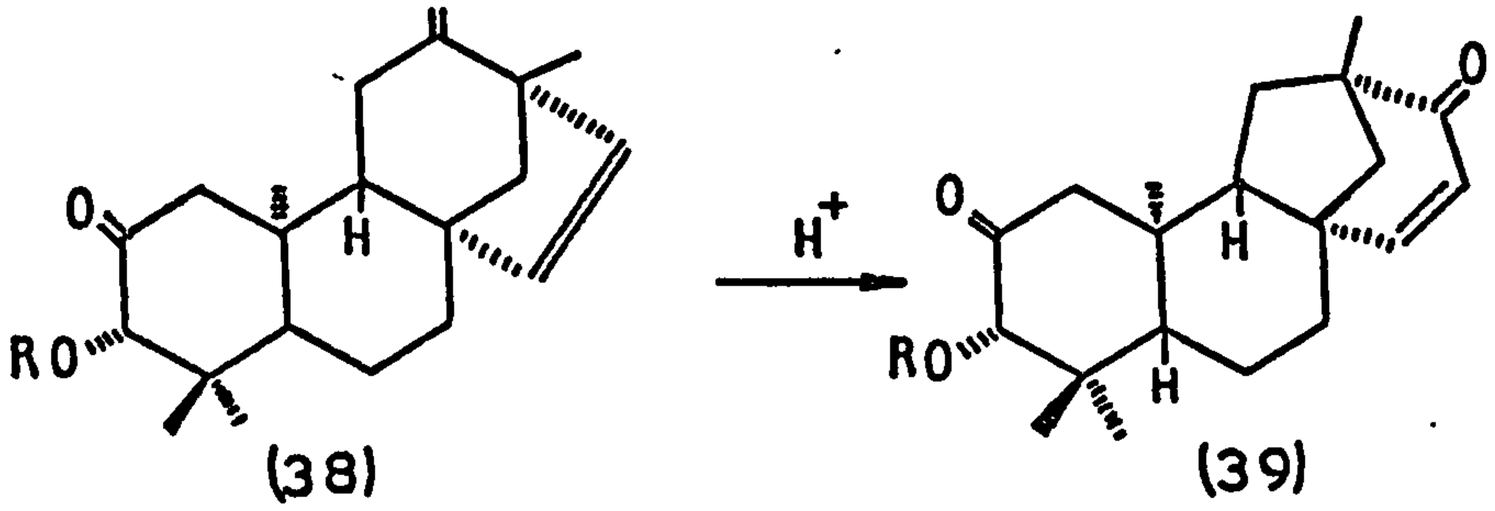
These results are particularly disturbing as it would appear that in our system no equilibration of intermediate carbonium ions occurs. It would also mean that the previously proposed mechanisms for the formation of the benzobarrelenone (3) from either the αβ-unsaturated ketone, mechanisms I and II (p.129), or from the vinyl ketone, mechanism III, are most probably incorrect. Recent work by Hart[143] on a related system, has shown that in trifluoroacetic acid an equilibrium mixture of ketones (34), (35), (36), and (37) could be obtained.



(34) (35) (36)

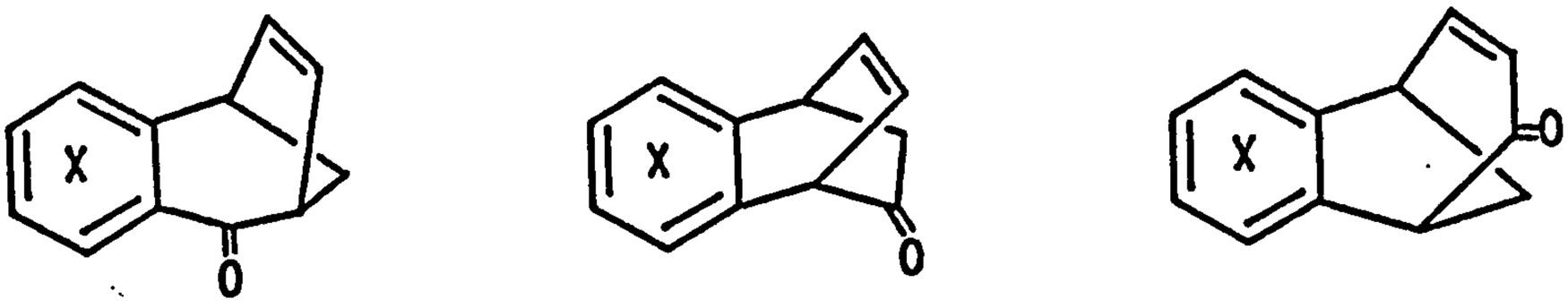
(37)

Also some recent work by Laing[144] shows that the beyer-15(16)-en-2,12-dione (38) rearranges to the αβ-unsaturated compound (39) in strong acid.



(38) (39)

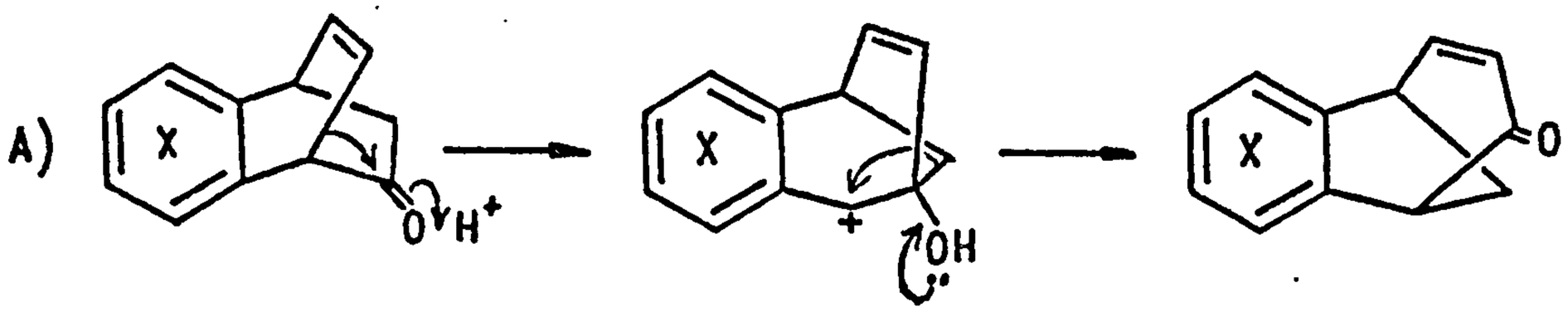
Some idea of thereluctance of the ketones (2) X=F, (3) X=F and (4) X=F to isomerise one to another was obtained from a study of the compounds in concentrated sulphuric acid over an extended period of time.



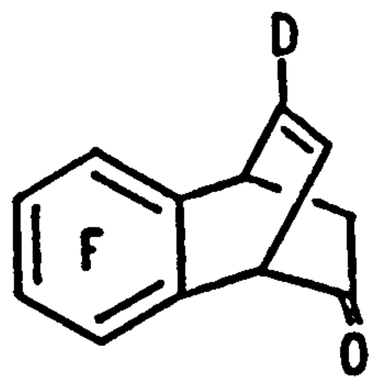
(2) (3) (4)

The compound (4) X=F, was recovered unchanged very nearly quantitatively after treatment in H_2SO_4 for 192 hours. The compound (3) X=F however did react and after 220 hours gave 11% unchanged starting material and 23% of αβ-unsaturated ketone (4) X=F, the other products in the reaction could not be obtained from the aqueous phase. The vinyl ketone (2) X=F, after 209 hours in concentrated sulphuric acid was considerably degraded, however there were no signs that either of the other ketones

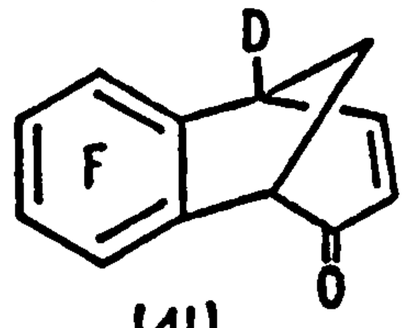
had been formed. Owing to the fact that the ketone (3) X=F did yield some αβ-unsaturated ketone (4) X=F it was necessary to determine the mechanism if possible. Some alternative mechanisms are :-



When the 5-deuterobenzobarrelenone (40) was reacted in concentrated H_2SO_4 for 192 hours, starting material was recovered, (10%) (unchanged by ^1H n.m.r. spectroscopy) together with the αβ-unsaturated ketone (41) (22%).

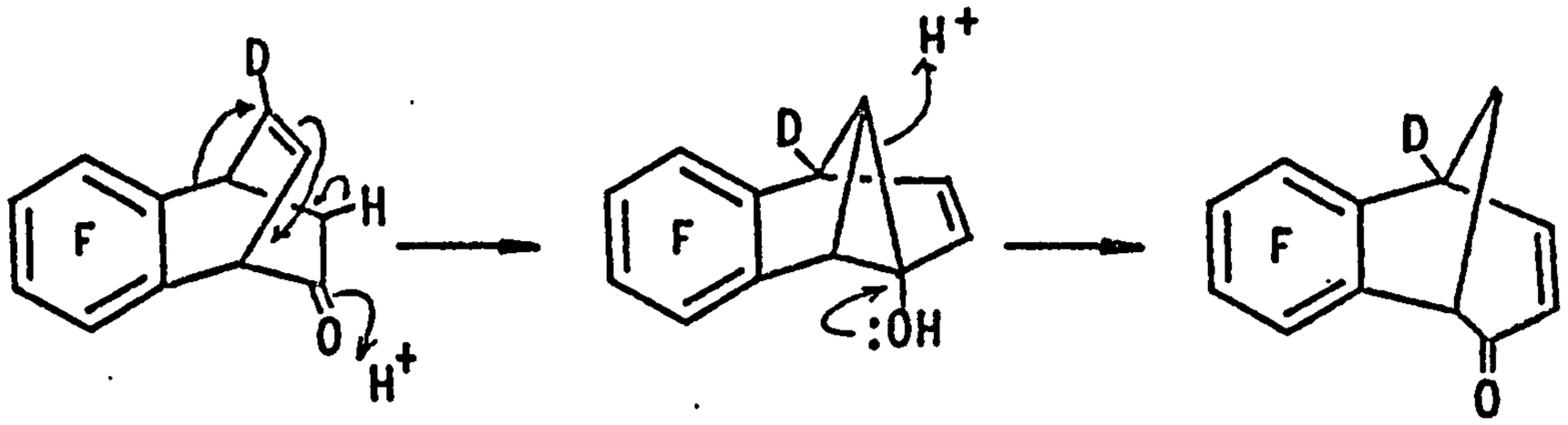


(40)



(41)

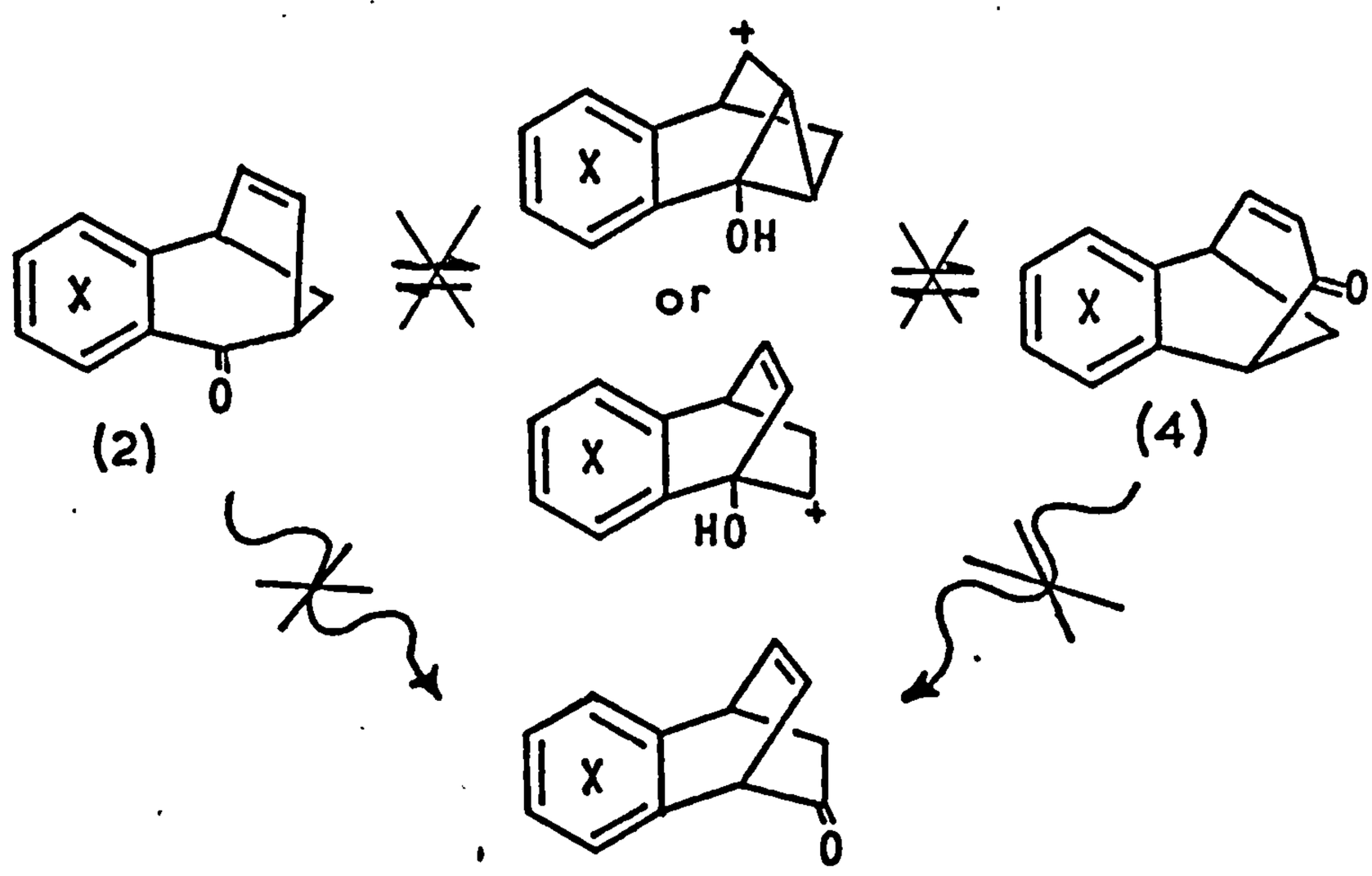
Mass spectrometry showed there was no loss of deuterium and ^1H n.m.r. spectroscopy showed the position of substitution. This result was therefore consistent with the mechanism C). The fact that only 5-deutero αβ-unsaturated ketone (41) was formed suggests the involvement of the carbonyl group in the rearrangement thus:-



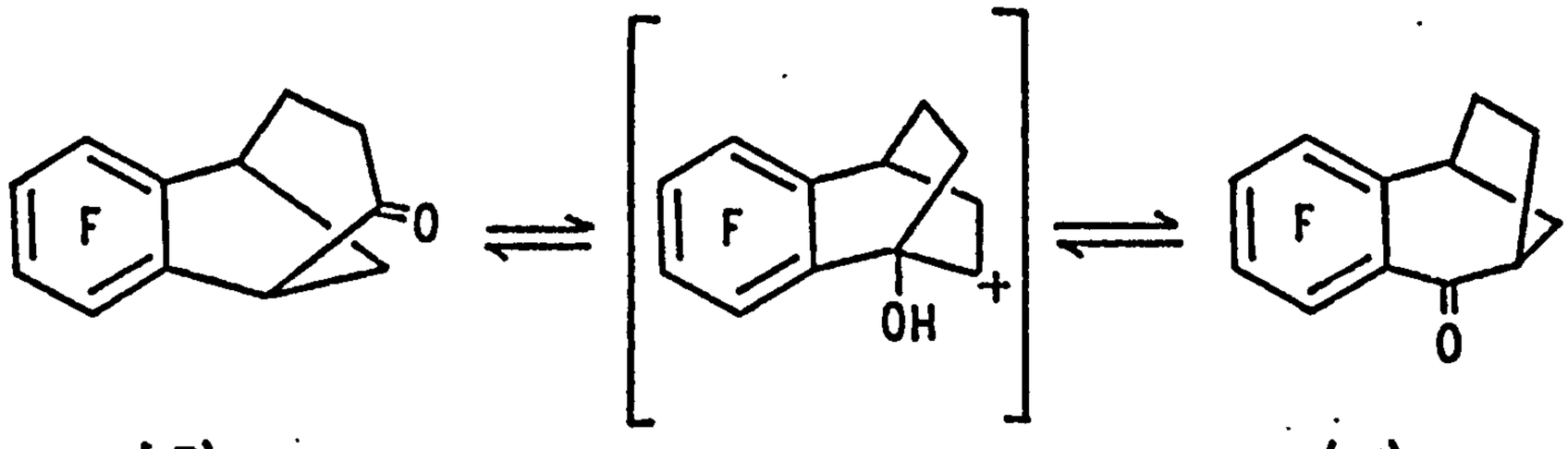
(40) (41)

No other mechanistic evidence was obtained for this reaction.

The results of these attempted equilibration studies suggest; 1) that the benzobarrelenone (3) was not formed from either the αβ-unsaturated- or vinyl ketones, 2) that the αβ-unsaturated- and vinyl ketones are not equilibrated through a common intermediate.



We have also briefly studied possible interconversions of the reduced vinyl ketone compound (14) and of the reduced αβ-unsaturated ketone, compound (15) thus:-



(15) (14)

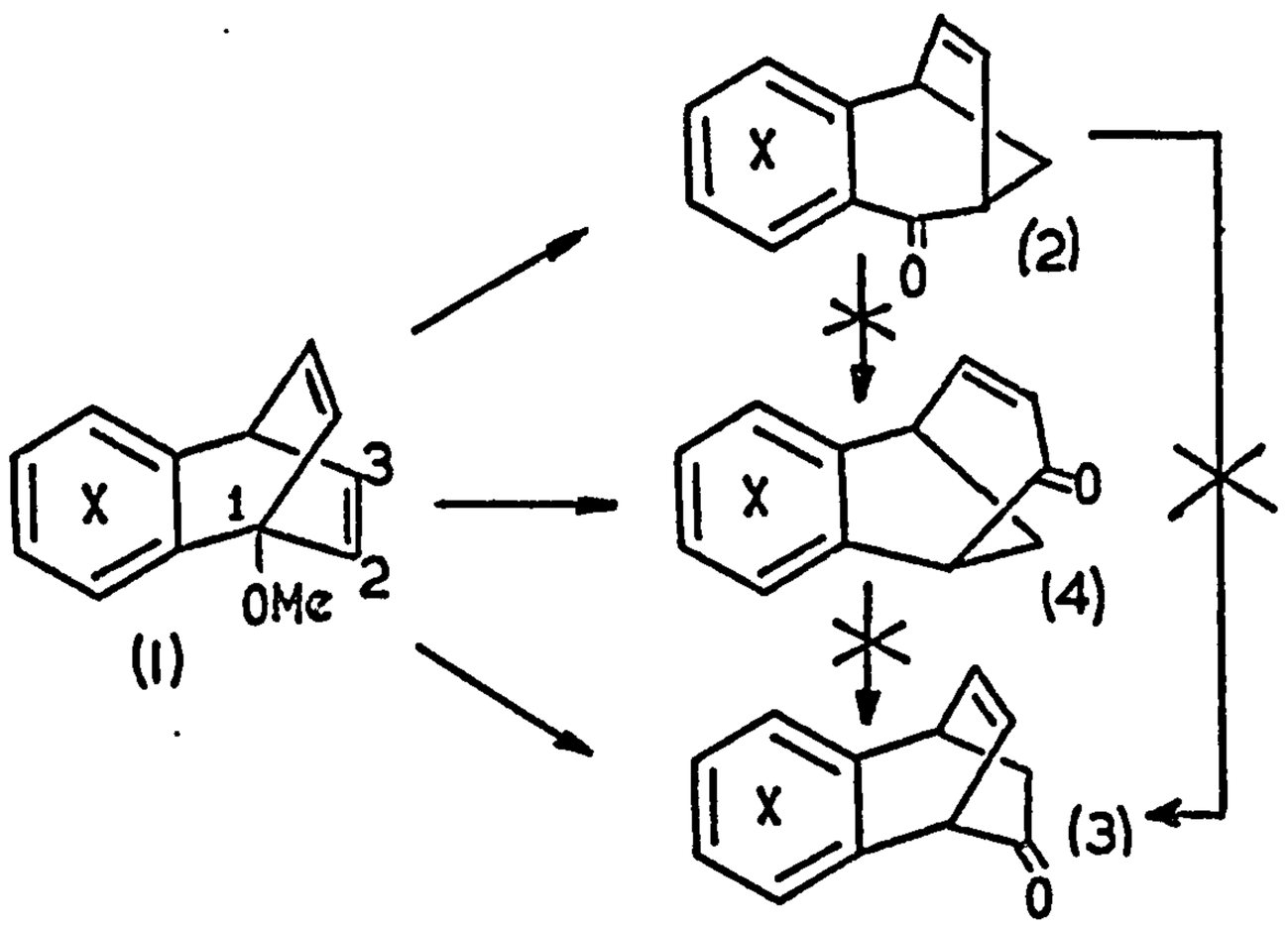
However both (14) and (15) can be recovered unchanged after treatment with either, trifluoroacetic acid heated under reflux for 18 hours, or with concentrated sulphuric acid after 20 hours at room temperature or fluorosulphonic acid at room temperature for 24 hours. Similar reduced compounds in the beyerene system do rearrange under acidic conditions. For example the compound (42) can be converted to the compound (43).[144]

(42) (43)

The only significant difference in this system to ours is the 17- methyl group. It is likely that the driving force for the rearrangement is therefore due to the increased stability of an intermediate carbonium ion by this methyl group.

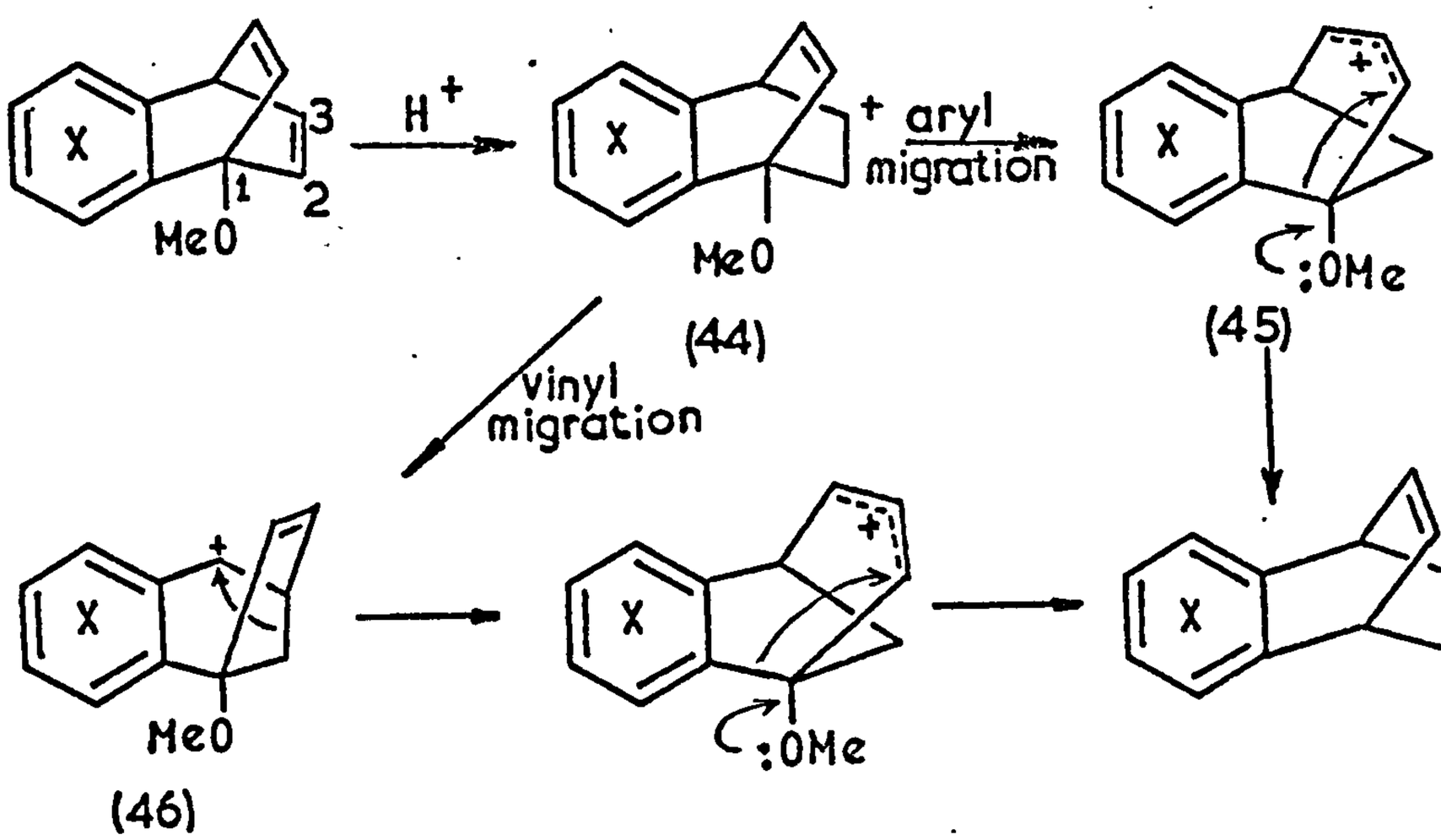
Solvolysis of the epimeric 1-methoxy-3-tosyloxy-(5,6)-tetrafluorobenzobicyclo[2.2.2]octadienes.

As the benzobarrelenone (3) was not apparently derived from the vinyl ketone (2) or the αβ-unsaturated ketone (4) we must consider other independent routes to account for its formation from the 1-methoxybenzobarrelene (1).

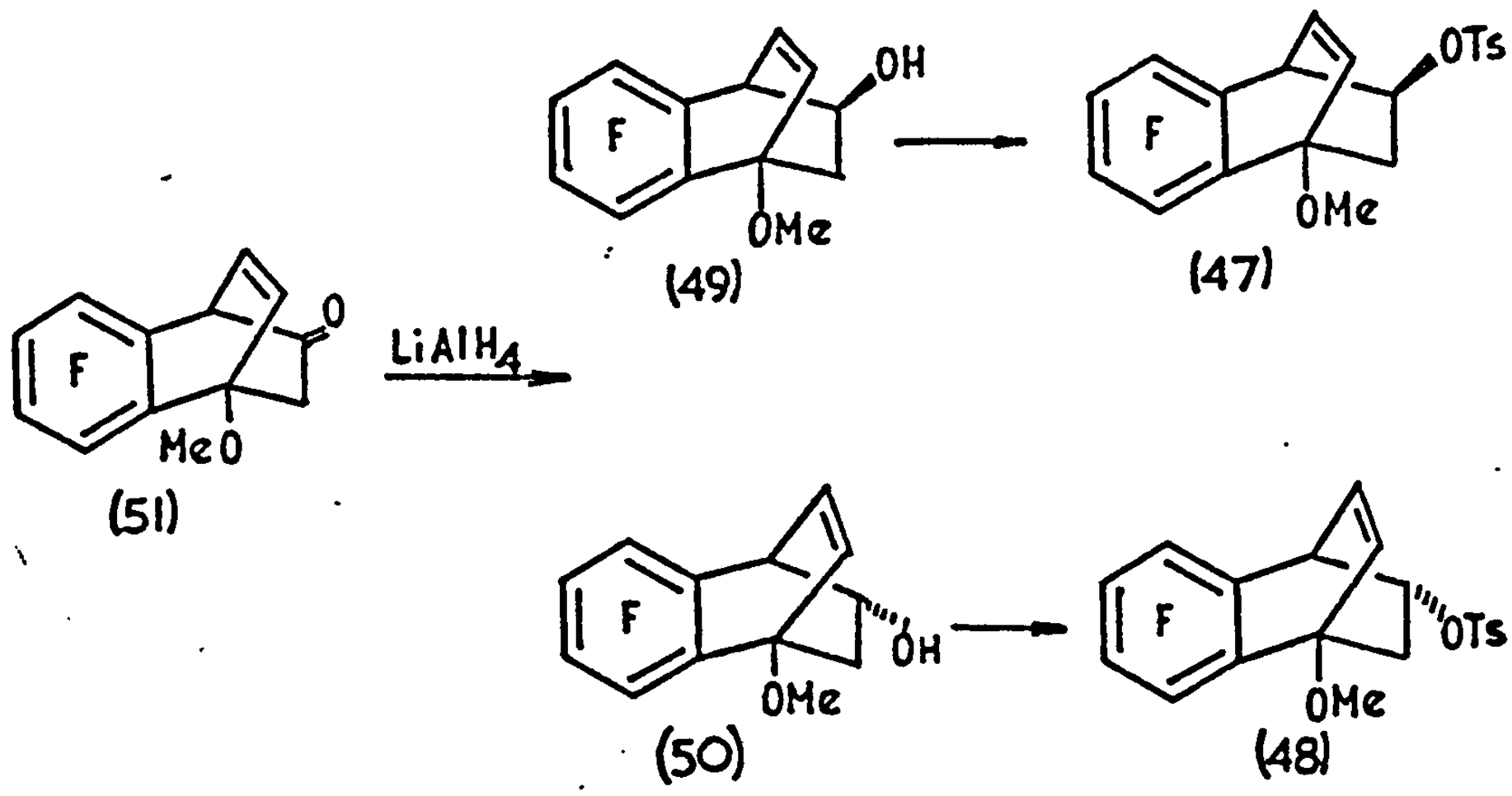


So far, we have only considered mechanisms which involve protonation of the barrelene double bond to form a carbonium ion at C_2. This was then thought to rearrange under the influence of the methoxy group. Protonation of the barrelene to form a carbonium ion at C_3 is, however, equally likely. The intermediate ion (44) could then rearrange to the benzobarrelenone (3) by a number of pathways.

Mechanism IV

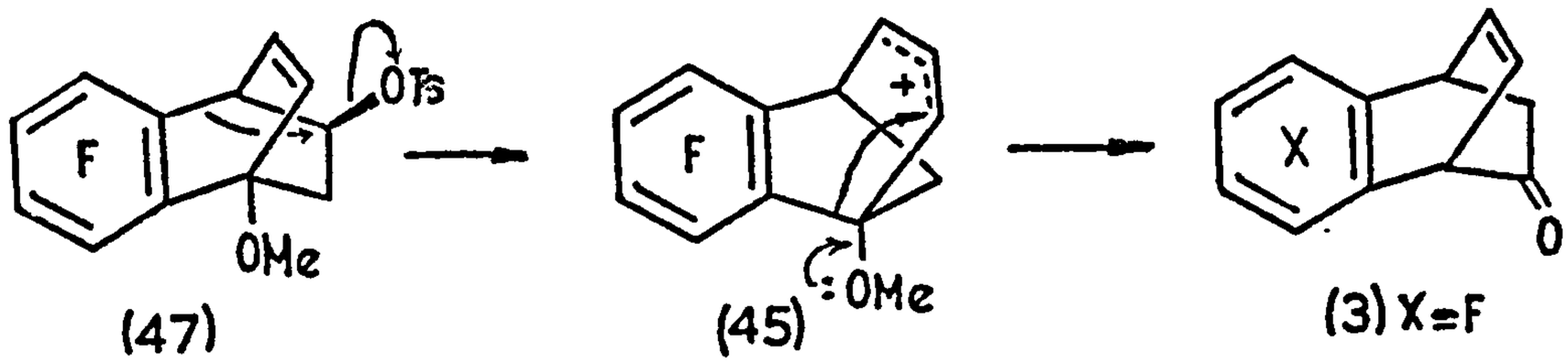


It was proposed to test these mechanisms by solvolytic studies of the 3-exo-tosylate (47) and of the 3-endo-tosylate (48). These two tosylates were prepared in the usual way from the alcohols (49) and (50). The alcohols were obtained by lithium aluminium hydride reduction of the 3-keto compound (51).

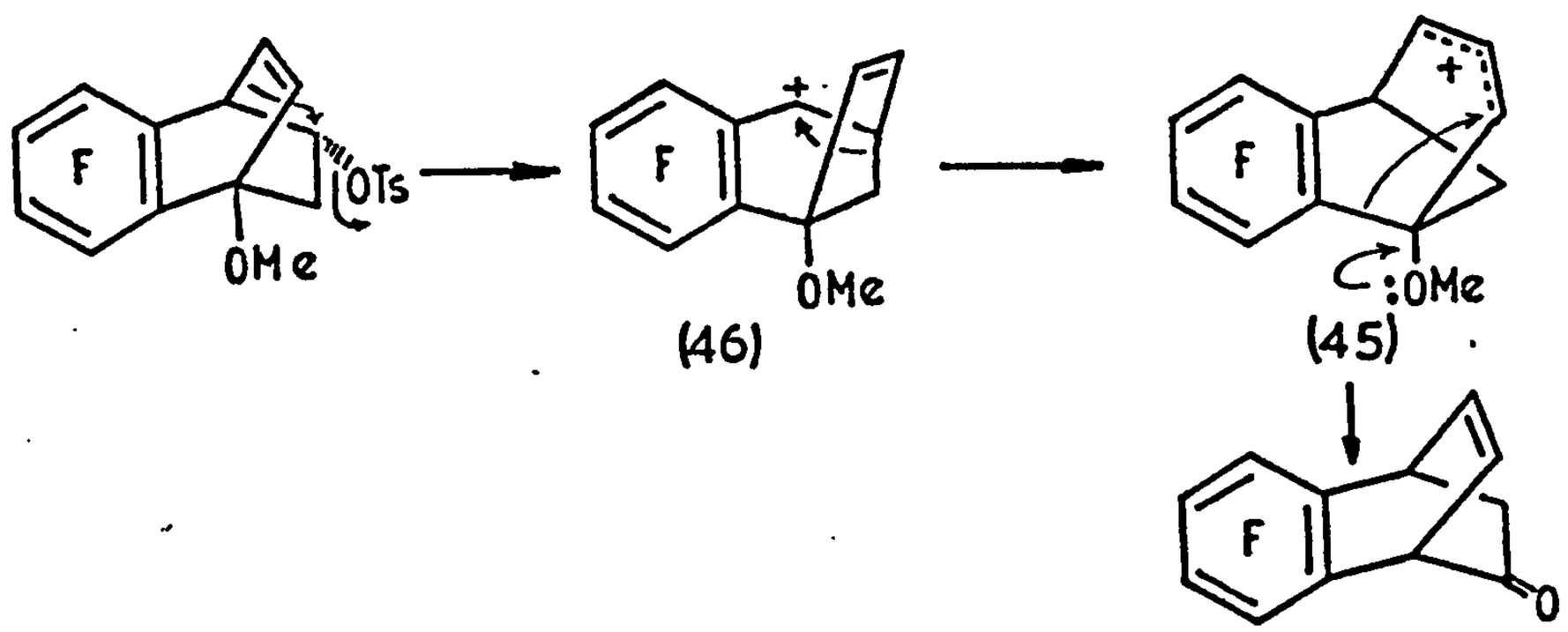


We hoped that the 3-tosylates would show high stereospecificity in their solvolyses and therefore the aryl-migration pathway versus the vinyl-migration pathway could be distinguished.

The 3-exo-tosylate should give the benzobarrelenone (3) X=F by aryl migration via the allylically stabilised cation (45) thus :-

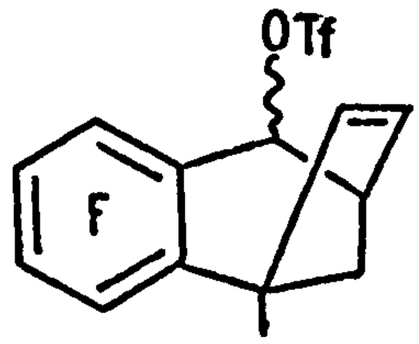


The 3-endo-tosylate should give the benzobarrelenone (3) X=F by 1,2-vinyl migration to form a benzylic cation (46); 1,2-alkyl-bridge migration would then lead to the same allylically stabilised ion (45), and hence to the barrelenone thus:-



In concentrated sulphuric acid both the 3-exo-tosylate (47) and the 3-endo-tosylate (48) gave benzobarrelenone (3) X=F, in 71 % and 60% yields respectively. However, in the more nucleophilic trifluoro-acetic acid, although the 3-exo-tosylate (47) gave the benzobarrelenone

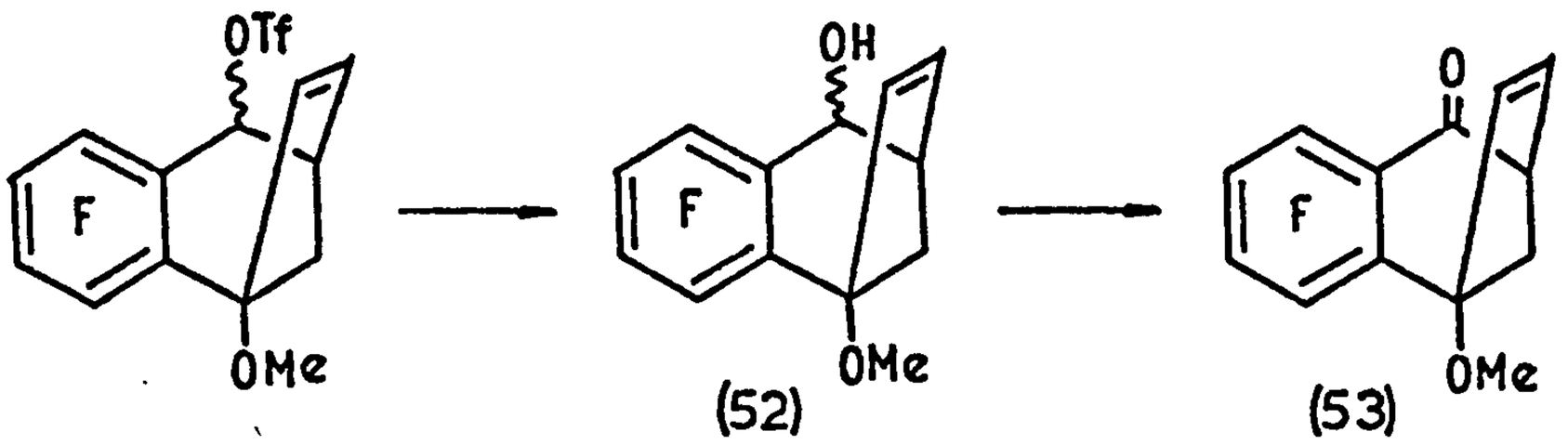
(3) X=F in 92% yield we were able to trap the intermediate (46) as the epimeric trifluoroacetates (51) when the 3-endo-tosylate (48) was solvolysed.



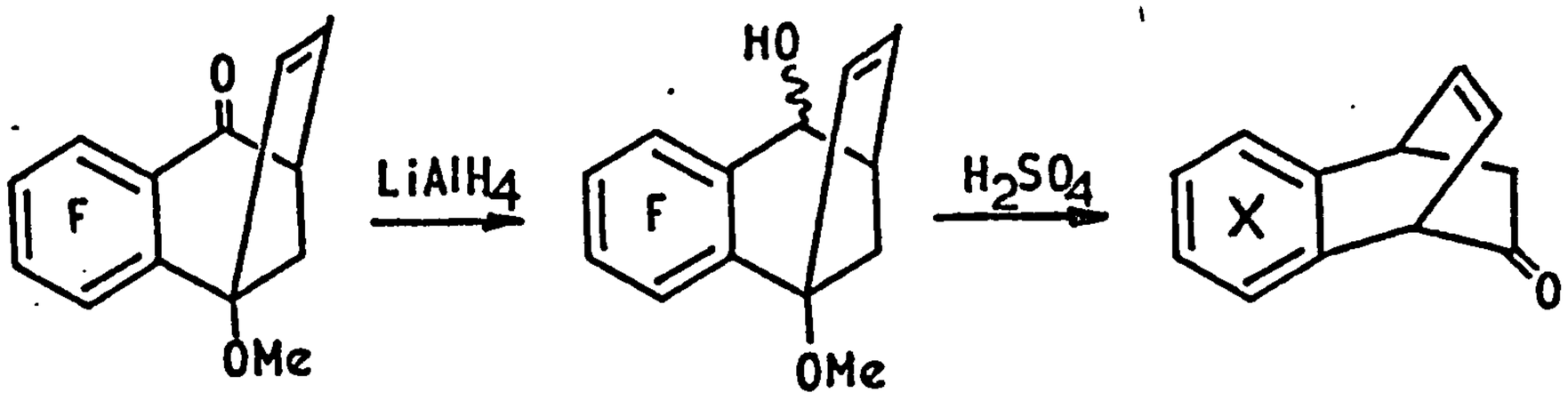
Tf = CF_3CO-

(51)

The epimeric trifluoroacetates (51) were characterised by hydrolysis to the epimeric alcohols (52) which were then oxidised with chromic oxide/pyridine to the known ketone (53) (reported later in this thesis).



When the ketone (53) was reduced with lithium aluminium hydride to the alcohols (54) and then treated with concentrated sulphuric acid the benzobarrelenone (3) X=F was formed.



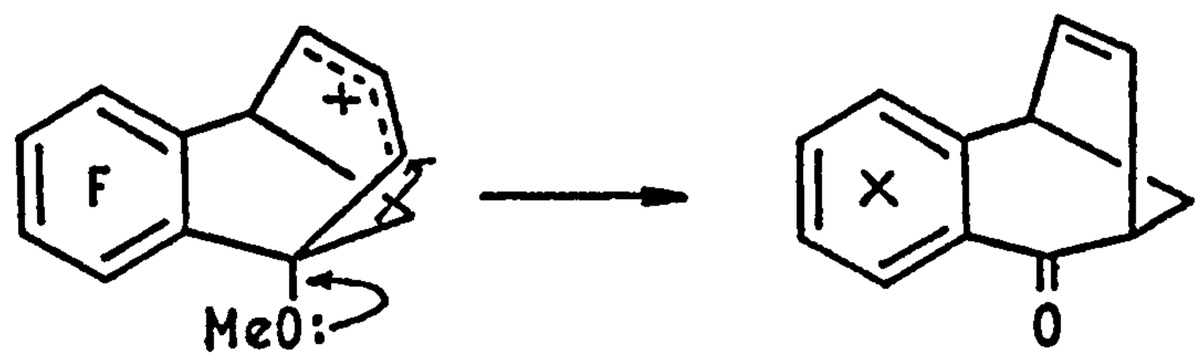
(53) (54) (3) X=F

The compounds (54) in concentrated sulphuric acid would be expected to form the benzylic cation (46) X=F which then could rearrange to the

benzobarrelenone.

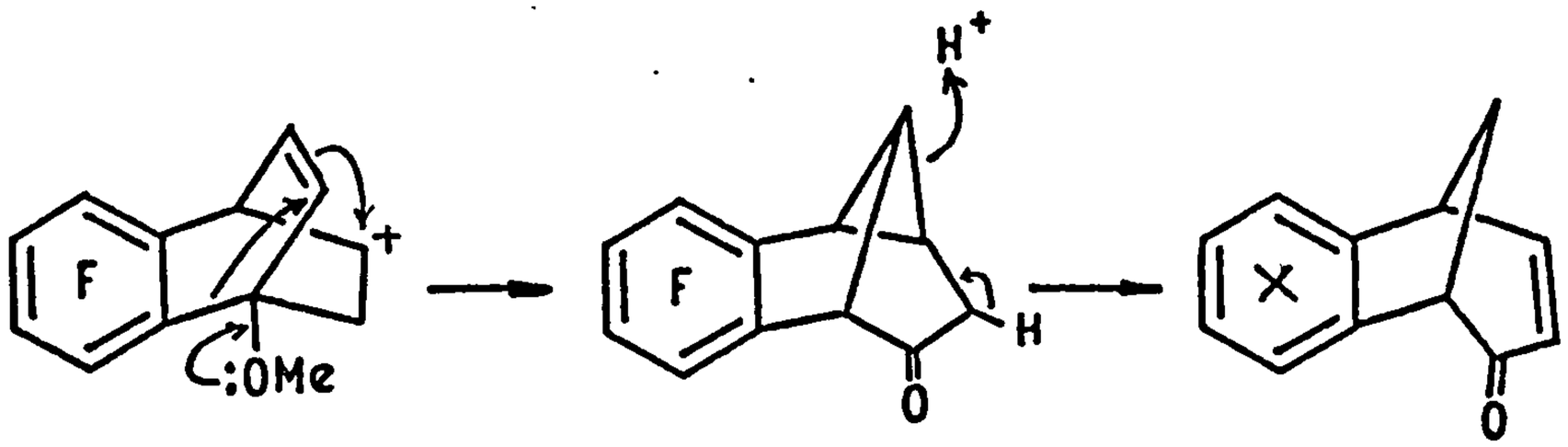
These reactions demonstrate that the benzobarrelenone (3) was most probably derived by initial rearrangement at the C_3 position. In all the solvolytic studies on the 3-tosylates, the vinyl ketone (2) X=F and the αβ-unsaturated ketone (4) X=F, were not detected, although in theory reasonable mechanistic routes to these compounds can be proposed.

For example the vinyl ketone (2) X=F, could be formed by an alkyl migration in the allylically stabilised ion (45) thus :-



(45) (2) X=F

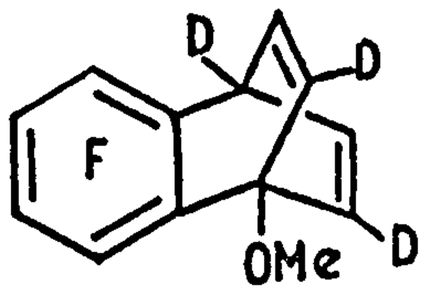
The αβ-unsaturated ketone (4) X=F, could be formed by the following mechanism:-



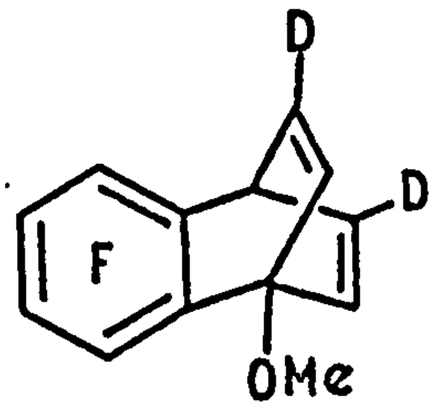
(4) X=F

Deuterated 1-methoxybenzobarrelenes

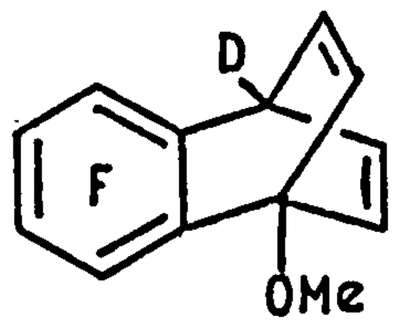
Undoubtedly the best way of studying the reaction mechanisms operating in the rearrangements of 1-methoxybenzobarrelenes in sulphuric acid has been the use of specifically deuterated 1-methoxybenzobarrelenes. Three deuterated compounds (54), (55), and (56), have been prepared, and their rearrangements studied.



(54)

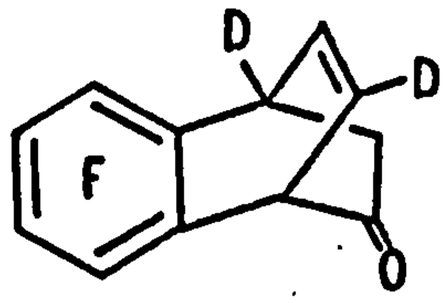


(55)

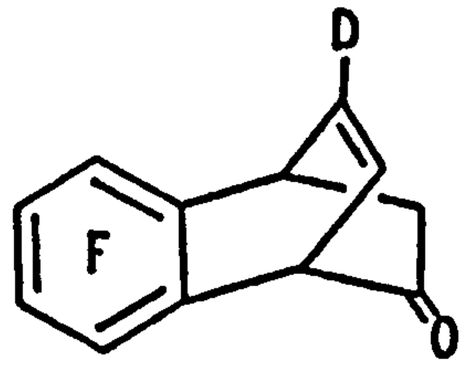


(56)

The three deuterated 1-methoxybenzobarrelenes were prepared by the reaction of tetrafluorobenzyne with the appropriately deuterated anisole. The benzobarrelenones (74) and (40) were obtained as minor products in the reaction of tetrafluorobenzyne with 3,5-dideuteroanisole and 4-deuteroanisole respectively.



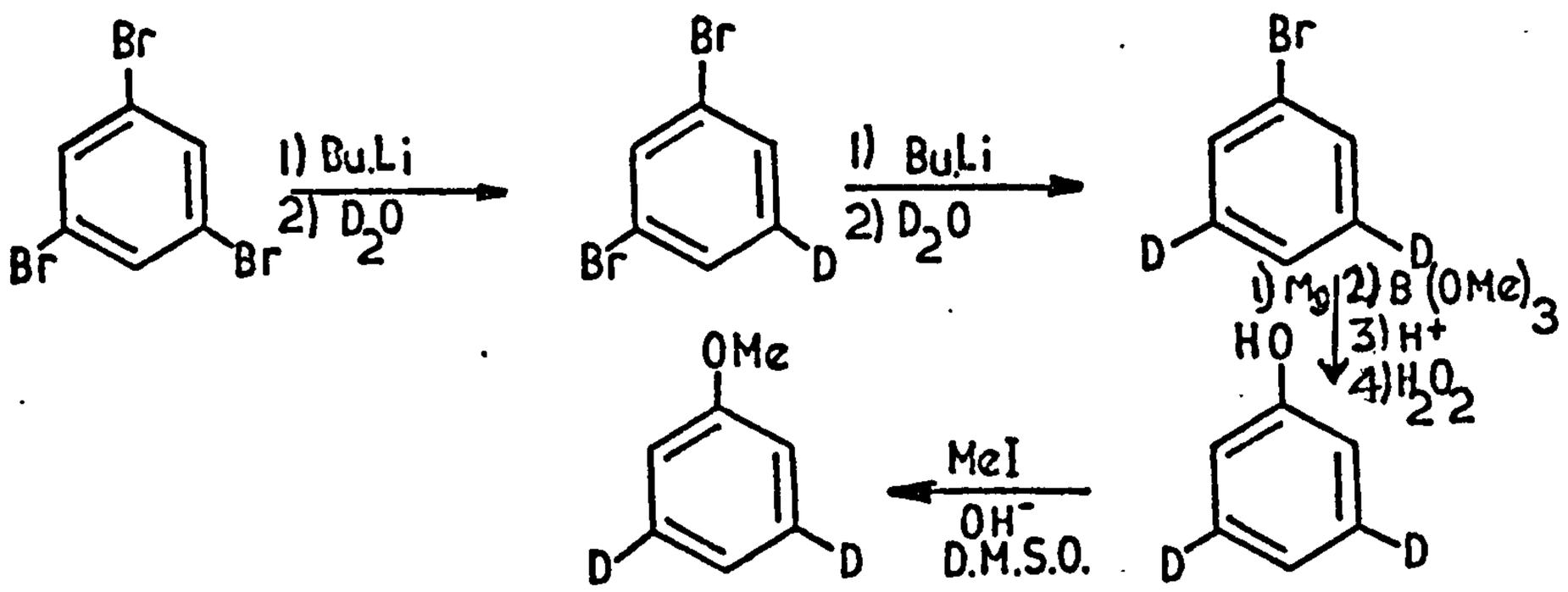
(74)



(40)

2,4,6-Trideuteroanisole was prepared in two steps from 2,4,6-tribromoanisole. The reaction of 2,4,6-tribromoanisole with n-butyl-lithium in light-petroleum gave, after quenching with deuterium oxide, 4-bromo-2,6-dideuteroanisole[1] The halogen-metal interconversion reaction of this product with n-butyl-lithium in ether followed by deuterolysis then gave 2,4,6-trideuteroanisole which was shown, by mass spectrometry, to contain $> 99\%$ d_3.

Methods of preparing deuterated anisoles or phenols usually involve exchange reactions,[145] for example 2,4,6-trideuterophenol (90% d_3, 10% d_2) has been prepared from sodium phenate by exchange with deuterium oxide.[146] These methods require a large molar excess of deuterium oxide. The very high incorporation of deuterium obtained in the 2,4,6-trideuteroanisole encouraged us to use a similar method for the preparation of 3,5-dideuteroanisole. The route that was chosen is outlined below.



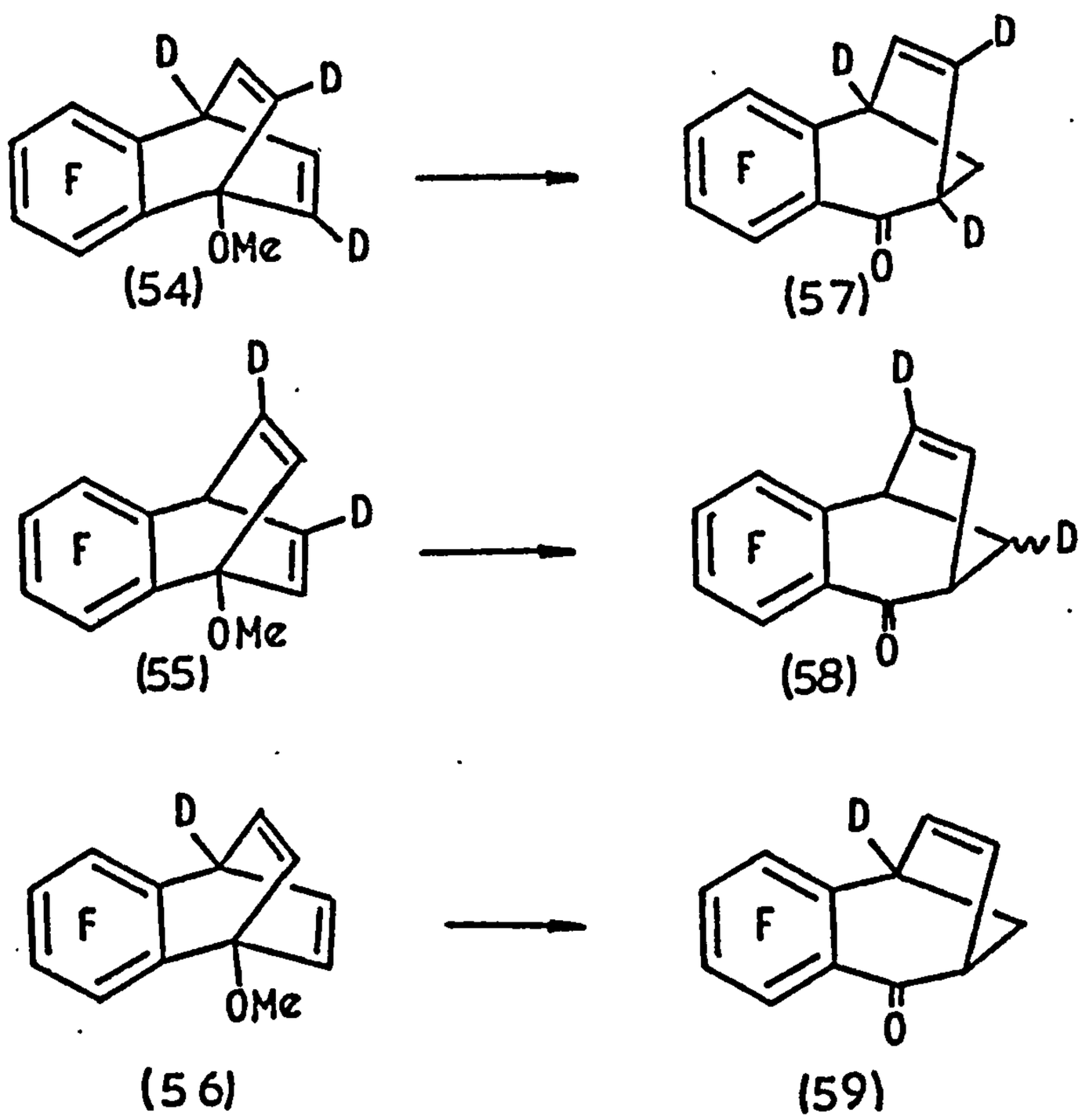
Bromo-3,5-dideuterobenzene has been prepared from 1,3,5-tribromobenzene via deuterolysis of the Grignard reagent.[164] The route that we used was not as successful as anticipated giving 3,5-dideuteroanisole, which was shown by mass spectrometry to contain 77% d_2, 19% d_1, and 4% d_o. 4-Deuteroanisole was prepared by deuterolysis of the Grignard reagent prepared from 4-bromoanisole. The deuterium content was determined by mass spectrometry and found to be 87% d_1 and 13% d_o.

The rearrangement of the adducts (54), (55), and (56) in sulphuric acid gave the corresponding vinyl ketones, benzobarrelenones and αβ-unsaturated ketones. The percentage of deuterium in these products was obtained by mass spectrometry. The position of deuteration was determined

by ^{1}H n.m.r. spectroscopy. The ^{1}H n.m.r. data for the products is shown in table 4 (p. 180) for the vinyl ketones, table 5 (p. 181) for the αβ-unsaturated ketones, and table 6 (p. 182) for the benzobarrelenones.

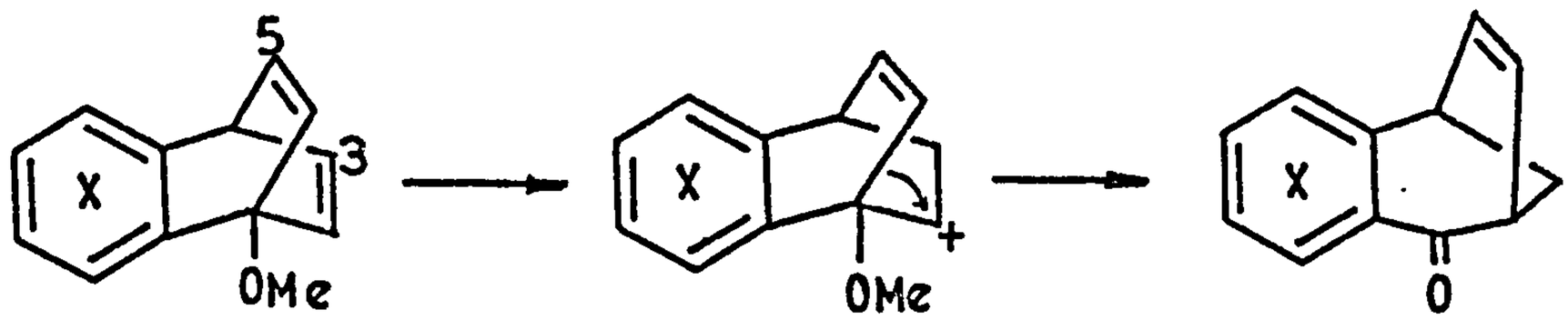
It is now possible to discuss the mechanistic details of the rearrangement of 1-methoxybenzobarrelenes in sulphuric acid with some degree of confidence.

Firstly the formation of the vinyl ketone. The deuteration results are represented pictorially below:-



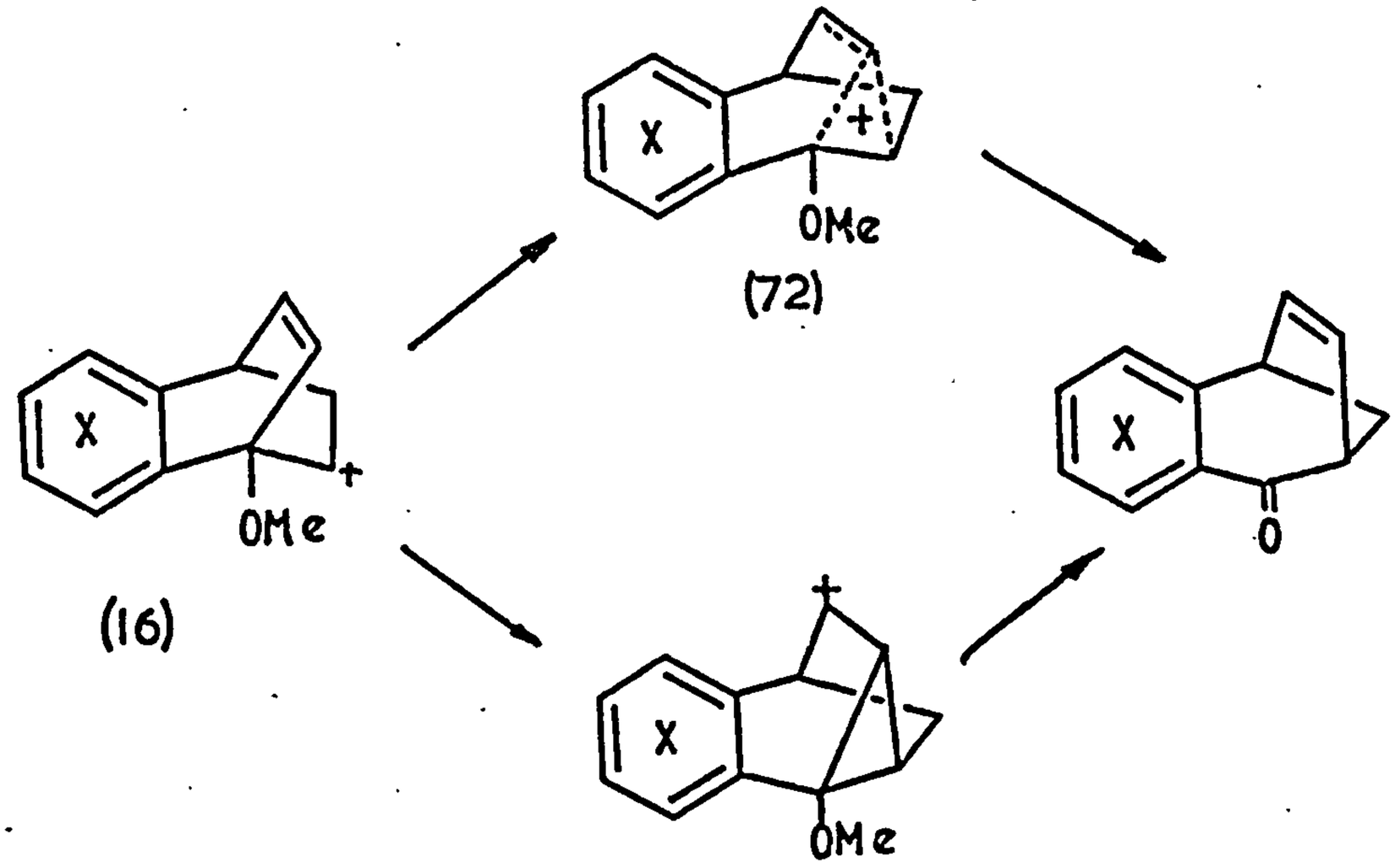
These results,together with the solvolytic studies of the 2-endo-tosylate (18) suggest that the vinyl ketone is formed from a carbonium ion intermediate (16) X=F, by migration of the vinyl bridge. The

intermediate ion being formed by protonation of the 1-methoxybenzobarrelene at C_3.



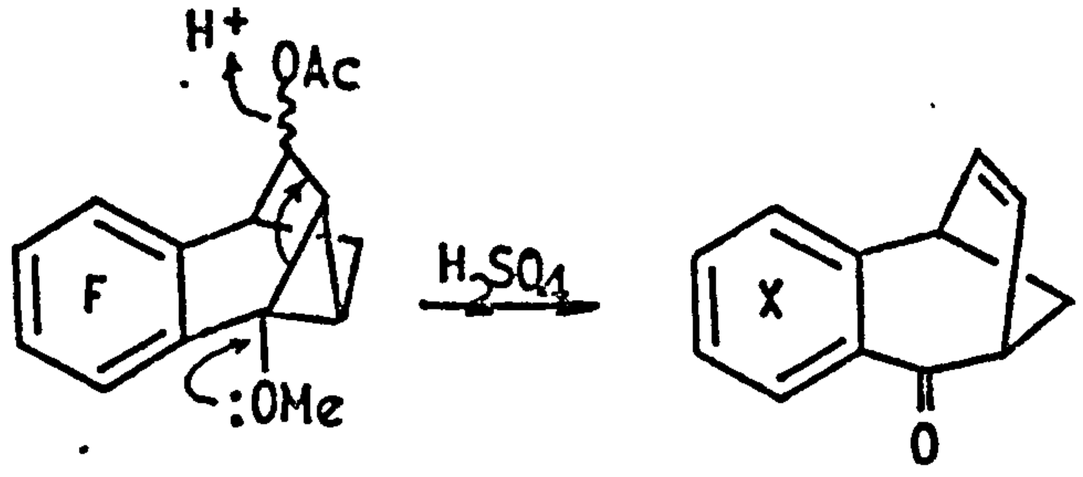
(1) (16) (2)

As no deuterium was lost during the rearrangement of the 3,5-dideutero-1-methoxybenzobarrelene (55), the ion (16) must rearrange rapidly. The 1,2-vinyl migration could also be represented as a collapse of a non-classical ion (72) or by rearranging a classical tricyclic ion (73).



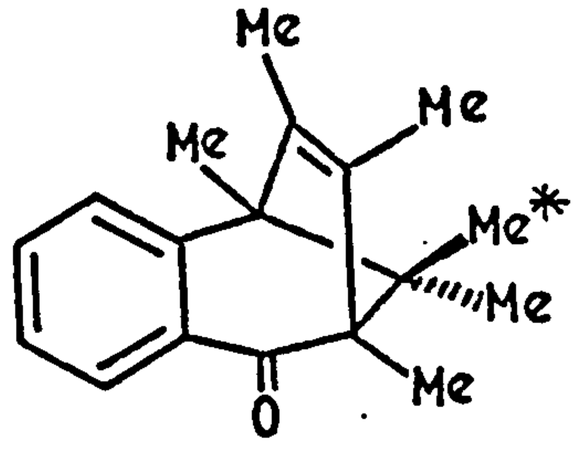
(73)

The methoxycyclopropyl structure present in (73) would be expected to be very reactive under acidic conditions.[147,148] It was hoped to be able to demonstrate the possible intermediacy of (73) by the acid catalysed rearrangement of (27). However it was not possible to prepare compound (27) (discussed previously on p. 127).



(27) (2) X= F

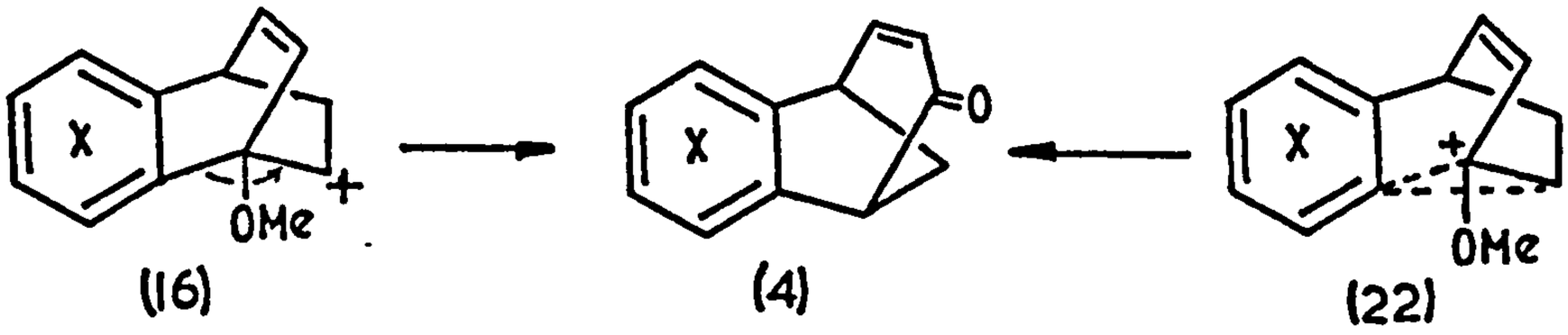
The deuteration results imply that there was no scrambling of the label during the rearrangement. Possible scrambling could occur via a degenerate cyclopropylcarbinyl cation. Degenerate cyclopropylcarbinyl cations have been observed in a related system. Hart[149] has shown that five of the six methyl groups in the compound (36) undergo deuterium exchange in deuterotrifluoroacetic acid; the 8-anti-methyl group (asterisk) remains unscathed.



(36)

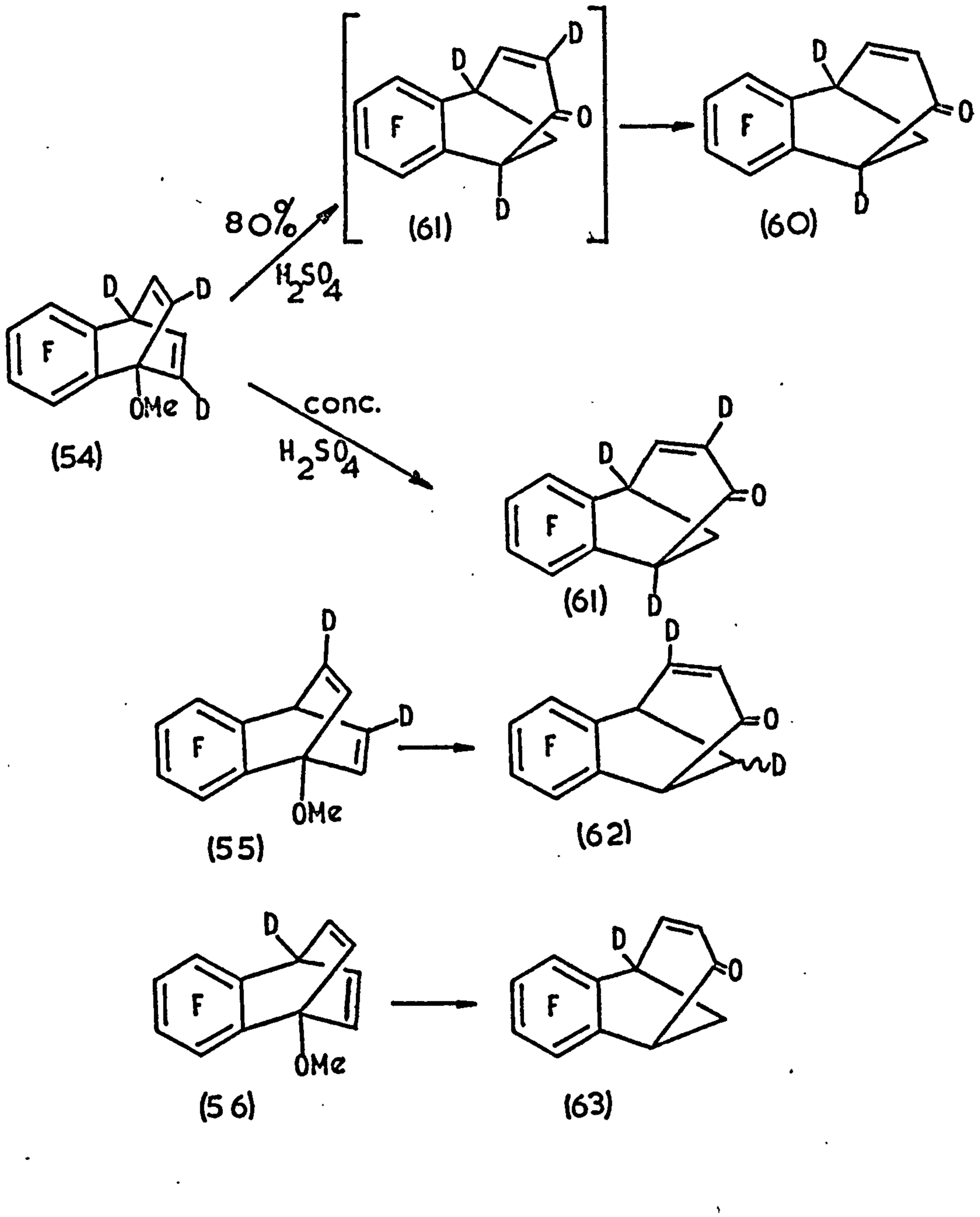
Other mechanisms of formation of the vinyl ketone (p. 144) cannot be accommodated by the present deuteration results.

The formation of the αβ-unsaturated ketone during the rearrangement of 1-methoxybenzobarrelenes appears to arise via an aryl-migration in the initially formed carbonium ion (16), or possibly involving an intermediate bridged ion (22).



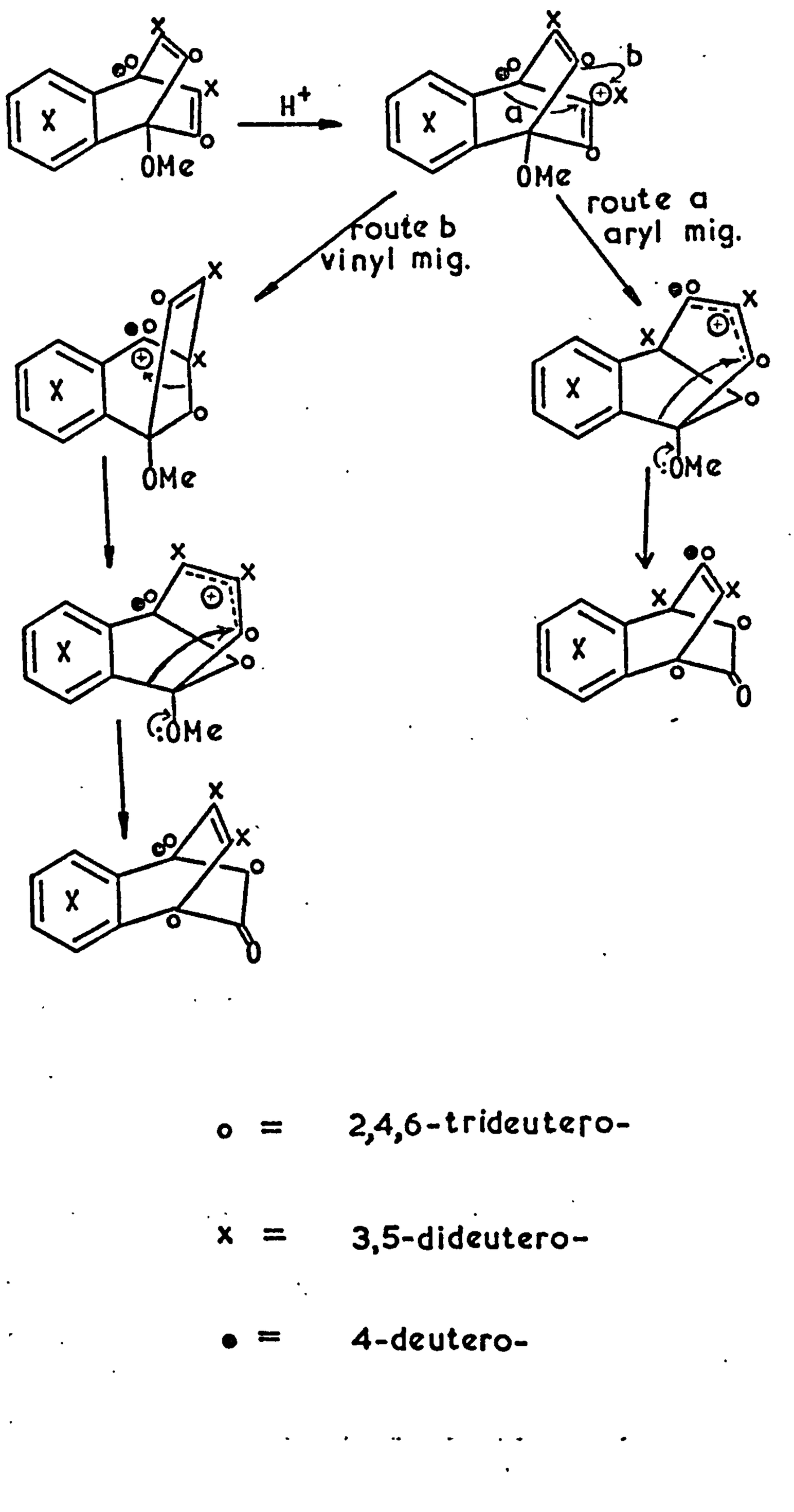
(16) (4) (22)

The deuteration results are in accord with these proposals (table 5. p. 181) and are represented pictorially below:-



Once again α-exchange in the αβ-unsaturated ketone (61) occurs to give the dideutero-αβ-unsaturated ketone (60) in 80% sulphuric acid at 80°.

The benzobarrelenones formed in the rearrangement of 1-methoxybenzobarrelenes appear to be derived by two pathways and further these pathways can vary depending on the reaction conditions.



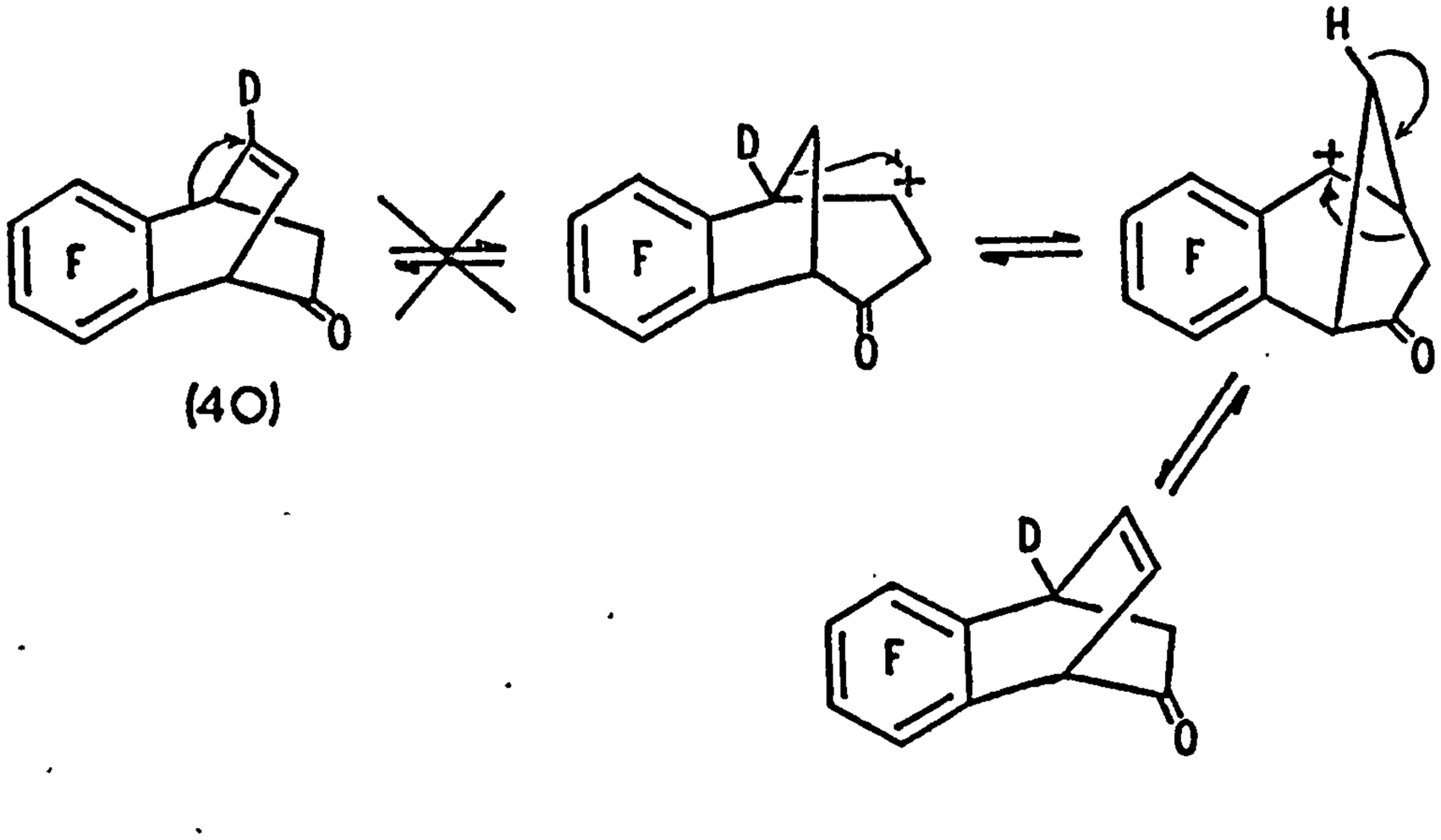
The ^1H n.m.r. spectroscopic data (table 6 p.182) shows the ratios of the vinyl to bridgehead to methylene protons. These ratios were obtained by averaging multiple integration values. It was possible to calculate the integration ratios by using the average deuteration levels (obtained by mass spectrometry) and finding the percentage pathways which would give the best fit with the observed values. The percentage pathways which gave the best fit with the observed values are shown below.

Starting material	Average deuteration levels	Reaction conditions	Percentage Pathway a.	Percentage Pathway b.
(54)	99% d_3	80% H_2SO_4 at 80°	55	45
(54)	99% d_3	Conc.H_2SO_4 at R.T.	79	21
(55)	5% d_o; 18% d_1; 77% d_2	Conc.H_2SO_4 at R.T.	80	20
(56)	12% d_o; 88% d_1	Conc.H_2SO_4 at R.T.	78	22

The results show that in concentrated sulphuric acid ca. 80% of the benzobarrelenone is derived by pathway a. (p. 151) and ca. 20% by pathway b.. In 80% sulphuric acid at 80° the ratio of the two pathways changes to 55% a. and 45% b. All the calculated integration values are within 5% of the observed values. A number of assumptions are made in the calculations. Thus, it has been assumed that there is no isotope effect and that protonation occurs equally rapidly to a double bond containing a deuterium atom and to one without deuterium present. Also that protonation occurs symmetrically to a double bond containing one

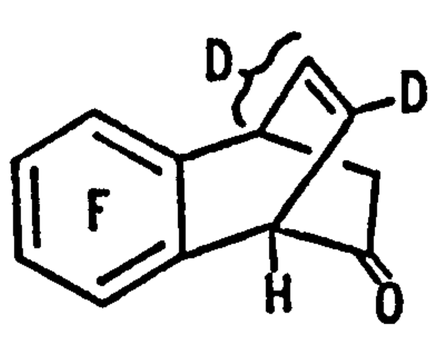
deuterium atom. As an added test, the deuterated benzobarrelenones from the rearrangements were converted to the corresponding naphthalenes by photolysis and the ^{1}H n.m.r. spectral integrations for the 1,4-protons were compared with those for the 2,3-protons (table 7 p.182). These results were then compared with the calculated values and are in very good agreement with one another. In the rearrangements which gave rise to the deuterated benzobarrelenones there was no evidence for loss of any of the deuterium.

It was also necessary to establish that there was no scrambling of the deuterium atoms in the benzobarrelenone under the reaction conditions. For this reason the 5-deuterio-benzobarrelenone (40) was dissolved in concentrated sulphuric acid at room temperature. After 3 hours the benzobarrelenone was recovered and was shown by ^{1}H n.m.r. spectroscopy to be completely unchanged.

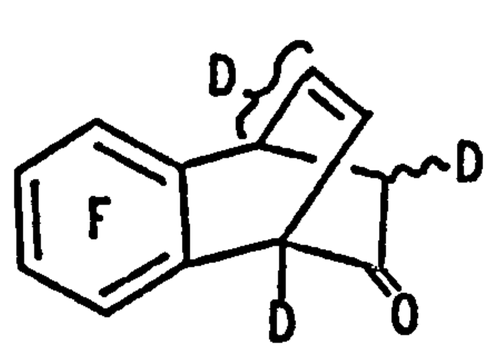


(40)

^{1}H N.m.r. spectra of the benzobarrelenones show resonances for the two bridgehead protons at the same chemical shift. It was important in the structure assignment of the deuterated benzobarrelenones to try and distinguish between these two protons. This was done using the chemical shift reagent, tris(dipivalomethanato)europium [$Eu(DPM)_3$].[150] The ^{1}H n.m.r. spectra of the benzobarrelenone (66) obtained from the rearrangement of the 3,5-dideutero-1-methoxybenzobarrelene (55) and the benzobarrelenone (65) from the rearrangement of 2,4,6-trideutero-1-methoxybenzobarrelene (54) were examined in the presence of $Eu(DPM)_3$. Compound (66) showed the expected large downfield shift of the C_1-proton, whereas the compound (65) showed no such shift.



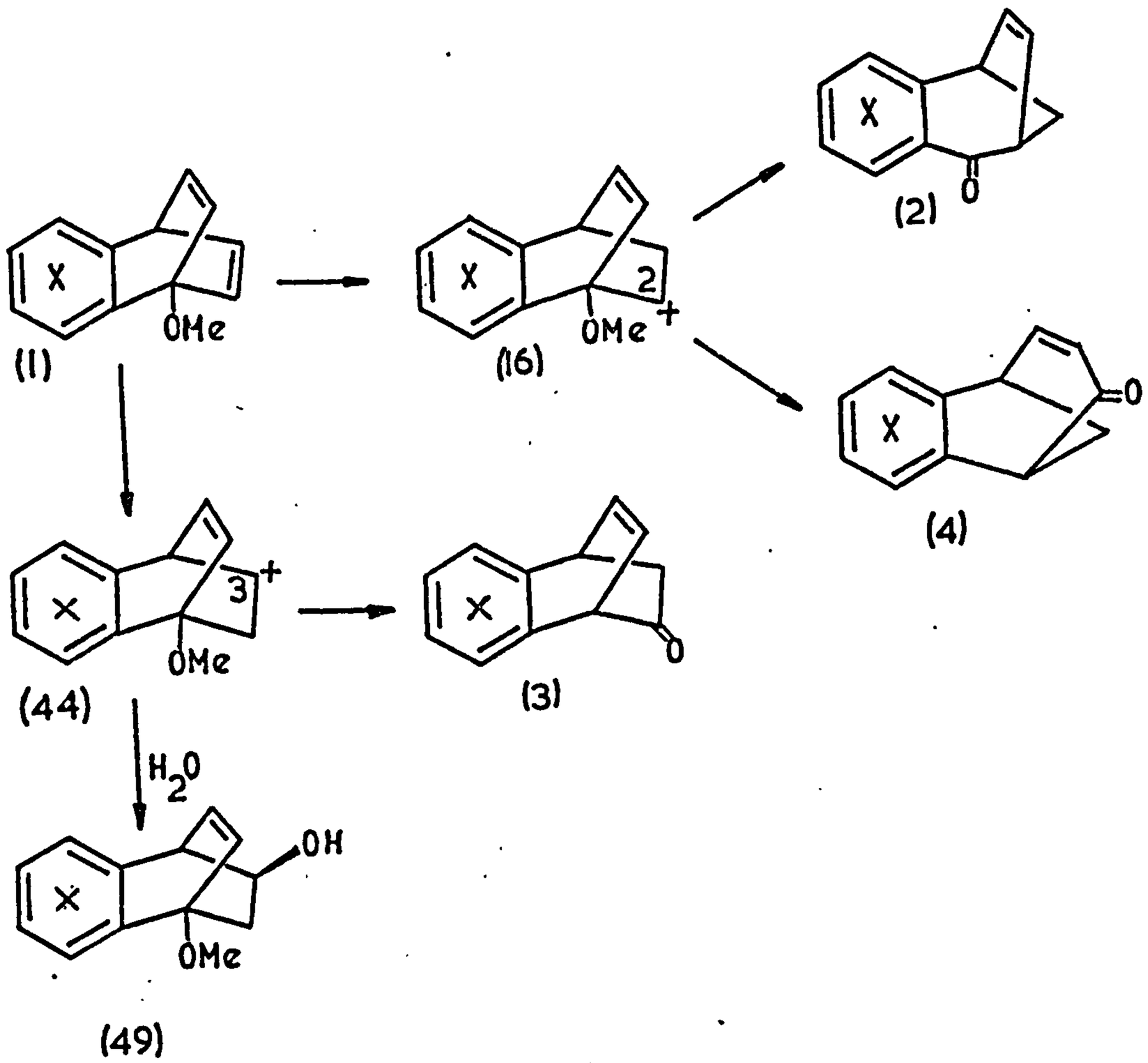
(66)



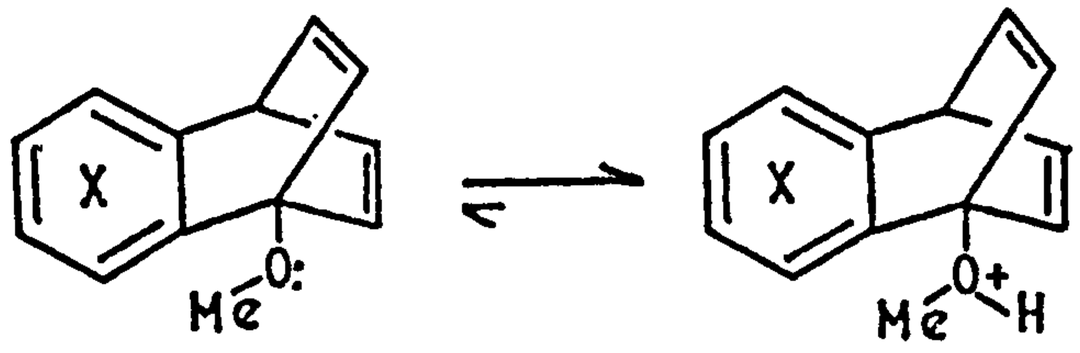
(65)

General conclusions on the reaction mechanism

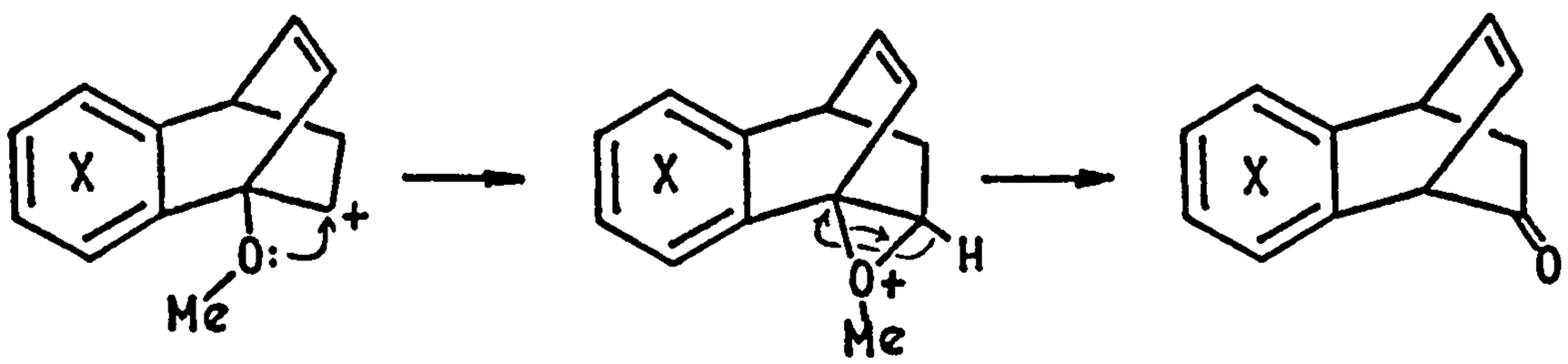
All the results obtained thus far indicate that in the rearrangement of the 1-methoxybenzobarrelenes (1) in concentrated sulphuric acid the vinyl ketone (2) and the αβ-unsaturated ketone (4) are derived irreversibly from a common carbonium ion intermediate (16). The benzobarrelenone (3) is derived by an independent route which involves rearrangement at position C-3.



Participation of the intermediate ion (44) has been observed in one experiment when 67% H_2SO_4 was used as the rearranging mixture and the ion was trapped as the 3-hydroxy compound (49). A pure sample of this was not obtained from the reaction mixture owing to contamination by other hydroxylated species. A possible explanation for the formation of the benzobarrelenone (3) as the major product in these reactions may involve inductive control. In strong acid solution the methoxy-group of the 1-methoxybenzobarrelene (1) will be almost completely protonated, thus precluding the methoxy group from acting as a "trigger" to the rearrangement reactions.



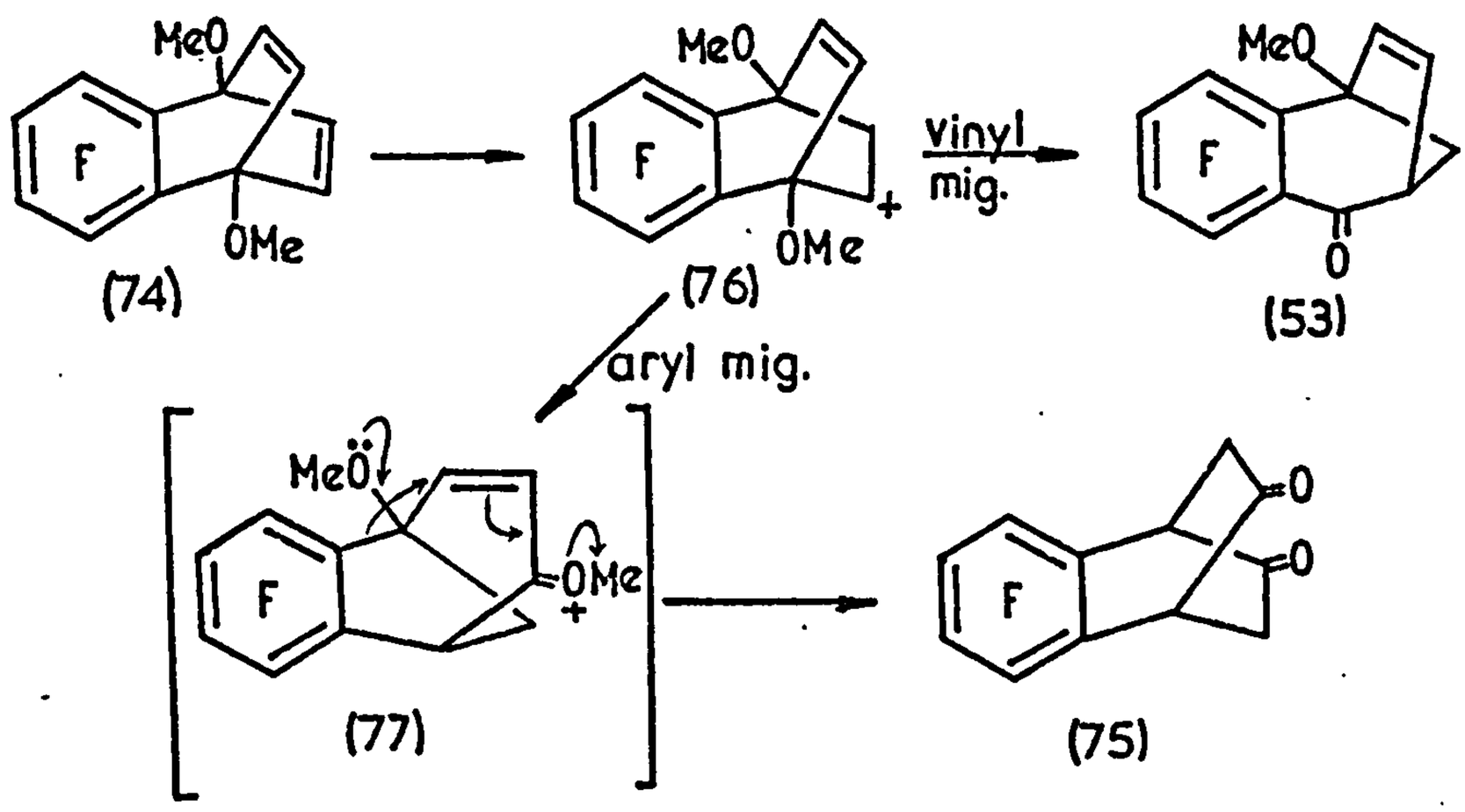
Some evidence for this idea was derived from the fact that in fluorosulphonic acid the 1-methoxybenzobarrelene (1) X=F gave the ratio of benzobarrelenone (3) X=F to the other two ketones (2), (4) X=F as ≃10:0.5. In concentrated sulphuric acid the ratio was ≃ 6:1 while in trifluoroacetic acid the ratio was ≃ 1:1. Other mechanisms which could account for the formation of the benzobarrelenone have been proposed by Barkhash.[52, 151] They involve anti-Bredt intermediates and hydride shifts and can be readily excluded by our deuterium labelling studies. Further results obtained in this laboratory[152] also exclude Barkhash's mechanisms. It has been shown that in the rearrangement of [1-^{14}C]-1-methoxytetrachlorobenzobarrelene to the benzobarrelenone the carbon attached originally to the methoxyl group becomes the carbonyl carbon in the product. The ^{14}C labelling result also eliminates any mechanisms which involve a 1,2-methoxy migration.



Similar 1,2-hydroxy shifts are known[153] although the strain present in the benzobarrelene system is likely to prohibit such rearrangements in our case. Some of the results so far discussed have been presented in a preliminary communication.[154]

Rearrangement of 1,4-dimethoxytetrafluorobenzobarrelene

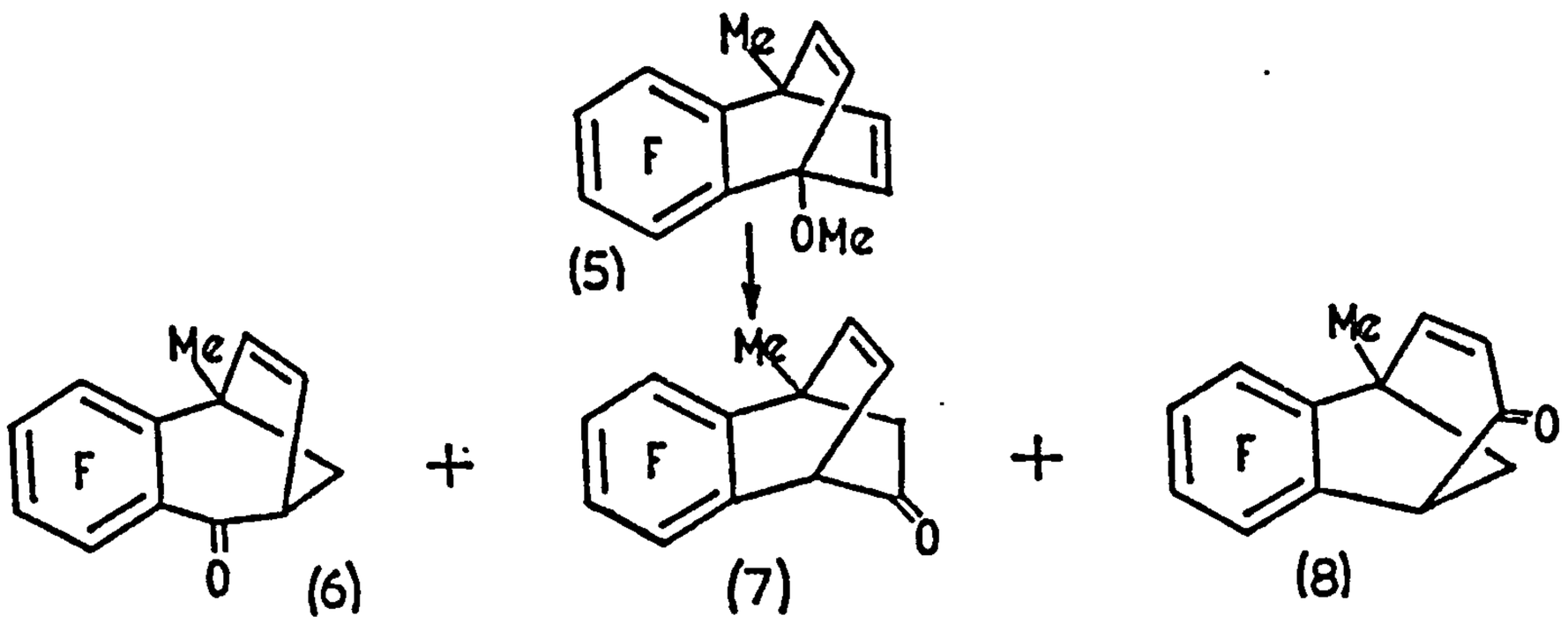
When the 1,4-dimethoxytetrafluorobenzobarrelene (74) was rearranged in 80% sulphuric acid, two products (75)and (53) were isolated in 20% and 18% yields respectively. The structure of compound (75) was readily assigned by a comparison with authentic material.[23] The structure of the compound (53) followed from its spectral properties which were similar to previously isolated vinyl ketones. The formation of these rearrangement products can be rationalised in terms of a protonation of a double bond in the benzobarrelene (74) to give a carbonium ion intermediate (76). Rearrangement of this ion by vinyl migration gives compound (53) and by aryl migration gives an unstable intermediate (77), which then rearranges further to the diketone (75).



Other pathways for the formation of (75) are possible but will not be discussed owing to lack of any mechanistic data on this reaction.

Rearrangement of 1-methoxy-4-methyltetrafluorobenzobarrelene.

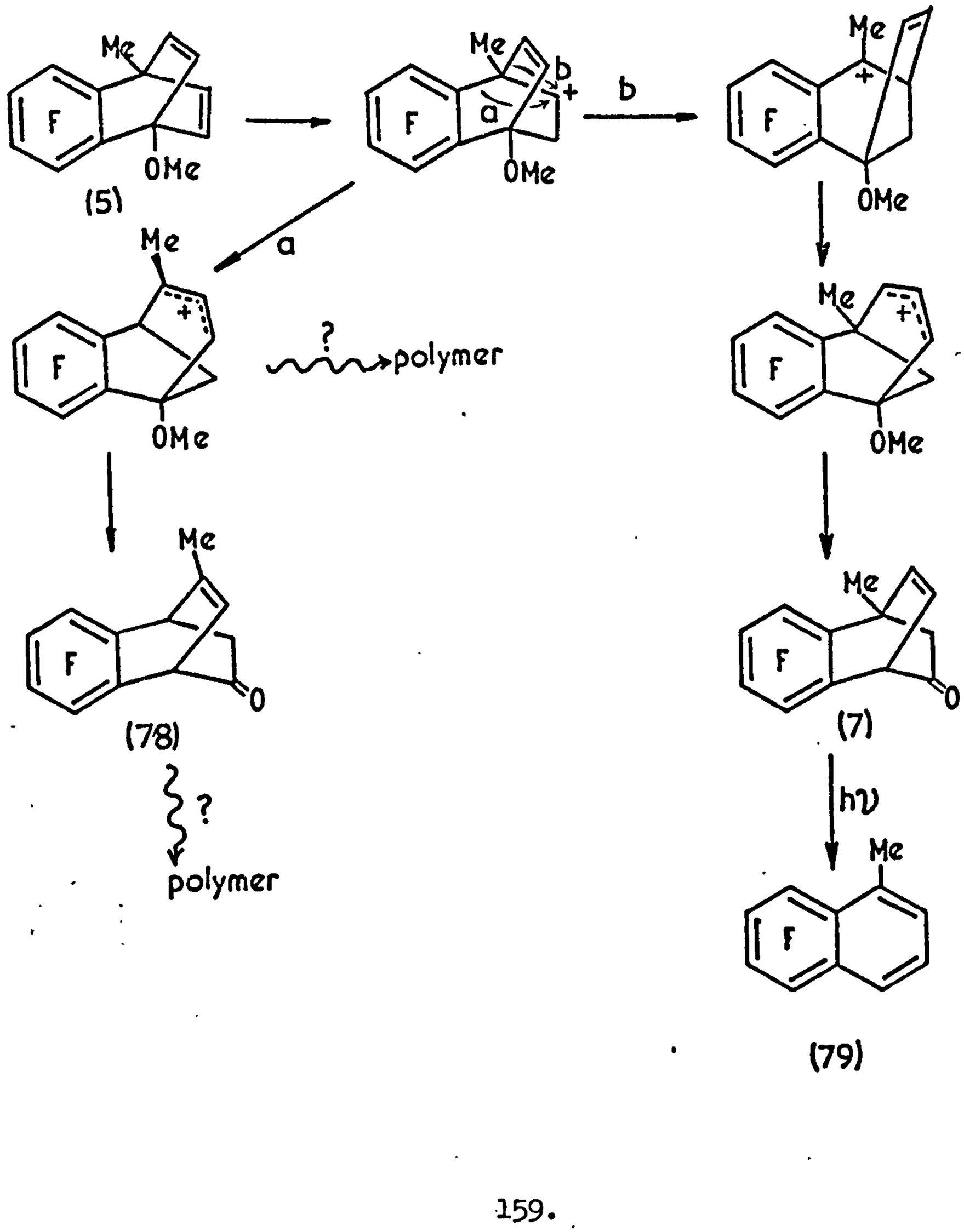
The rearrangement of the 1-methoxy-4-methyltetrafluorobenzobarrelene (5) was chosen for study,as it was thought that the 4-methyl group would have only a small effect on the reaction. The position of the methyl group in the products could act as a mechanistic probe. When the compound (5) was rearranged in sulphuric acid the products were shown to be (6), (7), and (8).



conc. H_2SO_4.	3 %	11 %	4 %
80% H_2SO_4.	0 %	54 %	6 %

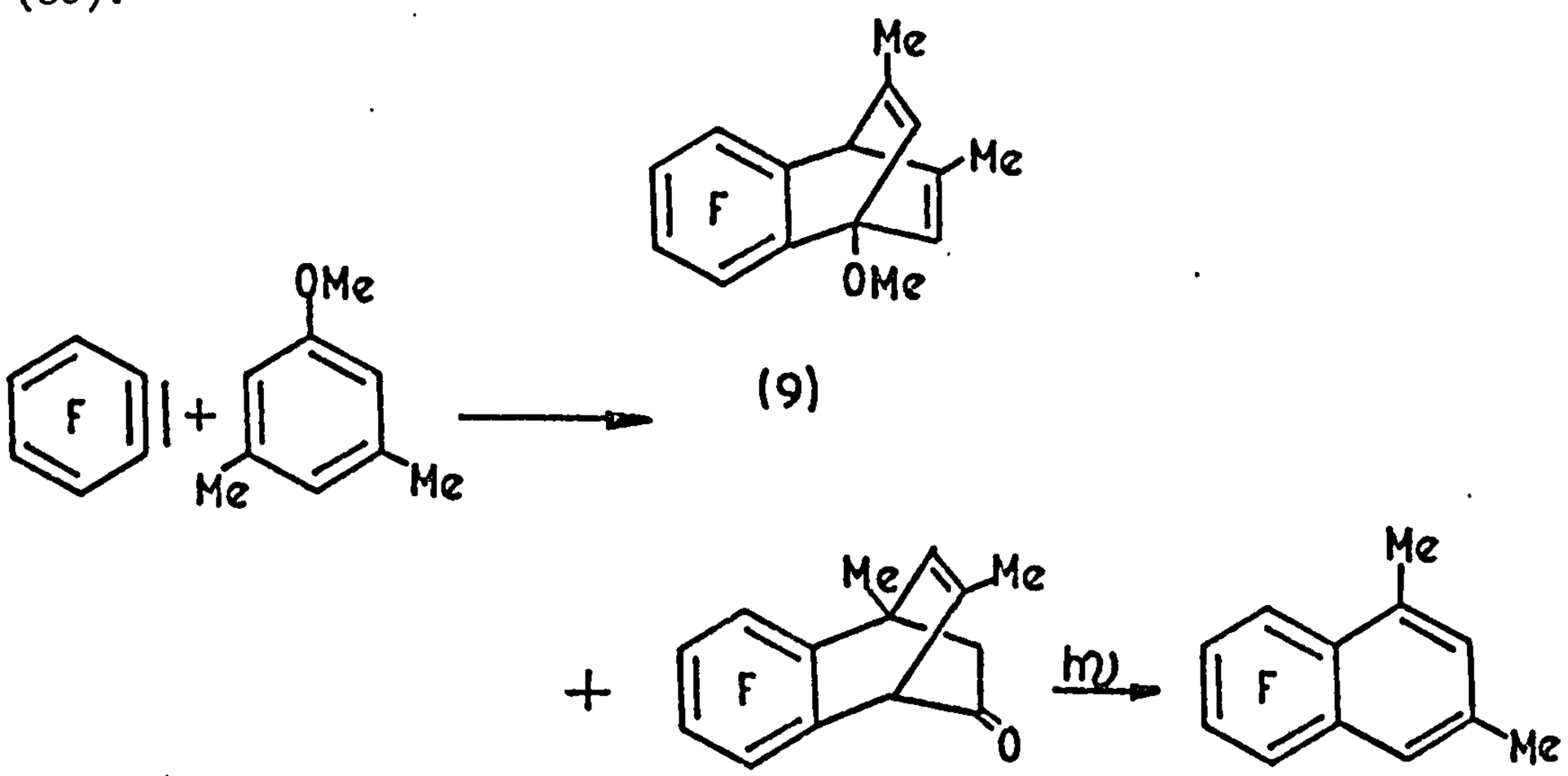
Both the vinyl ketone (6) and the αβ-unsaturated ketone (8) which contain a bridgehead methyl group are undoubtedly formed by the mechanisms previously proposed (p.128). However, it was anticipated that two benzobarrelenones (7) and (78) should be formed in this reaction if the previously proposed mechanisms are correct. The benzobarrelenone (7) was obtained and was characterised by photolysis to the known naphthalene (79).[13] On the other hand, the benzobarrelenone (78) was not observed in the reaction products. It was shown, however, that this ketone was unstable under the reaction conditions and formed a water soluble product. Attempts to characterise this product have sp

far failed, although it could be isolated from the acidic phase by basification with barium hydroxide, followed by the removal of the salts and the solvent. It appeared to be a polymeric hydroxy-compound. A similar product was also obtained from the concentrated sulphuric acid rearrangement of the compound (5). These results can be interpreted by the proposed mechanism particularly as the % yield of the benzobarrelenone (7), which was derived by pathway b, increases when more dilute sulphuric acid was used.



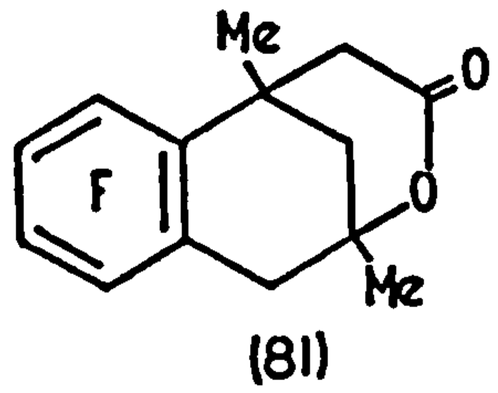
Rearrangement of 3,5-dimethyl-1-methoxytetrafluorobenzobarrelene.

The 3,5-dimethyl-1-methoxytetrafluorobenzobarrelene (9) was prepared by the reaction of tetrafluorobenzyne with 3,5-dimethylanisole. The minor product of this reaction was the 4,6-dimethylbenzobarrelenone (10), which was characterised by photolysis to the known naphthalene (80).[13]



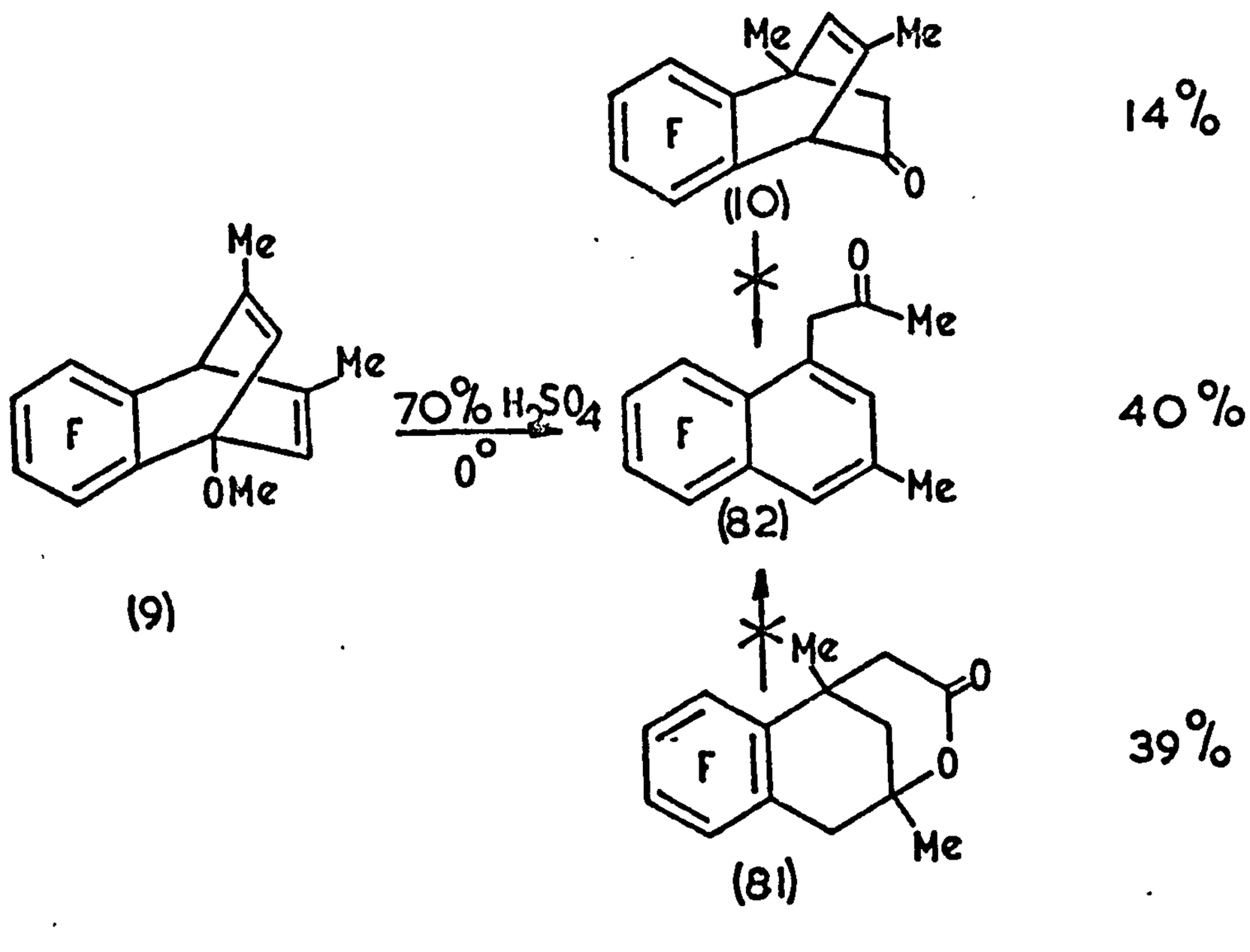
It was hoped that when the compound (9) was rearranged in strong acid the methyl groups would direct the protonation to form a carbonium ion initially at C-3.

When the compound (9) was dissolved in concentrated sulphuric acid and then immediately added to an excess of ice, a single product was obtained in quantitative yield. This compound was shown to have the structure (81).



(81)

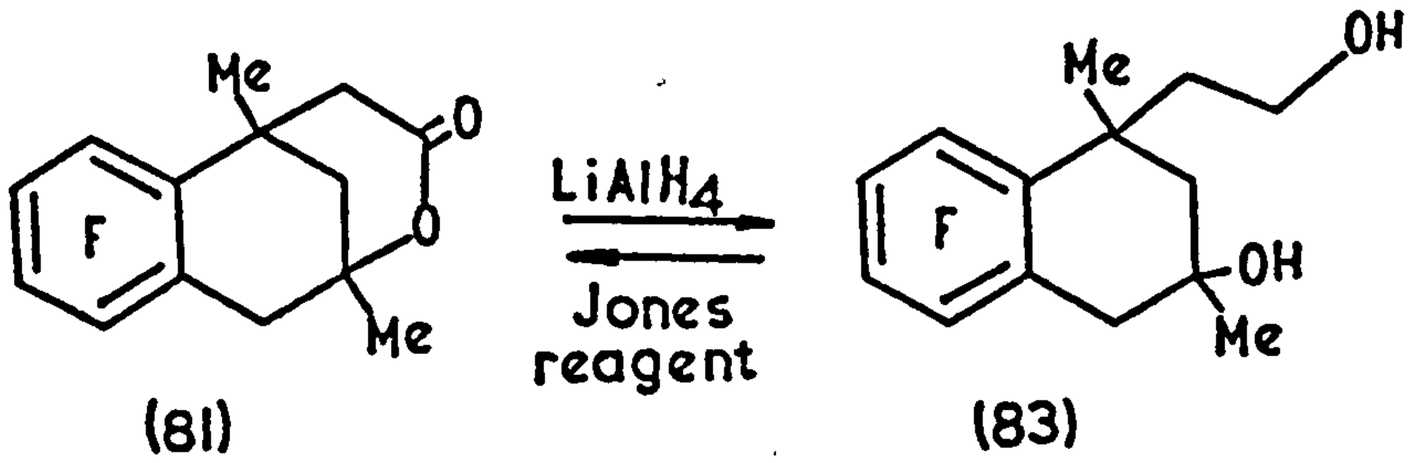
Obviously considerable rearrangement had taken place in the formation of the lactone (81) from the 3,5-dimethylbenzobarrelene (9). In an attempt to isolate some of the intermediates which led to the lactone, the rearrangement was studied under less vigorous conditions. When the compound (9) was heated under reflux for 6 hr. in trifluoroacetic acid two products were formed and were shown to be the 4,6-dimethylbenzobarrelenone (10) and the lactone (81). These products were isolated in 82% and 9.3% yields respectively. In order to test whether the 4,6-dimethylbenzobarrelenone (10) was a possible intermediate in the formation of the lactone it was dissolved in concentrated sulphuric acid and after work up gave a 94% yield of the lactone (81). The rearrangement of the 3,5-dimethylbenzobarrelene (9) was also studied at 0° in 70% sulphuric acid in the hope that possible carbonium ion intermediates might be trapped. The products of this reaction were the lactone (81), the benzobarrelenone (10), and a new product which was shown to be the ketone (82).



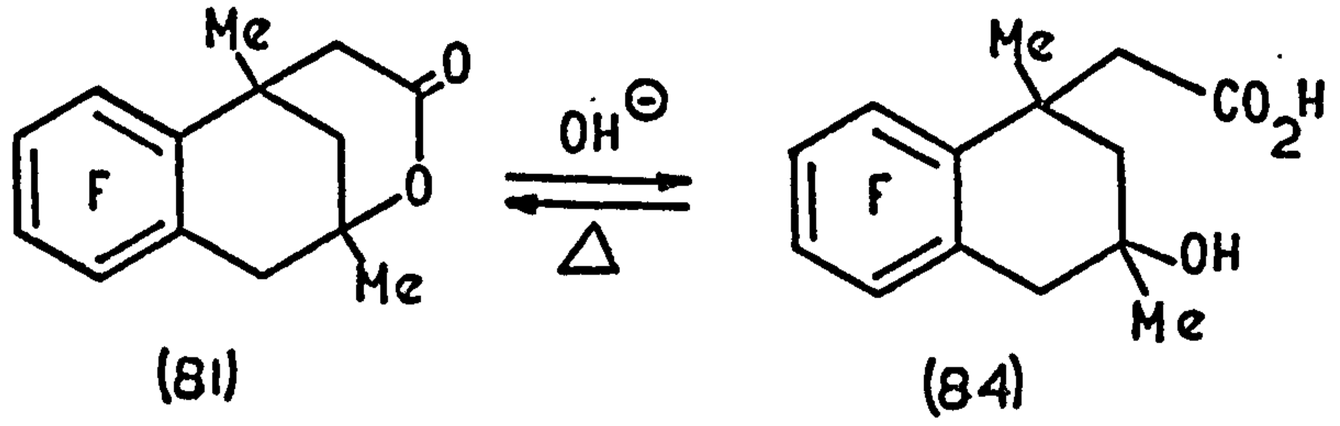
Neither the benzobarrelenone (10) nor the lactone (81) was converted to the ketone (82) under the reaction conditions. The structure of the compound (82) followed from its spectral data. I.r. spectroscopy showed a carbonyl absorption at 1725 $cm.^{-1}$. The u.v. spectrum indicated a tetrafluoronaphthalene chromophore at λ_{max} 275 (ϵ 5,470); 281 (6,020) and 290 (5,350) n.m.. The ^1H n.m.r. spectrum contained proton resonances at τ 2.15 - 2.35 (1H) which was assigned to the naphthalene peri proton, at τ 2.8 - 2.9 (1H) which was due to the other aromatic proton, at τ 5.9 a doublet (2H) which was due to the methylene group coupling with an aromatic fluorine atom (J_{HF} = 7 Hz.) and at τ 7.5 and τ 7.7 were resonances which were assigned to the two methyl groups. The ^1H n.m.r. of this compound (82) compared favourably with a similar compound prepared previously in these laboratories.[23]

The structure of the lactone was determined by chemical and spectroscopic methods.

Lithium aluminium hydride reduction of the lactone (81) gave a diol (83) which, on oxidation with Jones' reagent, regenerated the lactone. The lactone could be hydrolysed in base to give the hydroxy acid (84). This compound was readily converted back to the lactone by warming in chloroform.

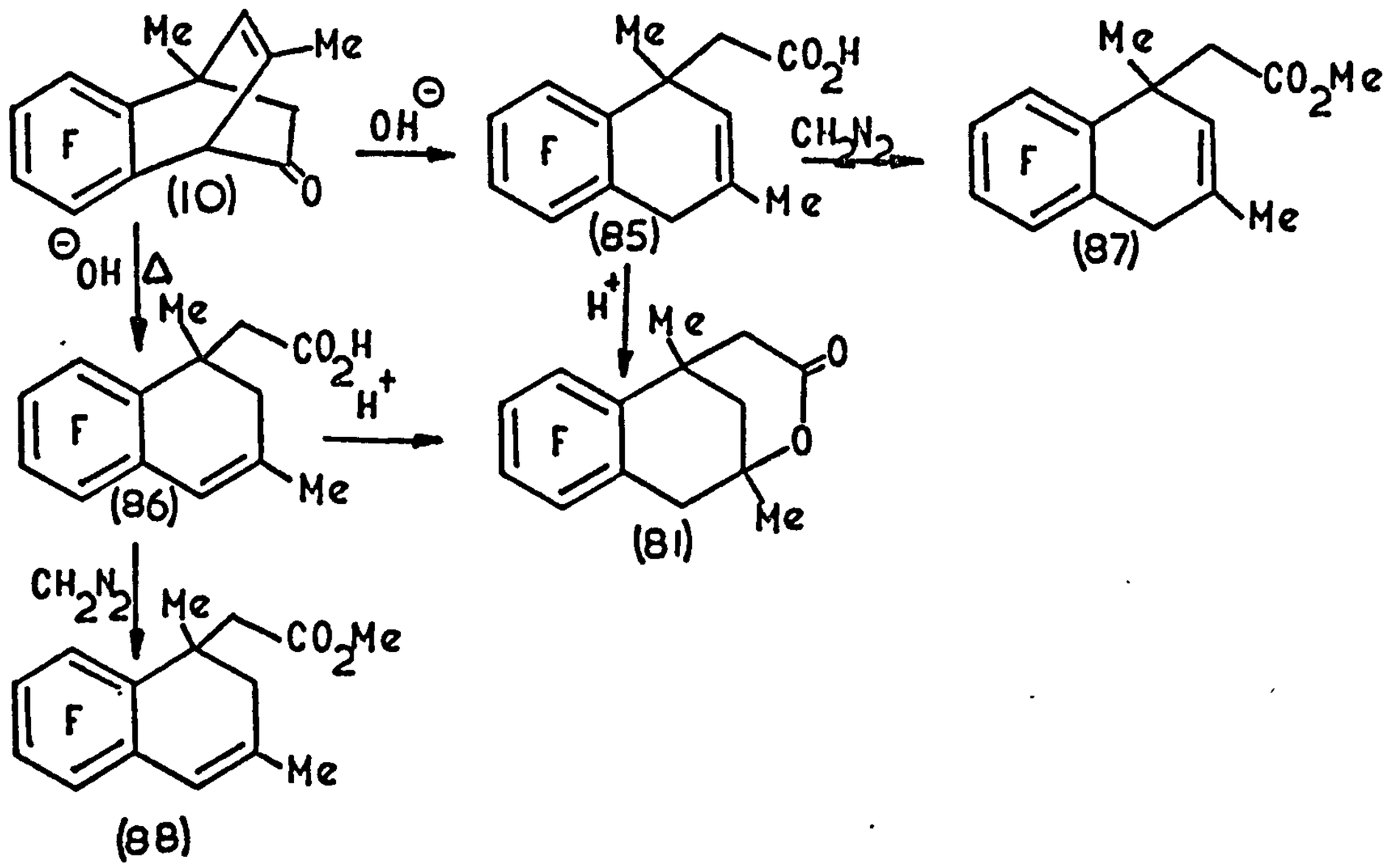


(81) (83)

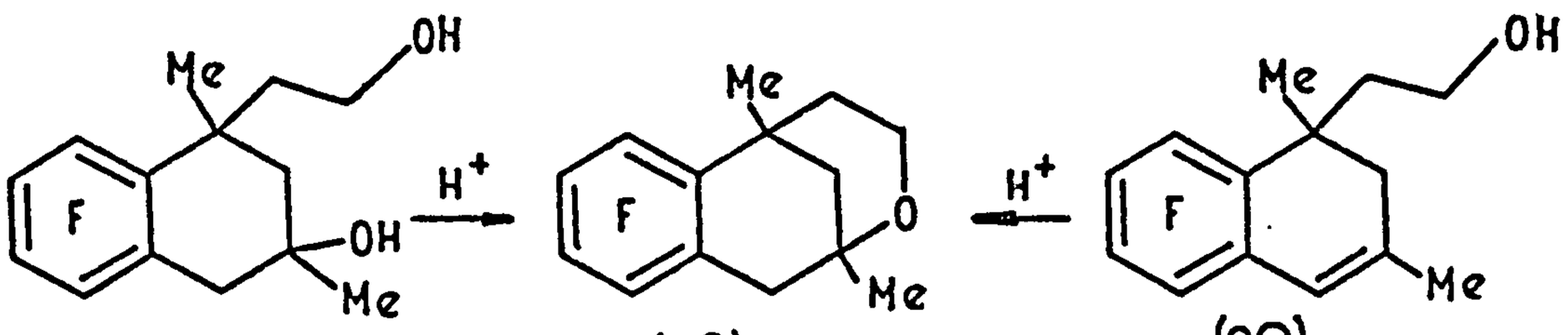


(81) (84)

The lactone was also formed from the unsaturated acids (85) and (86) by acid catalysed cyclisation.[155] The unsaturated acids (85) and (86) were obtained by hydrolysis of the benzobarrelenone (10) with sodium hydroxide. A similar hydrolysis reaction of a benzobarrelenone has been observed.[52]

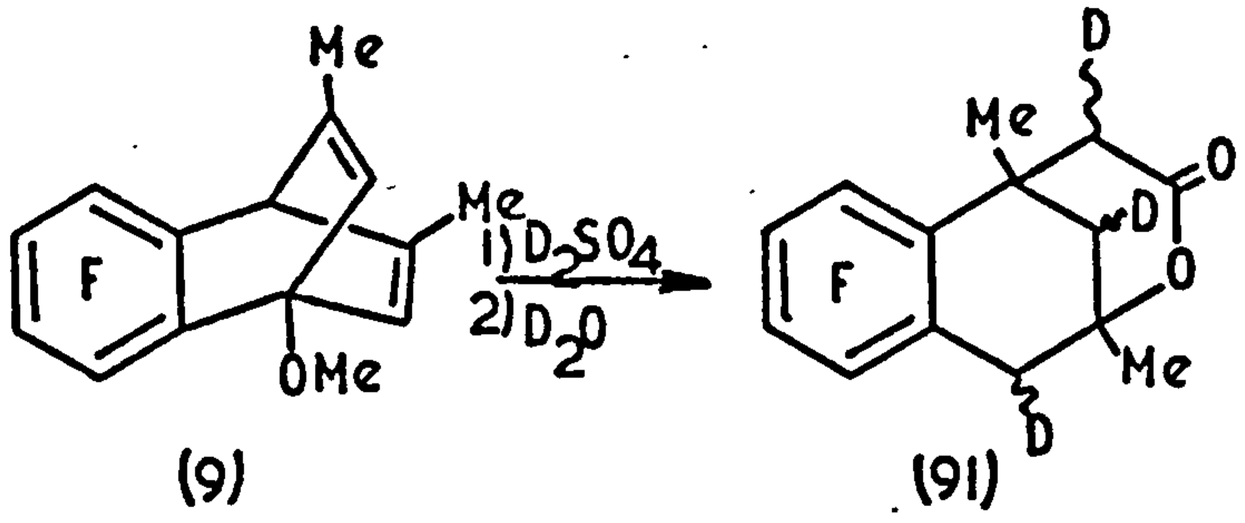


The diol (83),which was formed by lithium aluminium hydride reduction of the lactone, can be cyclised in the presence of phosphoric acid to give the cyclic ether (89). This ether (89) can also be prepared from the compound (90) under similar conditions.

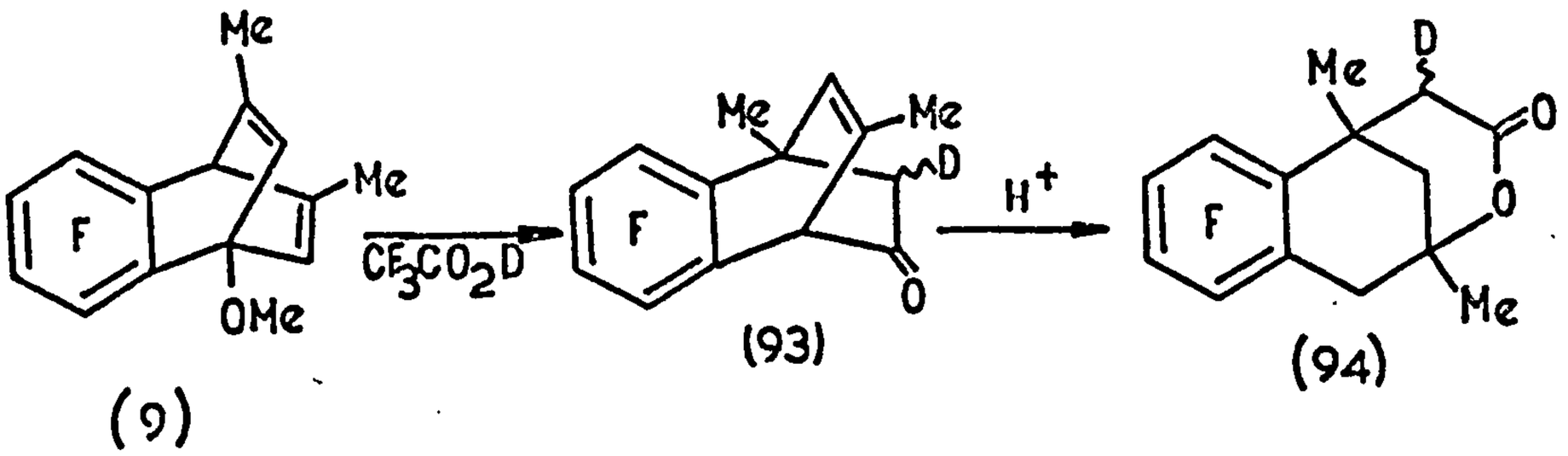


(83) (89) (90)

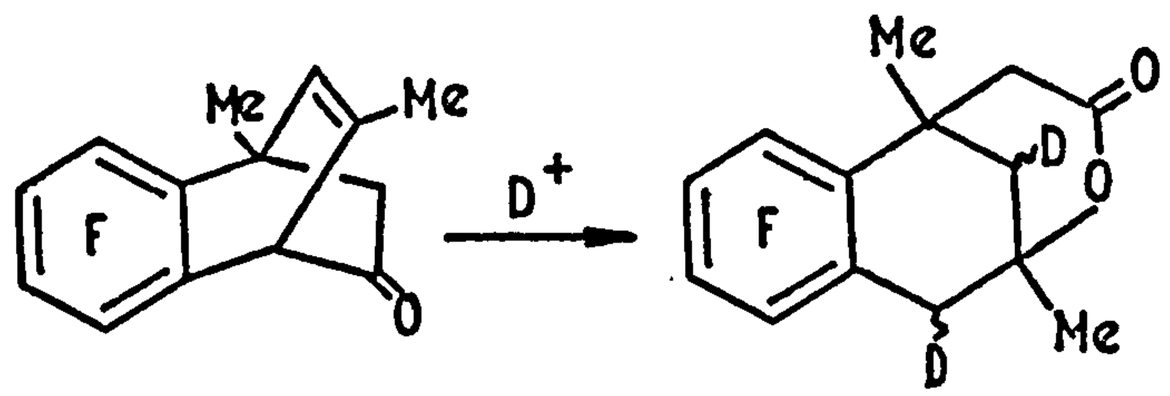
The rearrangement to give the lactone has been studied using deuterated solvents and deuterated starting material. The 3,5-dimethyl benzobarrelene (9) in dideuterosulphuric acid followed by quenching with deuterium oxide gave the lactone (91) which contained three deuterium atoms. Treatment of the benzobarrelenone (10) with dideuterosulphuric acid gave, after pouring into deuterium oxide, the d_2-lactone (92). Rearrangement of the d_1-benzobarrelenone (93) in concentrated sulphuric acid gave the d_1-lactone (94).



(9) (91)

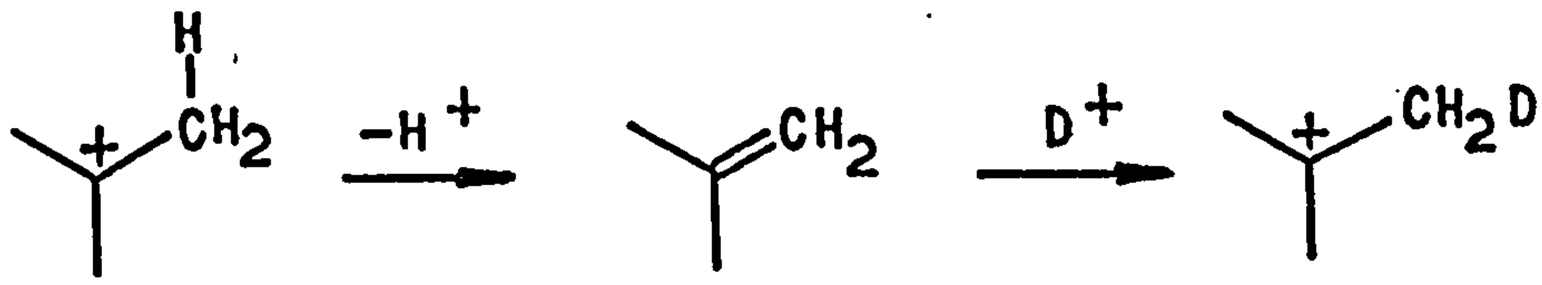


(9) (93) (94)



(10) (92)

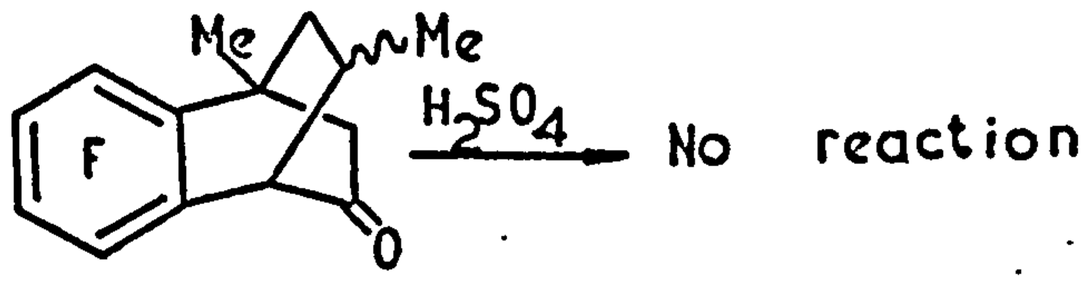
The deuteration levels in the products were shown by mass spectrometry. Owing to the very low relative abundance of the molecular ion derived from (81) in the mass spectra, accurate deuteration levels could not be obtained. The deuteration studies were also complicated by proton exchange in the methyl group, thus tending to increase the % of deuterium atom present. This exchange presumably occurs by a mechanism shown below:-



The 220 M.Hz. ^1H n.m.r. spectra of the deuterated lactones (91), (92), and (93) show that the deuterium incorporation was not stereospecific. The d_o lactone (81) shows three methylene quartets in the ^1H n.m.r. spectrum (n.m.r. I p. 169). The quartet at lowest field is due to

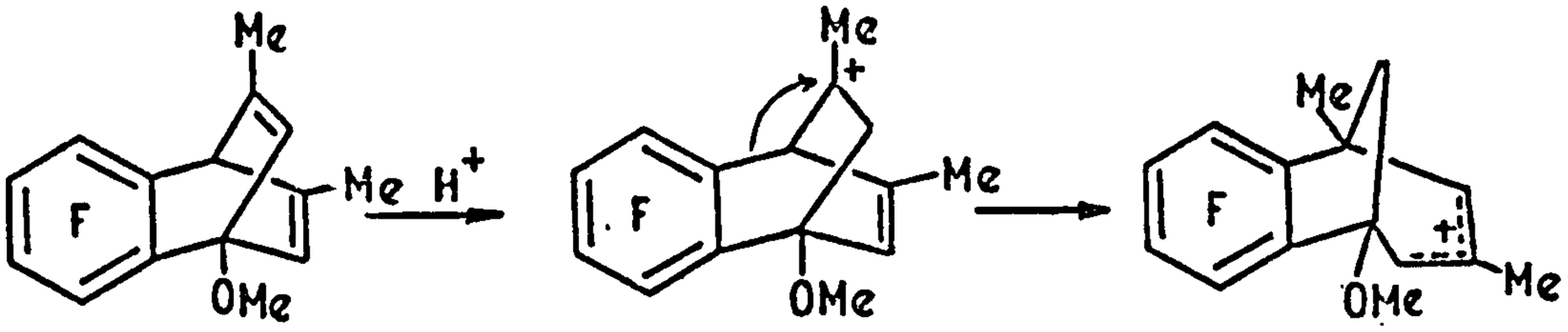
the benzylic protons, the next higher field quartet is due to the methylene protons adjacent to the carbonyl group and remaining methylene protons can be seen at highest field. The ^1H n.m.r. spectrum of the d_1-lactone (94) (n.m.r. II p. 170) shows the carbonyl "methylene" as two broadened singlets. If deuteration in the original benzobarrelenone (93) had been stereospecific only one broadened singlet would have been observed.

Similarly the ^1H n.m.r. spectrum of the d_2-lactone,(92) (n.m.r. III p. 171) shows two broadened singlets both for the benzylic "methylene" and for the methylene at highest field. Finally the spectrum of the d_3-lactone. (91) (n.m.r. IV p. 172) shows two broadened singlets for each of the three methylene groups. It has also been shown that the benzobarrelanones (95a)are recovered unchanged after treatment with concentrated sulphuric acid.

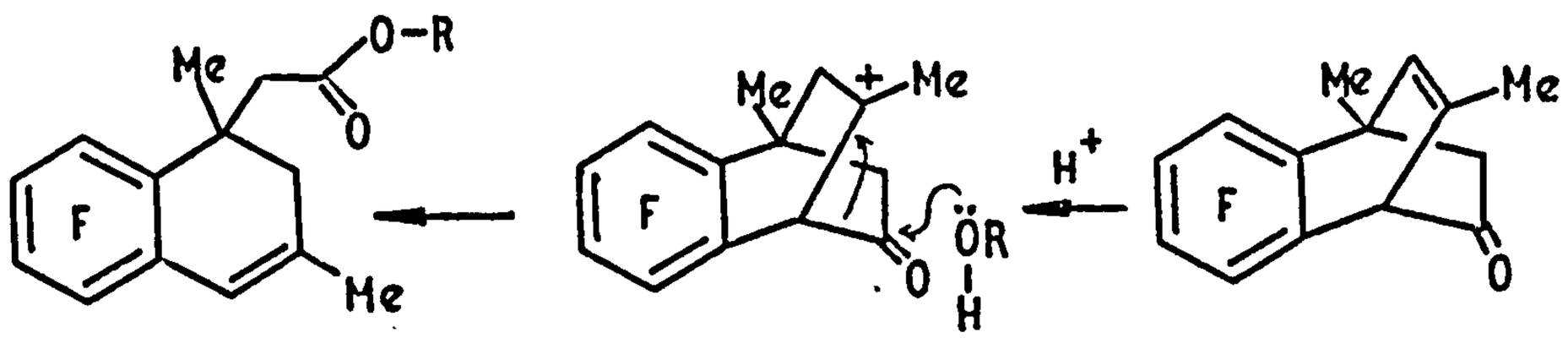


(95a)

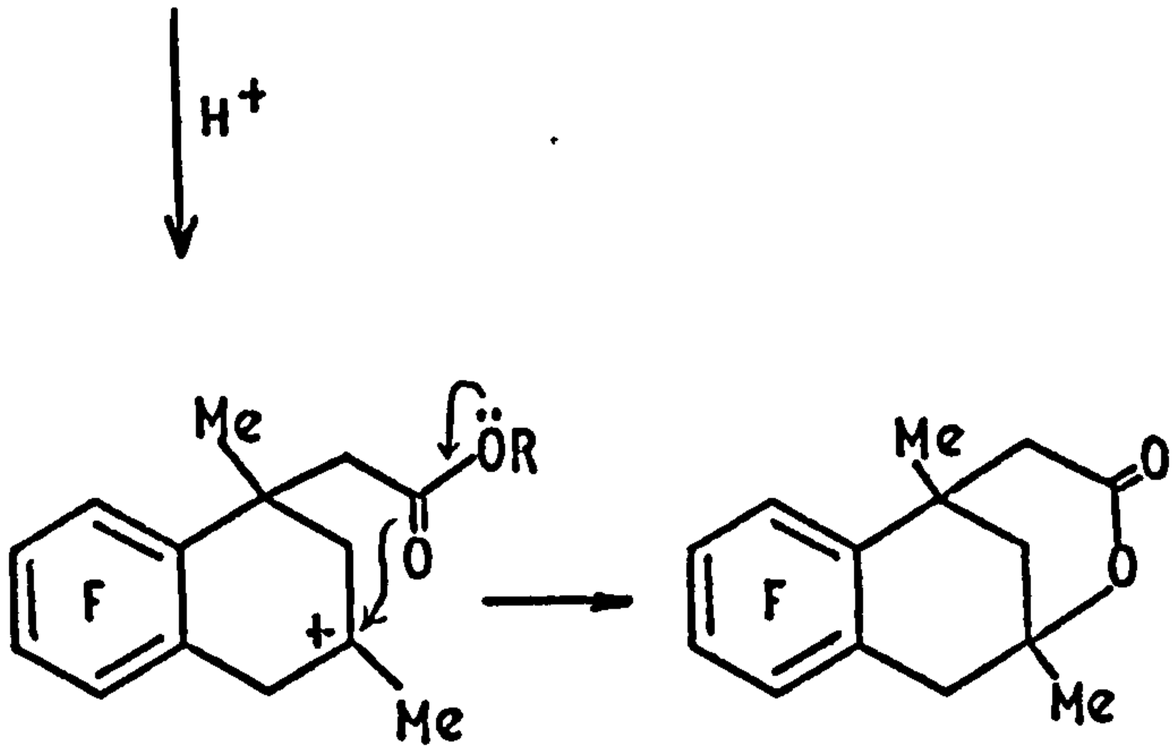
A mechanism which accounts for our results is shown below:



(9) (95)

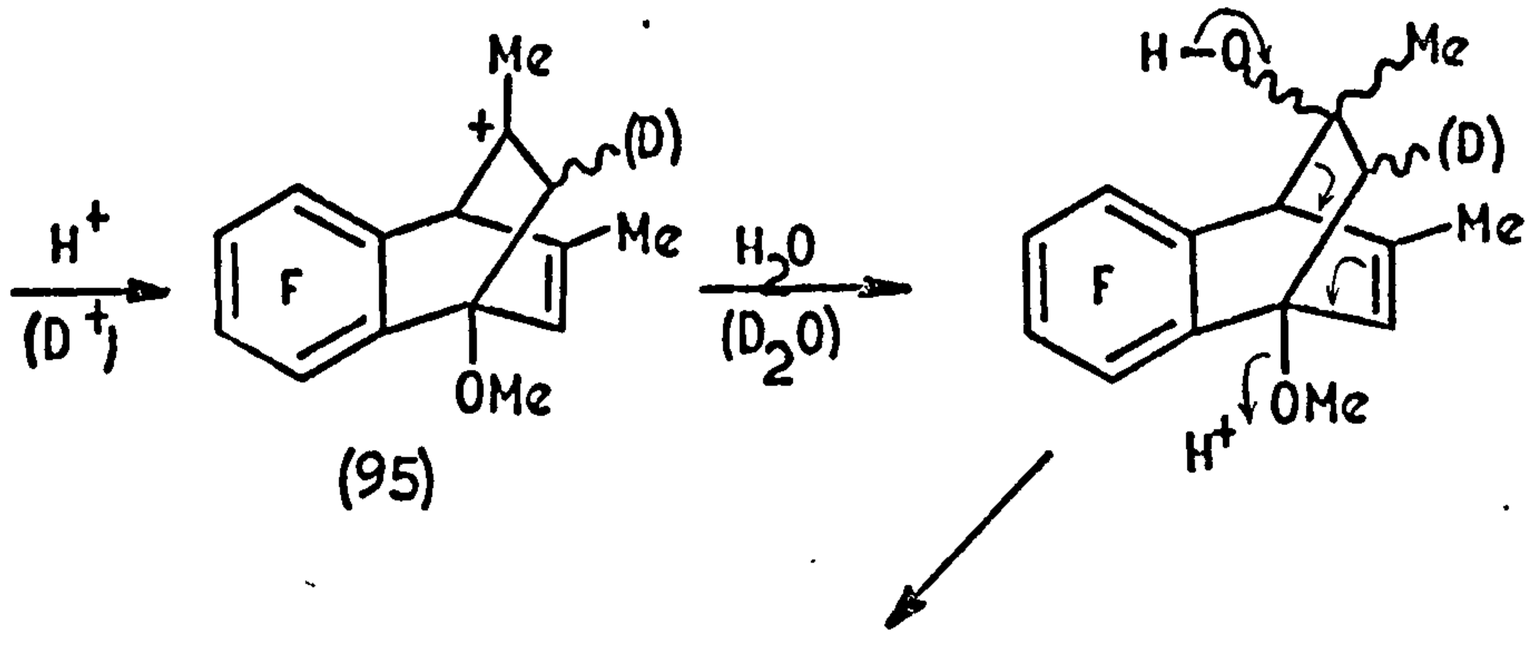


(10)

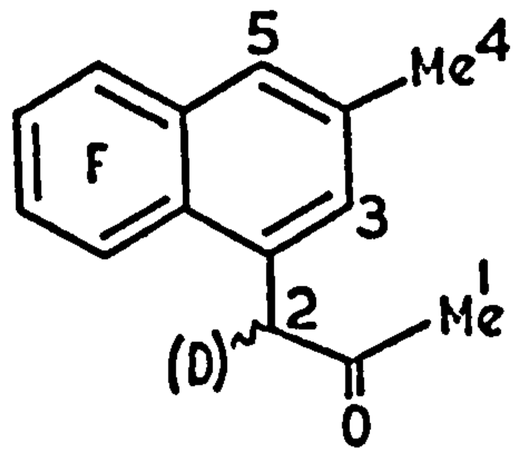


(81)

The formation of the naphthalene (82) during the rearrangement of the 3,5-dimethylbenzobarrelenone (9) in 70% H_2SO_4, is undoubtedly some evidence for the formation of the carbonium ion intermediate (95). A reasonable mechanism for the formation of the compound (82) is shown below:



(95)



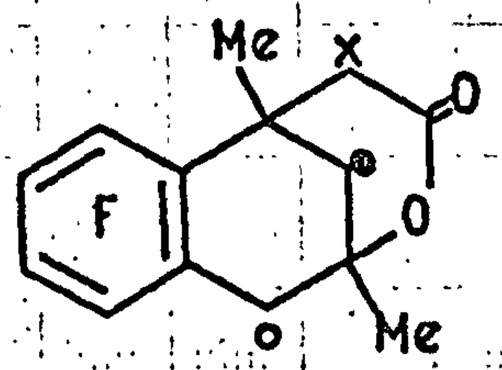
(82)

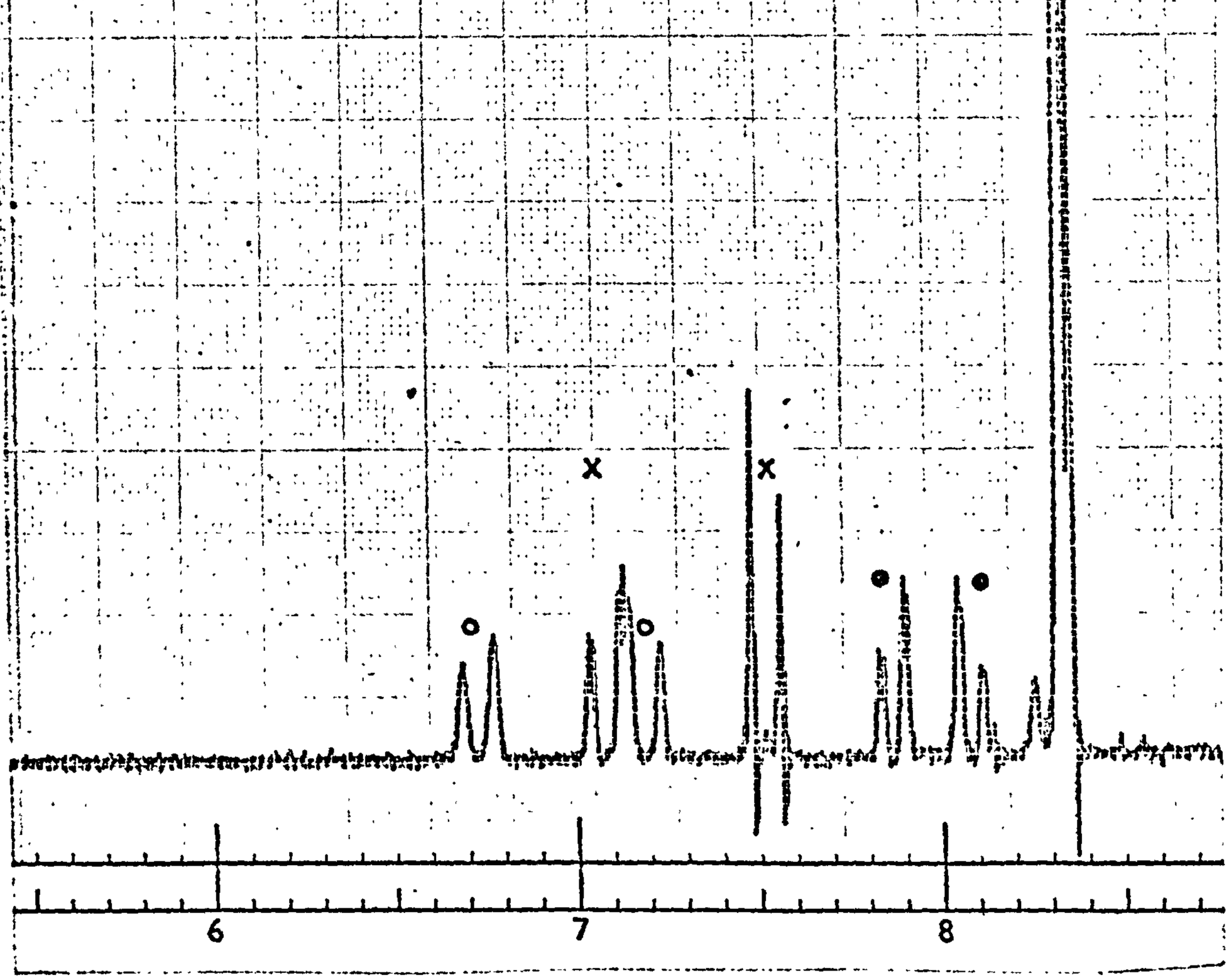
When the rearrangement was carried out in 70% D_2SO_4 a deuterium atom was incorporated into the methylene group. This incorporation was complicated by a small amount of deuterium exchange at other positions. ^1H N.m.r. spectroscopic integrals of the "d_1" naphthalene (82) are shown below:-

Protons	1	2	3	4	5
Integral Ratio:	2.5	.65	.71	2.9	1
Approx. Ratio:	3	1	1	3	1

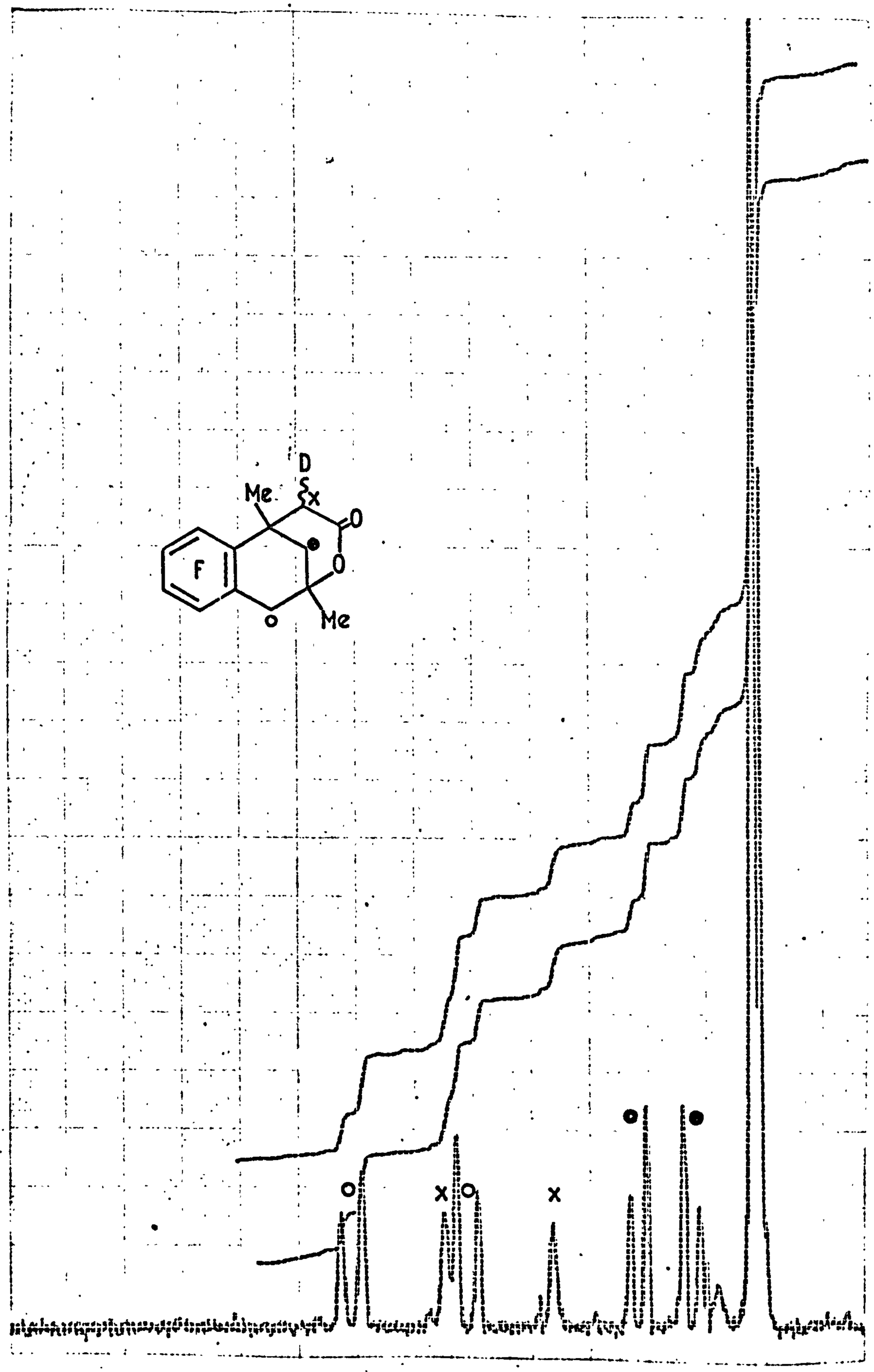
Some of the results of these rearrangement reactions have been presented in a preliminary communication.[156]

n.m.r. I

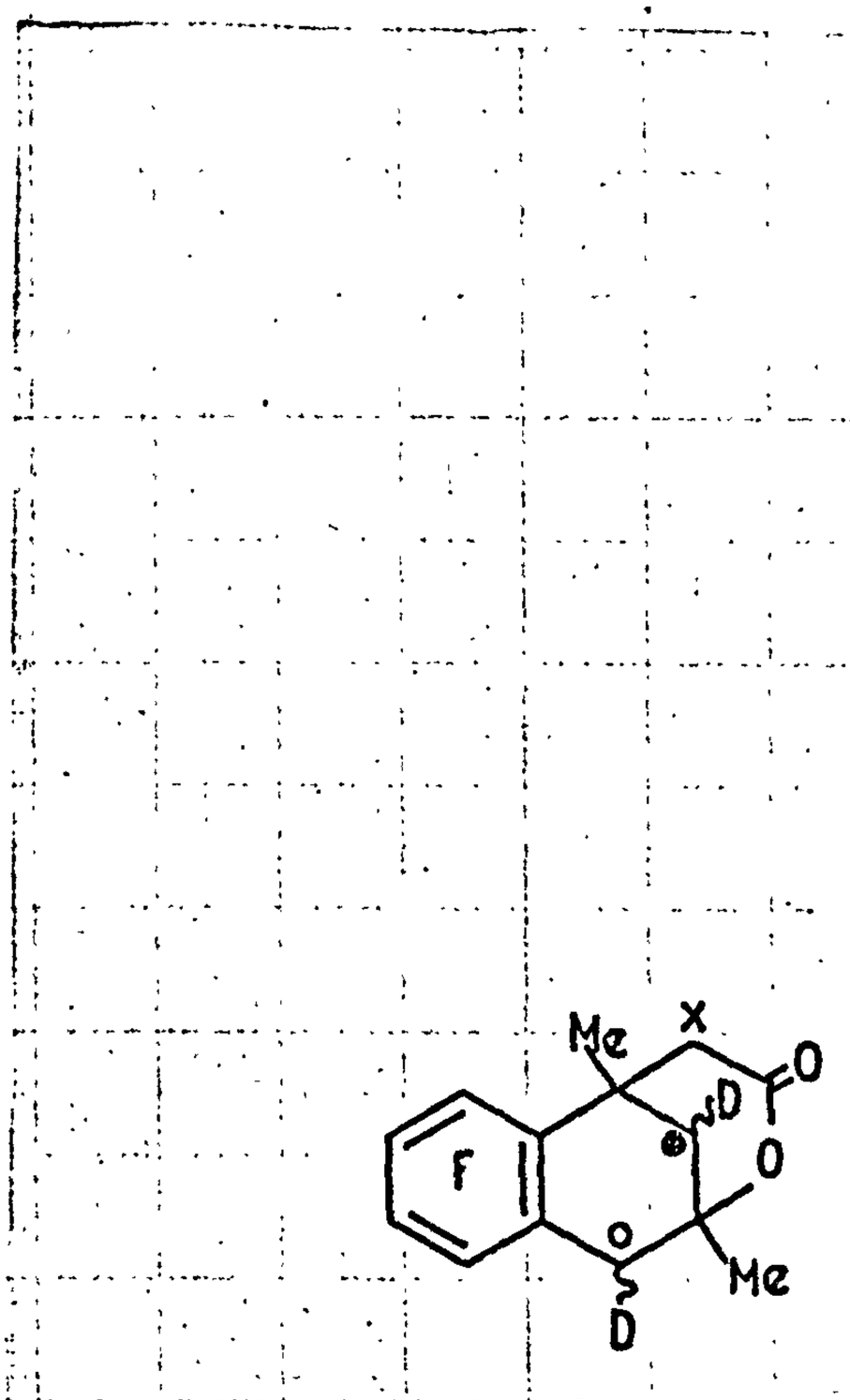




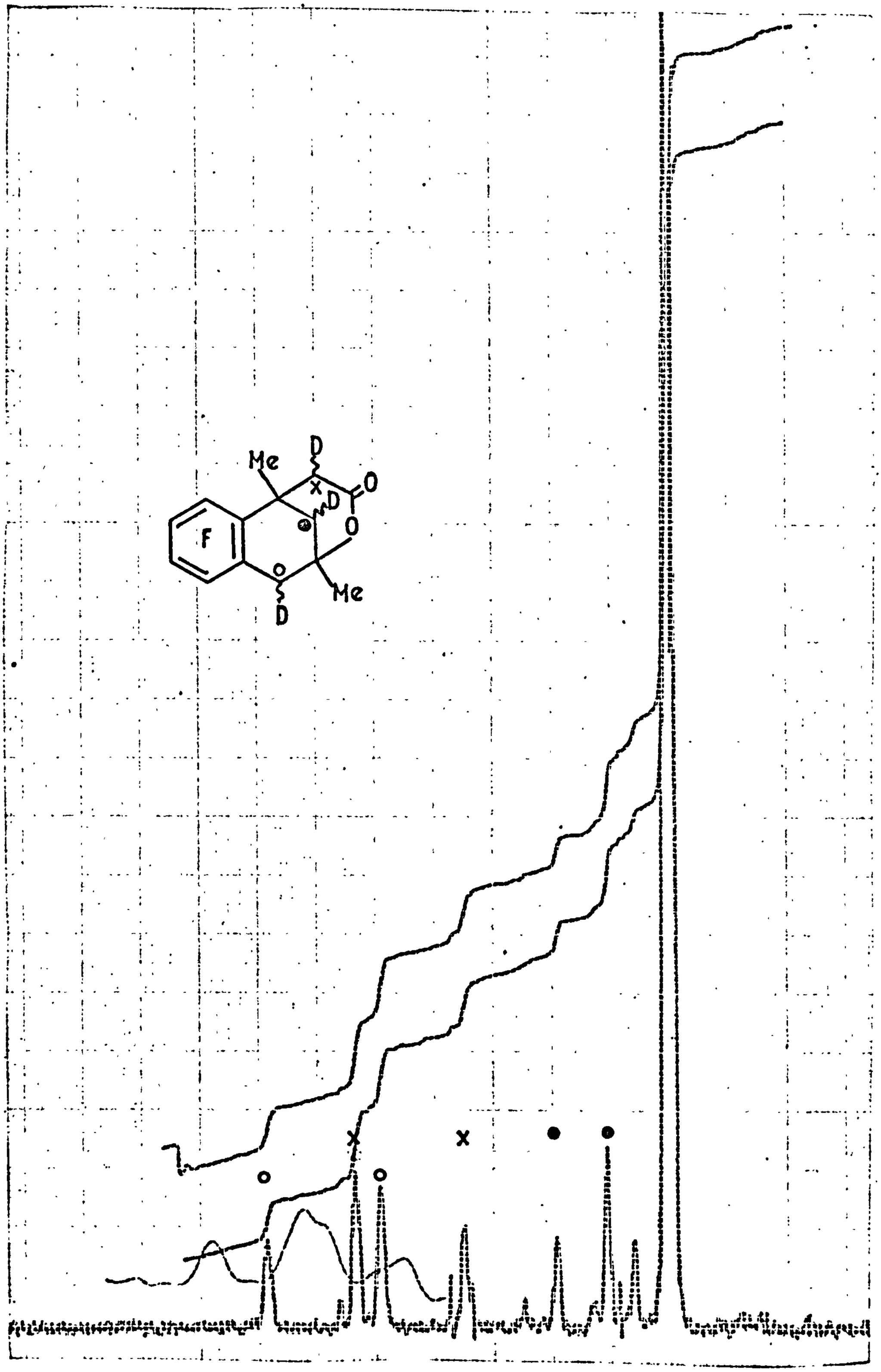
n.m.r. II



n.m.r. III

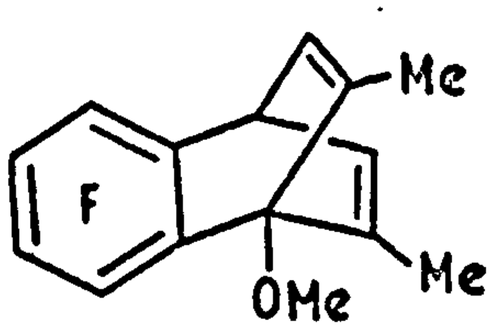


n.m.r. IV

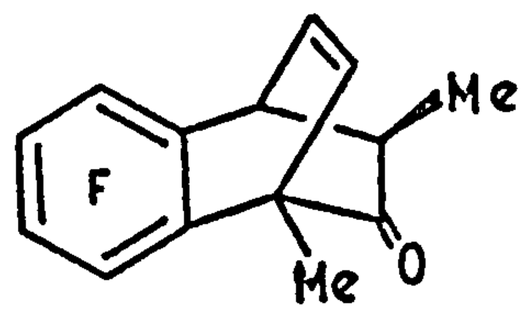


Rearrangement of 2,6-dimethoxy-1-methoxytetrafluorobenzobarrelene.

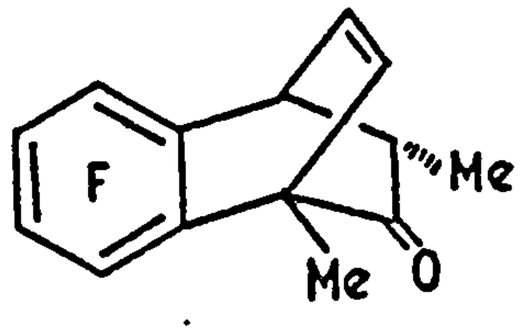
2,6-Dimethyl-1-methoxytetrafluorobenzobarrelene (11) was prepared in the usual manner by reacting tetrafluorobenzyne with 2,6-dimethylanisole. The minor products of the reaction were the two benzobarrelenones (96) and (97).



(11)

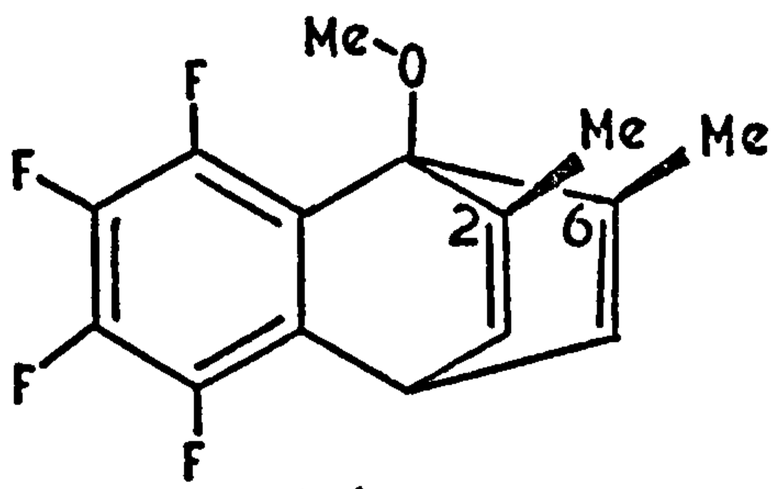


(96)



(97)

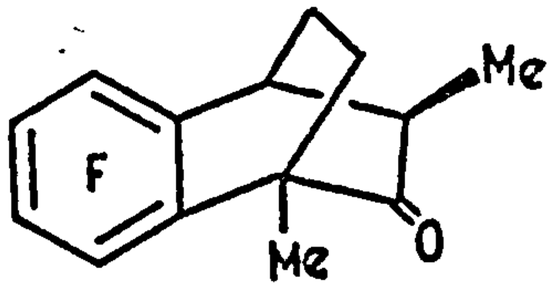
The ^{1}H n.m.r. spectrum of compound (11) shows $^{1}H—^{19}F$ spin-spin coupling of the methoxyl methyl group to an aromatic fluorine of 6 Hz.. This value was considerably higher than in 1-methoxytetrafluorobenzobarrelene (1) X=F, where the coupling was only 2.6 Hz. This high figure can be attributed to a buttressing effect of the 2- and 6-methyl groups, which force the methoxy-group closer to the peri-fluorine atom.



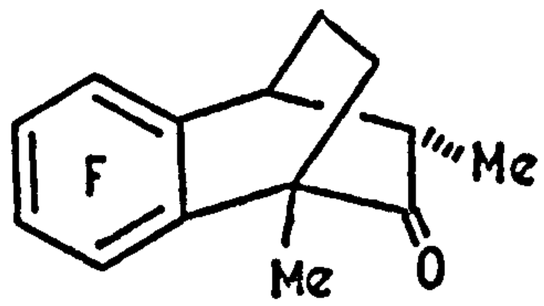
(11)

The structure assignment of the benzobarrelenones (96) and (97) was based on ^{1}H n.m.r. spectra. The 3-methyl group in the endo-isomer (97) was at higher field than in the exo-isomer (96) due to anisotropic shielding by the aryl ring. In order to exclude the possibility that

the shielding was due to the double bond in the benzobarrelenone, the ketones were reduced to the benzobarrelanones (98) and (99). ^{1}H N.m.r. spectroscopy then showed that the chemical shifts of the methyl groups were hardly changed.

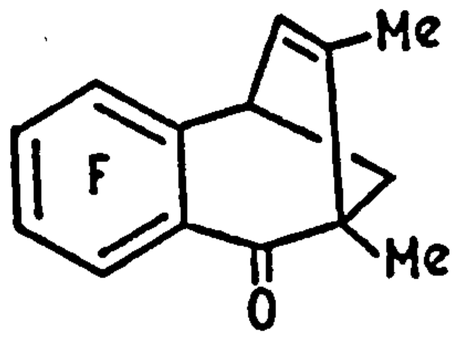


(98)

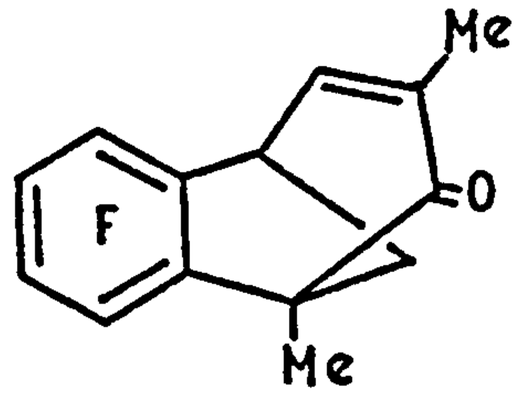


(99)

When the rearrangement of the 2,6-dimethyl-1-methoxybenzobarrelene (11) was studied it was found that in trifluoroacetic acid only two products were formed. These products were shown to be the vinyl ketone (12) and the αβ-unsaturated ketone (13) in 84% and 11% yields respectively.

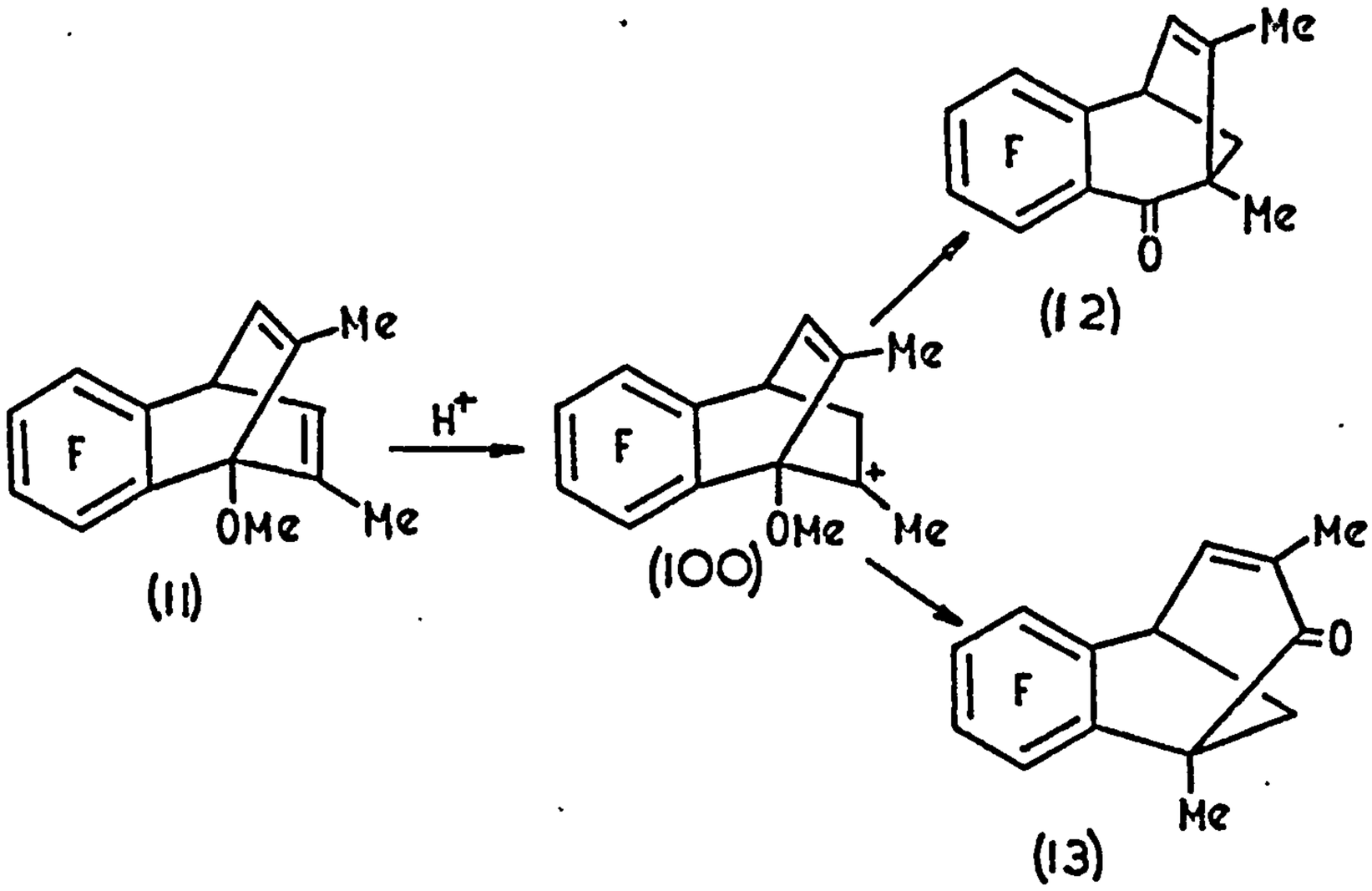


(12)

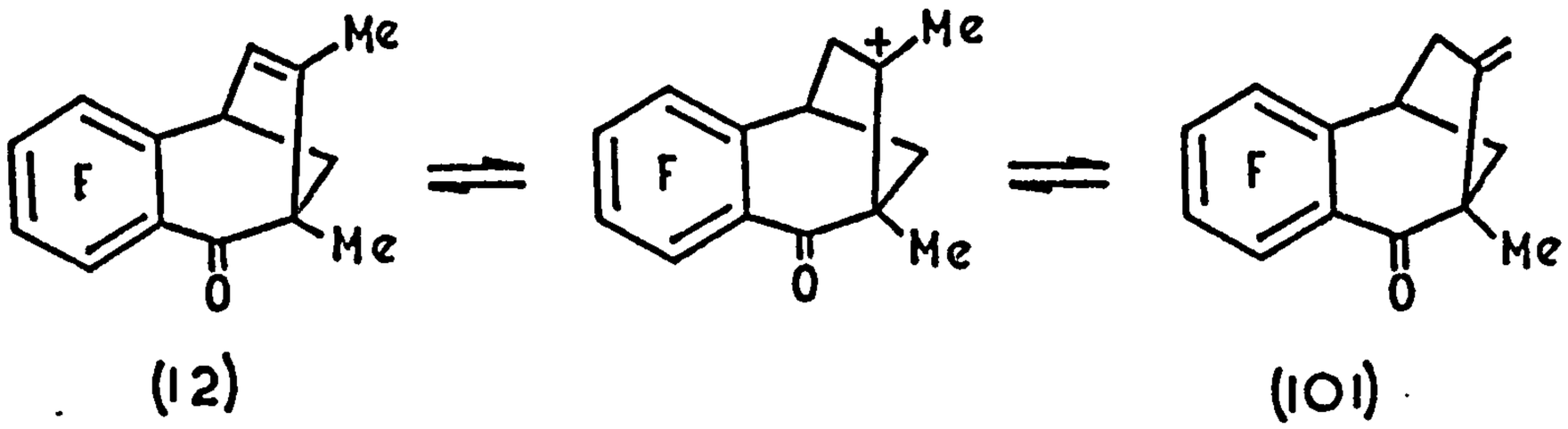


(13)

Products corresponding to the benzobarrelenones (96) and (97) could not be detected by g.l.c., t.l.c., nor by ^{1}H n.m.r. These results are in agreement with the previously proposed mechanism for the formation of vinyl and αβ-unsaturated ketones from a common intermediate. In this case protonation was directed by the methyl group to form the ion (100).



When the αβ-unsaturated compound (13) was dissolved in concentrated sulphuric acid in an attempt to equilibrate the system only starting material was recovered after 3 hours. Similarly there was no change after 18 hours in boiling trifluoroacetic acid. However, when the vinyl ketone (12) was heated under reflux in trifluoroacetic acid, the exo-cyclic methylene compound (101) was formed reversibly, in the ratio 1.3:1.



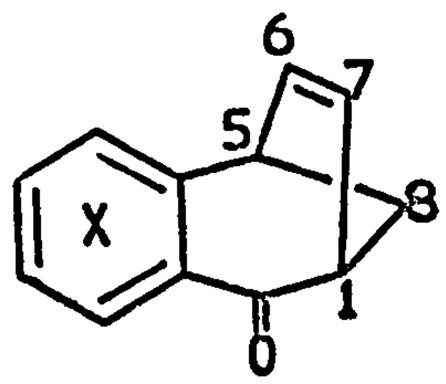
The rearrangement of the 2,6-dimethyl-1-methoxytetrafluorobenzobarrelene (11) in concentrated sulphuric acid is very complex and a large number of products are formed. This reaction is still under investigation.

General Conclusions.

It has been shown that the rearrangement of 1-methoxybenzobarrelenes in acid lead to a number of interesting products. Some attempt has been

made to establish mechanistic pathways for the rearrangements although more work still has to be done on this reactive system.

Table 1

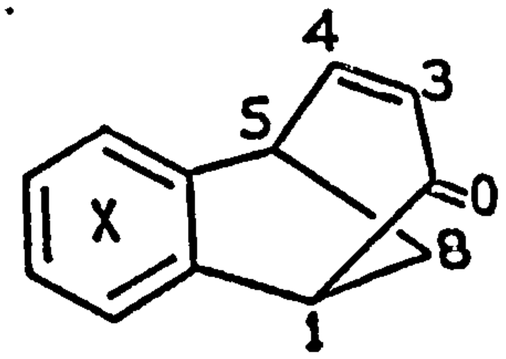


(2)

^{1}H n.m.r. spectra - chemical shift and coupling data

Compound	Protons					
	Aromatic	6	7	5	1	8
(2)X=F		3.3 (q.,1H) $J_{6,7}$=5.5 Hz. $J_{6,5}$= 3.5 Hz.	3.8 (q.,1H) $J_{7,6}$=5.5 Hz. $J_{7,1}$=3.5 Hz.	5.8-6.05 (m.,1H)	6.5-6.8 (m.,1H)	7.1-7.6 (m.,2H) J=14 Hz.
(2)X=Cl		3.27 (q.,1H) $J_{6,7}$=5.5Hz. $J_{6,5}$=3.5 Hz.	3.77 (q.,1H) $J_{7,6}$=5.5 Hz. $J_{7,1}$=3.5 Hz.	5.5-5.7 (m.,1H)	6.35-6.55 (m.,1H)	7.1-7.6 (m.,2H)
(2)X=H	2.05-2.3 (m., 1H) 2.6-3.1 (m.,3H)	3.31 (q.,1H) $J_{6,7}$=5.5 Hz. $J_{6,5}$=3.5 Hz.	3.90 (q.,1H) $J_{7,6}$=5.5 Hz. $J_{7,1}$=3.5 Hz.	6.3-6.5 (m.,1H)	6.5-6.7 (m.,1H)	7.15-7.6 (m.,2H)

Table 2

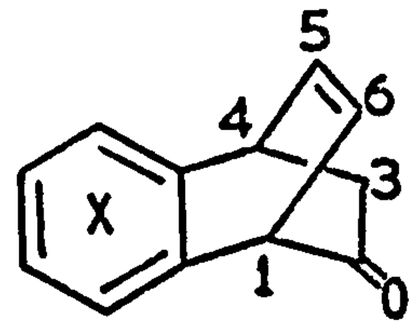


(4)

^{1}H n.m.r. spectra:- chemical shift and coupling data

Compound	Protons				
	Aromatic	4	3	1 - 5	8
(4)X=F		2.6 (q.,1H) $J_{4,3}$=10.3 Hz. $J_{4,5}$=7 Hz.	4.55 (q.,1H) $J_{3,4}$=10.3 Hz. $J_{3,1}$=1.5 Hz.	5.8-6.2 (m.,2H)	7.1-7.3 (m.,2H)
(4)X=Cl		2.54 (q.,1H) $J_{4,3}$=10 Hz. $J_{4,5}$= 7 Hz.	4.46 (q.,1H) $J_{3,4}$=10 Hz. $J_{3,1}$= 1.7 Hz.	5.75-6.2 (m.,2H)	7.1-7.3 (m.,2H)
(4)X=H	2.5-3.1 (m., 5H)		4.65 (q.,1H) $J_{3,4}$=10.3 Hz. $J_{3,1}$=1.7 Hz.	6.15-6.55 (m.,2H)	7.15-7.4 (m.,2H)

Table 3

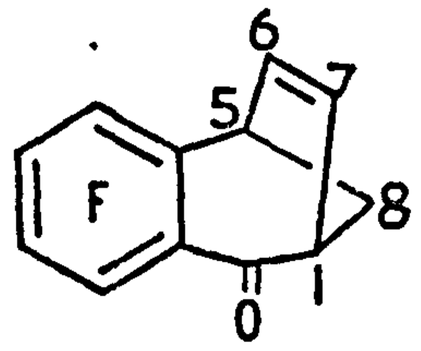


(3)

^{1}H n.m.r. spectra:- chemical shift and coupling data

Compound	Protons				
	Aromatic	5-6	1	4	3
(3)X=F		3.02-3.48 (m., 2H)	5.18 - 5.55 (m., 2H)		7.94 (8 lines of AB part of ABX 2H) J_{AB}=17 Hz. $J_{AX}=J_{BX}$= 2.5 Hz.
(3)X=Cl		3.0-3.5 (m.,2H)	5.05 (q.,1H) $J_{1,6}$=5 Hz. $J_{1,5}$=2 Hz.	5.1-5.3 (m.,1H)	7.9 (8 lines of AB part of ABX 2H) J_{AB}=17.5 Hz. $J_{AX}=J_{BX}$ = 3 Hz.
(3)X=H	2.55-2.95 (m.,4H)	3.05-3.6 (m.,2H)	5.57 (q.,1H) $J_{1,6}$=5.5 Hz. $J_{1,5}$=2.5 Hz.	5.6-5.9 (m.,1H) $J_{4,5}$=5.5 Hz. $J_{4,3}$=2.5 Hz. $J_{4,6}$=2.5 Hz.	7.9 (8 lines of AB part of ABX 2H) J_{AB}= 17.5 Hz. $J_{AX}=J_{BX}$=2.5 Hz.

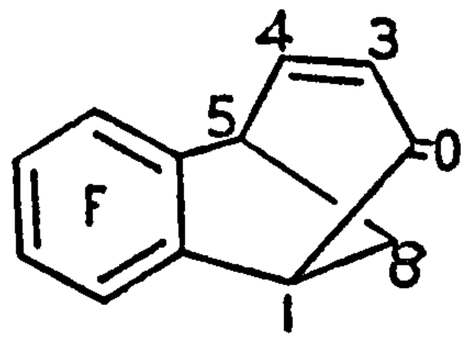
Table 4



Source of product.	Compound Number.	H_1	H_5	H_6	H_7	H_8
(54)d_3[a]	(57)	-	-	3.35 (broad s.,) (1H)	-	7.3-7.48 (AB q.) J_{AB}=14 Hz. (1H)
(55)d_2[a]	(58)	6.5-6.75 (m) (1H)	5.7-6.0 (m) (1H)	-	3.8 (d.) $J_{7,1}$=3.5Hz. (1H)	7.2-7.5 (m) (1H)
(56)d_1[a]	(59)	6.5-6.7 (m) (1H)	-	3.25 (d.) $J_{6,7}$=5.5 Hz. (1H)	3.7-3.9 (q.) $J_{7,6}$=5.5 Hz. $J_{7,1}$=3.5 Hz. (1H)	7.3-7.6 (m) (1H)

a. Rearranging medium :- Conc. H_2SO_4 at room temperature.

Table 5

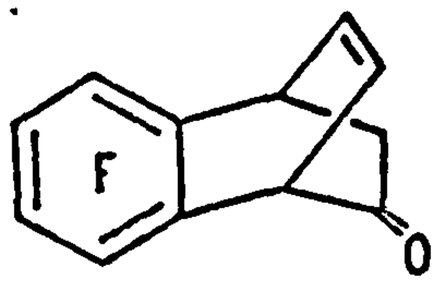


Source of product	Compound Number	H_1	H_3	H_4	H_5	H_8
(54)d_3 [b]	(60)	-	4.54 (d.) $J_{3,4}$=10 Hz. (1H)	2.65 (d.) $J_{4,3}$= 10 Hz. (1H)	-	7.25 (broad s.) (2H)
(54)d_3 [a]	(61)	-	-	2.65 (broad s.) (1H)	-	7.25 (broad s.) (2H)
(55)d_2 [a]	(62)	5.7-6.05 (m) (1H)	4.46 (broad s.) (1H)	-	5.7-6.05 (m) (1H)	7.23 (m) (1H)
(56)d_1 [a]	(63)	5.8-6.05 (m) (1H)	4.5 (q.) $J_{3,4}$= 10 Hz. $J_{3,1}$= 1.5 Hz (1H)	2.62 (d.) $J_{4,3}$=10 Hz. (1H)	-	7.2 (m) (2H)

a) Rearranging medium :- Conc. H_2SO_4 at room temperature.

b) Rearranging medium :- 80% H_2SO_4 at 80°.

Table 6

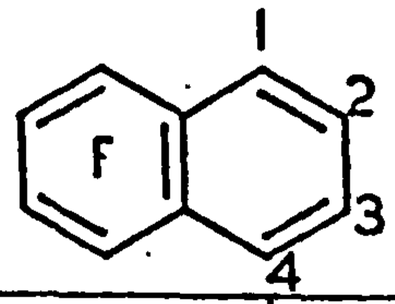


Source of compound	Compound Number		Proton Ratios		
			vinyl	bridgehead	methylene
(54)d_3 [b]	(64)	Found Calc.	2.54 2.64	1 1	1.9 1.82
(54)d_3 [a]	(65)	Found Calc.	1.52 1.53	1 1	1.3 1.27
(55)d_2 [a]	(66)	Found Calc.	1 1	1.3 1.35	2.13 2.07
(56)d_1 [a]	(67)	Found Calc.	1 1	1.32 1.37	1.54 1.52

a) Rearranging medium - Conc.H_2SO_4 at room temperature.

b) Rearranging medium - 80% H_2SO_4 at 80°.

Table 7



Source of compound	Compound Number		Proton Ratios	
			1,4	2,3
(64)	(68)	Found Calc.	1 1	2.6 2.64
(65)	(69)	Found Calc.	1 1	1.53 1.53
(66)	(70)	Found Calc.	1.35 1.35	1 1
(67)	(71)	Found Calc.	1.33 1.37	1 1

Experimental

The general procedures are as shown on p. 26. Concentrated sulphuric acid refers to Fisons analar reagent 98% H_2SO_4.

All the methoxy arenes were prepared from the corresponding phenol by methylation using standard procedures.

---

1. Reaction of tetrafluorobenzyne with anisole

Bromopentafluorobenzene (12.4 g., 0.05 mole) in ether (60 ml.) was added to magnesium (1.5 g.) in ether (10 ml.) at such a rate so as to maintain boiling of the solvent.

The mixture was heated under reflux for 45 min., anisole (22 g., 0.2 mole) was added, and the reaction temperature raised to 82° by removal of the ether by distillation and replacement with cyclohexane. After 3 hr. the solution was cooled and diluted with ether (100 ml.).

The ether solution was washed with 2N hydrochloric acid (2 x 100 ml.), water (100 ml.), and dried.

Removal of the solvent & excess anisole left an oil which was separated by chromatography on a column of silica (250 g.) using ether/light petroleum b.p. 40/60 (1 to 18) as eluant and gave a) 1-methoxy-(7,8)-tetrafluoro-benzobicyclo[2.2.2]octa-2,5,7-triene, (1) X=F (7.5 g., 58%); m.p. 79-80°, (from hexane) (lit.[13] 77°);

^1H n.m.r. τ (CCl_4) 2.86 - 3.35 (8 line AB of ABX, 4H);
4.68 - 5.05 (m., 1H); and 6.25 (d., 3H, J_{HF} = 2.6 Hz.);

υ_{max} 3015, 2950, 2850, 1635, 1490, 1340, 1227, 1215, 1195, 1077, 1040, 1008, 950, 930, 905, 855, 793, 730, 760, and 680 $cm.^{-1}$,

b) (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (3) X=F (1.2 g., 10%), m.p. 70 - 72°, (lit.[52] m.p. 72.5 - 73.5°). Identical by

its spectroscopic properties to material reported previously in this thesis, chapter I.

2. Rearrangement of 1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-2,5,7-triene

Method 1.

The compound, (1) X=F (1.5 g.) was dissolved in concentrated sulphuric acid (25 ml.) by shaking at room temperature. The solution was immediately poured onto crushed ice (150 g.) and the precipitate extracted with ether (5 x 25 ml.). Each of the ether extracts was washed with water until acid free; they were then combined and dried. The removal of drying agent and solvent left an oil which was separated by preparative t.l.c., using ether/light petroleum b.p. 40 - 60° as eluant, and gave in order of decreasing R_f

a) (3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (2) X=F, (71 mg., 5%);

m.p. 82 - 83° (from ethanol).

(Found: C, 59.35; H, 2.7%; M. [Mass spectrometry] 242;

$C_{12}H_6F_4O$ requires C, 59.5; H, 2.5%; M. 242);

^1H n.m.r. τ (CCl_4) 3.2 - 3.4 (q., 1H, $J_{6,7}$ = 5.5 Hz., $J_{6,5}$ = 3.5 Hz.); 3.7 - 3.9 (q., 1H $J_{7,6}$ = 5.5 Hz., $J_{7,1}$ = 3.5 Hz.); 5.8 - 6.05 (m., 1H); 6.5 - 6.8 (m., 1H); and 7.1 - 7.6 (m., 2H J_{AB} = 14 Hz.);

υ_{max} 3020, 2980, 2950, 1708, 1632, 1502, 1475, 1365, 1321, 1300, 1128, 1050, 950, 901, and 822 cm.$^{-1}$;

$\lambda_{max}^{Ethanol}$ 257 (ϵ 2100); 295 (940) n.m.,

b) (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (3) X=F, (910 mg., 64%); m.p. 71-73°, (from ethanol) (lit.[52] m.p. 72.5 - 73.5°);

^{1}H n.m.r. τ (CCl_4) 3.02 -.3.48 (m., 2H), 5.18 - 5.55
(m., 2H); 7.94 (8 lines of AB of ABX spectrum, 2H,
J_{AB} = 17 Hz., J_{AX} = J_{BX} = 2.5 Hz.);
υ_{max} 3080, 2940, 1738, 1500, 1421, 1386, 1334, 1310,1130, 1115, 1080,
1070, 1030, 917, 870, 750, and 717 cm.$^{-1}$,

c) (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one,
(4) X=F, (69 mg., 5%);
m.p. 74 - 75° (from hexane).
(Found: C, 59.6; H, 2.65%; M. [Mass spectrometry] 242;
$C_{12}H_6F_4O$ requires C, 59.5; H, 2.5% M. 242);
^{1}H n.m.r. τ(CCl_4) 2.6 (q., 1H, $J_{4,3}$ = 10.3 Hz.;
$J_{4,5}$ = 7 Hz.); 4.55 (q., 1H, $J_{3,4}$ = 10.3 Hz.;
$J_{3,1}$ = 1.5 Hz.); 5.8 - 6.2 (m., 2H); and
7.1 - 7.3 (m., 2H);
υ_{max} 2980, 2950, 2880, 1690, 1495, 1445, 1390, 1365, 1310, 1220, 1060,
960, 951, 881, and 831 cm.$^{-1}$,
λ_{max} 222 (ϵ 7890); 273 (900); and 350 (160) n.m..

Method 2.

Stirred fluorosulphonic acid (5 ml.) was cooled to -70° and compound (1) X=F, (500 mg.) was added. The mixture was allowed to warm to 0° and then poured cautiously onto crushed ice (60 g.). The white precipitate was filtered, washed with water and dried by vacuum desiccation.

The aqueous phase, after extraction with ether, gave a further quantity of product.

The crude product was examined by g.l.c. (column A) and was shown to be better than 96% pure, and after sublimation gave (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (3) X=F, (425 mg., 90%),

m.p. 69 - 71°; identical to previously prepared material by g.l.c., t.l.c., ^{1}H n.m.r., and i.r. spectroscopy.

Method 3.

The 1-methoxybenzobarrelene (1) X=F, (200 mg.) was dissolved in 80% sulphuric acid (5 ml.) at 80°. The mixture was shaken for 5 min. then poured onto ice, (15 g.), work as in experiment 2 method 1 gave

a) (7,6)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene (3) X=F, (125 mg., 66%), m.p. and mixed m.p. 69-70°; identical to previously prepared material;

b) (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (4) X=F, (11.4 mg., 6%), identical to previously prepared material.

3. Reaction of benzyne with anisole.

Benzene diazonium 2-carboxylate was prepared in the usual manner[157] from anthranilic acid (34.2 g., 0.25 mole), and was added to preheated anisole (300 g.) at 45°. The mixture was stirred at this temperature for 18 hr.. Removal of the anisole under reduced pressure gave a black oil which was separated by a column of alumina (1 Kg.) using benzene as eluant, and gave 1-methoxy-benzobicyclo[2.2.2]octatriene, (1) X=H, (650 mg., 1.5%), m.p. 37-38° (from light petroleum b.p. 40-60°). (Found: C, 84.2; H, 6.3%; M. [Mass spectrometry] 184; $C_{13}H_{12}O$ requires C, 84.7; H, 6.55%; M. 184);

^{1}H n.m.r. τ (CCl_4) 2.9 - 3.5 (m., 8H); 5.2 - 5.5 (m., 1H); and 6.28 (s., 3H);

υ_{max} 3067, 2983, 2938, 2816, 1619, 1579, 1457, 1329, 1227, 1155, 1132, 1080, 1017, 421, 857, 748, 698, and 685 cm.$^{-1}$.

A number of other products were present but were not characterised.

4. Preparation of 1-hydroxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene.

1-Methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene

(1) X=F, (3 g.) was dissolved in cyclohexane (100 ml.) and powdered aluminium bromide (3.9 g.) was added to the stirred solution. The mixture was heated under reflux for 5 hr., cooled and poured into water (400 ml.). The organic phase was separated and the aqueous phase extracted with ether (3 x 100 ml.). The combined organic phases were washed with water (2 x 100 ml.), dried, and after removal of solvent gave an oil (3.14 g.) which was eluted with benzene through a column of silica and gave 1-hydroxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene (33), (1.48 g., 53%), m.p. 102 - 104° (from hexane (lit.[52] m.p. 107 - 108°);

^{1}H n.m.r. τ (CCl_4) 3.05 - 3.4 (m., 4H); 4.7 - 5.0 (m., 1H); and 6.25 (d., 1H, J_{HF}= 5 Hz.);

υ_{max} 3250 (broad), 1500, 1482, 1400, 1330, 1195, 1115, 1075, 960, 855, 810, 715, and 675 cm.$^{-1}$.

5. Rearrangement of 1-hydroxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene (33).

The 1-hydroxy compound (33) was dissolved in sulphuric acid (experiment 2 method 1) and gave

a) (3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (2), X=F, (6%);

b) (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (3) X=F, (31%);

c) (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one,(4) X=F, (4.3%).

6. Attempted isomerisation of ketones (2), (3), and (4) X=F.

In trifluoroacetic acid.

(3,4)-Tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (2)

X=F (32 mg.) was heated under reflux in trifluoroacetic acid (5 ml.) for 111 hr.. Removal of the solvent gave only starting material as shown by t.l.c., g.l.c. (column A) and ^{1}H n.m.r. spectroscopy.

Similarly in boiling trifluoroacetic acid for 1 month,

(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (3)

X=F, gave no isomerisation,

and for 100 hr.

(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (4)

X=F, gave no isomerisation.

In sulphuric acid.

(3,4)-Tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one,(2) X=F, in concentrated sulphuric acid for 1 hr. at room temperature gave no isomerisation.

Similarly for 3 hr.

(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one,(3) X=F, gave no isomerisation,

and (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (4) X=F, gave no isomerisation.

7. Reduction of (6,7)-tetrafluorobicyclo[3.2.1]octa-3,6-diene-2-one.

The ketone (4) X=F, (60 mg.) in chloroform (15 ml.) was reduced with hydrogen in the presence of pre-reduced palladium on carbon catalyst (10% Pd/C).

Removal of the solvent and catalyst gave (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-6-ene-2-one,(15), (42 mg. 70%) m.p. 80-85° (from Hexane). Molecular weight by high resolution mass spectrometry:-

Measured mass:	244.0523
Expected formula:	$C_{12}H_8F_4O$
Calculated mass:	244.0522,

^{1}H n.m.r. τ ($CDCl_3$) 6 - 6.4 (m., 2H) and 7.1 - 8.3 (m., 6H);

$\upsilon_{max}^{CHCl_3}$: 2950, 2880, 1725, 1500, 1450, 1398, 1310, 1285, 1128, 1095, 1061, 943, and 892 cm.$^{-1}$.

8. Reduction of (3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one.

The ketone (2) X=F (40 mg.) in ethanol (10 ml.) was reduced with hydrogen in the presence of pre-reduced palladium on charcoal catalyst (4 mg., 10% Pd/C).

After removal of solvent and catalyst gave

(3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3-ene-2-one (14),

(38 mg., 95%), m.p. 74 - 75° (from ethanol).

(Found: C, 59.05; H, 3.35. $C_{12}H_8F_4O$ requires C, 59.00; H, 3.3%).

^{1}H n.m.r. τ ($CDCl_3$) 6.0 - 6.4 (m., 1H), 6.7 - 7.0 (m., 1H), and 7.4 - 8.9 (m., 8H).

$\upsilon_{max}^{CHCl_3}$: 2960, 2880, 1708, 1635, 1502, 1480, 1448, 1365, 1345, 1298, 1128, 1105, 1068, 1045, 1020, 944, 925, and 842 cm.$^{-1}$.

9. Rearrangement of (7,8)-tetrachlorobenzobicyclo[2.2.2]octa-2,5,7-triene (1) X=Cl.

Compound (1) X=Cl, (952 mg.) in concentrated sulphuric acid (25 ml.) gave after work up as in experiment 2 method 1

a) (3,4)-tetrachlorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (2) X=Cl, (29 mg., 3.2%),

m.p. 154 - 155° (from ethanol).

(Found: C, 46.9; H, 2.2; $C_{12}H_6Cl_4O$ requires C, 46.8; H, 1.95%).

^{1}H n.m.r. τ ($CDCl_3$) 3.27 (q., 1H, $J_{6,7}$ = 5.5 Hz; $J_{6,5}$ = 3.5 Hz.); 3.77 (q., 1H, $J_{7,6}$ = 5.5 Hz., $J_{7,1}$ = 3.5 Hz.); 5.5 - 5.7 (m., 1H); 6.35 - 6.55 (m., 1H); and 7.1 - 7.6 (m., 2H);

$\upsilon_{max}^{CHCl_3}$ 2970, 2945, 2870, 1708, 1535, 1360, 1321, 1295, 1220, 1138, 1070, 990, 905, 835, and 697 cm.$^{-1}$;

$\lambda_{max}^{Ethanol}$ 225 (ϵ30,200); 253 sh. (7,440); 268 sh. (5,216); 318 (1,830); and 328 (1,850) n.m.,

b) (7,8)-tetrachlorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (3) X=Cl, (688 mg., 76%),

m.p. 166-168° (from ethanol) (lit.[10a] m.p. 150°);

^{1}H n.m.r. τ ($CDCl_3$) 3.0 - 3.5 (m., 2H) 5.05 (q., 1H, $J_{1,6}$ = 5 Hz. $J_{1,5}$ = 2 Hz.); 5.1 - 5.3 (m., 1H); 7.9 (8 lines AB of ABX, 2H, J_{AB} = 17.5 Hz., J_{AX} = J_{BX} = 3 Hz.)

$\upsilon_{max}^{CHCl_3}$ 2960, 2930, 1740, 1380, 1310, 1270, 1140, 1125, 1075, 965, 900, and 690 cm.$^{-1}$;

c) (6,7)-tetrachlorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (4) X=Cl, (41 mg., 4.5 %),

m.p. 144 - 146° (from Hexane/benzene).

(Found: C, 46.95; H, 1.95; $C_{12}H_6Cl_4O$ requires C, 46.8; H, 1.95%);

^{1}H n.m.r. τ ($CDCl_3$) 2.54 (q., 1H, $J_{4,3}$ = 10 Hz., $J_{4,5}$ = 7 Hz.); 4.46 (q., 1H, $J_{3,4}$ = 10 Hz., $J_{3,1}$ = 1.7 Hz.); 5.75 - 6.2 (m., 2H); and 7.1 - 7.3 (m., 2H);

$\upsilon_{max}^{CHCl_3}$ 3020, 2985, 2950, 1700, 1680, 1370, 1310, 1290, 1220, 1130, 1095, 1028, 960, 840, 785, and 640 cm.$^{-1}$;

$\lambda_{max}^{Ethanol}$ 212 (ϵ 34,300) and 230 sh. (20,200) n.m..

10. Rearrangement of 1-methoxy-(7,8)-benzobicyclo[2.2.2]octa-2,5,7-triene (1) X=H.

Compound (1) X=H (300 mg.) in concentrated sulphuric acid gave after

work up as in experiment 2 method 1

a) (3,4)-benzobicyclo[3.2.1]octa-3,6-diene-2-one (2) X=H,(22 mg., 8%); oil;

^{1}H n.m.r. τ(CCl_4) 2.05 - 2.3 (m., 1H); 2.6 - 3.1

(m., 3H); 3.3, 3.35 (q., 1H, $J_{6,7}$ = 5.5 Hz; $J_{6,5}$ = 3.5 Hz.);

3.88, 3.93 (q., 1H, $J_{7,6}$ = 5.5 Hz.; $J_{7,1}$ = 3.5 Hz.);

6.3 - 6.5 (m., 1H); 6.5 - 6.7 (m., 1H); and 7.15 - 7.6 (m., 2H);

υ_{max} 3080, 2965, 1697, 1602, 1455, 1280, 1268, 1256, 1215, 906, 810,

720, and 688 cm.$^{-1}$.

Molecular weight by high resolution mass spectrometry:

Measured mass:	170.0729
Formula:	$C_{12}H_{10}O$
Calculated mass:	170.0732

b) (7,8)-benzobicyclo[2.2.2]octa-5,7-diene-2-one (3) X=H,

(139 mg., 50%); m.p. 54 - 55°, (after sublimation) (lit.[33]

m.p. 56 - 58°);

^{1}H n.m.r.τ($CDCl_3$) 2.55 - 2.95 (m., 4H); 3.05 - 3.6

(m., 2H); 5.57 (q., 1H, $J_{1,6}$ = 5.5 Hz., $J_{1,5}$ = 2.5 Hz.);

5.6 - 5.9 (m., 1H, $J_{4,5}$ = 5.5 Hz., $J_{4,6}$ = 2.5 Hz., $J_{4,3}$ = 2.5 Hz.);

7.5 - 8.3 (8 lines of AB part of ABX, 2H. J_{AB} = 17.5 Hz.,

$J_{3,4}$ = 2.5 Hz.);

υ_{max} 3080, 3015, 2930, 1735, 1470, 1460, 1410, 1334, 1300, 1145, 1120,

1080, 960, and 687 cm.$^{-1}$;

$\lambda^{Methanol}_{max}$ 217 (ϵ 3925); 261 sh. (824); 267 (965); 273 (896); 286 (545);

295 (565); 305 (312); and 317 sh. (216);

c) (6,7)-benzobicyclo[3.2.1]octa-3,6-diene-2-one (4) X=H,

(18 mg., 6.5 %), m.p. 55° (from hexane);

^{1}H n.m.r. τ (CCl_4) 2.5 - 3.1 (m., 5H); 4.65 (q., 1H, $J_{3,4}$ = 10 Hz., $J_{3,1}$ = 1.5 Hz.);
6.15 - 6.55 (m., 2H); and 7.15 - 7.4 (m., 2H);

υ_{max} 3010, 2970, 2880, 1680, 1463, 1368, 1280, 1220, 1096, 1026, and 883 cm.$^{-1}$,

$\lambda_{max}^{methanol}$ 211 (ϵ 8,280); 231 (7,450); and 348 (196)..

Molecular weight by high resolution mass spectrometry:

Measured mass:	170.0732
Formula:	$C_{12}H_{10}O$
Calculated mass:	170.0732

11. Attempted isomerisation of ketone (3) X=H.

The ketone (3) X=H, (50 mg.) was dissolved in concentrated sulphuric acid (1 ml.) at room temperature. After 2 min. the mixture was poured onto ice (5 g.), extracted with ether, and the ether layer washed with water and dried. Removal of the solvent gave a crystalline solid (44 mg., (90%) which was shown by t.l.c., ^{1}H n.m.r. spectroscopy and i.r. spectroscopy to be unreacted starting material.

12. Reduction of 1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (21).

The ketone (21),[23] (2g.,) in ether (25 ml.) was added dropwise to a suspension of lithium aluminium hydride (0.3 g.) in ether (25 ml.) and the mixture was stirred for 15 min.. Dilute sulphuric acid (80 ml., N/4) was added slowly and the organic phase was separated. The aqueous phase was extracted with ether (2 x 25 ml.) and the combined organic phases were washed with water and dried. Removal of the solvent gave an epimeric mixture of alcohols which were separated by preparative t.l.c. using 10% ether/90% benzene as eluant and gave a) 2-exo-hydroxy-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene (19), (1.1 g., 55%);

m.p. 113 - 115° (from ethanol).

(Found: C, 57.05; H, 3.7; $C_{13}H_{10}F_4O_2$ requires C, 56.95; H, 3.7%);

^{1}H n.m.r. τ($CDCl_3$) 3.2 - 3.5 (m., 2H); 5.6 - 5.9 (m., 1H);

5.95 - 6.2 (m., 1H); 6.27 (d., 3H, J_{HF}= 3 Hz.);

7.12 (broad s., 1H); 8.02 (q.d., 1H, $J_{3\ exo,\ 3\ endo}$ = 12.5 Hz., $J_{3\ endo,2}$ = 8 Hz; $J_{3\ endo,\ 4}$ = 3 Hz.); and

8.64 (d.t., 1H, $J_{3\ exo,\ 3\ endo}$ = 13 Hz., $J_{3\ exo,\ 2}$ = 3 Hz., $J_{3\ exo,4}$ = 3 Hz.);

υ_{max} 3530, 2920, 1500, 1485, 1460, 1375, 1357, 1325, 1260, 1190, 1170, 1130, 1085, 1037, 1010, 960, 867, 848, 797, and 710 cm.$^{-1}$, and

b) 2-endo-hydroxy-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene (20), (0.73 g., 37%);

m.p. 126 - 127° (from methanol).

(Found: C, 57.0; H, 3.6; $C_{13}H_{10}F_4O_2$ requires C, 56.95; H, 3.7%.);

^{1}H n.m.r. τ ($CDCl_3$) 3.3 - 3.5 (m., 2H); 5.6 - 5.9 (m., 1H)

5.98 (q., 1H, $J_{2,3\ exo}$ = 8 Hz., $J_{2,3\ endo}$ = 3 Hz.);

6.31 (d., 3H, J_{HF} = 2 Hz.); 7.1 (broad s., 1H);

7.88 (q.d., 1H, $J_{3\ exo,\ 3\ endo}$ = 12.5 Hz., $J_{3\ exo,\ 2}$ = 8.5 Hz., $J_{3\ exo,\ 4}$ = 3 Hz.); and 8.87 (d.t., 1H, $J_{3\ exo,\ 3\ endo}$ = 12.5 Hz., $J_{3\ endo,\ 4}$ = 3 Hz., $J_{3\ endo\ 2}$ = 3 Hz.);

υ_{max} 3580, 3000, 2950, 2845, 1500, 1485, 1360, 1320, 1290, 1117, 1070, 1030, 970, and 865 cm.$^{-1}$.

13. Preparation of 1-methoxy-2-endo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene.

The 2-endo alcohol (20) (500 mg.) was dissolved in dry pyridine (5 ml.) and cooled to 0°. A solution of p-toluene sulphonyl chloride (500 mg.) in pyridine (5 ml.) was added dropwise and the mixture was left

at 4^{o} for 5 days. Ether (50 ml.) was added to give a solution which was washed with firstly 2N. hydrochloric acid (3 x 25 ml.), then sodium carbonate solution (3 x 25 ml., 5%), and finally with water (2 x 25 ml.). The solution was dried, the solvents removed and the products separated by preparative t.l.c. (1:9 ether/benzene) gave,

a) Recovered starting material (157 mg.)

b) 1-methoxy-2-endo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzo-bicyclo[2.2.2]octa-5,7-diene (18) (293 mg., 55%);
m.p. 134 - 135° (from ethanol);
^{1}H n.m.r. $\tau(CDCl_3)$ 2.28 (d., 2H, (AA') J_{AB} = 8.5 Hz.);
2.66 (d., 2H, BB') J_{BA} = 8.5 Hz.); 3.2 - 3.6 (m., 2H);
5.1 (q., 1H, $J_{2,3\ exo}$ = 9 Hz., J = 2 Hz.); 5.6 - 5.85 (m., 1H);
6.58 (d., 3H, J_{HF} = 3 Hz.); 7.58 (s., 3H); 7.5 - 8.0 (m., 1H);
and 8.3 - 8.75 (m., 1H);
υ_{max} 2950, 2855, 1500, 1360, 1175, 1120, 1040, 1020, 1000, 955, 910, 872, and 860 $cm.^{-1}$.

A repeat experiment at room temperature gave the 2-endo tosylate in 87% yield.

14. Preparation of 1-methoxy-2-exo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene.

p-Toluene sulphonyl chloride (100 mg.) in pyridine (2 ml.) was added dropwise to a solution of the 2-exo alcohol (19) (100 mg.) in pyridine (2 ml.). The mixture was left to stand at room temperature for 4 days, work as in experiment 13 gave 1-methoxy-2-exo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene (17), (140 mg., 90%), m.p. 120 - 121° (from ethanol);
^{1}H n.m.r. τ ($CDCl_3$) 2.22 (d., 2H, (AA') J_{AB} = 8.5 Hz.);

2.65 (d., 2H, (BB') J_{BA} = 8.5 Hz.); 3.2 - 3.6 (m., 2H); 5.2 (q., 1H, $J_{2,3\ endo}$ = 8 Hz., $J_{2,3\ exo}$ = 2.5 Hz.); 5.6 - 5.9 (m., 1H); 6.55 (d., 3H, J_{HF} = 3 Hz.); 7.58 (s., 3H); 7.7 - 8.15 (m., 1H); and 8.15 - 8.55 (m., 1H); υ_{max} 2960, 2840, 1605, 1500, 1365, 1320, 1170, 1120, 1100, 1037, 990, 945, and 860 $cm.^{-1}$.

15. Solvolysis of 1-methoxy-2-exo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene (17).

The 2-exo-tosylate (17), (80 mg.) in trifluoroacetic acid (2 ml.) was heated under reflux for 2 hr.. Trifluoroacetic acid was removed from the cooled reaction mixture to leave a product which was separated from p-toluene sulphonic acid by preparative t.l.c. and gave (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (4) X=F, (44 mg., 98%) m.p. 73°.

The product had identical spectroscopic data with previously prepared material (experiment 2).

The 2-exo-tosylate (17), (100 mg.) in sulphuric acid (10 ml.) gave after work up (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (4) X=F, (21 mg., 37%), m.p. 73 - 74°.

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16. Solvolysis of 1-methoxy-2-endo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene (18).

The 2-endo-tosylate (18) (100 mg.) was dissolved in a mixture of glacial acetic acid (6 ml.), acetic anhydride (4 drops) and sodium acetate (4 mg.). The mixture was heated under reflux for 10 min., then at 80° for 12 hr.. The cooled reaction mixture was poured into water (50 ml.), and extracted with ether (4 x 10 ml.). The extracts were washed with sodium bicarbonate solution (2 x 20 ml., 10%), water (2 x 20 ml.) and dried. Removal of the solvent gave (3,4)-tetrafluorobenzobicyclo[3.2.1]-octa-3,6-diene-2-one, (2) X=F, (52 mg., 92%), m.p. 82 - 83°. The product had identical spectroscopic properties with the previously prepared material (experiment 2).

In a second experiment the 2-endo-tosylate (175 mg.) in the same solvolysis mixture after heating under reflux for 6 hr. gave, after work up (3,4-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (2) X=F, (66 mg., 67%) and 2-endoacetoxy -1-methoxy-(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-5,7-diene (28), (32 mg., 26%);

^{1}H n.m.r. τ ($CDCl_3$) 3.2 - 3.4 (m., 2H); 5.6 - 6.05 (m., 2H);
4.75 (q., 1H, J = 9 Hz. J = 2.5 Hz.)
5.6 - 5.9 (m., 1H); 6.37 (d., 3H, J_{HF} = 2 Hz.);
7.4 - 7.9 (m., 1H); 8.06 (s., 3H); and
8.65 - 9.0 (m., 1H);

ν_{max} 2950, 2840, 1740, 1500, 1375, 1355, 1230, 1120, 1110, 1040, 960, and 860 cm.$^{-1}$.

The 2-endo-acetyl-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene was hydrolysed in aqueous ethanol with sodium carbonate to give the 2-endo-hydroxy-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-5,7-diene (20), as shown by t.l.c. and ^{1}H n.m.r. spectroscopy.

17. Solvolysis of 2-exo-tosylate in ethanol/hydrochloric acid.

The 2-exo-tosylate (17), (50 mg.) was heated under reflux in ethanol (5 ml.) and concentrated hydrochloric acid (5 ml.) for 4 hr.. The mixture was poured into water (10 ml.), extracted with ether (3 x 10 ml.), and the combined extracts were washed with water and dried. Removal of the solvent left an oil which was subjected to preparative t.l.c. (20% ether/benzene) and gave 4-ethoxy-(6,7)-tetrafluorobenzobicyclo[3.2.1]oct-6-ene-2-one (23), (18 mg., 54%);

^{1}H n.m.r. τ (CCl_4) 5.9 - 6.7 (m., 5H); 7.2 - 8.3 (m., 4H); and 8.8 (t., 3H, J = 6.5 Hz.);

ν_{max} 2970, 2880, 1730, 1490, 1397, 1342, 1125, 1100, 1068, 958, and 883 cm.$^{-1}$.

Mass spectrometry: $M^+ = 288$

$C_{14}H_{12}F_4O_2$ requires M. = 288

18. Attempted isomerisation of ketones (2), (3), (4) X=F in concentrated sulphuric acid over an extended period of time.

(3,4)-Tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (2) X=F, (135 mg.) was dissolved in concentrated sulphuric acid (3 ml.) and the mixture was left to stand at room temperature for 209 hr.. The mixture was poured onto ice (20 g.), extracted with ether (3 x 10 ml.), and the extracts were washed with water and dried. Removal of the solvent gave a product (13 mg.) which by t.l.c. was a mixture and did not correspond to the ketones (2), (3), or (4) X=F, but by i.r. spectroscopy (ν_{max} 1730 cm.$^{-1}$) and its t.l.c. properties appears to be a lactone. ^{1}H n.m.r. spectroscopy showed the absence of the ketones, (2), (3), and (4) X=F. The product was not examined further.

Similarly (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (3) X=F, (500 mg.) in concentrated sulphuric acid (15 ml.) for 22 hr. gave

after work up and preparative t.l.c.

a) recovered starting material (54 mg., 11%);

b) (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (4) X=F, (115 mg., 23%). Identical to authentic material by t.l.c., i.r. spectroscopy and ^{1}H n.m.r. spectroscopy.

c) A crude fraction (16.5 mg.) by t.l.c. and i.r. spectroscopy (ν_{max} 1735 cm.$^{-1}$) appeared to be a lactone but was different from the lactone fraction isolated from ketone (2) X=F, in sulphuric acid. The product was not examined further.

(6,7)-Tetrafluorobenzobicyclo[3.2.1]octa-3,6]-diene-2-one (4) X=F (100 mg.) was dissolved in concentrated sulphuric acid and after 192 hr. gave only unchanged starting material (97 mg., 97%) after work up, as shown by t.l.c. and ^{1}H n.m.r. spectroscopy.

19. Reaction of 5-[^{2}H]-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (40) in sulphuric acid.

The ketone (40) (300 mg.) was dissolved in concentrated sulphuric acid (4 ml.) and after 192 hr. at room temperature was poured onto ice (20 g.). The usual work up and preparative t.l.c. gave

a) recovered starting material (29 mg., 10% unchanged as shown by ^{1}H n.m.r. spectroscopy.

b) 5-[^{2}H]-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (41) (67 mg., 22%).

^{1}H n.m.r. τ (CCl_4) 2.6 (d., 1H, $J_{4,3}$ = 10 Hz.); 4.52 (q., 1H, $J_{3,4}$ = 10 Hz., $J_{3,1}$ = 1.5 Hz.); 5.8 - 6.05 (m., 1H); and 7.1 - 7.3 (m., 2H).

Mass spectrometry: M^{+} 243

d_o = 13 ; d_1 87%.

20. Attempted isomerisation of ketones (14) and (15).

When the ketone (14) (30 mg.) was a) heated under reflux in trifluoroacetic acid (1.5 ml.) for 18 hr., or b) dissolved in fluorosulphonic acid (1.5 ml.) at room temperature for 20 hr., or c) dissolved in concentrated sulphuric acid (1.5 ml.) at room temperature for 24 hr., no isomerisation to ketone (15) was shown to occur by g.l.c. (column E).

Similarly the ketone (15) (30 mg.) could not be isomerised to ketone (14) using the above conditions.

21. Photolysis of (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (3) X=F.

The ketone (3) X=F, (200 mg.) was dissolved in ether (25 ml.) and photolysed in a nitrogen atmosphere using a medium pressure Hanovia U.V. lamp for 5 hr.. The heat of the lamp was sufficient to maintain a gentle boiling of the solvent. Removal of the ether gave a crystalline product which, after preparative t.l.c., gave 1,2,3,4-tetrafluoronaphthalene, (32) (134 mg., 81%);

m.p. 107 - 108° (from methanol) (lit.[124] 110 - 111°)

^{1}H n.m.r. τ (CCl_4) 1.8 - 2.2 (m., 2H); and 2.3 - 2.6 (m., 2H).

22. Deuteration of (6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (4) X=F.

The ketone (4) X=F (18 mg.) was dissolved in deuterio-sulphuric acid (0.5 ml.) and deuterium oxide (0.1 ml.). The mixture was warmed at 60° for 10 min., cooled, and deuterium oxide (1 ml.) added. The precipitate was filtered, washed with deuterium oxide (.5 ml.), then dried by vacuum desiccation and gave 3-[^{2}H]-(6,7)-tetrafluorobenzobicyclo[3.2.1]-octa-3,6-diene-2-one (30), (16 mg., 90%);

^{1}H n.m.r. τ (CCl_4) 2.63 (d., 1H, $J_{4,5}$ = 7 Hz.);

5.8 - 6.15 (m., 2H); and 7.1 - 7.3 (m., 2H).

Mass spectrometry: $M^+ = 243$

$d_o = 7$; $d_1 = 93\%$

23. Rearrangement of 1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-2,5,7-triene (1) X=F in deuteriosulphuric acid.

The compound (1) X=F, was dissolved in 80% deuterio-sulphuric acid (experiment 2, method 3) and gave :-

a) 3-[^{2}H]-(7,6)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (31) (60%);

^{1}H n.m.r. τ (CCl_4) 3.0 - 3.5 (m., 2H); 5.2 - 5.5 (m., 2H); 7.8 - 8.0 (m., 0.41 H); and 8.0 - 8.2 (m., 0.59 H.).

Mass spectrometry: $M^+ = 243$;

b) 3,8[$^2H_2$]-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (29), (4%);

^{1}H n.m.r. τ (CCl_4) 2.62 (d., 1H, $J_{4,5}$ = 7 Hz.); 5.8 - 6.05 (m., 2H); and 7.1 - 7.4 (m., 1H).

Mass spectrometry: $M^+ = 244$

$d_1 = 6$; $d_2 = 94\%$.

24. Photolysis of compound (31).

Gave 1,2,3,4-tetrafluoronaphthalene (32) (80%).

Mass spectrometry: $M^+ = 200$

$d_o = 100\%$.

25. Reduction of 1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-3-one (51).

The ketone (51)[23] (200 mg.) was reduced with lithium aluminium hydride in the usual manner (experiment 12) and gave a) 3-exo-hydroxy-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene (49) (118 mg., 59%), m.p. 99 - 100° (from methanol),

^{1}H n.m.r. τ ($CDCl_3$) 3.28 (d., 1H, $J_{6,5}$ = 8 Hz.); 3.64
(q., 1H, $J_{5,6}$ = 8 Hz., $J_{5,4}$ = 6 Hz.); 5.6 - 6.0
(m., 2H.), 6.39 (d., 3H, J_{HF} = 2 Hz.) 7.75 (q., 1H,
$J_{2\text{-exo, }2\text{-endo}}$ = 12 Hz., $J_{2\text{-endo},3}$ = 8 Hz.); 7.95 (broad s.,1H);
and 8.65 (q., 1H, $J_{2\text{-endo, }2\text{-exo}}$ = 12 Hz., $J_{2\text{-exo},3}$ = 3 Hz.).

ν_{max} 3450 broad, 2950, 2845, 1500, 1350, 1330, 1310, 1297, 1215,
1168, 1115, 1105, 1035, 995, 862, 802, 721, and 715 cm.$^{-1}$;

and b) 3-endo-hydroxy-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-5,7-diene (50) (79 mg., 39%); oil;

^{1}H n.m.r. τ ($CDCl_3$) 3.06 (d., 1H, $J_{6,5}$ = 8 Hz.);
3.49 (q., 1H, $J_{5,6}$ = 8 Hz., $J_{5,4}$ = 6 Hz.);
5.4 - 5.7 (m., 1H); 5.7 - 6.1 (m., 1H); 6.35
(d., 3H, J_{HF} = 2 Hz.); 7.67 (q., 1H, $J_{2\text{-exo, }2\text{-endo}}$ = 12 Hz.,
$J_{2\text{-exo},3}$ = 8 Hz.); 7.67 (broad s., 1H);
and 8.42 (q., 1H, $J_{2\text{-exo, }2\text{-endo}}$ = 12 Hz., $J_{2\text{-endo},3}$ = 3 Hz.)

ν_{max} 3400 broad, 2960, 2850, 1500, 1375, 1325, 1290, 1210, 1170, 1120,
1060, 1030, 960, 865, 790, 727, and 708 cm.$^{-1}$.

26. Preparation of 1-methoxy-3-exo (and -3-endo)-toluene-p-sulphoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,6-diene.

By the method previously described (experiment 14) an epimeric mixture of 1-methoxy-3-hydroxy compounds gave the tosylates after preparative t.l.c.

a) 1-methoxy-3-exo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzo-bicyclo[2.2.2]octa-5,7-diene (47), (42%).
m.p. 95° (from ethanol).

(Found: C, 56.25; H, 3.6; $C_{20}H_{16}F_4O_4S$ requires C, 56.1; H, 3.8%);

^{1}H n.m.r. τ ($CDCl_3$) 2.26 (d., 2H, (AA') J_{AB} = 8.5 Hz.); 2.65 (d., (BB') J_{BA} = 8.5 Hz.); 3.17 (d., 1H, $J_{6,5}$ = 8 Hz.) 3.65 (q., 1H, $J_{5,6}$ = 8 Hz., $J_{5,4}$ = 6 Hz.); 5.2 - 5.7 (m., 2H); 6.43 (d., 3H, J_{HF} = 3 Hz.); 7.56 (s., 3H); 7.78 (q., 1H, J = 13 Hz., $J_{2\text{-endo},3}$ = 7.5 Hz.); and 8.28 (q., 1H, $J_{2\text{-exo, 2-endo}}$ = 13 Hz., $J_{2\text{-exo, }3}$ = 2.5 Hz.);

ν_{max} 3020, 2950, 2850, 1610, 1490, 1370, 1300, 1175, 1120, 1095, 1040, 950, 925, and 865 cm.$^{-1}$,

and b) 1-methoxy-3-endo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene (48), (27%);

m.p. 91 - 92° (from methanol).

(Found: C, 56.15; H, 3.95; $C_{20}H_{16}F_4O_4S$ requires C, 56.1; H, 3.8%);

^{1}H n.m.r. τ ($CDCl_3$) 2.26 (d., 2H, (AA') J_{AB} = 8.5 Hz.); 2.65 (d., 2H, (BB') J_{BA} = 8.5 Hz.); 3.25 (d., 1H, $J_{6,5}$ = 8 Hz.); 3.7 (q., 1H, $J_{5,6}$ = 8 Hz., $J_{5,4}$ = 6 Hz.); 5.0 - 5.35 (m., 1H); 5.45 - 5.7 (m., 1H); 6.43 (d., 3H, $J_{H,F}$ = 3 Hz.); 7.74 (q., 1H, $J_{2\text{-exo, 2-endo}}$ = 13 Hz., $J_{2\text{-exo},3}$ = 8 Hz.); and 8.38 (q., 1H, $J_{2\text{-exo, 2-endo}}$ = 13 Hz., $J_{2\text{-endo, }3}$ = 3 Hz.);

ν_{max}^{KBr} 3015, 2985, 2960, 2935, 2855, 1600, 1500, 1385, 1365, 1345, 1210, 1190, 1175, 1090, 1040, 945, 910, 860, 820, and 665 cm.$^{-1}$.

27. Solvolysis of 1-methoxy-3-endo-toluene-p-sulphonyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,6-diene (48).

The 1-methoxy-3-endo-tosylate (48) (100 m g.) was dissolved in concentrated sulphuric acid (2 ml.) at room temperature then immediately poured onto ice (10 g.). The solution was extracted with ether (3 x 7 ml.) and the combined extracts were washed with water (3 x 2 ml.). The organic phase was dried and after removal of solvent gave (7,8)-tetra-

fluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (3) X=F,(34 mg., 60%), m.p. 70 - 72° mixed m.p. 70 - 72°, identical to an authentic sample by ^{1}H n.m.r. and i.r. spectroscopy.

28. Solvolysis of 1-methoxy-3-exo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,6-diene.

The 1-methoxy-3-exo-tosylate (47) (33 mg.) was dissolved in concentrated sulphuric acid (1 ml.). Work up as in the previous experiment gave (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (3) X=F (12.2 mg., 71%); m.p. and mixed m.p. 69 - 72° identical to an authentic sample by t.l.c., and i.r..

29. Solvolysis of 1-methoxy-3-exo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,6-diene.

The 1-methoxy-3-exo-tosylate (47) (100 mg.) in trifluoroacetic acid (3 ml.) was heated under reflux for 3 hr.. Removal of the solvent gave a crystalline product which was heated with light petroleum b.p. 40-60° and filtered. The light petroleum insoluble fraction was shown to be p-toluene sulphonic acid (by ^{1}H n.m.r. i.r. spectrometry). Removal of the solvent from the filtrate gave (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (3) X=F, (52.1 mg., 92%), m.p. 69 - 72°, identical to previously prepared material (experiment 1) by its t.l.c., g.l.c. properties, and by its i.r. and ^{1}H n.m.r. spectra.

30. Solvolysis of 1-methoxy-3-endo-toluene-p-sulphonyloxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,6-diene (50).

The 1-methoxy-3-endo-tosylate (50), (100 mg.) was solvolysed in trifluoroacetic acid (3 ml.) for 90 min., and after work up as in experiment 29 gave 1-methoxy-4-trifluoroacetyloxy-(2,3)-tetrafluorobenzobicyclo[3.2.1]octa-2,6-diene (51), (68 mg., 79%), oil;

^{1}H n.m.r. τ ($CDCl_3$) 3.45 (d., 1H, $J_{7,6}$ = 6 Hz.); 4.04 (m., 2H);
6.2 - 6.8 (m., 4H); and 7.2 - 7.8 (m., 2H);

υ_{max} 2960, 2850, 1793, 1510, 1485, 1370, 1340, 1225, 1160, 1038, 925, 833, and 760 cm.$^{-1}$.

Mass spectrometry: M^+ = 370.

$C_{15}H_9F_7O_3$ requires M. 370.

The 1-methoxy-4-trifluoroacetyl compound (51), was hydrolysed at room temperature with sodium carbonate in aqueous ethanol and gave 1-methoxy-4-hydroxy-(2,3)-tetrafluorobenzobicyclo[3.2.1]octa-2,6-diene, (52), (100%),

υ_{max} 3400, 2950, 2840, 1500, 1480, 1360, 1335, 1215, 1165, 1110, 930, and 835 cm.$^{-1}$.

This crude 4-hydroxy compound (52), (43 mg.) was dissolved in dichloromethane (1 ml.) and added dropwise to a solution of chromium trioxide (90 mg.), pyridine (140 mg.) in dichloromethane (2 ml.).

The solution was stirred for 15 min., chloroform (4 ml.) added, and then washed with 1N sodium hydroxide (5 ml.), 1N hydrochloric acid (5 ml.), and sodium bicarbonate (5 ml., 5%). The solvent was removed from the dried organic phase to give a crystalline solid (45 mg.). Recrystallisation from hexane gave 1-methoxy-(2,3)-tetrafluorobenzobicyclo[3.2.1]octa-2,6-diene-4-one, (53), (31 mg., 73%) m.p. 64 - 65° mixed m.p. 63 - 65°, identical by t.l.c., ^{1}H n.m.r. and i.r. spectroscopy to an authentic sample.

31. Reduction of 1-methoxy-(2,3)-tetrafluorobenzobicyclo[3.2.1]octa-2,6-diene-4-one and rearrangement of the product.

The ketone (53) (10 mg.) was reduced with lithium aluminium hydride (10 mg.) in the usual manner (experiment 12) and gave an epimeric mixture

of alcohols 1-methoxy-4-hydroxy-(2,3)-tetrafluorobenzobicyclo[3.2.1]octa-2,6-diene (54) (8.7 mg. 87%);

$\nu_{max}^{CHCl_3}$ 3400, 2950, 2840, 1500, 1480, 1360, 1325, 1290, 1165, 1110, 1040, 930, and 835 cm.$^{-1}$.

The product (8.7 mg.) was dissolved in concentrated sulphuric acid (0.2 ml.), poured onto ice (1 g.), extracted with ether (4 x 1 ml.). The ether extracts were washed with water (4 x 1 ml.), dried; removal of the solvent gave (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (6.7 mg., 87%) m.p. 68 - 71°.

The compound was identical by t.l.c., g.l.c., (column A, and column F), and i.r. spectrometry, to an authentic sample.

32. Rearrangement of 1-methoxy-(7,8)-tetrafluorobicyclo[2.2.2]octa-triene in 67% H_2SO_4.

The compound (1) X=F, (500 mg.) was dissolved in sulphuric acid (15 ml., 67%) at 80°. The mixture was stirred for 15 min., then poured onto ice (50g.). The aqueous mixture was extracted with chloroform (4 x 10 ml.). The organic extracts were washed with water, dried, then evaporated under reduced pressure to give an oil which was separated by preparative t.l.c.. The products were in order of decreasing R_f

a) (3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (2) X=F, (28 mg., 6%); b) (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (3) X=F, (142 mg., 30%); c) (6,7)-tetrafluorobenzobicyclo[3.2.1]-octa-3,6-diene-2-one, (4) X=F, (18 mg., 4%);

d) 3-exo-hydroxy -1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene, (49), (92 mg., 17%); identified by comparison of ^{1}H n.m.r. and i.r. spectra with authentic material (this sample was contaminated with other minor products which could not be easily removed);

e) a mixture of other hydroxy compounds (63 mg.) which could not be separated.

33. Preparation of 2,4,6-[$^2H_3$]anisole.

2,4,6-Tribromophenol was methylated by the Gillis method[90] and gave 2,4,6-tribromoanisole (97%). 2,4,6-Tribromoanisole was then dimetallated with n-butyl lithium in light petroleum b.p. 40-60° by the method described by Gilman.[158] The addition of deuterium oxide in tetrahydrofuran gave, after work up, 4-bromo-2,6-[$^2H_2$]anisole (69%). The 4-bromo-2,6-[$^2H_2$]anisole was then metallated with n-butyl lithium in ether by the method of Gilman,[159] the addition of deuterium oxide in tetrahydrofuran gave, after work up, 2,4,6-[$^2H_3$]anisole (65%); ^1H n.m.r. (CCl_4) 2.84 (broad s., 2H) and 6.27 (s., 3H).

34. Preparation of 2,4,6-[$^2H_3$]-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene.

By the method previously described (experiment 1) using a .9 mole excess of the 2,4,6-[$^2H_3$]anisole gave 2,4,6-[$^2H_3$]-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene, (54), (34%); ^1H n.m.r. τ (CCl_4) 3.2 (broad s., 2H) and 6.3 (d., 3H, J_{HF} = 3 Hz.).

Mass Spectrometry: M^+ 259.

99% d_3

35. Preparation of 3,5-[$^2H_2$]anisole.

1,3,5-Tribromobenzene in ether was metallated with n-butyl lithium[160] and, after the addition of deuterium oxide in tetrahydrofuran, gave [^2H]-3,5-dibromobenzene (42%). The [^2H]-3,5-dibromobenzene was treated with n-butyl lithium in ether,[161] and after the addition of deuterium oxide in tetrahydrofuran gave 3,5-[$^2H_2$]-bromobenzene (67%); ^1H n.m.r. τ (CCl_4) 2.4 - 2.6 (m., 1.8 H); and 2.7 - 2.9 (m., 1H).

3,5-[$^2H_2$]-Bromobenzene was oxidised to 3,5-[$^2H_2$]-phenol by the method described by Hawthorne.[162]

3,5-[$^2H_2$]-Phenylmagnesium bromide, (from 3,5-[$^2H_2$]-bromobenzene (17.1 g.), and magnesium (3.2 g.)) in ether (70 ml.) was added to a solution of trimethyl borate[163] (11.4 g.) in ether (140 ml.), pre-cooled to -80°. The addition took 1 hr., after which time the mixture was allowed to warm to room temperature. Dilute hydrochloric acid (70 ml., 10%) was added dropwise (ca. 10 min.) under a nitrogen atmosphere with vigorous stirring. The stirring was stopped and the aqueous phase separated by means of a stopcock in the bottom of the reaction vessel. The ethereal layer was washed twice with water (70 ml.). Hydrogen peroxide (100 ml., 10%) was added over 10 min. with vigorous stirring. After 1½ hr. the layers were again separated and the ethereal phase was washed with ferrous ammonium sulphate (2 x 10%, 50 ml.). The ether layer was extracted with sodium hydroxide (4 x 25 ml., 8%). Acidification of the basic extract gave 3,5-[$^2H_2$]-phenol (5 g., 49%). The 3,5-[$^2H_2$]phenol was methylated by the Gillis procedure[90] and gave, after distillation, 3,5-[$^2H_2$]anisole (86%).

Mass spectrometry: M^+ 110

d_o = 4; d_1 = 19; and d_2 = 77%.

36. Preparation of 3,5-[$^2H_2$]-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-2,5,7-triene.

By the method previously described (experiment 1) gave

a) 3,5-[$^2H_2$]-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene (55), (37%);

^1H n.m.r.τ(CCl_4) 2.9 - 3.1 (m., 2H); 4.7 - 5.0 (m., 1H); and 6.3 (d., 3H, J_{HF} = 3 Hz.).

Mass spectrometry: M^+ 258

d_o = 6; d_1 = 18; d_2 = 76%.

and b) 4,6-[$^2H_2$]-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (74), (4%);

^1H n.m.r. τ (CCl_4) 3.05 - 3.25 (m., 1H); 5.1 - 5.3 (m., 1H); and 7.71 - 8.0 (AB q., 2H, J_{AB} = 17 Hz.).

Mass spectrometry: M^+ 244

d_1 5; d_1 19; d_2 76%.

37. Preparation of 4-[^2H]anisole.

p-Bromoanisole (37.4 g., 0.2 mole) in ether (150 ml.) was added to magnesium (5 g.) in ether (50 ml.) at such a rate so as to maintain boiling of the solvent. The mixture was heated under reflux for 30 min., cooled, and deuterium oxide (12 ml., 0.6 mole) in tetrahydrofuran (60 ml.) added. After 4 hr. stirring, the mixture was filtered through a celite pad and washed with water (2 x 100 ml.). Removal of the solvent from the dried solution gave, after distillation, 4-[^2H]anisole (75%);

^1H n.m.r. τ (CCl_4) 2.78 (d., 2H, (AA') J_{AB} = 9 Hz.), and 3.18 (d., 2H (BB') J_{BA} = 9 Hz.).

Mass spectrometry: M^+ 109

d_o = 13; d_1 = 87%.

38. Preparation of 4-[^2H]-1-methoxy-(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-2,5,7-triene.

By the method previously described (experiment 1) gave

a) 4-[^2H]-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene (56), (56%);

^1H n.m.r. τ (CCl_4) 3.0 (d., 2H, (AA') J_{AB} = 7 Hz.); 3.23 (d., 2H, (BB') J_{BA} = 7 Hz.); and 6.29 (d., 3H, J_{HF} = 3 Hz.).

Mass spectrometry: M^+ 257

d_o = 11; d_1 = 89%.

b) 5-[^{2}H]-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (40), (9%);

^{1}H n.m.r. τ (CCl_4) 3.1 - 3.55 (m.,); 5.15 - 5.45 (m., 2H);
and 7.98 (8 lines of AB part of ABX, 2H).

Mass spectrometry: M^+ 243

d_o 14; d_1 = 86%..

39. Rearrangement of 2,4,6-[$^2H_3$]-1-methoxy-(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-2,5,7-triene.

The compound (54) was rearranged in sulphuric acid (experiment 2, method 1) and gave :-

a) 1,5,7-[$^2H_3$]-(3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (57), (5.3%);

^{1}H n.m.r. τ (CCl_4) 3.35 (broad s., 1H) and
7.3 - 7.48 (AB q., 2H J_{AB} = 14 Hz.).

Mass spectrometry: M^+ = 245

d_3 99%

b) [$^2H_3$]-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one,(65), (53%);

^{1}H n.m.r. Ratio of proton resonances
vinyl 1.52 : bridgehead 1 : methylene 1.3

Mass spectrometry: M^+ = 245

d_3 99%

c) 1,3,5-[$^2H_3$]-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (61), (5.7%);

^{1}H n.m.r. (CCl_4) 2.65 (broad s., 1H) and 7.25 (broad s., 2H).

Mass spectrometry: M^+ = 245

d_2 = 4%; d_3 = 96%.

40. Photolysis of Compound (65).

Gave $[^2H_2]$-5,6,7,8-tetrafluoronaphthalene, (69)

^1H n.m.r. Ratio of proton resonances

1,4 protons : 2,3 protons

1 : 1.53

Mass spectrometry : $M^+ = 202$

d_2 99%.

41. Rearrangement of 1-methoxy-2,4,6-$[^2H_3]$-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-2,5,7-triene.

The compound (54) was rearranged in sulphuric acid (experiment 2, method 3) and gave :-

a) $[^2H_3]$-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one,(64), (66%);

^1H n.m.r. Ratio of proton resonances

vinyl 2.54 : bridgehead 1 : methylene 1.9

Mass spectrometry: $M^+ = 245$

d_3 99%

b) 1,5-$[^2H_2]$-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (60), (6%);

^1H n.m.r. τ (CCl_4) 2.65 (d., 1H, $J_{4,3}$ = 10 Hz.); 4.54 (d., 1H, $J_{3,4}$ = 10 Hz.); and 7.25 (broad s., 2H).

Mass spectrometry: $M^+ = 244$

d_2 99%.

42. Photolysis of compound (64).

Gave $[^2H_2]$-5,6,7,8-tetrafluoronaphthalene (68).

^1H n.m.r. Ratio of proton resonances

1,4 protons : 2,3 protons

1 : 2.6

Mass spectrometry: $M^+ = 202$; d_2 99%.

43. Rearrangement of 1-methoxy-3,5-[$^2H_2$]-(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-2,5,7-triene.

The compound (55) was rearranged in sulphuric acid (experiment 2, method 1), and gave :-

a) 6,8-[$^2H_2$];(3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (58), (5.5%);

^1H n.m.r. τ (CCl_4) 3.8 (d., 1H, $J_{7,1}$ = 3.5 Hz.); 5.7 - 6.0 (m., 1H); 6.5 - 6.75 (m., 1H); and 7.2 - 7.5 (m., 1H).

Mass spectrometry: M^+ = 244

d_o = 5; d_1 = 17; d_2 = 78%,

b) [$^2H_2$]-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (66), (56%);

^1H n.m.r. Ratio of proton resonances

vinyl 1 : bridgehead 1.3 : methylene 2.13

Mass spectrometry: M^+ = 244

d_o 5; d_1 19; d_2 76%

c) 4,8-[$^2H_2$]-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (62), (5%);

^1H n.m.r. τ(CCl_4) 4.46 (broad s., 1H); 5.7 - 6.05 (m., 2H); and 7.23 (m., 1H).

Mass spectrometry: M^+ = 244

d_o 4; d_1 19; d_2 77%.

44. Photolysis of compound (66)

Gave [$^2H_2$]-5,6,7,8-tetrafluoronaphthalene (70)

^1H n.m.r. Ratio of proton resonances

1,4 protons : 2,3 protons

1.35 : 1

Mass spectrometry: M^+ = 202

d_o 5; d_1 18; d_2 77%.

45. Rearrangement of 4-[^{2}H]-1-methoxy-(7,8)-tetrafluorobenzobicyclo [2.2.2]octa-2,5,7-triene.

The compound (56) was rearranged in sulphuric acid (experiment 2, mwthod 1) and gave:-

a) 5-[^{2}H]-(3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (59), (5.3%);

^{1}H n.m.r. τ (CCl_4) 3.25 (d., 1H, $J_{6,7}$ = 5.5 Hz.);
3.7 - 3.9 (q., 1H, $J_{7.6}$ = 5.5 Hz., $J_{7,1}$ = 3.5 Hz.);
6.5 - 6.7 (m., 1H); and 7.3 - 7.6 (m., 2H).

Mass spectrometry: M^+ = 243

d_o 13 ; d_1 87%

b) [^{2}H]-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (67), (61%);

^{1}H n.m.r. Ratio of proton resonances

vinyl 1 : bridgehead 1.32 : methylene 1.54

Mass spectrometry: M^+ = 243

d_o 11; d_1 89%

c) 5-[^{2}H]-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (63), (5%);

^{1}H n.m.r. τ (CCl_4) 2.62 (d., 1H, $J_{4,3}$ = 10 Hz.);
4.5 (q., 1H, $J_{3,4}$ = 10 Hz., $J_{3,1}$ = 1.5 Hz.)
5.8 - 6.05 (m., 1H); and 7.2 (m., 2H).

Mass spectrometry: M^+ 243

d_o = 13; d_1 = 87%.

46. Photolysis of compound (67).

Gave, [^{2}H]-5,6,7,8-tetrafluoronaphthalene (71)

^{1}H n.m.r. Ratio of proton resonances

1,4-protons : 2,3-protons

1.33 : 1

Mass spectrometry: M^+ 201

d_o 11 ; d_1 = 89%

47. Rearrangement of 1,4-dimethoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-2,5,7-triene (74).

The dimethoxy compound (74)[23] (300 mg.) was dissolved in sulphuric acid (12.5 ml., 80%) at 60° and after 30 min. the cooled mixture was poured into water (150 ml.). The aqueous phase was extracted with ether (4 x 25 ml.); the ether extracts were washed with water, combined, and dried over magnesium sulphate.

Removal of the solvent and drying agent gave a mixture of products which were separated by preparative t.l.c. using ether/light petroleum b.p. 40-60° (1 to 1) as eluant and gave a) 1-methoxy-(2,3)-tetrafluorobenzo-bicyclo[3.2.1]octa-2,6-diene-4-one, (53), (50 mg., 18%); m.p. 63 - 65° (from methanol).

(Found: C, 57.2; H, 2.90%; M. [Mass spectrometry] 272;

$C_{13}H_8F_4O_2$ requires C, 57.3; H, 2.95%; M. 272);

^{1}H n.m.r. τ (CCl_4) 3.43 (d., 1H, $J_{7,6}$ = 5.5 Hz.);

3.9 (q., 1H, $J_{6,7}$ = 5.5 Hz., $J_{6,5}$ = 3.5 Hz.); 6.37 - 6.75

(m., 1H); 6.6 (d., 3H, J_{HF} = 0.5 Hz.); and 7.05 - 7.55

(m., 2H);

$\nu_{max}^{CHCl_3}$ 2943, 2838, 1708, 1623, 1493, 1473, 1353, 1323, 1305, 1266,

1160, 1119, 1043, 1008, 920, 868, and 810 cm.$^{-1}$,

$\lambda_{max}^{Ethanol}$ 210 (ϵ13,200); 249 (4300); and 296 (1900) n.m.,

and b) (7,8)-tetrafluorobenzobicyclo[2.2.2]octa-7-ene-2,5-dione (75)

(55mg., 20%), m.p. 165 - 167° (after sublimation)

(lit.[23] m.p. 161 - 164°), mixed m.p. 163 - 166°;

^{1}H n.m.r. ($CDCl_3$) 5.75 (m., 2H);and 7.4 (8 lines of AB part of

ABX; 4H, J_{AB} = 18 Hz., J_{AX} = J_{BX} = 3.0 Hz.);

$\nu_{max}^{CDCl_3}$ 3030, 2920, 1745, 1500, 1403, 1390, 1320, 1120, 1070, 1027, 941, 888, and 863 cm.$^{-1}$.

48. Rearrangement of 1-methoxy-4-methyl-tetrafluorobenzobicyclo[2.2.2]octatriene (5).

The compound (5),[23] (850 mg.) was dissolved in concentrated sulphuric acid (15 ml.) as in experiment 2 method 1, and gave :-

a) 5-methyl-(3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one,(6), (26 mg., 3%);

m.p. 82° (from hexane).

(Found: C, 60.5; H, 3.1; $C_{18}H_8F_4O$ requires C, 60.95; H, 3.15%);

^{1}H n.m.r.$\tau(CCl_4)$ 3.6 (d., 1H, $J_{6,7}$ = 5.5 Hz.); 3.96 (q., 1H, $J_{7.6}$ = 5.5 Hz., $J_{7,1}$ = 3.5 Hz.); 6.5 - 6.8 (m., 2H); 7.34 (d., 1H, $J_{8\ SYN,\ 8\ ANTI}$ = 12 Hz.); 7.7 (q., 1H, $J_{8\ SYN,\ 8\ ANTI}$ = 12 Hz. $J_{8\ ANTI,1}$ = 5 Hz.); and 7.25 (d., 3H, J_{HF} = 6.5 Hz.).

$\nu_{max}^{CHCl_3}$ 2945, 1710, 1625, 1490, 1465, 1355, 1300, 1118, 1070, 990, 975, 895, and 850 cm.$^{-1}$

$\lambda_{max}^{Ethanol}$ 230 (ϵ 6540); 235 (5640); 258 (2940); and 296 (1660) n.m.,

b) 4-methyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one,(7) (90 mg., 11%);

m.p. 58 - 59° (from methanol).

Found: C,61.15; H, 3.05; $C_{13}H_8F_4O$ requires C, 60.95; H, 3.15%);

^{1}H n.m.r.$\tau(CCl_4)$ 3.2 - 3.7 (m., 2H); 5.2 - 5.45 (m., 1H); 8.08 (d., 3H, J_{HF} = 5 Hz.) and 7.9 - 8.1 (m., 2H);

υ_{max}^{KBr} 3060, 2995, 2900, 1740, 1490, 1390, 1335, 1302, 1285, 1165, 1135, 1110, 1085, 1050, 990, 908, 865, 783, 755, and 716 cm.$^{-1}$

$\lambda_{max}^{Ethanol}$ 213 (ϵ 11,210); 266 (715); 281 (350); 295 (405); 304 (360); and 315 sh. (250) n.m.,

c) 5-methyl-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one,(8), (31 mg., 4%);

m.p. 54° (from hexane).

(Found: C, 61.15; H, 3.15; $C_{13}H_8F_4O$ requires C, 60.95; H, 3.15%);

^{1}H n.m.r. τ (CCl_4) 2.88 (d., 1H, $J_{4,3}$ = 10 Hz.);

4.6 (q., 1H $J_{3,4}$ = 10 Hz., $J_{3,1}$ = 1.5 Hz.);

5.8 - 6.0 (m., 1H); 7.2 - 7.4 (m., 2H); and 7.26 (d., 3H, J_{HF} = 1.5 Hz.);

$_{max}$ 2970, 2940, 2880, 1690, 1490, 1390, 1280, 1110, 1070, 1047, 1023, 964, 894, 880, 838, and 714 cm.$^{-1}$,

d) a glassy solid (282 mg.),

^{1}H n.m.r. τ (D.M.S.O. d_6) 5.3 - 6.8 (broad m.) and 7.5 - 9.2 (broad m.),

υ_{max}^{KBr} 3450 (broad), 2950, 1640, 1500, 1400, 1330, 1315, 1290, 1200, 1120, 1050, 1025, and 770 cm.$^{-1}$.

49. Rearrangement of 1-methoxy-4-methyl-tetrafluorobenzobicyclo[2.2.2]-octa-triene (5).

The compound (5) (200 mg.) was dissolved in sulphuric acid (80%) as in epxeriment 2 method 3, and gave :-

a) recovered starting material (12 mg.),

b) 4-methyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one,(7), (95 mg., 54%), identical to an authentic sample by ^{1}H n.m.r. spectroscopy.

c) 5-methyl-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one,(8),

(10 mg., 5.6 %), identical to an authentic sample by ^{1}H n.m.r. spectroscopy.

Photolysis of 4-methyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (7).

By the usual method gave 1-methyl-5,6,7,8-tetrafluoronaphthalene, (79), (94%), m.p. 93 - 94° (from ethanol), (lit.[13] m.p. 95 - 97°).

^{1}H n.m.r. $\tau(CCl_4)$ 2.0 - 2.3 (m., 1H); 2.4 - 2.8 (m., 2H); 7.2 (d., 3H, J_{HF} = 7.4 Hz.).

50. Rearrangement of 5-methyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (78).

The ketone (78), (400 mg.) was dissolved in concentrated sulphuric acid (4 ml.) at room temperature. The mixture after 10 min., was poured onto ice (40 g.). The aqueous phase was extracted with ether (2 x 10 ml.). The ether extracts,after washing, drying, and removal of the solvent, gave a mixture of products (8 mg.), none of which corresponded to starting material (by t.l.c.). The aqueous phase was neutralised to pH 7. by the addition of saturated barium hydroxide solution.

The precipitated salts were filtered off through a 'hyflo' super-cel pad. Water was removed from the filtrate to give a glass (550 mg.).

^{1}H N.m.r. $\tau(CDCl_3)$ 6.2 - 7.0 (broad m.)

ν_{max}^{KBr} 3450 (broad), 2960, 1740, 1640, 1500, 1400, 1200, 1060, 1050, and 770 cm.$^{-1}$.

51. Reaction of tetrafluorobenzyne with 3,5-dimethyl anisole.

The Grignard reagent was formed from bromopentafluorobenzene (0.1 mole) experiment 1), and this was decomposed at 80° in the presence of 3,5-dimethyl anisole (0.6 mole); after work up gave

a) 3,5-dimethyl-1-methoxy-tetrafluorobenzobicyclo[2.2.2]octa-triene,(9),

(11.4 g., 40%);

m.p. 83.5° (from ethanol).

(Found: C, 63.4; 4.3% M. [Mass spectrometry] 284

$C_{15}H_{12}F_4O$ requires C, 63.45; H, 4.25%, M. 284).

^1H n.m.r. τ ($CDCl_4$) 3.4 - 3.6 (m., 2H); 5.45 - 5.6

(m., 1H); 6.31 (d., 3H, J_{HF} = 2 Hz.);

and 8.09 (d., J = 1.5 Hz.);

$\nu_{max}^{CHCl_3}$ 2970, 2940, 2915, 2842, 1670, 1630, 1480, 1442,

1370, 1300, 1277, 1135, 1110, 1098, 1067, 1010, 992, 950, 910,

and 838 cm.$^{-1}$,

b) 4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (10), (5.95 g., 22%);

m.p. 62 - 64° (from hexane).

(Found: C, 62.3; H, 3.85; $C_{14}H_{10}F_4O$ requires C, 62.25; H, 3.75%);

^1H n.m.r. τ (CCl_4) 3.75 - 3.95 (m., 1H); 5.4 - 5.6 (m., 1H);

and 7.85 - 8.2 (m., 8H);

$\nu_{max}^{CHCl_3}$ 2980, 2945, 2910, 1740, 1490, 1375, 1310, 1170, 1115, 1050,

987, 920, 880, 847, and 815

λ_{max} 265 (ϵ 659); 295 (415); 305 (385);

and 314 sh. (267) n.m..

52. Photolysis of 4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-5,7-diene-2-one.

By the method previously described (experiment 21) gave 5,7-dimethyl-1,2,3,4-tetrafluoronaphthalene, (80), (84%); m.p. 84 - 85° (from ethanol) (lit.[13] m.p. 83.5°);

^1H n.m.r. τ (CCl_4) 2.45 (broad s., 1H);

2.9 (broad s., 1H); 7.27 (d., 3H,

J_{HF} = 7.5 Hz.); and 7.55 (s., 3H).

53. Rearrangement of 3,5-dimethyl-1-methoxy-tetrafluorobenzobicyclo-[2.2.2]octa-triene (9) in sulphuric acid.

The compound (9) (2 g.) was dissolved in concentrated sulphuric acid (35 ml.) and the mixture was poured immediately onto ice (150 g.). The precipitate was filtered, washed with water until acid-free, dried by vacuum desiccation and gave 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzo-bicyclo[3.3.1]non-2-ene-7-one, (81), (2.02 g., 100%), m.p. 170 - 171° (from ethanol).

(Found: C, 58.2; H, 4.2; F, 26.4% M. [Mass spectrometry] 288

$C_{14}H_{12}F_4O_2$ requires C, 58.35; H, 4.2; F, 26.35%; M. 288);

^{1}H n.m.r. τ ($CDCl_3$) 6.6 - 8.4 (m., 6H); 8.38 (s., 3H); and

8.4 (d., 3H, J_{HF} = 1.5 Hz.);

ν_{max} 2940, 1730, 1515, 1475, 1381, 1335, 1127, 1070, 957, 905, and 850 cm.$^{-1}$,

$\lambda_{max}^{Ethanol}$ 262 (ϵ 660) n.m..

54. Rearrangement of 3,5-dimethyl-1-methoxy-tetrafluorobenzobicyclo-[2.2.2]octa-triene (9) in aqueous sulphuric acid.

The compound (9) (200 mg.) was added to stirred sulphuric acid (10 ml., 70%) at 0°.

The solution, after 3 hr. at this temperature, was poured onto ice (20 g.), extracted with ether (3 x 10 ml.) and the ethereal extracts were washed with water. The extracts were dried, and removal of the solvent left an oil (194 mg.) which was separated by preparative t.l.c. using 30% ether/70% light petroleum b.p. 40 - 60° as eluant. The products were in order of decreasing R_f a) recovered starting material (19 mg. 1%) identical by t.l.c., g.l.c., and i.r. spectroscopy to an authentic sample; b) 4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (10), (24 mg., 14%) identical by t.l.c., g.l.c., and ^{1}H n.m.r.

spectroscopy to an authentic sample;

c) 3-methyl-1-(2'-oxopropanyl)-5,6,7,8-tetrafluoronaphthalene,(82), (69 mg., 40%).

m.p. 104.5° (from hexane),

(Found: C, 61.6; H, 3.7% M. [mass spectrometry] 270

$C_{14}H_{10}F_4O$ requires C, 62.25; H, 3.75% M. 270);

^1H n.m.r. $\tau(CDCl_3)$ 2.15 - 2.35 (m., 1H); 2.8 - 2.9 (m., 1H);

5.8 (d., 2H, J_{HF} = 7 Hz.); 7.5 (broad s., 3H); and 7.7 (s., 3H);

$\upsilon_{max}^{CHCl_3}$ 2925, 1725, 1670, 1625, 1495, 1375, 1160, 1130, 1085,

and 868 cm.$^{-1}$;

λ_{max} 275 (ϵ 5,470); 281 (6,020); and 290 (5,350) n.m.

Molecular weight by high resolution mass spectrometry:-

Measured mass = 270.0667

Possible formula = $C_{14}H_{10}F_4O$

Calculated mass = 270.0668

d) 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]non-2-ene-7-one (81) (71 mg., 39%), identical by m.p., t.l.c., and ^1H n.m.r. spectroscopy to an authentic sample.

55. Reaction of ketone (10) in aqueous sulphuric acid.

The ketone (10) (300 mg.) was reacted in aqueous sulphuric acid using the conditions previously described (experiment 54), gave after work up: a) unreacted starting material (149 mg., 53%); b) lactone (81), (148 mg., 46%).

56. Reaction of the lactone (81) in aqueous sulphuric acid.

The lactone (81) (50 mg.) was reacted as in experiment 54 and gave, after work up, unchanged starting material (50 mg.) as shown by t.l.c. and ^1H n.m.r. spectroscopy.

57. Rearrangement of 3,5-dimethyl-1-methoxy-tetrafluorobenzobicyclo-[2.2.2]octa-triene (9) in trifluoroacetic acid.

The compound (9), (300 mg.) in trifluoroacetic acid (10 ml.) was heated under reflux for 6 hr.. Removal of the solvent gave an oil which was separated by preparative t.l.c. and gave a) 4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (10), (234 mg., 82%), by m.p., mixed m.p., t.l.c., g.l.c., and ^{1}H n.m.r. spectroscopy was identical to an authentic sample;

and b) 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]non-2-ene-7-one, (81), (28 mg., 9.3%), by m.p., t.l.c., and i.r. spectroscopy was identical to an authentic sample.

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1 In a similar experiment a chloroform solution of compound (9) was added to trifluoroacetic acid/sulphuric acid (1:1) at 0° and gave, after work up, the same two products :- (10) (87%) and (81) (12%).

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58. Rearrangement of 4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-5,7-diene-2-one (10).

The ketone (10) was dissolved in concentrated sulphuric acid as in experiment 53 and gave 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]non-2-ene-7-one, (81), (94%) identical by t.l.c. and ^{1}H n.m.r. spectroscopy to an authentic sample.

59. Reduction of 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]-non-2-ene-7-one (81).

The lactone (81) (500 mg.) was reduced with lithium aluminium hydride in ether by the usual method (experiment 12), and gave 1,3-dimethyl-3-hydroxy-1-(2'-hydroxyethyl)-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydronaphthalene, (83), (490 mg., 97%);

m.p. 105 - 106° (from ethanol).

(Found: C, 57.5; H, 5.55%; M. [Mass spectrometry] 292

$C_{14}H_{16}F_4O_2$ requires C, 57.55; H, 5.5%; M. 292)

^{1}H n.m.r. τ ($CDCl_3$) 5.7 - 6.1 (m., 2H, exchanged in D_2O)

6.1 - 6.5 (m., 2H); 6.8 - 8.9 (m., 6H);

8.6 (d., 3H, J_{HF} = 2.5 Hz.); and 8.65 (s., 3H);

$\nu_{max}^{CHCl_3}$ 3350 (broad), 2960, 2940, 1650, 1510, 1465, 1373, 1325, 1298, 1185, 1157, 1130, 1070, 1005, 945, 930, and 867 cm.$^{-1}$.

60. Oxidation of 1,3-dimethyl-3-hydroxy-1-(2'-hydroxyethyl)-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydronaphthalene, (83).

The diol (83) (100 mg.) was dissolved in acetone (10 ml.) and a solution of chromium trioxide in sulphuric acid (Jones' reagent*) was added dropwise until a yellow colour remained for 5 min.. Water (20 ml.) was added and precipitated product was collected, washed, and dried. The product was shown by t.l.c. and ^{1}H n.m.r. spectroscopy to be 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]non-2-ene-7-one, (81), (100 mg., 100%).

61. Hydrogenation of 4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-5,7-diene-2-one (10).

By the usual method (experiment 8) at 0° gave an epimeric mixture of 4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]oct-7-ene-2-ones, (95a), (99%);

^{1}H n.m.r. τ ($CDCl_3$) 6.1 - 6.3 (m., 1H) 7.6 - 6.9 (m., 5H)

8.35 (d., 3H, J_{HF} = 6 Hz.); 8.85 (d., 1H);

J = 7 Hz.); and 9.18 (d., 2H, J = 7 Hz.).

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* Jones' reagent:- chromium trioxide (26.72 g.) was dissolved in concentrated sulphuric acid (23 ml.) and the mixture diluted with water (to 100 ml.).

62. Attempted rearrangement of the epimeric mixture (95a).

The ketones (95a) (100 mg.) were dissolved in concentrated sulphuric acid (2 ml.) at room temperature. The mixture, after 1 hr., was worked up as usual (experiment 53) and gave recovered starting material (99%) as shown by t.l.c. ^{1}H n.m.r.

63. Hydrolysis of 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]-non-2-ene-7-one (81).

The lactone (81) (586 mg.) in ethanol (10 ml.) and 2N sodium hydroxide (15 ml.) was heated under reflux for 10 min..

The cooled reaction mixture was poured into water (15 ml.) and concentrated hydrochloric acid added until the pH reached 7. The mixture was extracted with ether (3 x 10 ml.) and the ether extracts washed and dried. Removal of the solvent gave fraction 1 (350 mg.). The aqueous phase was acidified to pH 2 and again extracted with ether (3 x 10 ml.). Removal of the solvent gave fraction 2 (203 mg.) which, by i.r. spectroscopy was identical to fraction 1.

The combined fractions were recrystallised and gave 1,3-dimethyl-3-hydroxy-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydronaphth-1-ylacetic acid, (84), (310 mg., 50%), m.p. 126-127° (from chloroform);

υ_{max}^{KBr} 3350 (broad), 2950, 1722, 1648, 1513, 1465, 1415, 1390, 1352, 1330, 1300, 1242, 1178, 1156, 1120, 1070, 930, and 860 $cm.^{-1}$..

Mass spectrometry: M^{+} 306

$C_{14}H_{14}F_4O_3$ requires M. 306.

The compound (84) was readily converted to the lactone (81) by heating in a solution of chloroform for 30 min.. Even in the solid state it was converted slowly to the lactone (81) (1 week).

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64. Preparation of 1,4-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid (85).

The ketone (10) (100 mg.) was dissolved in tetrahydrofuran (0.4 ml.), 2N sodium hydroxide (1.75 ml.) and the solution was stirred at room temperature for 39 hr.. Water (3 ml.) was added and the aqueous phase was washed with ether (5 ml.).

Concentrated hydrochloric acid was added dropwise to the aqueous phase until acid,then extracted with ether (3 x 3 ml.). The extracts were combined, washed with water, and dried. Removal of the solvent left an oil, which was shown to be 1,4-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid, (85), (107 mg., 100%);

^{1}H n.m.r. τ ($CDCl_3$) 0.7 - 1.2 (broad s., 1H);
4.6 - 4.8 (m., 1H); 6.7 - 6.9 (m., 2H); 6.95 (d., 1H J_{AB} = 14.5 Hz.);
and 7.45 (d., 1H. J_{BA} = 14.5 Hz.) 8.2 (s., 3H); and 8.56 (d., 3H
J_{HF} = 1.5 Hz.);

υ_{max} 3400 - 2600 broad, 2930, 1720, 1515, 1480, 1450, 1380, 1305, 1235, 1104, 1055, 985, 955, 905, and 850 cm.$^{-1}$.

65. Methylation of 1,4-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid (85).

The acid (85) (100 mg.) was dissolved in ether (1 ml.) and diazomethane in ether was added until a faint yellow colour persisted for 1 min.. Removal of the solvent gave methyl-1,4-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetate, (87), (106 mg., 100%);

^{1}H n.m.r. τ ($CDCl_3$) 4.6 - 4.8 (m., 1H); 6.5 (s., 3H);
6.7 - 6.9 (m., 2H); 6.92 (d., 1H, J_{AB} = 15 Hz.);
7.45 (d., 1H, J_{BA} = 15 Hz.); 8.15 (s., 3H); and 8.56
(d., 3H; J_{HF} = 1.5 Hz.);

υ_{max} 2950, 1745, 1515, 1488, 1450, 1380, 1200, 1170, 1100, 1060, 980, 955, and 845 cm.$^{-1}$.

Molecular weight by high resolution mass spectrometry:-

Measured mass: 302.0900

Possible formula: $C_{15}H_{14}F_4O_2$

Calculated mass: 302.0930

66. Preparation of 1,2-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid.

The ketone (10) (500 mg.) was heated under reflux in 2N sodium hydroxide (15 ml.) and tetrahydrofuran (5 ml.) for 18 hr.. Work up as in experiment 64 gave 1,2-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid, (86), (450 mg., 84%);

^1H n.m.r. τ ($CDCl_3$) -0.15 - - 0.4 (broad s., 1H);

3.5 - 3.7 (m., 1H); 6.8 - 7.8 (m., 4H);

8.05 (s., 3H); and 8.52 (d., 3H, J_{HF} = 3 Hz.);

υ_{max} 3500 - 2500 (broad), 2980, 2930, 1720, 1515, 1505, 1480, 1450, 1390, 1330, 1115, 1075, 995, 880, 845, and 765 cm.$^{-1}$.

Mass spectrometry: M^+ = 288

$C_{14}H_{12}F_4O_2$ requires M. = 288

67. Methylation of 1,2-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid (86).

The acid (86) was methylated with diazomethane by the method as in experiment 65 and gave methyl-1,2-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetate, (88) as an oil;

^1H n.m.r. τ($CDCl_3$) 3.5 - 3.7 (m., 1H); 6.4 (s., 3H);

7.0 - 7.85 (m., 4H); 8.08 (broad s., 3H); and

8.59 (d., 3H, J_{HF} = 3 Hz.);

υ_{max} 2960, 2920, 1745, 1505, 1478, 1440, 1388, 1210, 1075, 1015, 995, and 880 cm.$^{-1}$.

Molecular weight by high.resolution mass spectrometry:-

Measured mass: 302.0939

Possible formula: $C_{15}H_{14}F_4O_2$

Calculated mass: 302.0930

68. Cyclisation of 1,4-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid.

The acid (85) (100 mg.) was dissolved in concentrated sulphuric acid (5 ml.) and after 5 min. poured onto ice (10 g.). Work up as in experiment 53 gave 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo-[3.3.1]non-2-ene-7-one, (81), (100 mg., 100%), identical by t.l.c., i.r. spectroscopy, and ^1H n.m.r. spectroscopy to an authentic sample.

69. Cyclisation of 1,2-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid (86).

The acid (86) (130 mg.) was dissolved in concentrated sulphuric acid (2 ml.) and after 5 min. poured onto ice (15 g.). Work up as in experiment 53 gave 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo-[3.3.1]non-2-ene-7-one (81), (125 mg., 96%), identical by t.l.c. and ^1H n.m.r. spectroscopy to an authentic sample.

70. Reduction of 1,2-dihydro-1,3-dimethyl-5,6,7,8-tetrafluoronaphth-1-ylacetic acid (86).

The acid (86) (1 g.) was reduced with lithium aluminium hydride by the usual method (experiment 12) and gave 1,3-dimethyl-1-(2'-hydroxy-ethyl)-5,6,7,8-tetrafluoro-1,2-dihydronaphthalene, (90), (804 mg., 85%); ^1H n.m.r. $\tau(CDCl_3)$ 3.5 - 3.75 (m., 1H); 6.4 (t., 2H, J = 7 Hz.); 6.6 - 6.9 (broad s., 1H, exchangeable in D_2O); 7.7 - 8.3 (m., 4H); 8.15 (broad s., 3H); and 8.68 (d., 3H, J_{HF} = 4 Hz.);

ν_{max} 3350 (broad), 2980, 2940, 1660, 1505, 1475, 1382, 1330, 1215, 1080, 1050, 1008, 982, 930, 880, and 840 cm.$^{-1}$.

71. Cyclisation of 1,3-dimethyl-1-(2'-hydroxymethyl)-5,6,7,8-tetrafluoro-1,2-dihydronaphthalene (90).

The alcohol (90) (300 mg.) in orthophosphoric acid (6 ml., 88%) was shaken at room temperature for 4 days. The mixture was poured into water (50 ml.), extracted with ether (5 x 10 ml.), and the extracts were washed with water until acid-free. Removal of solvent from the dried solution gave 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo-[3.3.1]non-2-ene, (89), (270 mg.,90%).

(Found: C, 61.45; H, 5.1 % M. [Mass spectrometry] 274,

$C_{14}H_{14}F_4O$ requires C, 61.3; H, 5.15%; M. 274);

^{1}H n.m.r. τ ($CDCl_3$) 6.05 - 7.0 (m., 2H); 7.1 - 7.3 (m., 2H); 8.1 - 8.8 (m., 4H); 8.5 (d., 3H J_{HF} = 5.5 Hz.); and 8.77 (s., 3H).

ν_{max} 3000, 2970, 2940, 2880, 1645, 1505, 1465, 1375, 1260, 1113, 1100, 1067, 1055, 1005, 948, 915, and 865 cm.$^{-1}$.

72. Cyclisation of 1,3-dimethyl-3-hydroxy-1-(2'-hydroxyethyl)-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydronaphthalene (83).

The diol (83) (100 mg.) was dissolved in orthophosphoric acid (3 g.) and heated at 100° for 1 hr.. The cooled mixture was poured onto ice (10 g.). Work up as in experiment 71 followed by preparative t.l.c. gave 1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]-non-2-ene, (89), (38 mg., 40%), identical by t.l.c., i.r. spectroscopy, and ^{1}H n.m.r. spectroscopy to an authentic sample.

73. Reaction of tetrafluorobenzyne with 2,6-dimethylanisole.

The Grignard reagent was formed from bromopentafluorobenzene (0.05 mole) (experiment 1) and this was decomposed at 80° in the presence

of 2,6-dimethylanisole (0.15 mole.). The products were separated by elution through a column of silica using light petroleum b.p. 40 - 60° and gave :-

a) 2,6-dimethyl-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octatriene, (11), (6.1 g., 43%), b.p. 110° at 4 m.m.

(Found: C, 63.3; H, 4.1% M. [Mass spectrometry] 284;

$C_{15}H_{12}F_4O$ requires C, 63.45; H, 4.25% M. 284),

^1H n.m.r. τ (CCl_4) 3.6 - 3.9 (m., 2H); 5.22 (d.t., 1H,

$J_{4,3} = J_{4,6} = 6$ Hz., $J_{4,F} = 2$ Hz.);

6.18 (d., $J_{HF} = 6$ Hz.); and 8.07 (d., 6H, J = 1.5 Hz.);

ν_{max}^{KBr} 3063, 2968, 2928, 2853, 1628, 1500, 1478, 1444, 1289, 1226,

1158, 1108, 1065, 1038, 961, 809, and 762 cm.$^{-1}$.

b) A mixture of ketones after elution with chloroform.

These were separated by preparative t.l.c. using 10% ether/90% light petroleum b.p. 60 - 80° as the eluant and gave 1,3-exo-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one, (96),

(1.25 g., 9%), m.p. 85 - 87° (from ethanol).

(Found: C, 62.05; H, 3.95; $C_{14}H_{10}F_4O$ requires C, 62.25; H,3.75%);

^1H n.m.r. and 220 M.Hz. τ (CCl_4) 3.43 (q., 1H, $J_{5,6}$ =

$J_{5,4} = 6.5$ Hz.), 3.84 (q., 1H, $J_{6,5}$ = Hz., $J_{6,4} = 2$ Hz.);

5.6 - 5.7 (m, 1H); 8.1 (q.d., 1H, $J_{3,4} = 2$ Hz., $J_{3,3\text{-Me}} = 7$ Hz.);

8.21 (d., 3H, $J_{HF} = 5.5$ Hz.); 8.8 (d., 3H, J = 7 Hz.);

$\nu_{max}^{CHCl_3}$ 2990, 2945, 2880, 1728, 1490, 1452, 1390, 1380, 1317, 1120,

1045, 977, 920, 890, 860, 818, and 700 cm.$^{-1}$.

$\lambda_{max}^{Ethanol}$ 266 (ϵ650); 295 (275); 304 (270); and 315 sh. (190) n.m.,

and 1,3-endo-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-5,7-diene-2-one (97), (2 g., 14%), m.p. 58 - 60° (from ethanol).

(Found: C, 62.05; H, 3.8%);

^{1}H n.m.r. at 220 M.Hz. $\tau(CCl_4)$ 3.25 (q., 1H, $J_{5,6} = J_{5,4}$ = 6.5 Hz.); 3.74 (q., 1H, $J_{6,5}$ = 6.5 Hz., $J_{6,4}$ = 2 Hz.); 5.6 - 5.7 (m., 1H); 7.77 (q., 1H, $J_{3,4}$ = 2.5 Hz., $J_{3,3\text{-Me}}$ = 7 Hz.) 8.16 (d., 3H, J_{HF} = 5.5 Hz.); and 9.1 (d., 3H $J_{3\text{-Me},3}$ = 7 Hz.);

$\nu_{max}^{CDCl_3}$ 2990, 2950, 2880, 1730, 1500, 1450, 1380, 1320, 1115, 1050, 965, 887, and 858 cm.$^{-1}$,

$\lambda_{max}^{Ethanol}$ 267 (ϵ 680); 298 (380); 306 (385); and 315 sh. (300) n.m..

74. a. Hydrogenation of 1,3-exo-dimethyl-(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-5,7-diene-2-one (96).

By the usual method (experiment 8) gave 1,3-exo-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]oct-7-ene-2-one (98),

m.p. 80 - 83° (from ethanol);

^{1}H n.m.r. $\tau(CCl_4)$ 6.25 - 6.5 (m., 1H); 7.5 - 8.5 (m., 5H); 8.42 (d., 3H, J_{HF} = 5.5 Hz.); and 8.75 (d., 3H, $J_{3\text{-Me},3}$ = 7 Hz.),

$\nu_{max}^{CHCl_3}$ 2970, 2883, 1729, 1622, 1500, 1390, 1335, 1120, 1050, 1025, 965, 918, and 890 cm.$^{-1}$.

b. Hydrogenation of 1,3-endo-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-5,7-diene-2-one (97).

By the usual method (experiment 8) gave 1,3-endo-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]oct-7-ene-2-one,(99);

m.p. 68 - 69° (from ethanol).

(Found: C, 61.95; H, 4.4; $C_{14}H_{12}F_4O$ requires C,61.8; H,4.45%);

^{1}H n.m.r. $\tau(CCl_4)$ 6.25 - 6.5 (m., 1H); 7.4 - 8.5 (m., 5H); 8.45 (d., 3H, J_{HF} = 6 Hz.); and 9.1 (d., 3H, $J_{3\text{-Me},3}$ 7 7 Hz.);

$CHCl_3$ 2965, 2945, 2885, 1730, 1500, 1390, 1385, 1345, 1115, 1050, 920, 890, 870, and 853 $cm.^{-1}$.

75. Rearrangement of 2,6-dimethyl-1-methoxy-(7,8)-tetrafluorobenzobicyclo[2.2.2]octa-triene (11).

The compound (11), (1 g.) was dissolved in trifluoroacetic acid (40 ml.) at room temperature. The mixture was stirred for 10 min. and then the trifluoroacetic acid was removed by evaporation under reduced pressure. The remaining oil was separated by preparative t.l.c. using 20% ether/80% light petroleum b.p. 40 - 60° as eluant and gave, in order of decreasing R_f

a) 1,7-dimethyl-(3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (12), (794 mg. 84%),
m.p. 50 - 51° (from ethanol).

(Found: C, 62.2; H, 3.8%; M. [Mass spectrometry] 270;
$C_{14}H_{10}F_4O$ requires C, 62.25; H, 3.75%; M. 270).

^1H n.m.r. τ ($CDCl_3$) 3.6 - 3.85 (m., 1H); 5.9 - 6.15 (m., 1H), 7.25 - 7.75 (m., 2H); 8.35 (d., 3H, J = 1.5 Hz.); and 8.69 (s., 3H);

ν_{max} 2980, 2940, 2875, 1707, 1620, 1504, 1477, 1450, 1440, 1380, 1365, 1325, 1291, 1268, 1005, 971, 941, 894, 843, 810, and 737 $cm.^{-1}$;

$\lambda_{max}^{Ethanol}$ 234 (ϵ 6,780); 264 (1830); 275 (1740); and 295 (1280) n.m.,

b) 1,3-dimethyl-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one, (13), (103 mg., 11%),
m.p. 49 - 51° (from hexane).

(Found: C, 62.15; H, 3.8% M. [Mass spectrometry] 270;
$C_{14}H_{10}F_4O$ requires C, 62.25; H, 3.75%; M. 270);

^1H n.m.r. τ (CCl_4) 2.8 - 3.1 (m., 1H, $J_{4,5}$ = 7 Hz.); 5.95 - 6.3 (m., 1H); 7.45 (d., 2H, $J_{8,5}$ = 2.5 Hz.); and 8.4 - 8.45 (m., 6H);

$\upsilon_{max}^{CHCl_3}$ 2938, 2873, 1688, 1500, 1486, 1448, 1378, 1316, 1098, 1053, 1043, 1018, 961, 946, 898, and 874 cm.$^{-1}$.

$\lambda_{max}^{Ethanol}$ 229 (ϵ 9,100); 273 (1,740); and 348 (130) n.m..

76. Isomerisation of 1,7-dimethyl-(3,4)-tetrafluorobenzobicyclo[3.2.1]-octa-3,6-diene-2-one (12).

The ketone (12) (100 mg.) in trifluoroacetic acid (9 ml.) was heated under reflux for 24 hr.. Removal of the solvent gave an oil which by g.l.c. (column E) was a mixture of two components in the ratio 1.25 : 1. These two components were separated by preparative t.l.c. using 20% ether/light petroleum b.p. 40 - 60° as eluant and gave in order of decreasing R_f :-

a) starting material (49 mg., 49%) as shown by t.l.c., g.l.c., and ^{1}H n.m.r. spectroscopy;

b) 1-methyl-7-methylene-(3,4)-tetrafluorobenzobicyclo[3.2.1]oct-3-ene-2-one, (101), (39 mg., 39%);

m.p. 60 - 61° (from hexane).

(Found: C, 62.5; H, 3.8%; M. [Mass spectrometry] 270;

$C_{14}H_{10}F_4O$ requires C, 62.25; H, 3.75%; M. 270),

^{1}H n.m.r. τ ($CDCl_3$) 4.75 - 5.0 (m., 1H); 6.1 - 6.4 (m., 1H);

6.8 - 7.6 (m., 2H); 7.8 - 8.0 (m., 2H);

and 8.65 (s., 3H);

υ_{max} 2980, 2945, 1703, 1635, 1510, 1470, 1367, 1340, 1290, 1140, 1093, 1010, 990, 937, 905, 825, and 730 cm.$^{-1}$,

$\lambda_{max}^{Ethanol}$ 208 (ϵ 11,200); 242 (11,500); 290 (2,215); and 337 (305) n.m..

77. Isomerisation of 1-methyl-7-methylene-(3,4)-tetrafluorobenzobicyclo[3.2.1]oct-3-ene-2-one (101).

The ketone (101) (4 mg.) in trifluoroacetic acid was heated under reflux for 24 hr.. Evaporation of the solvent gave a mixture (4 mg.)

which was shown by g.l.c. (columnsF and E) to be 1,7-dimethyl (3,4)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (12) and starting material in the ratio 1.27 : 1.

78. Attempted isomerisation of 1,3-dimethyl-(6,7)-tetrafluorobenzobicyclo[3.2.1]octa-3,6-diene-2-one (13).

The ketone (13) was dissolved in either boiling trifluoroacetic acid (for 18 hr.) or concentrated sulphuric acid at room temperature (for 3 hr.), and gave unchanged starting material as shown by g.l.c., and t.l.c.

79. Rearrangement of 3,5-dimethyl-1-methoxytetrafluorobenzobicyclo-[2.2.2]octa-triene (9) in D_2SO_4.
(150 mg.)

The compound (9) was dissolved in D_2SO_4 (1 ml.) and after 3 min. the mixture was poured into deuterium oxide (4 ml.). The precipitate was filtered, washed with deuterium oxide (1 ml.) and dried. Recrystallisation from benzene/hexane gave 4,8,9-[$^2H_3$]-1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]non-2-ene-7-one, (91); (152 mg.).

^1H N.m.r. n.m.r. IV p. 172.

Mass spectrometry M^+. = 291.

80. Rearrangement of 4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo[2.2.2]-octa-5,7-diene-2-one (10) in D_2SO_4.

The ketone (10) (100 mg.) was dissolved in D_2SO_4 (0.6 ml.). The solution was poured into deuterium oxide (3 ml.), the precipitate was filtered, washed with deuterium oxide (1 ml.) and then dried. Recrystallisation from ethanol gave 4,9-[$^2H_2$]-1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]non-2-ene-7-one, (92), (90 mg.).

^1H N.m.r. n.m.r. III p. 171.

Mass spectrometry: M^+ = 290.

81. Rearrangement of 3-[^{2}H]-4,6-dimethyl-(7,8)-tetrafluorobenzobicyclo-[2.2.2]octa-5,7-diene-2-one (93) in H_2SO_4.

The compound (9) (300 mg.) was heated under reflux in deuterotrifluoro acetic acid (10 ml.) for 1½ hr.. The mixture was cooled and the solvent removed under reduced pressure. The remaining solid was purified by preparative t.l.c. and gave 3-[^{2}H]-4,6-dimethyl-(7,8)-tetrafluorobenzo-bicyclo[2.2.2]octa-5,7-diene-2-one,(93), (200 mg.).

Compound (93) (90 mg.) was dissolved in concentrated sulphuric acid (0.9 ml.) and gave, after work up as in the previous experiment, 8-[^{2}H]-1,5-dimethyl-6-oxa-(2,3)-tetrafluorobenzobicyclo[3.3.1]non-2-ene-7-one, (94), (90.3 mg.).

^{1}H N.m.r. n.m.r. II p. 170.

Mass spectrometry: M^+ = 289.

82. Rearrangement of 3,5-dimethyl-1-methoxy-tetrafluorobenzobicyclo-[2.2.2]octa-triene (9) in 70% D_2SO_4.

The compound (9) (200 mg.) was dissolved in 70% D_2SO_4 (8.75 ml.) at 0°. The mixture, after 3 hr., was poured onto ice (20 g.) and extracted with ether (4 x 7 ml.).

The ether extracts were washed and dried. Evaporation of the solvent left an oil which was separated by preparative t.l.c. and gave a) recovered starting material (53 mg.) and b) 3-methyl-1-(1'-[^{2}H]-2'-oxopropanyl)-5,6,7,8-tetrafluoronaphthalene, (82), (25 mg.).

^{1}H N.m.r. at 100 M.Hz. ($CDCl_3$) 2.2 - 2.35 (broad s., 1H); 2.9 - 3.0 (broad s., 7H); 5.7 - 5.9 (m., .65H); 7.5 (s., 2.9 H) and 7.75 (s., 2.5 H)

Mass spectrometry: M^+ = 271.

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