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THERMOLYSIS OF PENTAFLUOROPHENYL ALLYL ETHER AND RELATED COMPOUNDS

by

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(Van Mildert College)

A thesis submitted to the University of Durham for
the Degree of Doctor of Philosophy

1977

To My Parents

Abstract

This work is concerned with the involvement of the two possible intramolecular Diels-Alder adducts which can be formed from a 2-allyl-3,5-cyclohexadienone produced by the Claisen rearrangement of a phenyl allyl ether. One of these adducts has been invoked to account for the ortho-ortho′ transformation.

Pentafluorophenyl allyl ether was chosen as the starting material, as it was envisaged that the fluorine atoms would a) block enolisation in the dienone intermediates; b) make the proposed Diels-Alder reaction more favourable by furnishing an electron deficient diene; and c) would help to stabilise small ring systems in the product.

The thesis is divided into five parts. Chapter one reviews the literature and traces the mechanistic development of the Claisen rearrangement and the ortho-ortho′ transformation.

In Chapters two and three the isolation and characterisation of aromatic, bicyclic and tricyclic decomposition products, from the two possible intramolecular Diels-Alder adducts, are discussed.

Chapters four and five describe the Claisen rearrangement in pentafluorophenyl 2-methylprop-2-enyl and pentafluorophenyl 2-methylbut-3-en-2-yl ethers and suggest that the products formed can be accounted for by a mechanistic scheme which could be general.

Acknowledgements

I would like to thank Dr. G.M. Brooke for his encouragement and unfailing support throughout the supervision of this work, and Professor W.K.R. Musgrave for his interest. I am grateful to Dr. R.S. Matthews for some n.m.r. measurements and Dr. H.M.M. Shearer for an X-ray crystal structure.

Assistance from the technical staff is appreciated, in particular Mr. R. Hart and Mr. T. Holmes. I am also indebted to Mrs. B. McGonigle for the presentation of the typescript and to my wife Ailsa for considerable help in the final preparation of this thesis.

MEMORANDUM

The work in this thesis was carried out in the Chemistry Laboratories of the University of Durham between October 1974 and July 1977. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

Notes to Reader

Throughout this thesis a number of abbreviations have been used regularly, these are: infra-red spectroscopy (i.r.); ultra-violet spectroscopy (u.v.); gas-liquid chromatography (g.l.c.); nuclear magnetic resonance spectroscopy (n.m.r.) and thin layer chromatography (t.l.c.).

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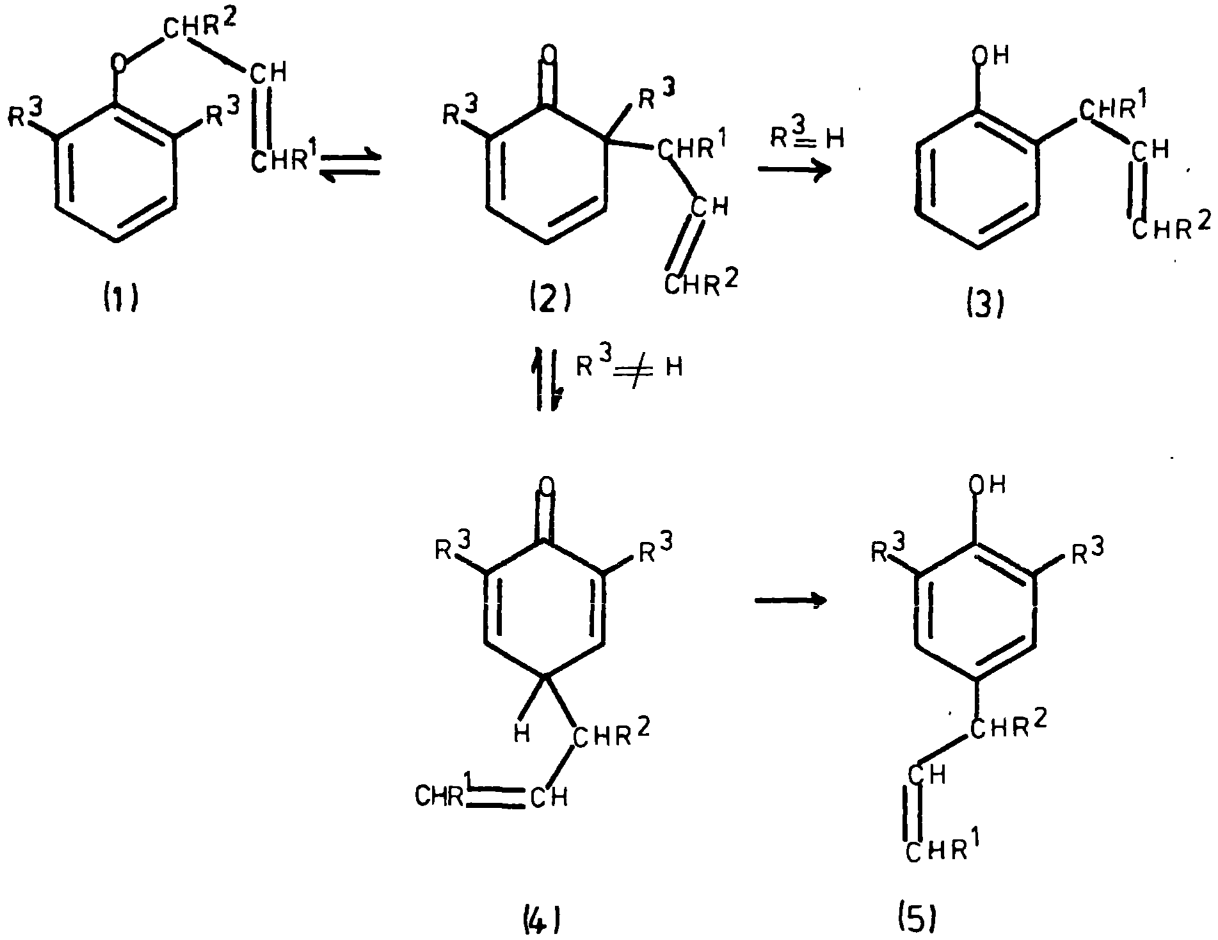
APPENDICES

The Claisen Rearrangement

Chapter I

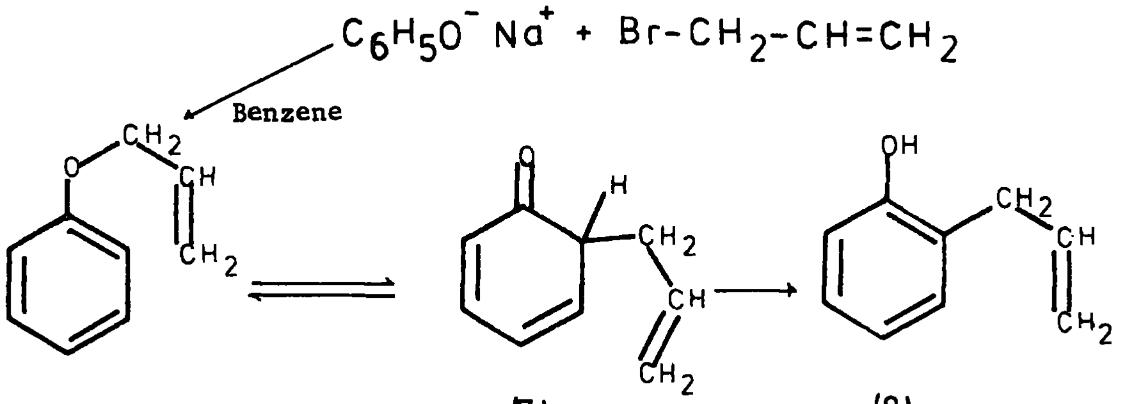
1.1 Introduction

The aromatic Claisen rearrangement involves the thermal transformation of an allyl phenyl ether (1) to a 2-allylcyclohexa-3,5-dienone (2), a rearrangement which has been extensively reviewed.[1] The 2-allylcyclohexa-3,5-dienone (2), usually termed the ortho-dienone, rapidly enolises to the ortho substituted phenol (3). When the ortho-positions in the allyl phenyl ether are substituted (i.e. R^3 = Alkyl) this enolisation can not occur; the ortho-dienone rearranges to give the 4-allylcyclohexa-2,5-dienone (4), usually termed the para-dienone by a Cope rearrangement, the overall transformation being designated the para Claisen rearrangement. The para-dienone, once formed, rapidly enolises to the para-substituted phenol (5).



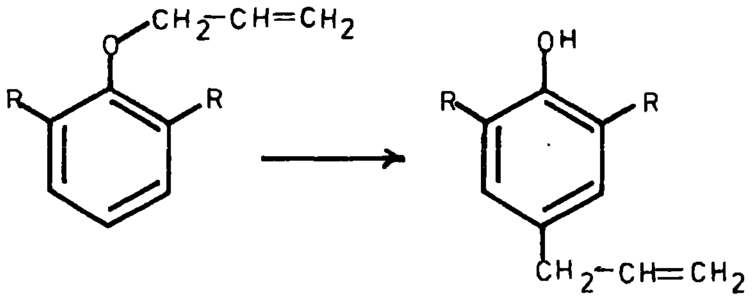
1.2 The Historical Development of the Claisen Rearrangement

When sodium phenoxide was reacted with allyl bromide in warm benzene, it was expected that allyl phenyl ether (6) would be the product.[2] However, ortho-allyl phenol (8) was recovered and this was thought to be derived from an intermediate ortho-dienone (7).[3]



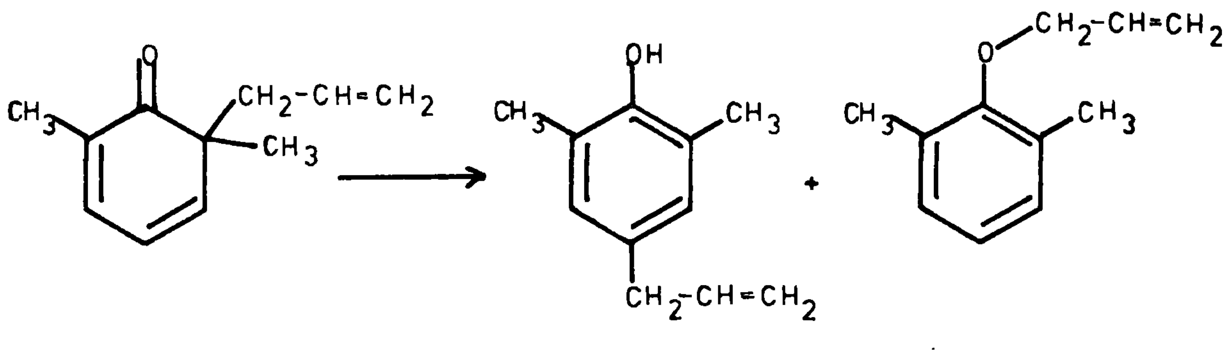
(6) (7) (8)

Further experiments showed that if both ortho positions in allyl phenyl ether were substituted, then a para-substituted phenol (9) was formed.[4]



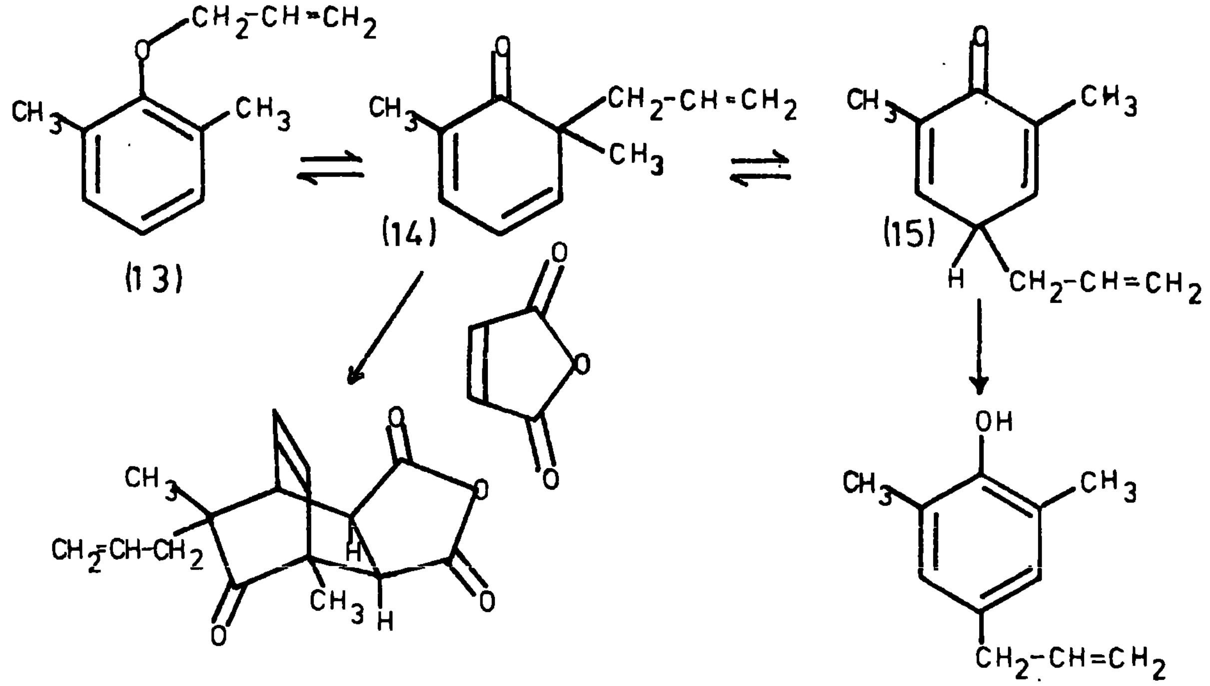
(9)

The importance of the ortho-dienone in the Claisen rearrangement was stressed by the conversion of (10) into the para-allyl phenol (11) and the allyl ether (12).[5] This demonstrated that the ortho-dienone must be an intermediate in the Claisen rearrangement, and that the reaction must occur reversibly.



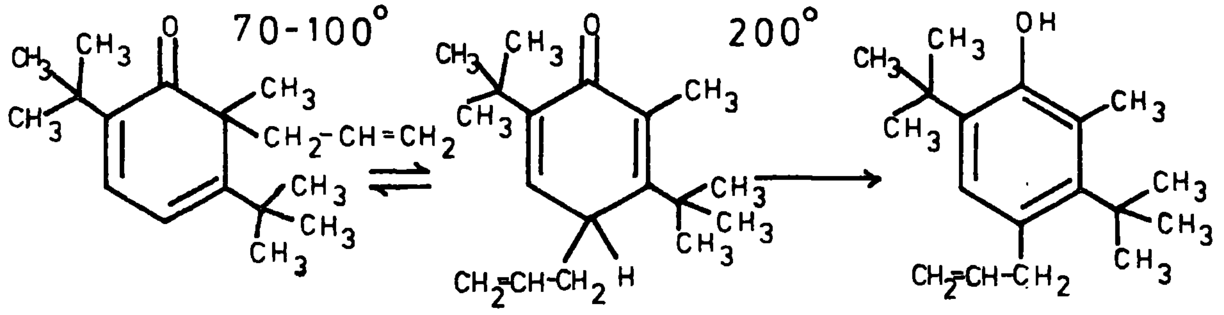
(10) (11) (12)

The intermediacy of an ortho-dienone in the thermolysis of an ether was confirmed by trapping it from the reaction mixture, using a Diels-Alder reaction with maleic anhydride as the dienophile.[6] Using 2,6-dimethylphenyl allyl ether (13) [the methyl groups prevent the ortho-dienone (14) undergoing enolisation] an equilibrium was set up between the ether (13) and the dienones (14) and (15).



An excess of maleic anhydride ensured that reasonable quantities of the adduct were produced, since the removed dienone was replaced by the re-establishment of the equilibrium.

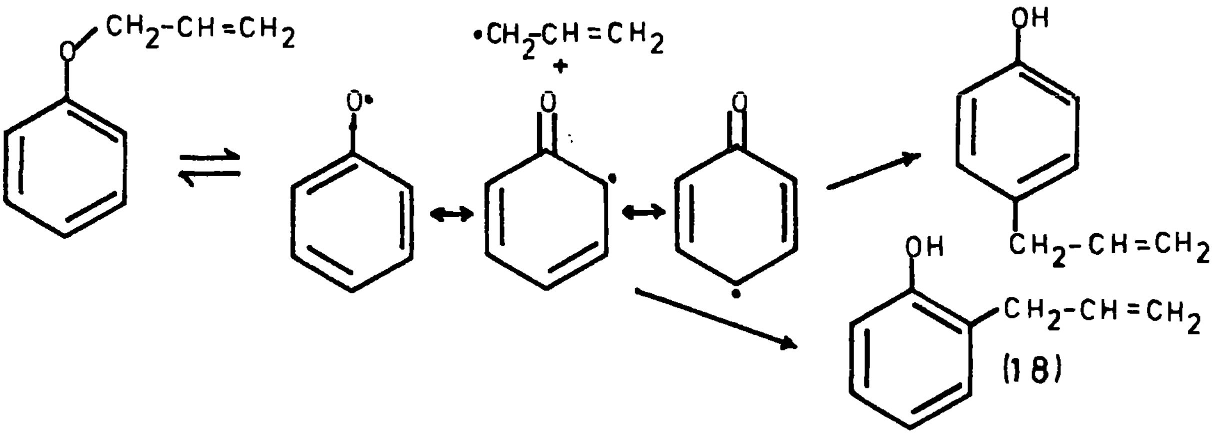
The fact that para-dienones are indeed intermediates in the formation of para-phenols was shown recently using the stable 2-allyl-2-methyl-3,6-di[1,1-dimethyl ethyl] cyclohexa-3,5-dienone (16).[7] This ortho-dienone (16) rearranged to the para-dienone (17) between 70-100°C. The latter was



(16) (17)

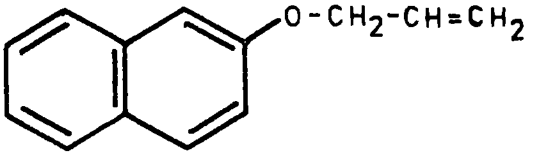
stable with respect to enolisation up to 200°, due to the large steric strain which develops in the aromatised product as a result of having an adjacent allyl and 1,1-dimethyl ethyl group in the same plane.

Once the reaction path had been established there was great interest in the reaction mechanism. Claisen postulated that the rearrangement involved the participation of radicals (Scheme 1). The relatively high concentration of the ortho-substituted phenol (18) was explained, simply, in terms of a steric argument, the ortho position being much nearer the allyl group than the para position.



Scheme 1

However, the rearrangement was shown to be intramolecular by the lack of crossover products.[8] When 2-naphthyl allyl ether (19) and phenyl (γ-phenyl allyl) ether (20) were heated together, allyl naphthols and



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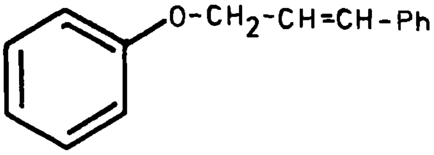
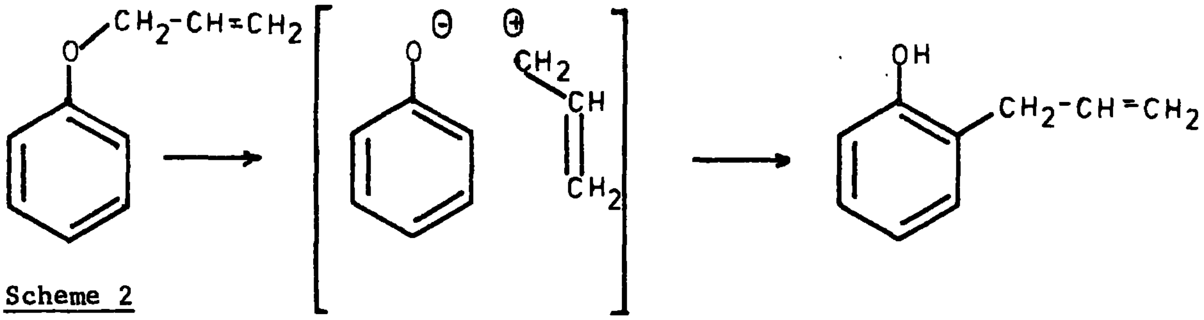


(20)

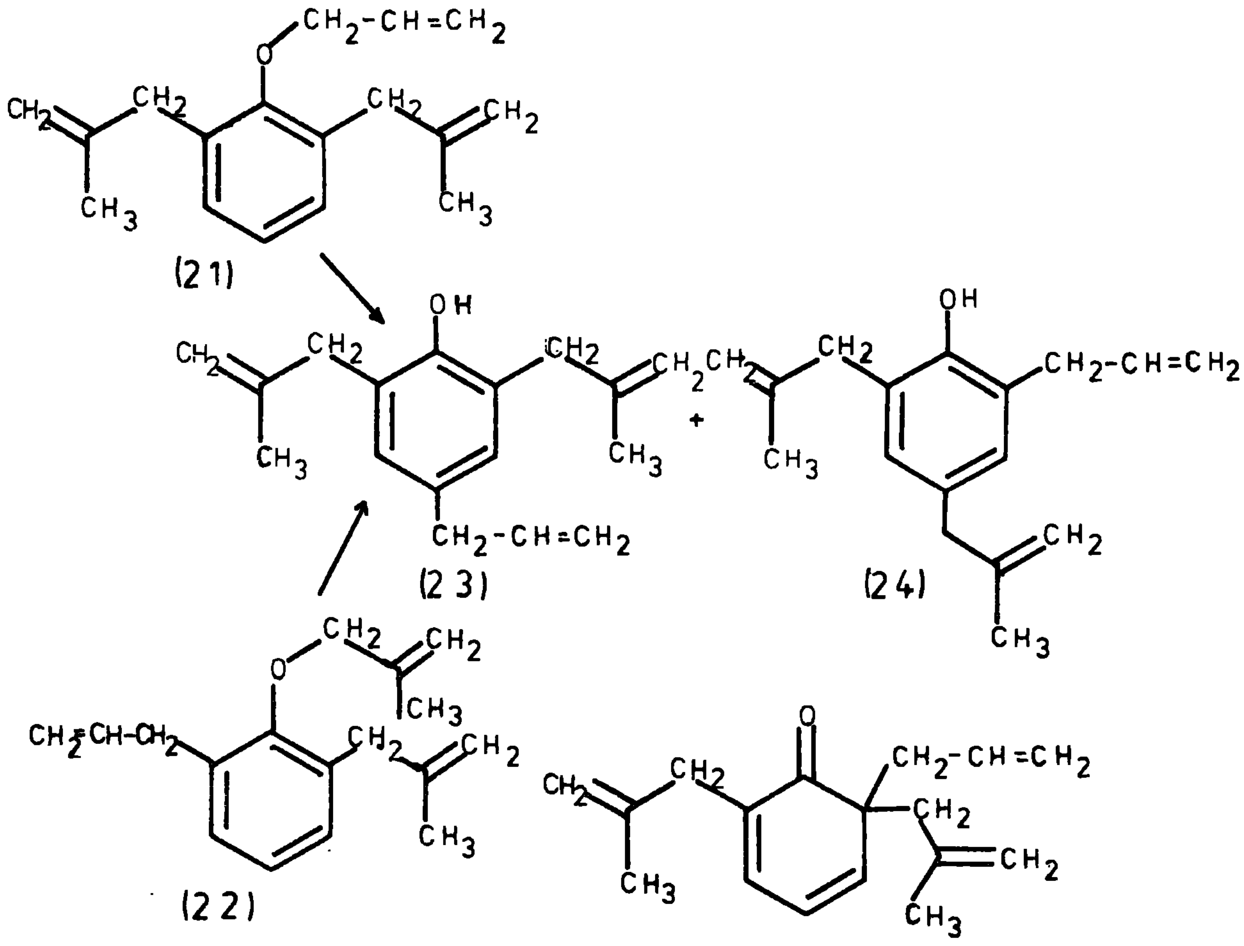
phenyl allyl phenols were the only products. The idea of radicals being involved was therefore abandoned since it was unreasonable to expect a radical reaction to be intramolecular.[9]



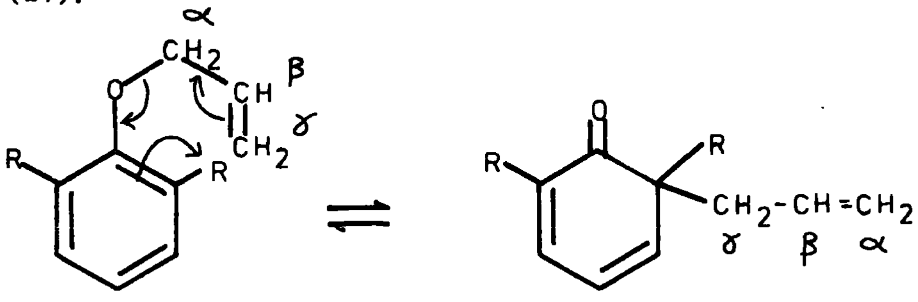
Scheme 2

Dewar proposed that an ionisation occurred and the ions were thought to be held together in a complex which collapsed to give the product (scheme 2).[10]

However, ethers (21) and (22) rearrange to give identical product distribution - 59% (23), 41% (24), a result for which the migration of the ortho substituent could not be explained by Dewer's theory. It was postulated that the results could be explained if the ortho-dienone (25) was a common intermediate.[11]


(21) (22) (23) (24) (25)

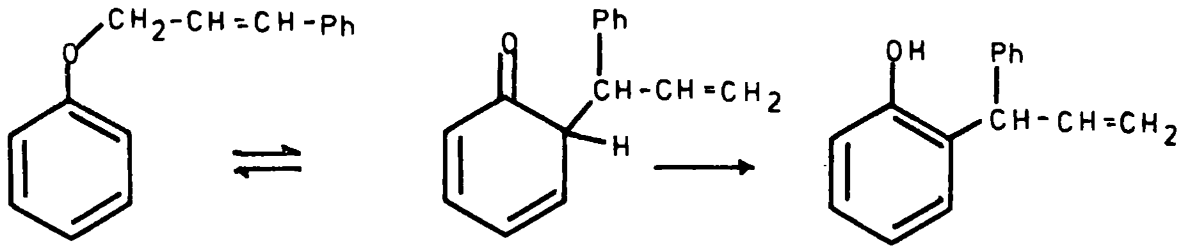
Hurd and Pollack, earlier, had envisaged that the rearrangement occurred by concerted electron transfers, and that the migrating group moved around the ring position in a cartwheel fashion (scheme 3).[3] A consequence of this mechanism is that the allyl group is inverted during the transformation to the ortho position: the γ carbon of the allyl group in the ether (26) becomes the α carbon of the allyl group in the ortho-dienone (27).



(26) (27)

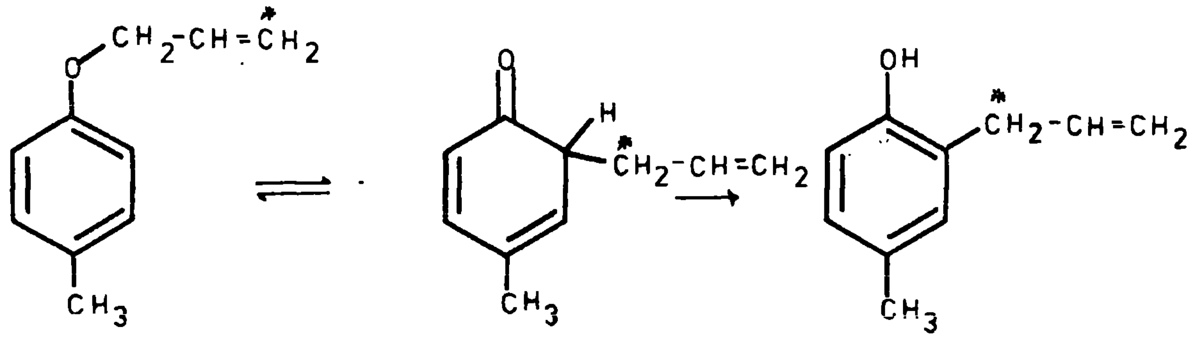
Scheme 3

This mechanism was examined by labelling the allyl group - either at the α or γ position - in order to establish whether inversion did indeed occur. This was first investigated using (γ-phenyl-allyl) phenyl ether (28), when it was noted that the phenyl group of the allyl chain had been transformed to the α position in the ortho-phenol (29).[8]



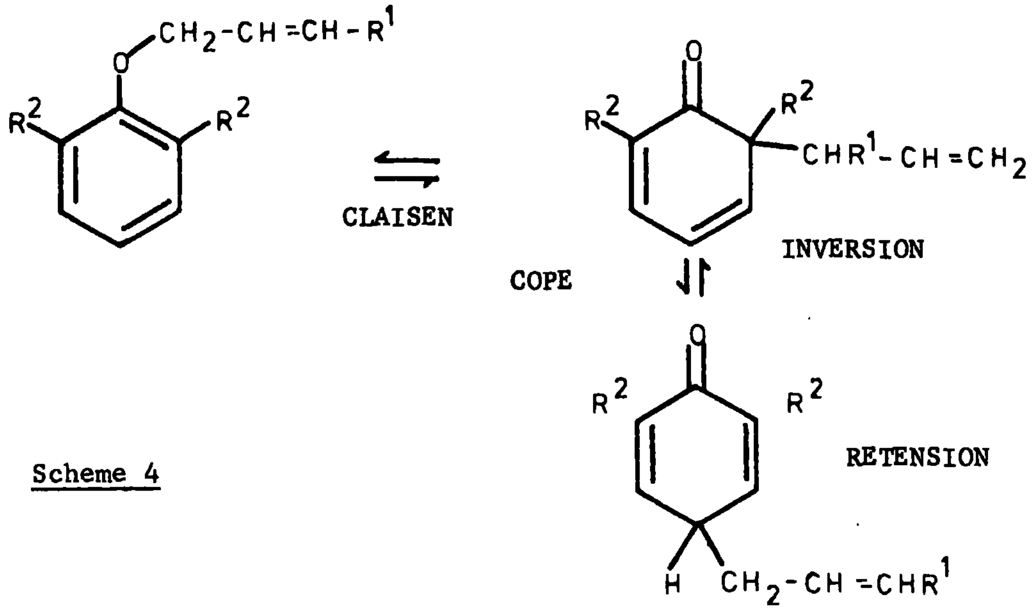
(28) (29)

Schmid was able to show, quite elegantly, that inversion occurred using the ^{14}C-labelled material (30).[12] The methyl substituent was present to prevent para-substituted phenol formation, which would have complicated the study.



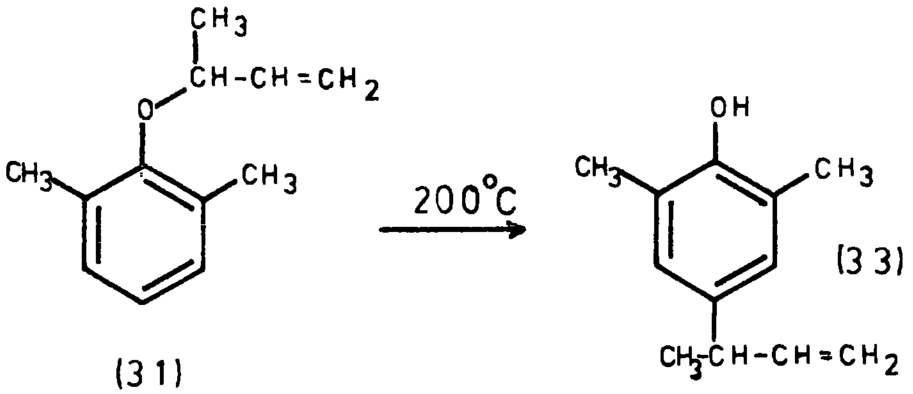
(30)

Thus the mechanism for the Claisen rearrangement had been elucidated and it was expected that the para Claisen rearrangement (phenyl allyl ether → para-allyl phenol) should be very similar. It was expected that two allyl migrations should leave the allyl steric chemistry retained (scheme 4).

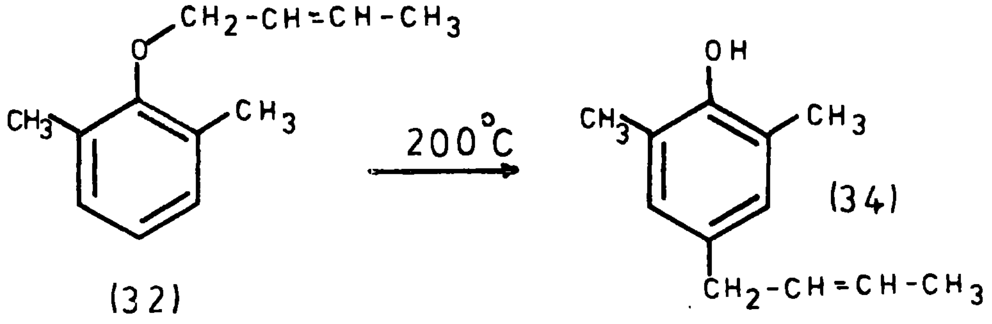


Scheme 4

The stereochemistry of the para-allyl phenol with respect to that of the allyl phenyl ether has been extensively studied.[13] It was observed that ethers (31) and (32) rearrange to give para-substituted phenols (33) and (34) respectively, in which the stereochemistry of the allyl group was indeed retained.[14] Thus the mechanism of the para rearrangement was shown to be similar to the ortho rearrangement.



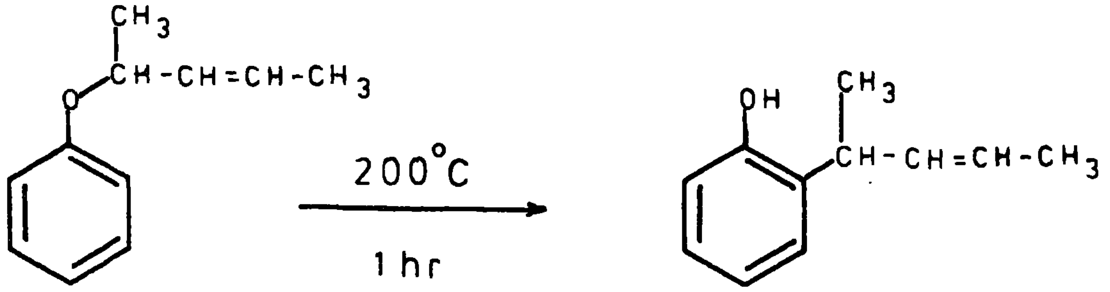
(31) (33)



(32) (34)

1.3 Stereochemistry and nature of the Transition State

The stereochemistry of the Claisen rearrangement was first investigated by Alexander and Kluiber.[15] They noted that when optically active $\alpha\gamma$-dimethyl-allyl phenyl ether (35) was heated for 1 hour, the resulting ortho $\alpha\gamma$-dimethyl-allyl phenol (36) was also optically active. Since the activity was not destroyed then the stereochemistry of the transition state must be selective.



$\alpha^{25}D$ - 0.10°

(35)

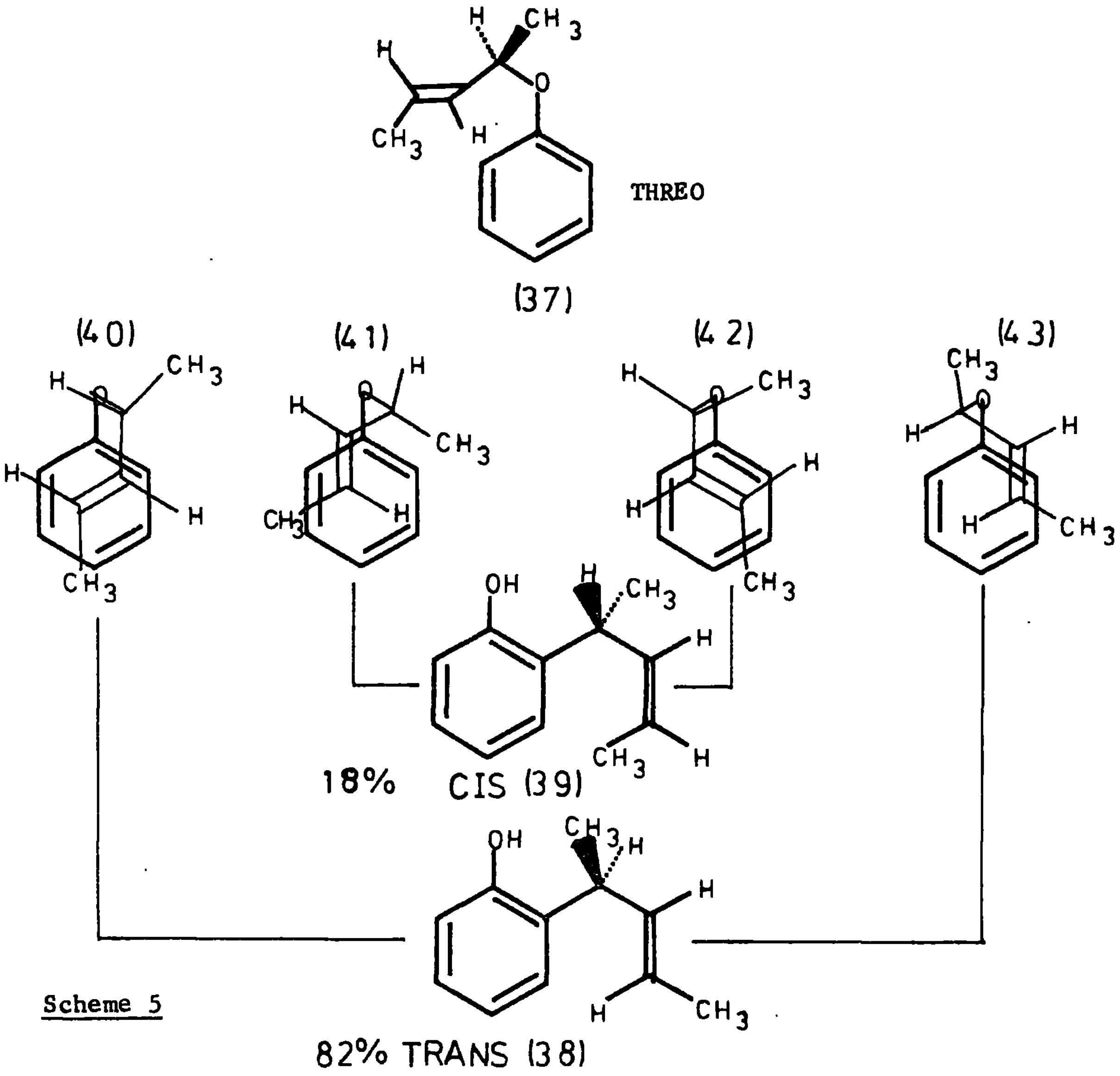
$\alpha^{25}D$ + 0.48°

(36)

Since there were six atoms involved in the concerted electron transfer it was proposed that the transition state was based on a six membered ring, and that the two extreme forms approximating to the chair and boat conformations of cyclohexane.[16]

Trans phenyl 1-methyl-but-2-en-1-yl ether (37) rearranges in mesitylene to give trans (38) and cis (39) 2[1-methyl-but-2-en-1-yl]phenol in the ratio 82:18 (scheme 5).[17] The predominance of the trans (38) product was explained in terms of relative thermodynamic stability, trans alkenes being more stable than cis alkenes.[18] The product distribution can be predicted by consideration of transition state stability.

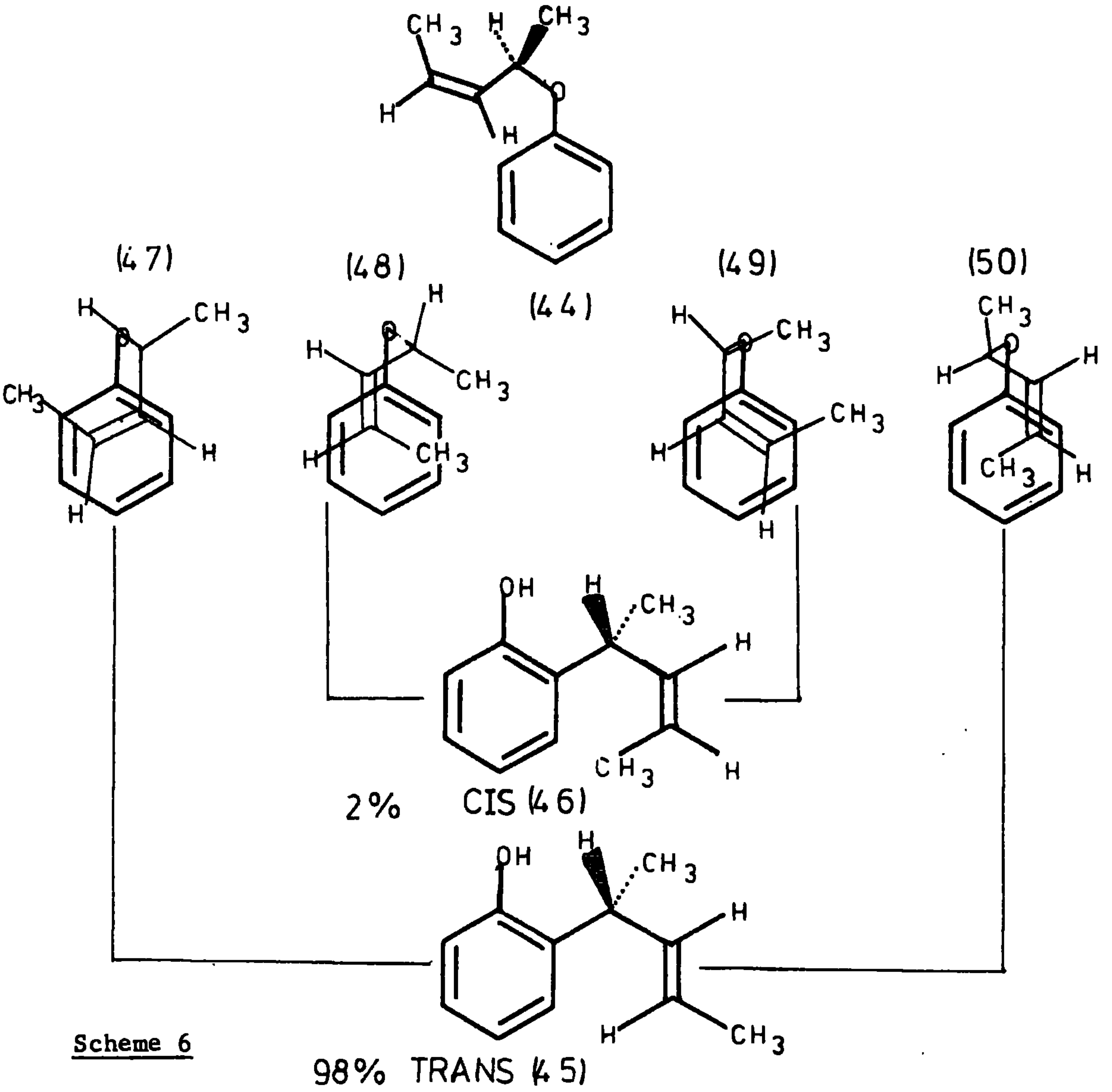
For each enantiomorph (scheme 5) four possible transition state conformers exist, two chair forms (41 and 43) and two boat forms (40 and 42). Consideration of steric interactions, especially axial-axial, predicts (43) to be more stable than (41), (40) to be more stable than (42) and



Scheme 5

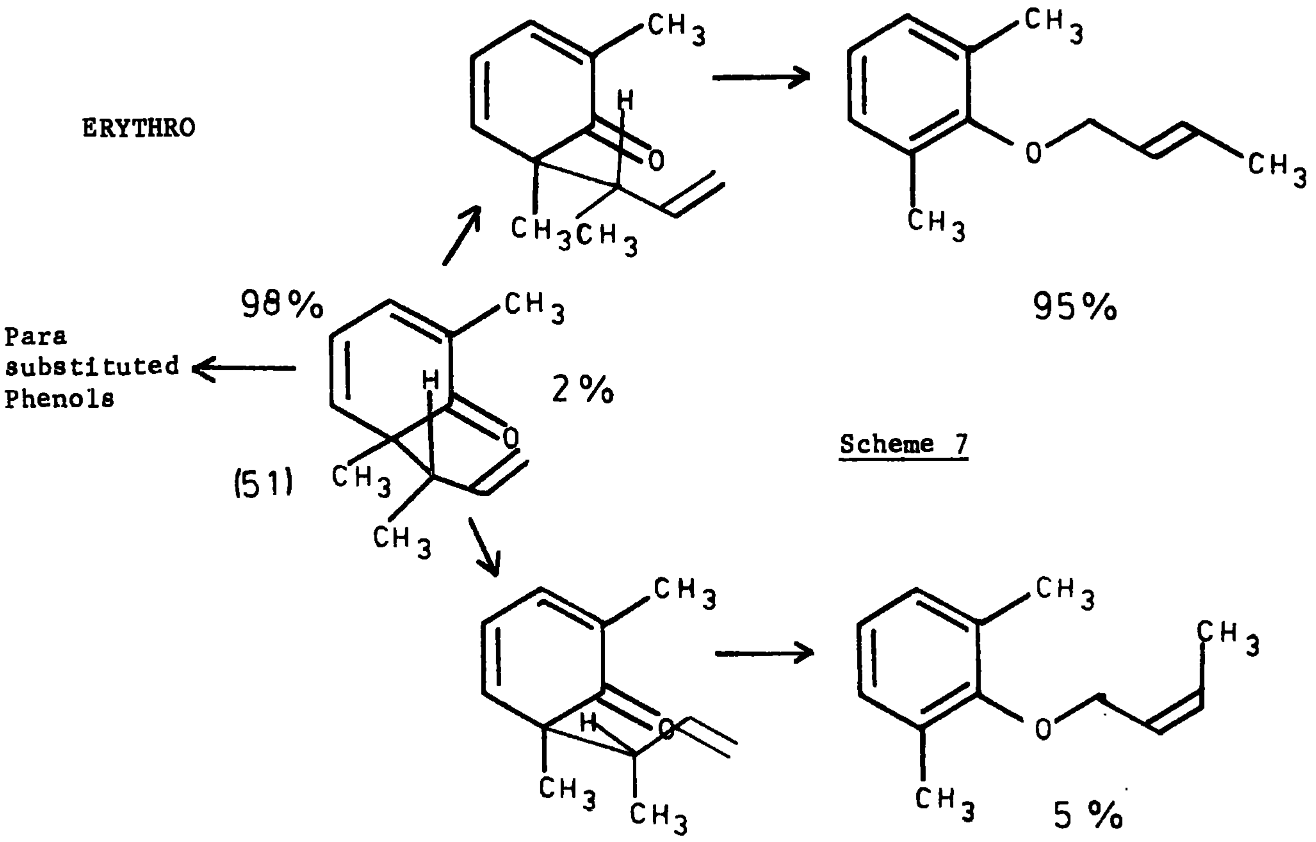
that the trans product will predominate. Cis phenyl 1-methyl-but-2-en-1-yl ether (44) rearranges to give trans (45) and cis (46) products in the ratio 98:2 (scheme 6).[16] High steric interference in transition state conformers (48) and (49) restricts the amount of the cis alkene formed.

Since it was not possible to stop the reaction once the dienones were formed, then no consideration can be made of the relative contributions of chair and boat conformers. (Each product molecule can be derived from either a boat or chair transition state). 2,6-Di-substituted ortho-dienones may undergo two possible reactions: Cope rearrangement to form



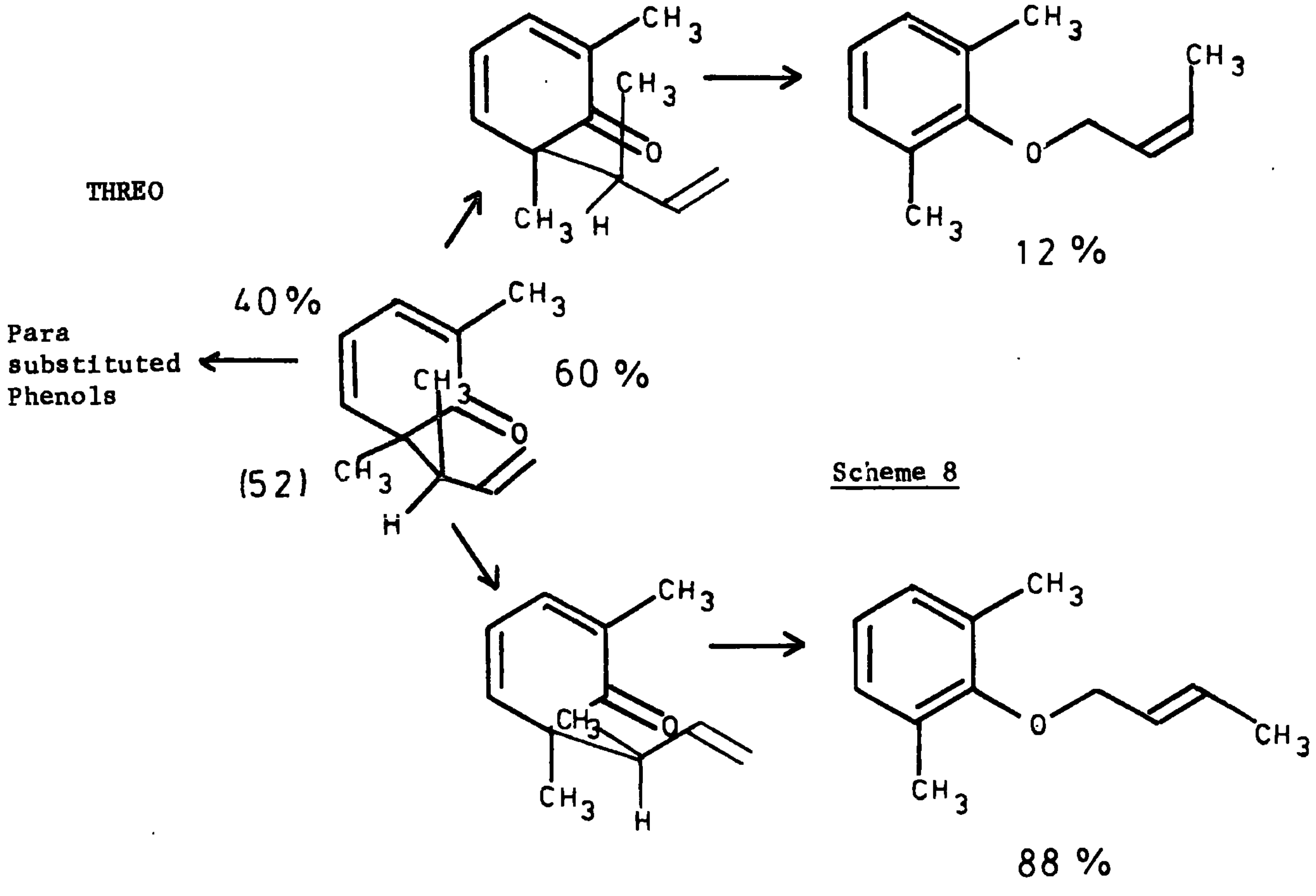
Scheme 6

a para dienone and a retro-Claisen rearrangement to generate an ether. Erythro-2-(α methyl allyl)-2,6-dimethylcyclohexa-3,5-dien-1-one (erythro 1) (51) rearranges to a mixture of para phenols (98%) and a mixture of trans + cis crotyl-2,6-dimethyl phenyl ether (2%) (scheme 7). The products with a trans configuration, formed by a chair conformer, predominate (95%). Threo-2-(α-methyl allyl)-2,6-dimethyl-cyclohexa-3,5-dien-1-one (threo -1) (52) also rearranges to give crotyl -2,6-dimethyl phenyl ether in which the trans isomer predominates (88%) (scheme 8). However, analysis of the activated complex configurations shows that the trans alkene must be derived from a boat type conformation.



(51)

Scheme 7



(52)

Scheme 8

Secondary orbital symmetry effects predict preference for the chair conformation over the boat conformation.[19,20] When, however, the chair conformation leads to the less thermodynamically stable product, or if pseudo diaxial 1,3-interaction in the chair conformation is high, then the boat conformation is preferred.

1.4 Sigmatropic Rearrangements

The Claisen rearrangement is, in Woodward-Hoffmann terminology, a sigmatropic shift of order [3,3].[21] The order(i,j) refers to the extent of migration of a sigma bond along the π-electron system during a concerted electron and bond reorganisation; i-1 is the distance travelled along the π system and j is the number of atoms used in the migrating group. Using phase relationships of the highest occupied molecular orbitals in the migrating group and the π electron system, it can be shown that thermal changes are allowed if $(i+j) = 4n+2$, and photochemically excited changes are symmetry allowed with $(i+j) = 4n$.

The π electron system of an allyl radical can be described by three molecular orbitals ψ_1, ψ_2, ψ_3, using Huckel molecular orbital theory.

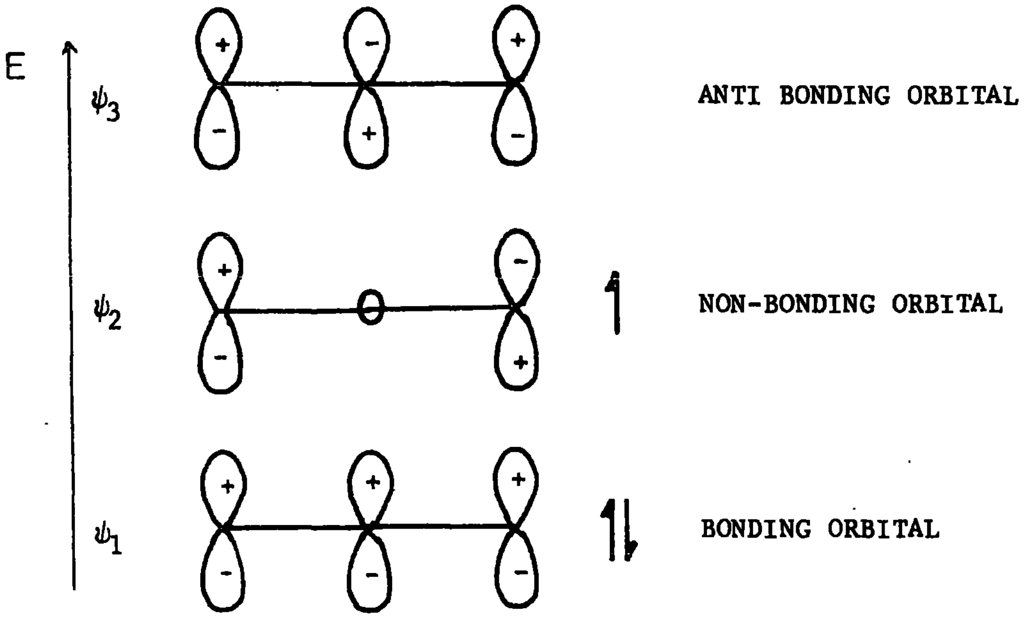


Fig. 1

The three orbitals are described in order of increasing energy as Bonding, Non-Bonding and Antibonding, and are represented in Fig. 1, the positive and negative signs referring to the phase of the wave function. Each molecular orbital can accommodate no more than two paired electrons; ψ_2, the non-bonding orbital, is the highest occupied molecular orbital.

The π electron system of the phenoxyl radical can be described in terms of seven molecular orbitals, of which ψ_4 is the highest occupied (with one electron) - Fig. 2.[22] In the Claisen rearrangement and subsequent reactions only the coefficients at the oxygen, the ortho and the para positions are of interest. Thus $\psi_4{}'$ (Fig. 2) can be used instead of ψ_4 when considering overlap.

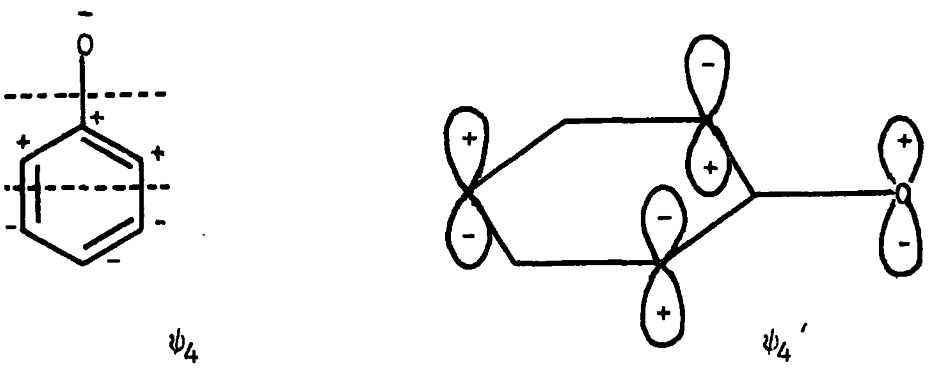


Fig. 2 ψ_4 $\psi_4{}'$

The stereochemical requirements for intramolecular allylic rearrangements demand that bond breaking and bond formation both occur on the same face of the allyl group, i.e. a suprafacial migration. For the allyl radical there is a change of phase between atoms 1 and 3 in ψ_2. For the phenoxyl radical the phase changes between the oxygen atom and the ortho position, and the phase changes again between the ortho and para positions.

Bonding can only occur between molecular orbitals of the same phase, and assuming the rearrangement must occur suprafacially, then Fig. 3 shows why the 3,3 shift is thermally allowed, whilst a 1,3 shift is thermally forbidden. Fig. 4 shows that a 3,3 shift in the Cope or para-Claisen rearrangement is thermally allowed.

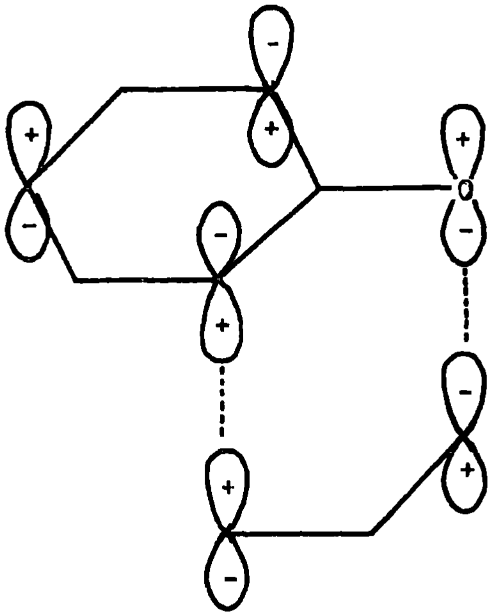


Fig. 3

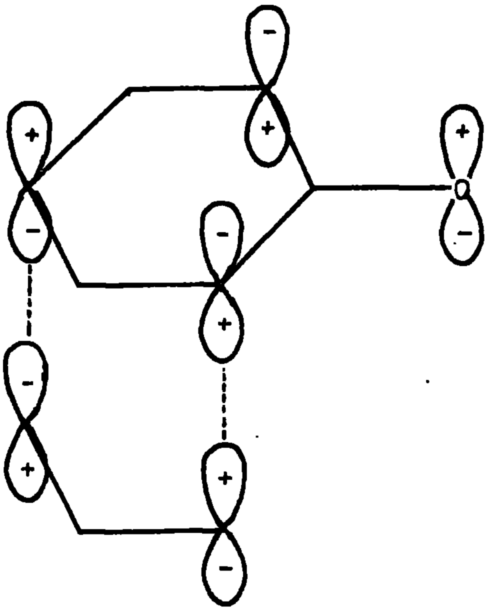
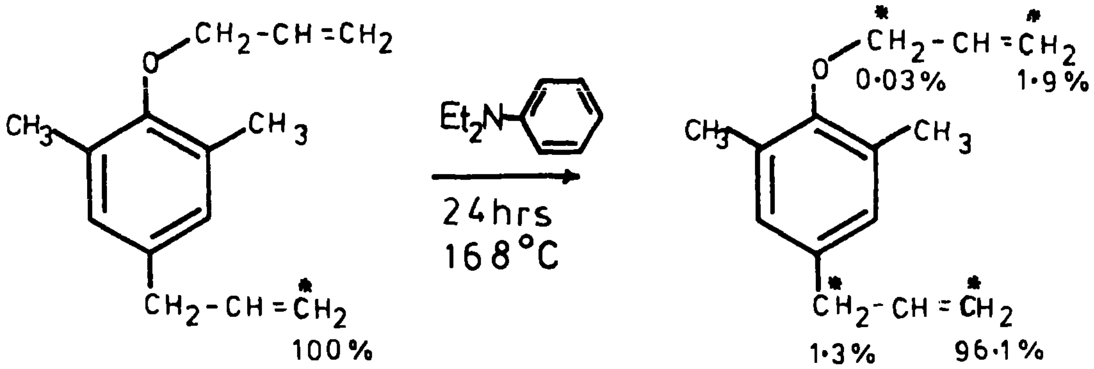


Fig. 4

1.5 The ortho-ortho′ rearrangement

The ortho-ortho′ rearrangement is the transfer of the migrating group from one ortho position to the other ortho position. It was first proposed to explain the results of the thermal rearrangement of ether (53)-^{14}C labelled at the γ position of the para-substituted allyl group.[23]

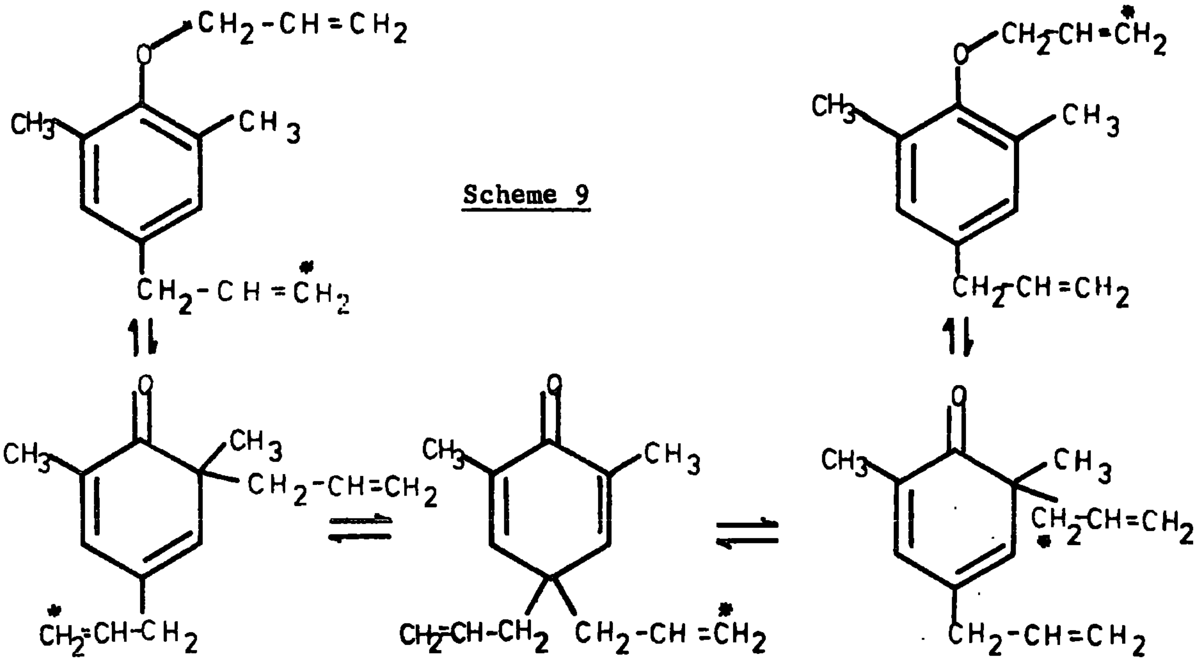


(53)

Equat. 1

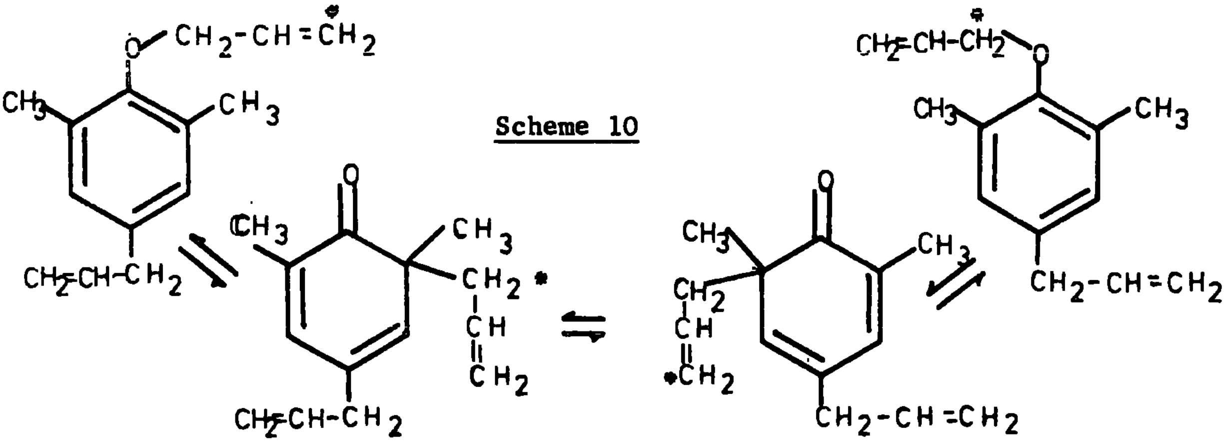
Ether (53) was heated in diethylaniline for 24 hours and then analysed for radioactivity (Equat. 1). Both oxygen allyl and para allyl groups were found to contain activity, and moreover, the activity was scrambled between the α and γ positions.

The location of active carbons in the previously unlabelled γ positions



Scheme 9

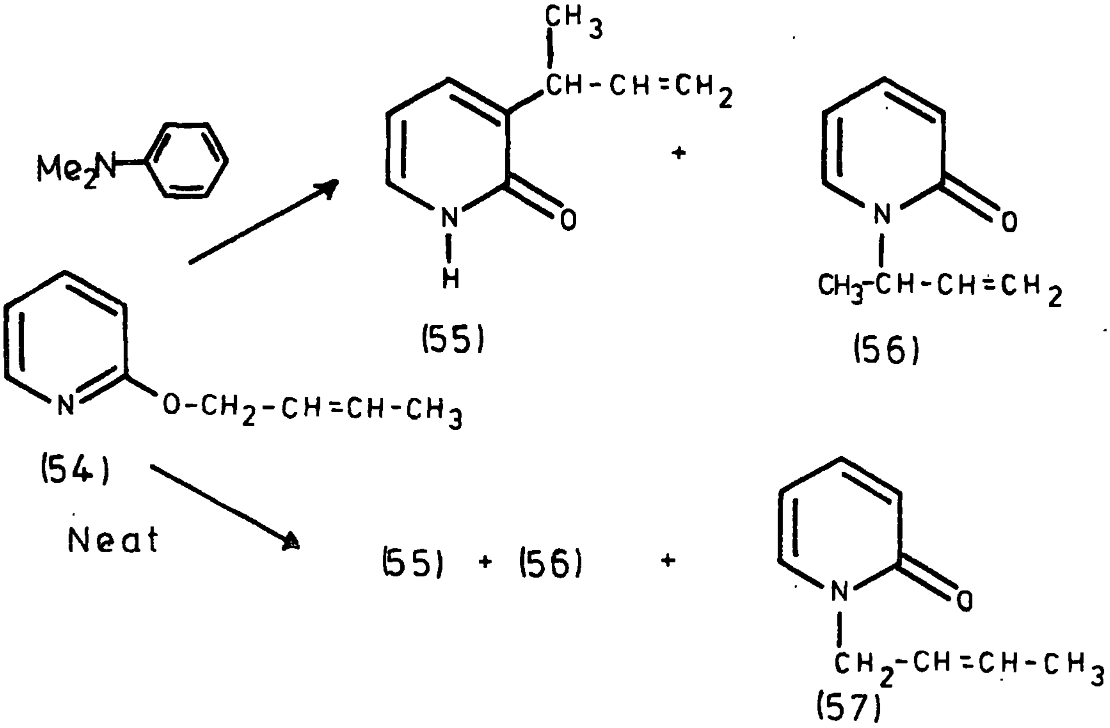
of the o-allyl and para allyl groups was readily explained by well established sigmatropic migrations (scheme 9). On the other hand the presence of activity in the α-position in both o-allyl and para-allyl groups could not be explained by established mechanisms. It was proposed that the scrambling could be explained by invoking an ortho-ortho′ shift



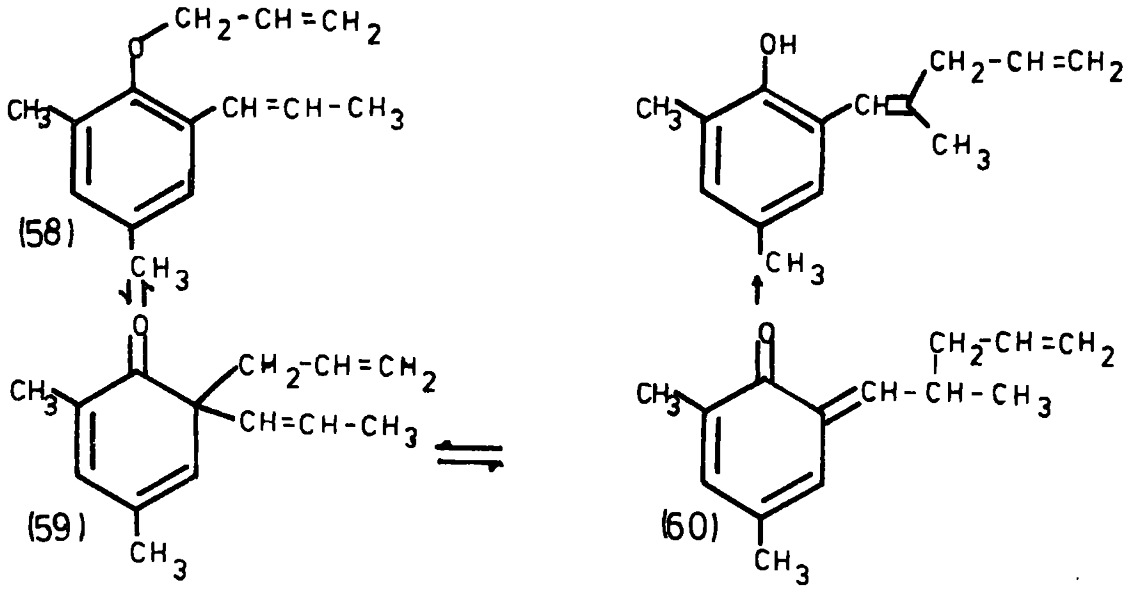
Scheme 10

of the labelled allyl group in accordance with (scheme 10).[24]

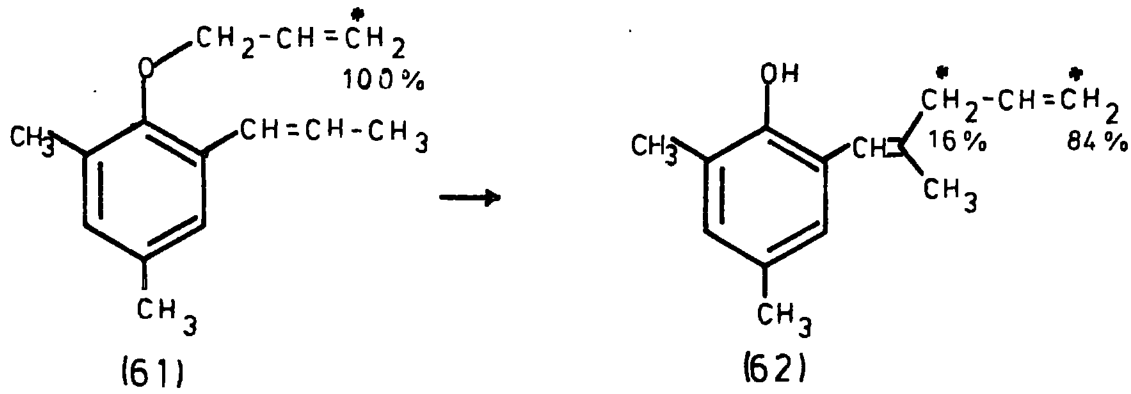
A further example of an ortho-ortho′ shift was observed in the thermal rearrangement of γ-methylallyl 2-pyridyl ether (54).[25] When the ether (54) was heated in N,N dimethylaniline the dienones (55) and (56) were produced. However, when ether (54) was heated in the absence of solvent, in addition to the 3,3 rearrangement products (55) and (56), dienone (57) was also isolated. It was proposed that (57) was derived from (55) by an ortho-ortho′ transformation. In addition to the dienone products, a large amount of the cleaved phenol was produced in both the reactions. It was suggested that the high phenol concentration was linked with the presence of the ortho-ortho′ product; the ease of removal of the allyl radical from the ortho-ortho′ transition state was thought to be responsible for the high phenol concentration.[26]



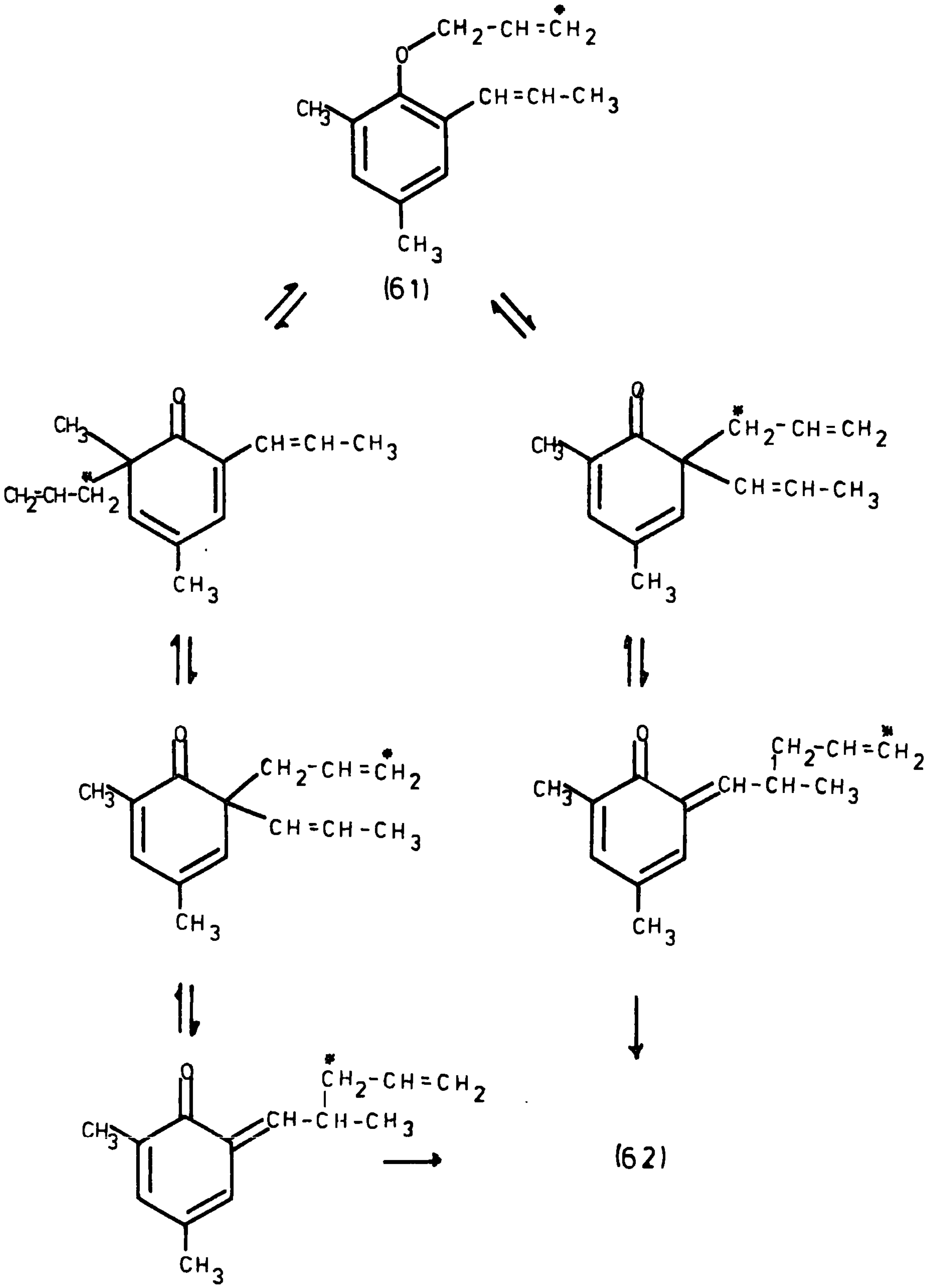
The "out-of-ring Claisen rearrangement" has also been investigated.[27] The ether (58) rearranges to the dienone (59) and the latter undergoes a 3,3 rearrangement to the dienone (60) rather than the competing para-Claisen



since enolisation is not possible at the blocked para position. The ether (61), with ^{14}C labelling in the α position of the allyl group, rearranged to the phenol (62), in which the radioactive label was



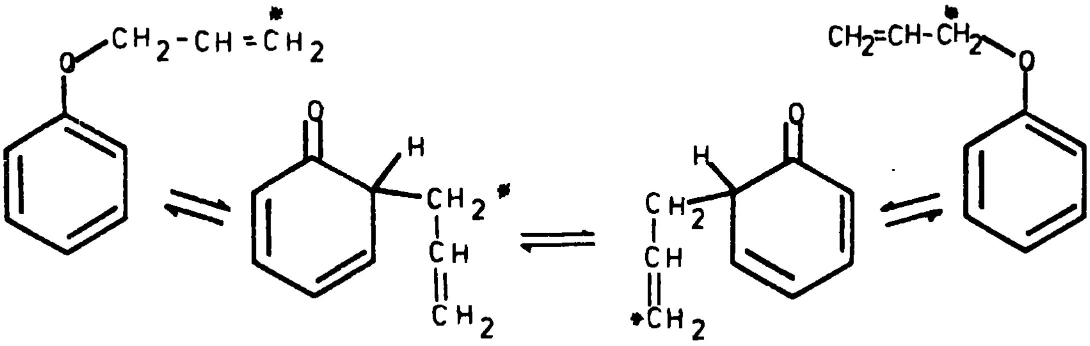
distributed between the α and γ positions of the allyl group in the ratio 16:84. Schmid also explained this result invoking an ortho-ortho′ transformation (Scheme 11).[27]



Scheme 11

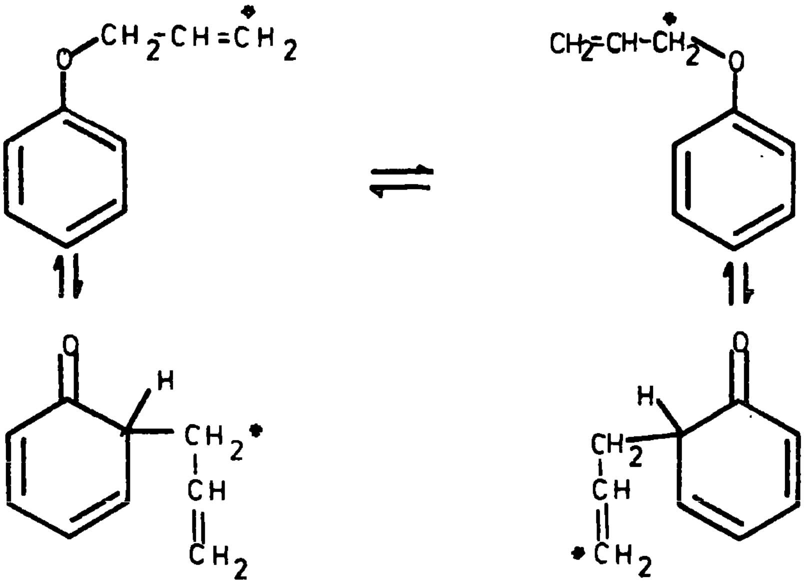
1.6 Mechanism of the ortho-ortho′ migration

There are several possible mechanisms for the ortho-ortho′ rearrangement - the transformation of an allyl group from one ortho position to the other ortho position (Scheme 12).



Scheme 12

If the initial ether could isomerise, then in a subsequent Claisen rearrangement both ortho isomers would be produced without having to invoke an o-o′ migration (Scheme 13). However, this isomerisation would

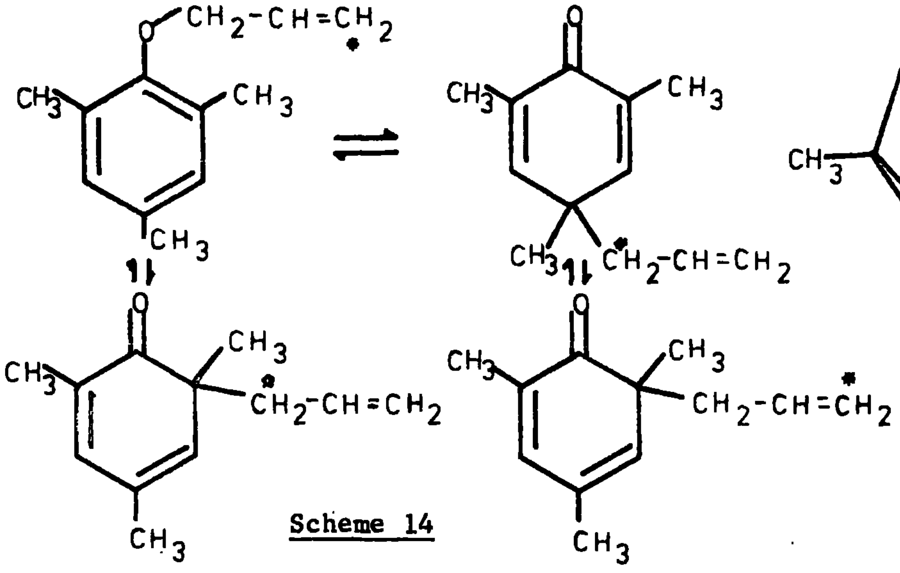


Scheme 13

involve a suprafacial 1,3 shift which is thermally forbidden by Woodward-Hoffmann rules.

Isomerisation in the initial ether may be the result of cleavage and recombination, rather than a concerted mechanism. However, it is well established that the Claisen rearrangement is intramolecular.

The scrambling of the label in Scheme 12 could be explained by invoking a 3,5 shift directly linking the γ-carbon of the allyl group with the para position. If the 3,5 shift occurred concurrently with 3,3-shifts then two ortho dienone isomers, with differing labelling pattern would be produced. It was thought that 3,5 shifts might occur by a concerted mechanism (Fig. 5), (Scheme 14).



Scheme 14

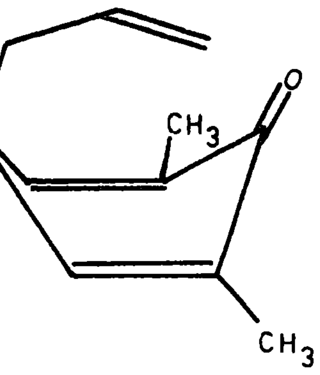
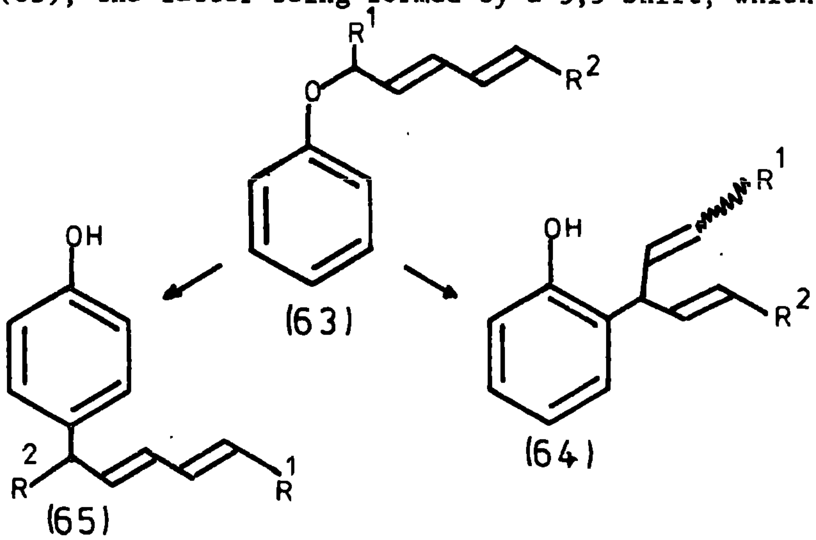


Fig. 5

The first direct transformation of a migrating group from the oxygen to the para position was observed when ether (63) was transformed into phenols (64) and (65), the latter being formed by a 5,5 shift, which is



thermally allowed by Woodward-Hoffmann rules.[28] This can be seen by looking at the Huckel molecular orbitals involved. The π system of the pentadienyl radical can be described in terms of five molecular orbitals ψ_1, ψ_2, ψ_3, ψ_4, ψ_5, represented in Fig. 6. Each of these molecular orbitals can accommodate only two paired electrons, thus ψ_3 is the highest occupied molecular orbital.

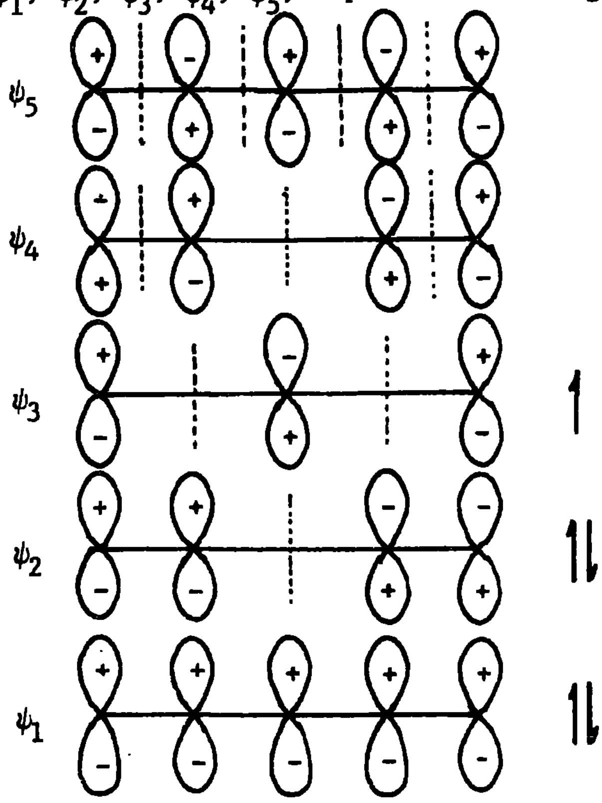


Fig. 6

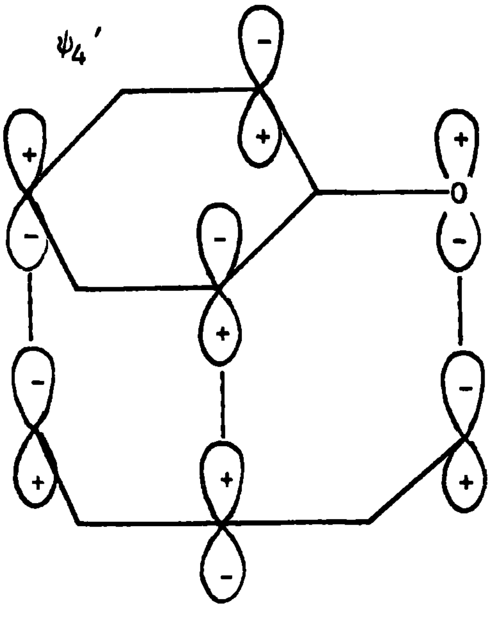
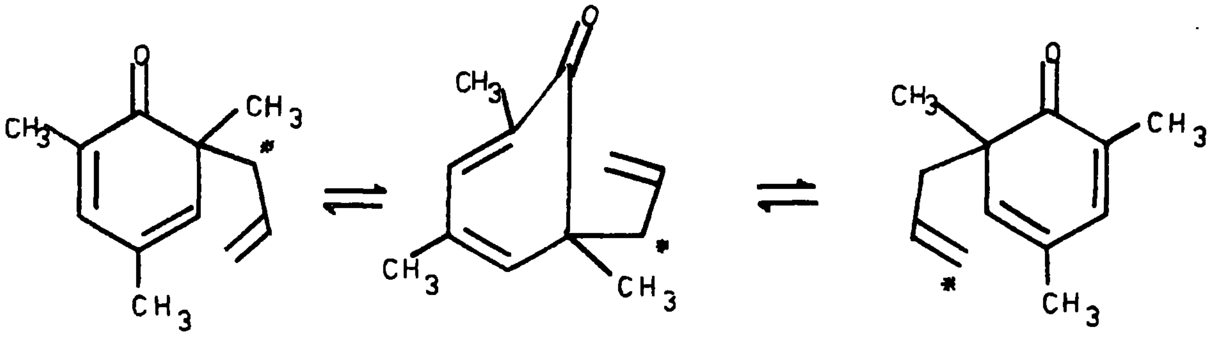


Fig. 7

Considering the interaction between ψ_3 of the pentadienyl radical and ψ_4' of the phenoxyl radical, it is clear that 5,5 shifts are thermally allowed (Fig. 7). Inspection of the highest occupied molecular orbital of the allyl radical and ψ_4' of the phenoxyl radical, shows that a 3,5 shift is symmetry forbidden (Fig. 8).

Schmid originally proposed that the ortho-ortho′ transformation could occur by a concerted mechanism (Scheme 15).[29] However, the direct ortho-ortho′ transformation, occurring by a concerted mechanism, is seen to be



Scheme 15

forbidden by consideration of the interaction of the molecular orbitals involved (Fig. 9).

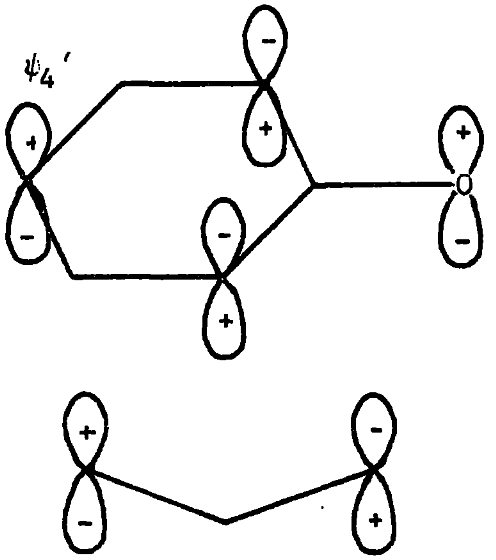


Fig. 8

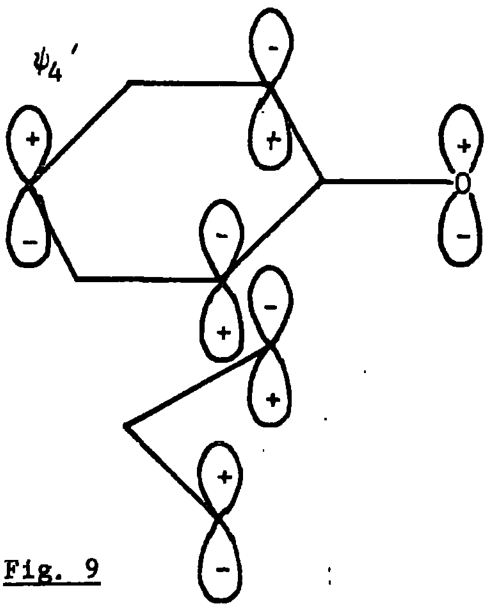
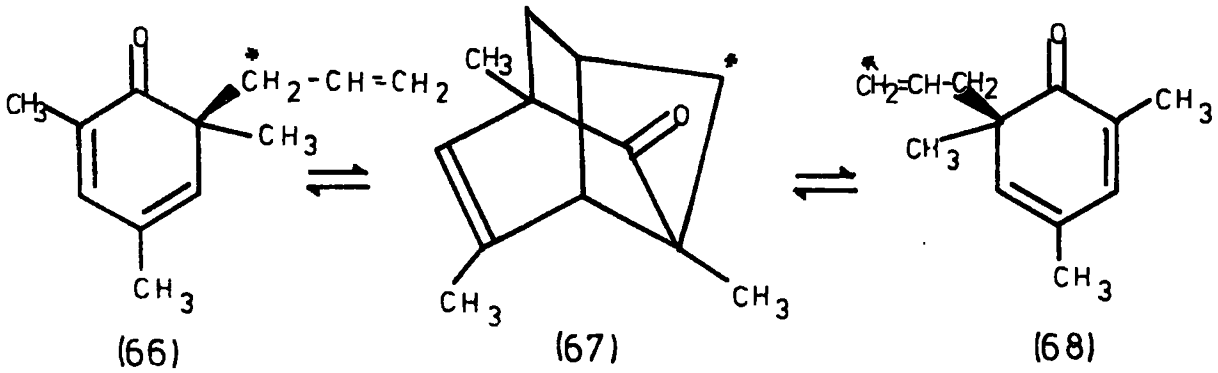


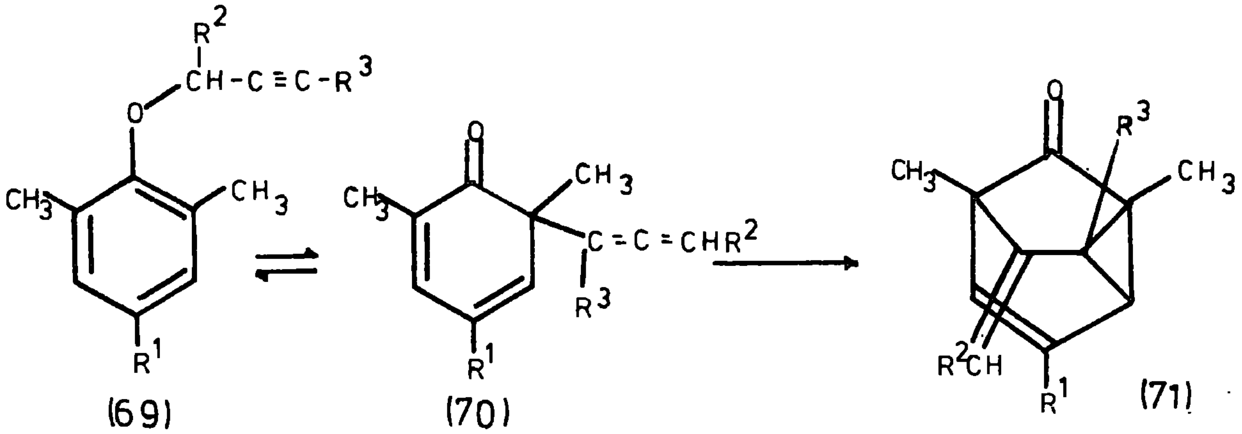
Fig. 9

In the ortho-dienone there is a 4π system in the ring and a 2π system in the side chain, an appropriate arrangement for an intramolecular Diels-Alder addition. It became clear that the o-o′ rearrangement could be explained by invoking the intermediacy of an intramolecular Diels-Alder adduct (67).[22]

Cleavage of the four membered ring in (67), a well established non-concerted process results in the formation of the rearranged ortho isomer (68).

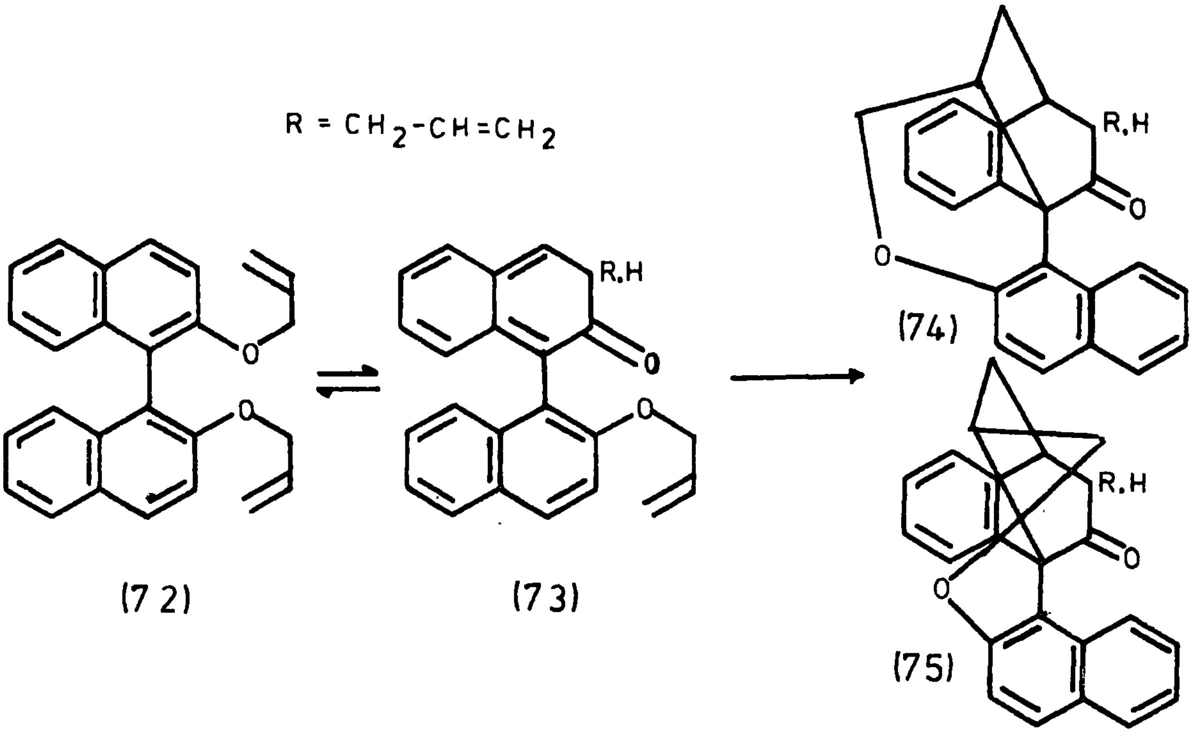


Evidence for the above proposal, in which all the steps are well documented in the literature, came from work with the acetylene derivative (69) when a stable Diels-Alder adduct (71) was isolated.[30]



The dienone intermediate (70) formed has an allene side chain and it is the 1,2 π bond (rather than the 2,3 π bond - the interaction invoked to explain the o-o′ transformation) which interacts with the 4π system of the ring. Clearly the dienone intermediate (66) formed from the allyl ether differs from the dienone (70) only in the number of 2π electron sites available. Thus, formation of intramolecular Diels-Alder adducts from dienone (66) could not be considered an impossibility.

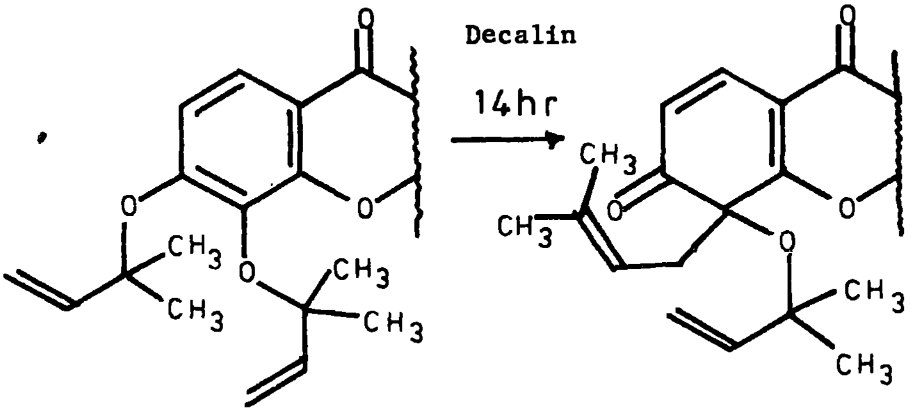
Intramolecular Diels-Alder adducts in systems related to phenyl allyl ether have been isolated. The ether (72) rearranged to the dienone (73), in which the 2π system of non rearranged ring interacts with the 4π system



(72) (73) (74) (75)

of the rearranged ring to form adducts (74) and (75).[31]

On heating the ether (76) in refluxing decalin for 14 hours it was found that one of the 2-methyl-3-buten-2-yl groups had migrated to form the dienone (77).[32] In the dienone (77) there is competition between the



(76) (77)

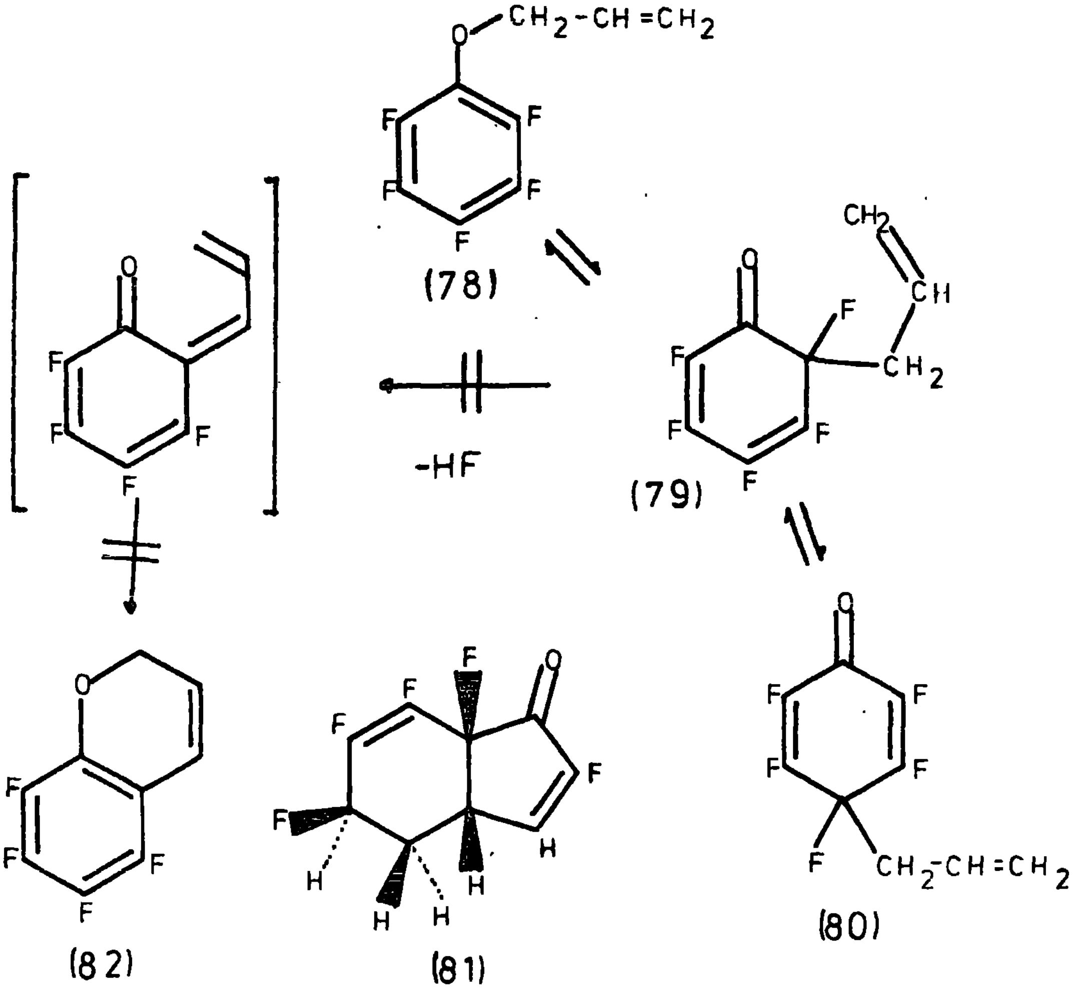
2π systems for Diels-Alder adduct formation. The 4π system preferentially combines with the non migrating 2-methyl-3-buten-2-yl moiety to form an adduct containing a five membered ring. An adduct containing a four membered ring would have been formed if the 3-methyl-2-buten-1-yl moiety had been used in adduct formation, and it is the steric and overlap difficulties associated with the smaller ring that controls the reaction pathway.

Chapter 2

Flow pyrolyses of Pentafluorophenyl Prop-2-enyl (78) and [2,3,3-$^{2}H_{3}$] Prop-2-enyl (86) Ethers

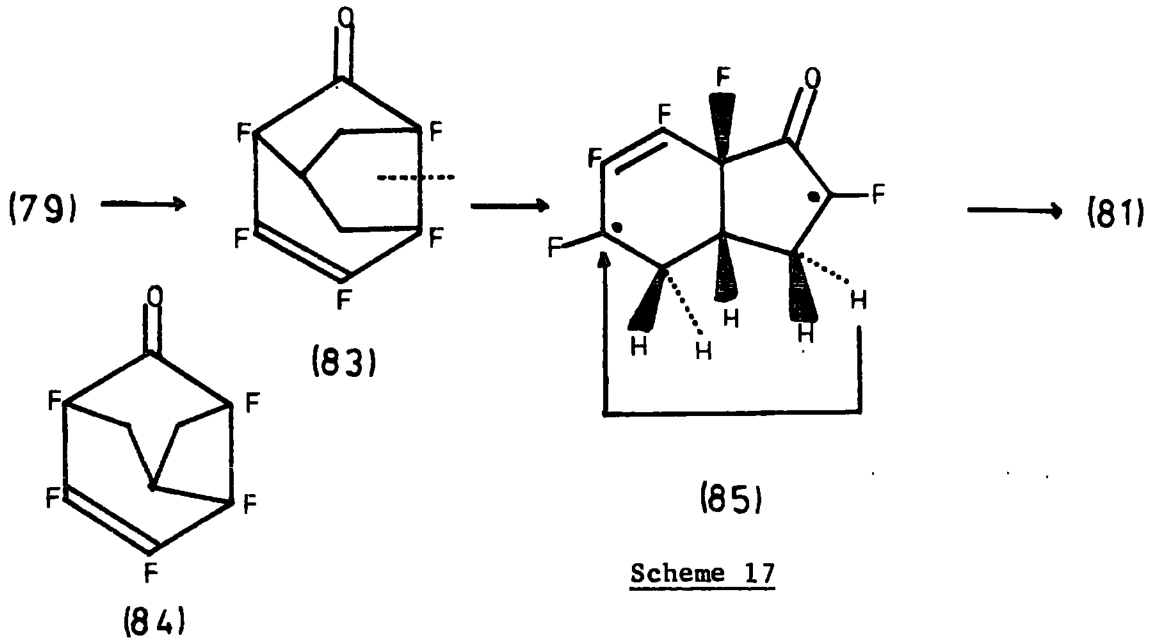
2.1 Introduction

This work was started in 1969, originally to devise a simple synthesis of 5,6,7,8-tetrafluorochromen (82) which could be then oxidised to 6-carboxy-2,3,4,5-tetrafluorophenoxyacetic acid, a precursor for the synthesis of 4,5,6,7-tetrafluorobenzo[b]furan derivatives.[33] Flow pyrolysis of pentafluorophenyl prop-2-enyl ether (78) at 365° gave the para-dienone 2,3,4,5,6-pentafluoro-4-(prop-2-enyl)-2,5-cyclohexadienone (80).[34] It was envisaged that the chromen (82) would be formed by the dehydrofluorination of the orthodienone (79) (formed as an intermediate in the above pyrolysis) followed by an electrocyclic ring closure (Scheme 16).



Scheme 16

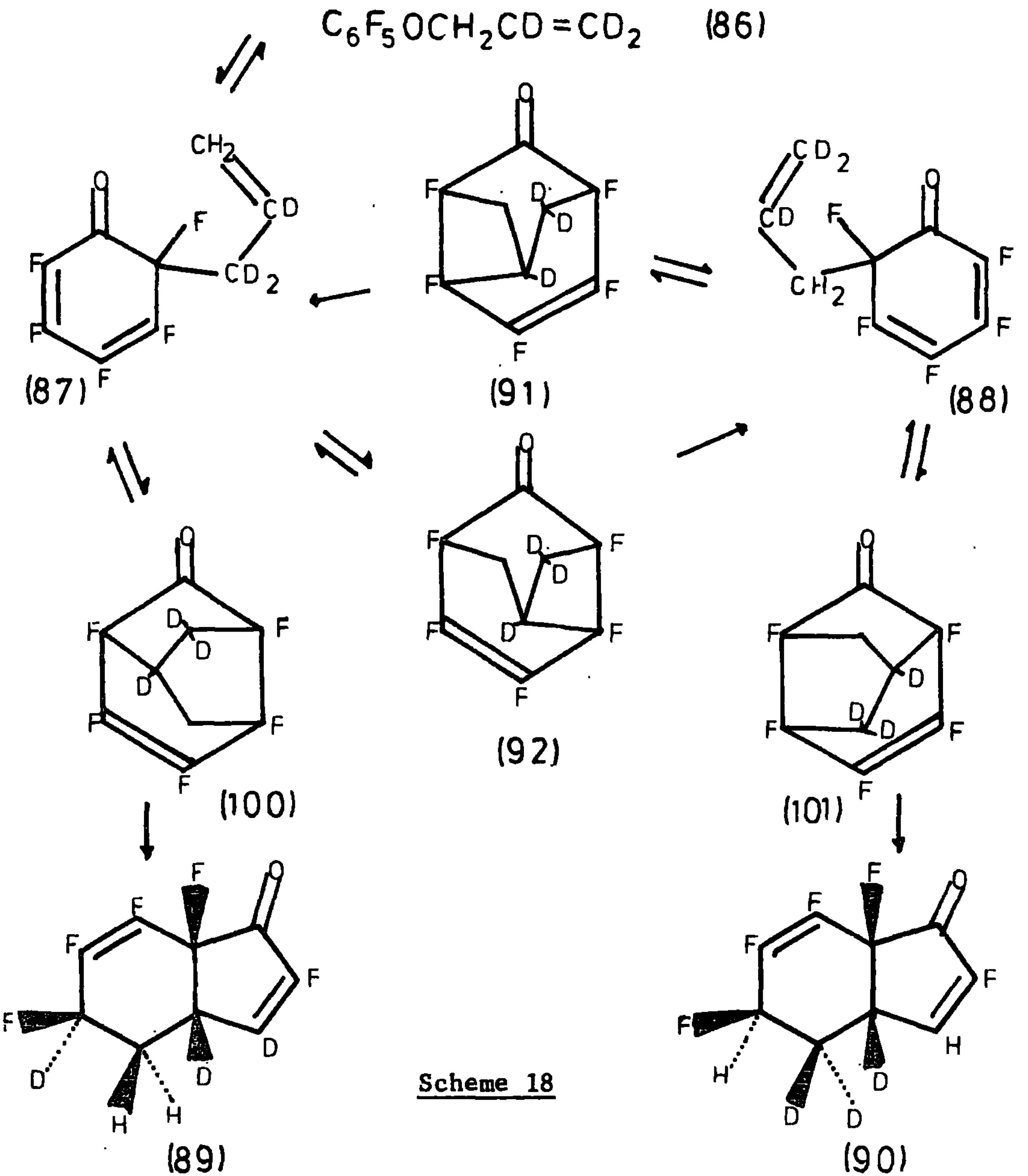
Distillation of the ether (78) in vacuo through a quartz tube packed with silica fibre heated to 480° did not produce (82) but a complex mixture, of which the major component (33%) was shown to be 2,5β,6,7,7aβ-pentafluoro-3aβ,4,5,7a-tetrahydroinden-1-one (81).[35,36] It was envisaged that the inden-1-one (81) was produced from (83), one of the two possible Diels-Alder adducts [(83) and (84)] originating from (79) (Scheme 17).



Scheme 17

The cleavage of a C-C bond in (83) followed by a hydrogen migration in the diradical (85) thus formed, was the proposed mechanism for the formation of (81).

Pentafluorophenyl $[2,3,3-^{2}H_3]$prop-2-enyl ether (86) was pyrolysed under the same conditions, in order to test the mechanism. The inden-1-one separated contained not only $[3,3a\beta,5\alpha-^{2}H_3]$-2,5,6,7,7aβ-pentafluoro-3a,4,5,7a-tetrahydroinden-1-one (89), the expected product from (87) but also $[3a\beta,4,4-^{2}H_3]$-2,5β,6,7,7aβ-pentafluoro-3a,4,5,7a-tetrahydroinden-1-one (90), formed in the ratio (9:10) respectively. It was proposed that (90) must be derived from the orthodienone (88), formed from (87) by an ortho-ortho rearrangement in which the Diels-Alder adducts (91) and (92) are involved (Scheme 18). In order to explain the product distribution it was



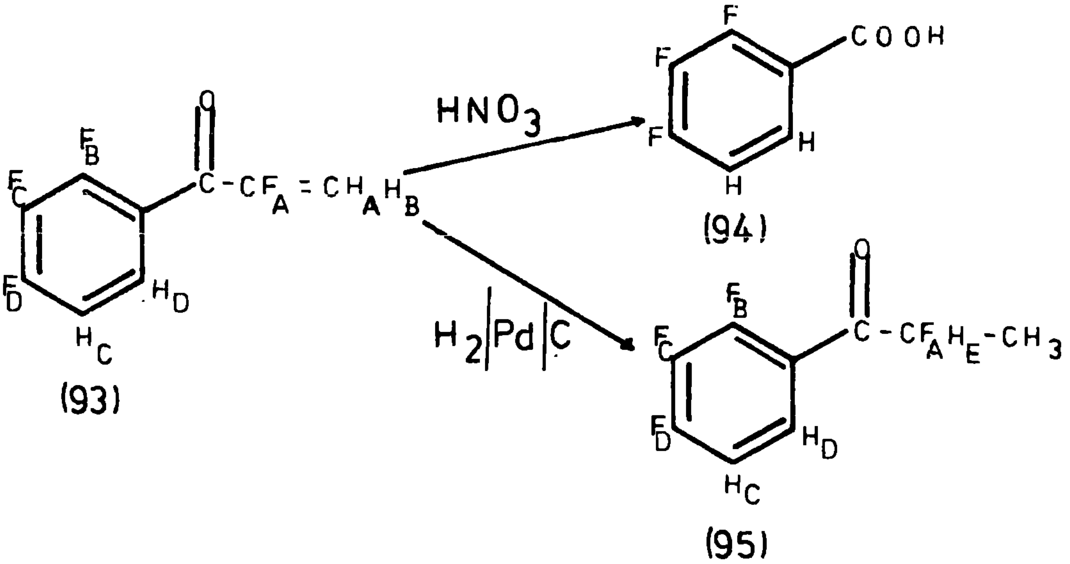
Scheme 18

proposed that the ortho-ortho′ rearrangement attained equilibrium very rapidly in comparison with the subsequent formation of products.

2.2 Isolation of 1-Fluorovinyl 2,3,4-Trifluorophenyl Ketone (93)

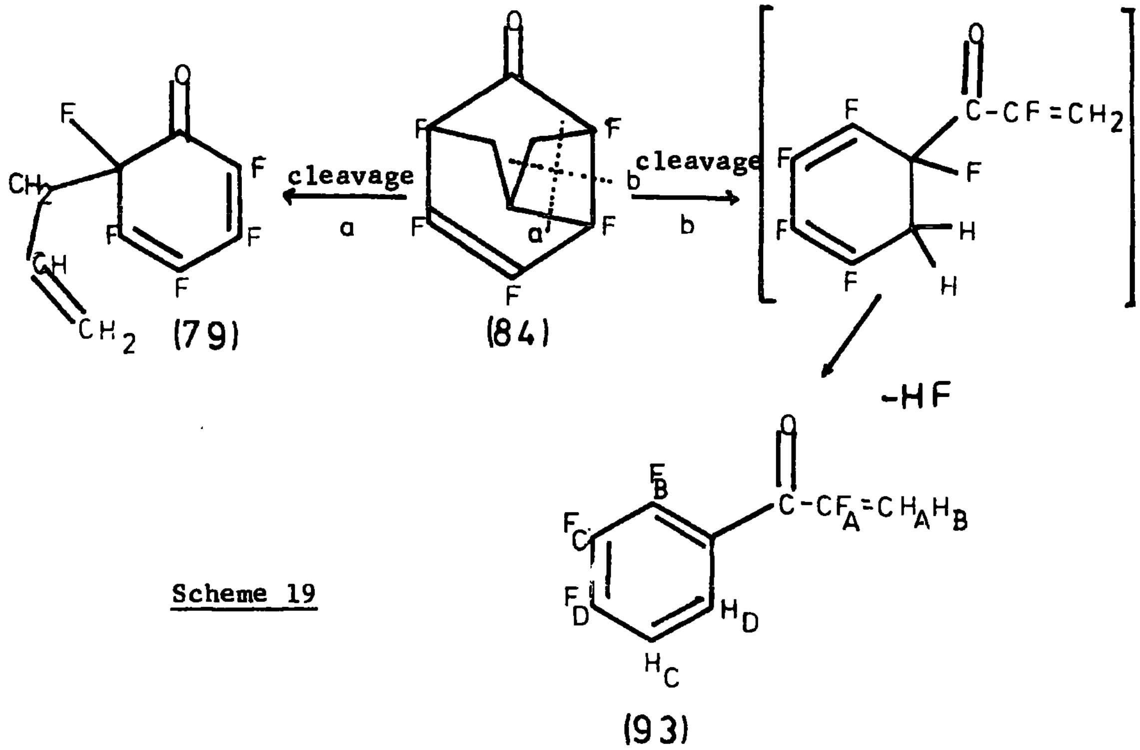
Pentafluorophenyl prop-2-enyl ether (78) was distilled through a silica tube packed with silica fibre at 440°C. The inden-1-one (81) was removed by precipitation at -10°C and then filtration. Coupled g.l.c.-mass spectrometry revealed that the complex residue contained: the ether (78); the 2,5-dienone (80), two components isomeric with (78) [which have not yet been identified], and a component with M^+204 (starting material - HF) which was the major component (40%). This material, which polymerised rapidly in air, was isolated by chromatography on silica and shown to be 1-fluorovinyl 2,3,4-trifluorophenyl ketone (93) on the basis of spectroscopic data and further chemical reactions.

The u.v. and i.r. spectra were consistent with the presence of a conjugated ketone. The ^{1}H n.m.r. spectrum showed two aromatic and two vinylic absorptions.While the aromatic absorption could not be resolved, the vinylic absorption clearly showed the presence of 45.0 and 12.0 Hz coupling constants which were due to H-F coupling. The ^{19}F n.m.r. spectrum showed four absorptions: one vinylic fluorine containing 45.0 [$J(F_A$, anti-$H_A)$] and 12.0 [$J(F_A$, syn-$H_B)$] Hz coupling constants, and three due to aromatic fluorine atoms. One of the aromatic ^{19}F absorptions (F_C) contained two coupling constants of 20.5 Hz, consistent with adjacent ortho fluorine (F_B and F_D) atoms. The ketone (93) was oxidised with fuming nitric acid to give an acid which was unambiguously identified as 2,3,4-trifluorobenzoic acid (94) on the basis of elemental analysis, mass spectroscopy and the magnitude of J_{FF}, J_{HF} and J_{HH} coupling constants in the ^{19}F and ^{1}H n.m.r. spectra.



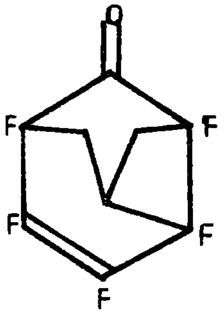
Catalytic hydrogenation of the ketone (93) gave 1-fluoroethyl 2,3,4-trifluorophenyl ketone (95) identified on the basis of elemental analysis, mass spectroscopy and the presence of a J_{gem} HF (48.0 Hz) in the ^{19}F n.m.r. spectrum. Both the ketones (93) and (95) showed large through space F,F-coupling constants $J(F_A,F_B)$, 17.0 and 15.5 Hz, respectively, which indicate rigid conformations in these molecules.

The formation of the vinyl ketone (93) can be explained by invoking the opening of the four-membered ring of the Diels-Alder adduct (84) by the mode alternative to the one involved in the degenerate ortho-ortho′ rearrangement followed by loss of HF (Scheme 19).

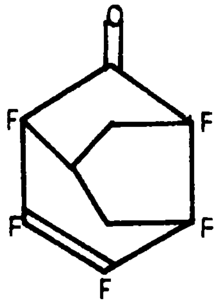


Scheme 19

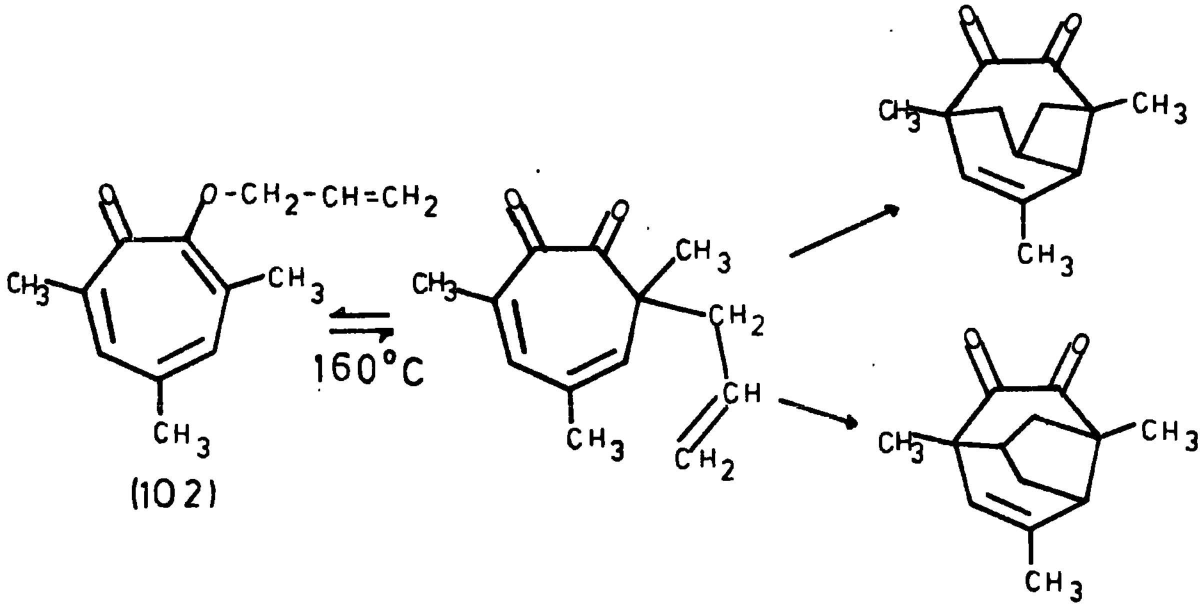
The formation of the vinylic ketones and the inden-1-ones is proposed to involve the intermediacy of Diels-Alder adducts (84) and (83) respectively. Adducts analogous to (83) and (84) have been isolated during the thermolysis of allyl tropylone ether (102) and allyl tropyl ether (103).[37,38]

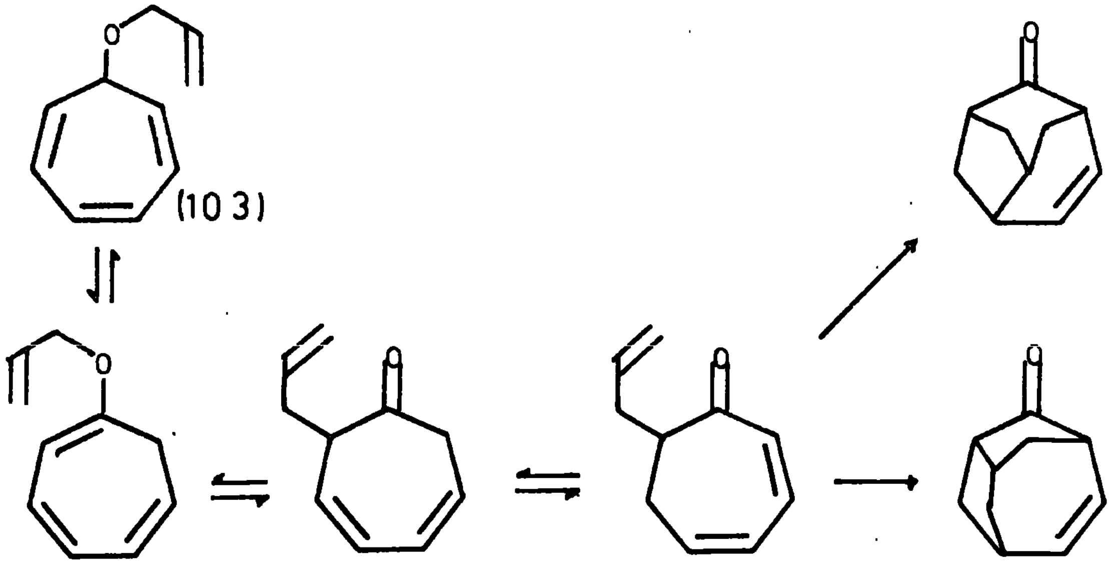

O
F
F
F
F
F

(84)

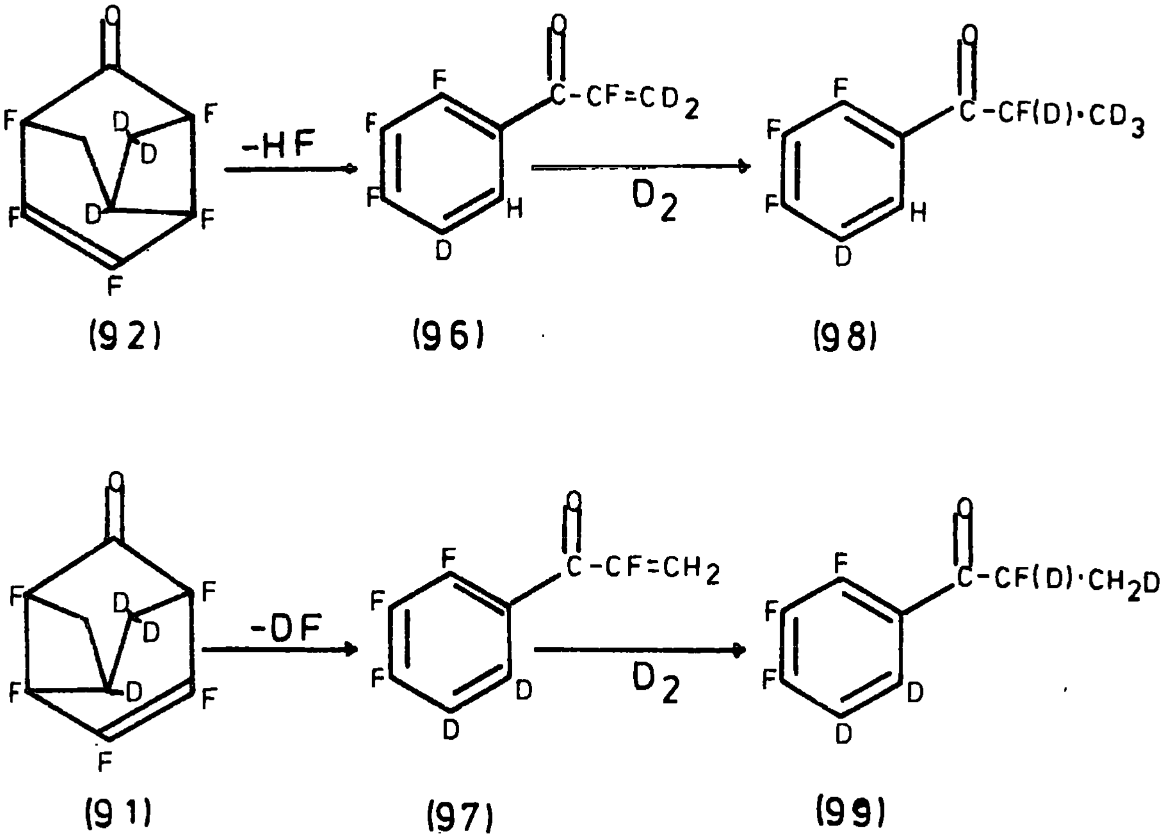

O
F
F
F
F
F

(83)


O-CH2-CH=CH2
CH3
CH3
CH3
160°C
(102)
CH3
CH3
CH2
CH
CH2
CH3
CH3
CH3
CH3
CH3
CH3
CH3


O
(103)
O
O
O
O
O

In order to test the mechanism proposed for the formation of the vinylic ketone, pentafluorophenyl $[2,3,3-{}^{2}H_{3}]$prop-2-enyl ether (86) was pyrolysed under conditions identical with (78). The vinylic ketone was isolated as before and immediately reduced with deuterium in order to produce a stable product with a simplified ^{1}H n.m.r. spectrum. Two compounds (98) and (99) were obtained in the ratio 1:1.1 respectively (identified from the intensities of the aromatic and CH_2 absorptions in the ^{1}H n.m.r. spectrum), indicating that the pyrolysis products were the unsaturated ketones (96) and (97), which must have been produced from the internal Diels-Alder adducts (92) and (91) respectively (Scheme 20).

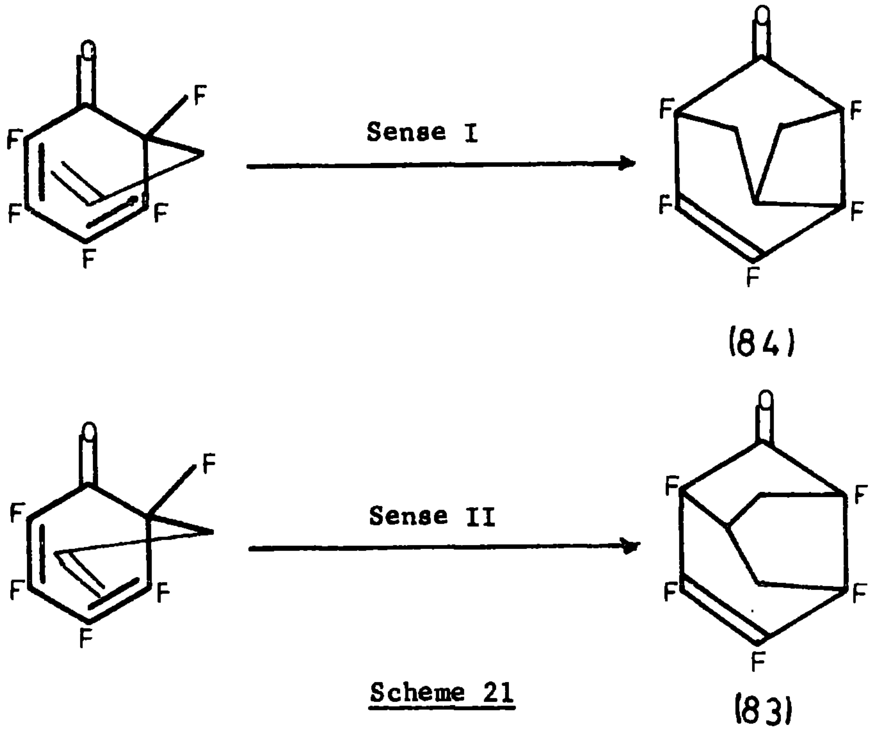


Scheme 20

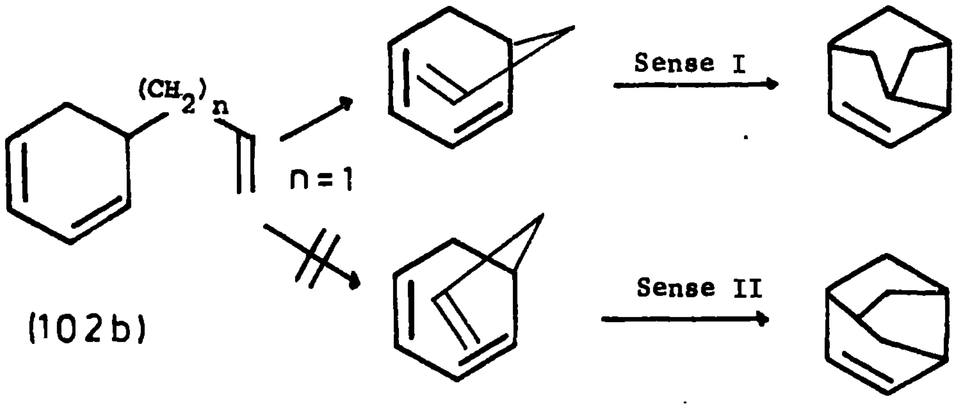
Compounds (89) and (90) (Scheme 18) were also isolated and found to be present in the ratio 1:1. The identical isomer distribution in the inden-1-ones (89) and (90) and vinylic ketones (96) and (97) indicate that they were formed from common precursors, the 2,4-dienones (87) and (88).

Furthermore, the equilibrium between (87) and (88) must be established very rapidly in comparison to the formation of the vinylic ketones (96) and (97), and thus cleavage of bonds a in (84) occurred more easily than cleavage of bonds b (Scheme 19).

The equal proportions of the two inden-1-ones (89) and (90) indicated that the formation of the Diels-Alder adducts (91) and (92) [which lead to the vinylic ketones (96) and (97)] must occur more readily than the formation of the Diels-Alder adducts (100) and (101) (Scheme 18), [which lead to the inden-1-ones]. Inspection of molecular models confirms that the formation of adduct (84) should occur more readily than the formation of (83) due to the high torsional strain in sense II (Scheme 21). Experimental evidence for this observation is born out by the exclusive additions by sense I in concerted intramolecular Diels-Alder reactions involving cyclohexadienes (102b).[39] Sense II addition is only seen when a two step process involving a diradical intermediate is possible.[40] With (103b) it is thought that allylic and oxa pentadienylic stablization of the radical

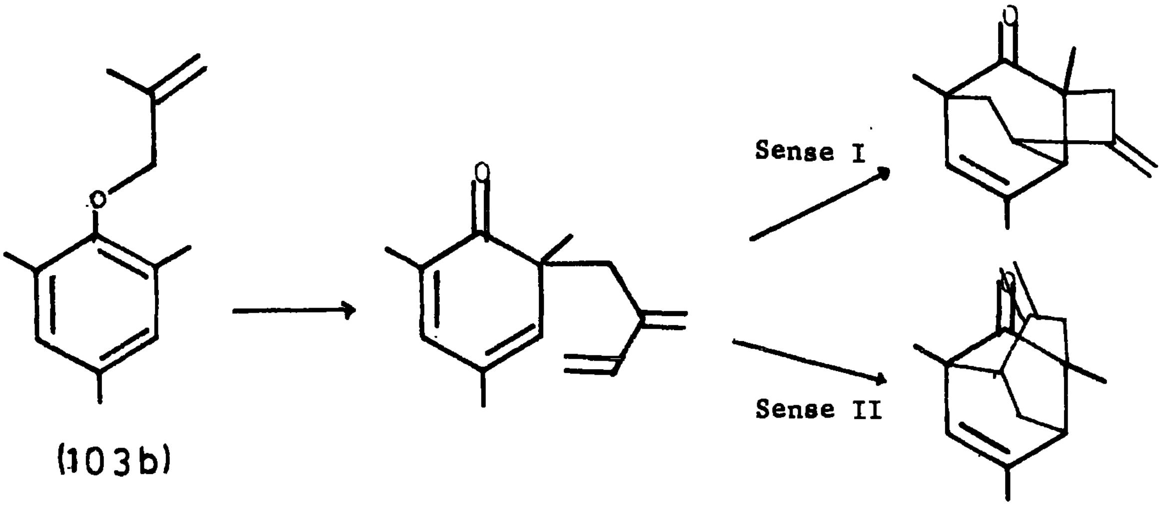


Scheme 21



(102b)

transition state is responsible for the formation of the sense II product.[41]



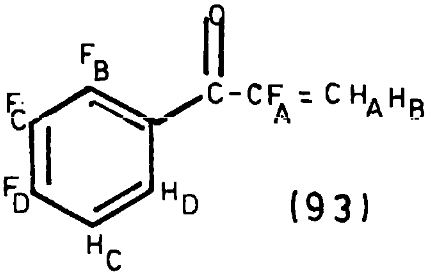
(103b)

Thus it is concluded that the formation of (83), the Diels-Alder adduct responsible for the formation of the inden-1-one (81) must occur by a non-concerted, two step process involving radicals.

Chapter 2 Experimental

2.3 Flow pyrolysis of Pentafluorophenyl Prop-2-enyl Ether (78)

The ether (78) (19.4g) was distilled during 4 h from a vessel at 70°C through a silica tube (20 cm x 1.5 cm diam.) packed with silica fibre and heated to 440°C, into a trap cooled by liquid air, connected to a high vacuum system (0.001 mm Hg). The liquid product (18.8g) was cooled to -10°C to precipitate 2,5β,6,7,7aβ-pentafluoro-3aβ,4,5,7a-tetrahydroinden-1-one (81) which was filtered off, and the filtrate was washed with water to remove HF. Examination of this product by coupled g.l.c.-mass spectrometry (v.g. micromass 12B instrument) indicated a complex mixture with one component, M^+204 (starting material - HF), present in significant amount(40%). Chromatography of the mixture (6.0g) on silica (70 cm x 3.5 cm diam.) (carbon tetrachloride as eluant) gave an impure sample of this component, 1-fluorovinyl 2,3,4-trifluorophenyl ketone (93) (1.4g), b.p. 42° at 0.03 mm Hg, as a slow moving material which rapidly polymerised in the absence of solvent and so was immediately hydrogenated or oxidised. The ^{19}F n.m.r. spectrum $[(CD_3)_2CO]$ showed signals at 115.1 (F_A), 128.1 (F_D), 134.2 (F_B) and 160.3 (F_C) p.p.m. upfield from internal $CFCl_3$ [J(F_A,anti-H_A) 45.0, J(F_A,syn-H_B) 12.0, J(F_A,F_B) 17.0, J(F_B,F_C) 20.5, J(F_B,F_D) 12.0, J(F_B,H_C) 6.0, J(F_B,H_D) 3.0, J(F_C,F_D) 20.5, J(F_C,H_C) 6.0, J(F_C,H_D) 3.0, J(F_D,H_C) 9.0, J(F_D,H_D) 5.5 Hz]. The ^1H n.m.r. $[(CD_3)_2CO]$ showed r 2.3 - 3.3 (complex multiplet, H_C and H_D), 4.38 (anti - H_A), and 4.43 (syn - H_B); V_{max}1692 cm^{-1} (C = O); λ_{max} (cyclohexane) 252 nm (ε 14,700).



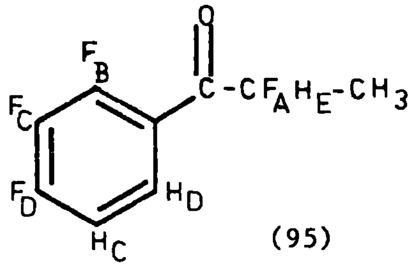
(93)

2.4 Flow pyrolysis of Pentafluorophenyl [2,3,3-$^2H_3$] Prop-2-enyl Ether (86)

The ether (86) (6.0g) was pyrolysed as in the previous experiment to give a product separated by chromatography on silica (CCl_4 as eluant) into 1-fluoro[2,2-$^2H_2$]-vinyl 2,3,4-trifluoro[5-$^2H_1$]phenyl ketone (96) and 1-fluorovinyl 2,3,4-trifluoro[5,6-$^2H_2$]phenyl ketone (97) (0.8g); this was not distilled, but was treated immediately with deuterium. The slower moving components on the column were eluted with ether and finally separated by preparative t.l.c. on kieselgel GF_{254} (chloroform as eluant) to give a mixture of [3,3aβ,5α-$^2H_3$]-2,5,6,7,7aβ-pentafluoro-(89) and [3aβ,4,4-$^2H_3$]-2,5β,6,7,7aβ-pentafluoro - 3a,4,5,7a-tetrahydroinden-1-one (90) in the ratio 1:1 {from the intensities of the ^1H n.m.r. signals [$(CD_3)_2CO$] at τ4.65 and 7.59 respectively}.

2.5 1-Fluoroethyl 2,3,4-trifluorophenyl ketone (95)

The crude vinyl ketone (93) (1.7g) in ethyl acetate (30 ml) was hydrogenated at atmospheric pressure over palladium-charcoal (0.5g; 10% w/w) at room temperature until ca. 1 mol equiv. of gas had been absorbed. The catalyst was filtered off, the solution evaporated, and the residue purified by preparative g.l.c. (di-isodecyl phthalate, 178°C) to give 1-fluoroethyl 2,3,4-trifluorophenyl ketone (95), m.p. 46-47°C (from ethanol-water) (Found: C, 52.7; H, 2.6; F, 36.1%; M^+, 206. $C_9H_6F_4O$ requires C, 52.4; H, 2.6; F, 36.8%; M, 206). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed signals at 128.7 (F_D), 133.3 (F_B), 162.3 (F_C) and 184.4 (F_A) p.p.m. upfield from internal $CFCl_3$. [J(F_A, H_E) 48.0, J(F_A, vic H) 23.0, J(F_A, F_B) 15.5, J(F_B, F_C) 20.0, J(F_B, F_D) 12.0, J(F_C, F_D) 19.0, J(F_C, H_C) 6.5,



(95)

$J(F_C, H_D)$ 1.5, $J(F_D, H_C)$ 9.2, $J(F_D, H_D)$ 6.2 Hz]. The ^1H n.m.r. spectrum ($CDCl_3$) showed τ2.52 (H_D), 2.90 (H_C), 4.54 (H_E) and 8.56 (CH_3) [$J(H_E, CH_3)$ 7.0 Hz]; ν_{max} 1705 cm^{-1} (C=O).

2.6 Reactions of 1-Fluorovinyl 2,3,4-Trifluoro[5,6-$^2H_2$]phenyl ketone (97) and 1-Fluoro[2,2-$^2H_2$]vinyl 2,3,4-Trifluoro[5-$^2H_1$]phenyl ketone (96) with Deuterium

The crude mixture of ketone (96) and (97) (see above), in ethyl acetate, was treated at atmospheric pressure with deuterium over palladium-charcoal, and the product was isolated by preparative t.l.c. as before. The ^1H n.m.r. spectrum [$(CD_3)_2CO$] showed signals for ring protons H-6 and H-5 and side-chain protons H-1 and H-2, with relative intensities 1:0.23:1.71:2.19, which indicated the presence of both 1-fluoro[1,2,2,2-$^2H_4$] ethyl 2,3,4-trifluoro[5-$^2H_1$]phenyl ketone (98) and 1-fluoro[1,2-$^2H_2$]ethyl 2,3,4-trifluoro[5,6-$^2H_2$] phenyl ketone (99) in the ratio 1:1 respectively in which 11% overall exchange of H for D at ring position 5 and 82% overall exchange of H for D at side-chain position 1 had occurred. A separate experiment showed that these exchange reactions could be induced on the silica by moisture in the environment (the silica, the solvent, or the atmosphere).

2.7 2,3,4-Trifluorobenzoic Acid (94)

The crude vinyl ketone (93) (0.14g) was heated under reflux with nitric acid (10 cm^3; 70% w/w) for 2 hours. The mixture was diluted with water and extracted with ether, and the dried ($MgSO_4$) extracts were evaporated. Sublimation of the residue at 120°C and 0.05 mm Hg and recrystallisation from toluene-petroleum (b.p. 60-80°C) gave 2,3,4-trifluorobenzoic acid (0.043g), m.p. 136.5-137°C. (Found: C, 48.0; H 2.0; F, 32.7%; M^+, 176. $C_7H_3F_3O_2$ requires C, 47.7; H, 1.7; F, 32.3%; M, 176).

The ^{19}F n.m.r. spectrum (Et_2O) showed signals at 130.4 (F-4), 132.1 (F-2), and 163.0 (F-3) upfield from external $CFCl_3$ [J(F-2, F-3) 19.0, J(F-2, F-4) 12.5, J(F-3, F-4) 19.0, J(F-2, H-5) 2.5, J(F-2, H-6) 7.0, J(F-3, H-5) 6.5, J(F-3, H-6) 2.5, J(F-4, H-5) 8.5, J(F-4, H-6) 6.0 Hz]. The ^1H n.m.r. spectrum (Et_2O) showed τ2.52 (H-6) and 3.21 (H-5) [J(H-5, H-6) 9.0 Hz]; ν_{max} 1690 cm^{-1} (C=O).

Chapter 3

Static Thermolysis of Pentafluorophenyl Prop-2-enyl ether (78)

3.1 Introduction

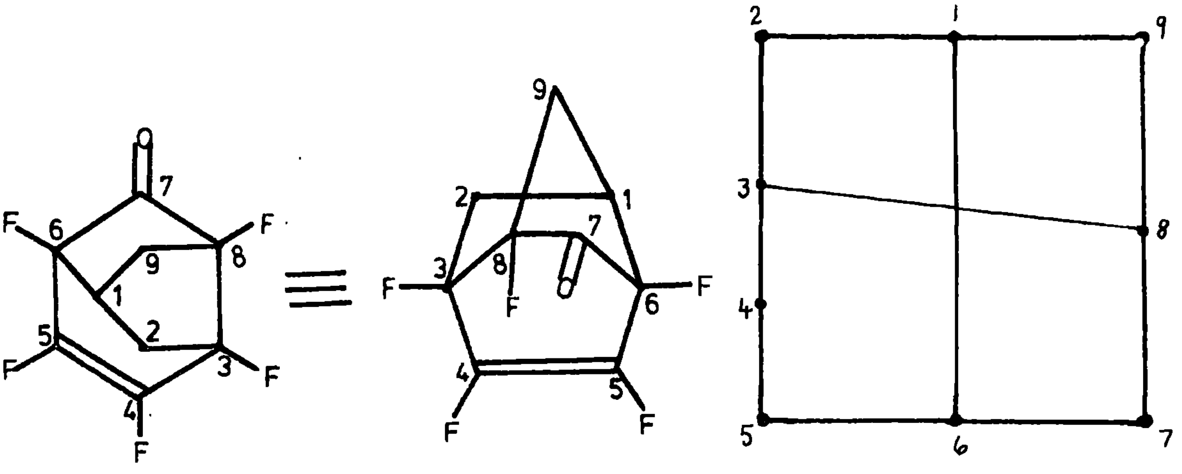
It was shown that the formation of products (81) and (93) from flow pyrolyses with pentafluorophenyl prop-2-enyl ether (78) could be rationalised by invoking the intermediacy of the intramolecular Diels-Alder adducts (83) and (84) respectively. (Scheme 17 and Scheme 19, Chapter 2). To confirm these mechanisms an attempt was made to isolate the Diels-Alder adducts (83) and (84). Clearly the reaction conditions had to be modified to inhibit the decomposition of the adducts, and so the temperature was reduced while the period of heating was lengthened.

Discussion

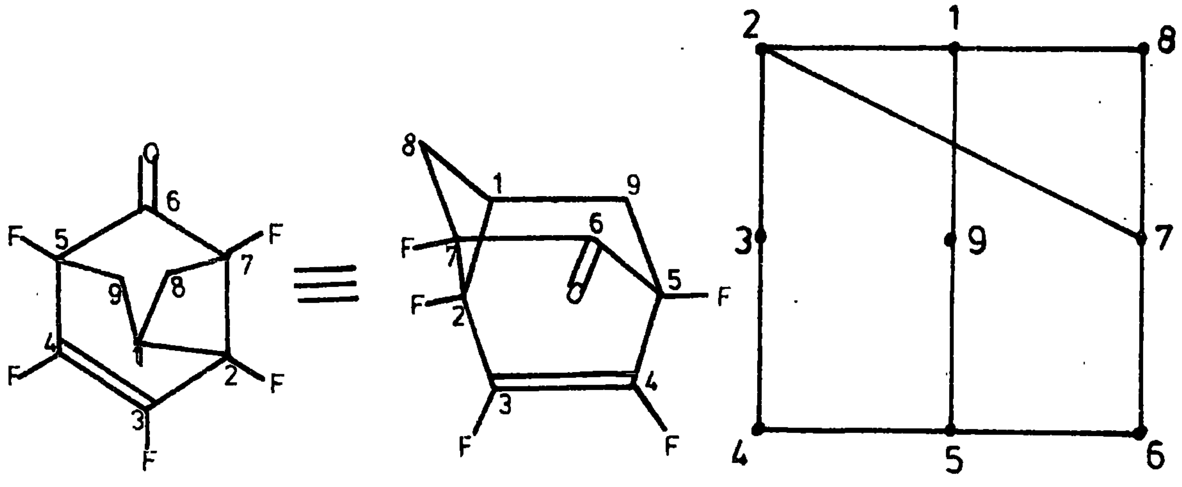
The ether (78) was sealed in a 10 litre bulb, under reduced pressure (.001mm Hg), and heated in an oven at 141-143°C for 13 days. The product was washed from the bulb with diethyl ether and separated into three parts: a volatile component (39%), shown by g.l.c analysis to be starting material (78) and the para-dienone (80) in the ratio 2:1 respectively (from the ratio of CH_2 absorptions in ^1H n.m.r. spectrum); a material (24%) which sublimed at room temperature (0.001mm Hg) and whose i.r. spectrum showed it was a ketone; and a material (37%) which sublimed at 40° (0.001mm Hg), the i.r. spectrum of which showed it was a hydroxy-compound (104).

3.2 Characterisation of the Ketone

Mass spectroscopy and elemental analysis revealed that the ketone was isomeric with the ether (78), M^+224. The i.r. spectrum showed characteristic absorptions at 1760 (CF=CF) and 1700 cm^{-1} (C=O). The ^{19}F n.m.r. spectrum showed five distinct absorptions, the chemical shifts of which indicated that two of the fluorines were olefinic in nature and the remaining three, at very high field, were in bridge-head positions. The ketone could be a Diels-Alder adduct, either (83) or (84), on the strength of these observations.



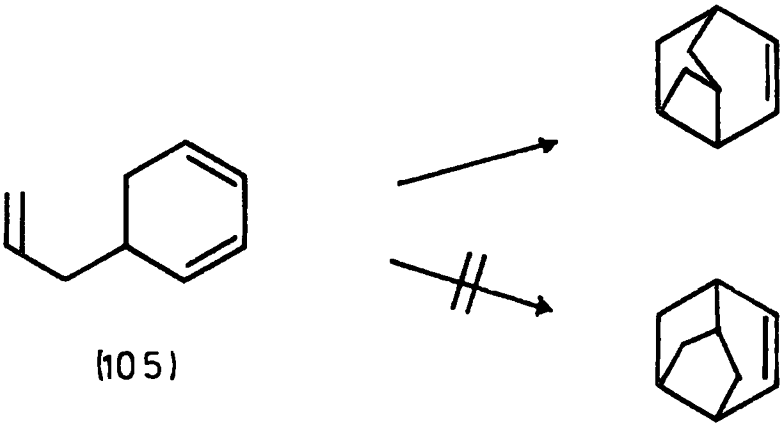
(83)



(84)

Examination of the ^{19}F n.m.r. spectrum revealed the presence of coupling constants 18.5 and 16.0 Hz, found in the absorptions at 193.2 and 212.4 p.p.m. respectively, which were due to H-F interaction. Although complete analysis of the ^{1}H n.m.r. proved impossible, it was clear that both the above constants must be contained within the CH_2 absorption at τ 6.72, and thus two of the bridge-head fluorines are coupled to the same CH_2 group. A common coupling constant of 10.0 Hz was found in the ^{1}H absorption at τ 7.65 and the ^{19}F absorption at 193.2 p.p.m. Therefore, one fluorine (at 193.2 p.p.m.) is coupled to both the single hydrogen and one of the methylene groups (at τ 6.72) which is also coupled to a second fluorine (at 212.4 p.p.m.).

Although an unambiguous structural assignment can not be made, the n.m.r. coupling constant data is more consistent with the structure (84), 2,3,4,5,7-pentafluorotricyclo [3.3.1.$0^{2,7}$]non-3-en-6-one. An X-ray crystal structure is expected to confirm this assignment, which is also corroborated by evidence in the literature. Indirect support for this assignment, however, comes from the thermolysis of 5-allylcyclohexa-1,3-diene (105) at 225°, which in addition to Cope rearrangement products gave only one Diels-Alder adduct - tricyclo[3.3.1.$0^{2,7}$]non-3-ene (106).[42] The absence of tricyclo[4.3.$0^{1,6}$.$0^{3,8}$]non-4-ene (107) [the analogue of which in this work would be (83)] was explained in terms of the high torsional strain present in the transition state for formation of (107), as outlined in Chapter 2.



(105)

(106)

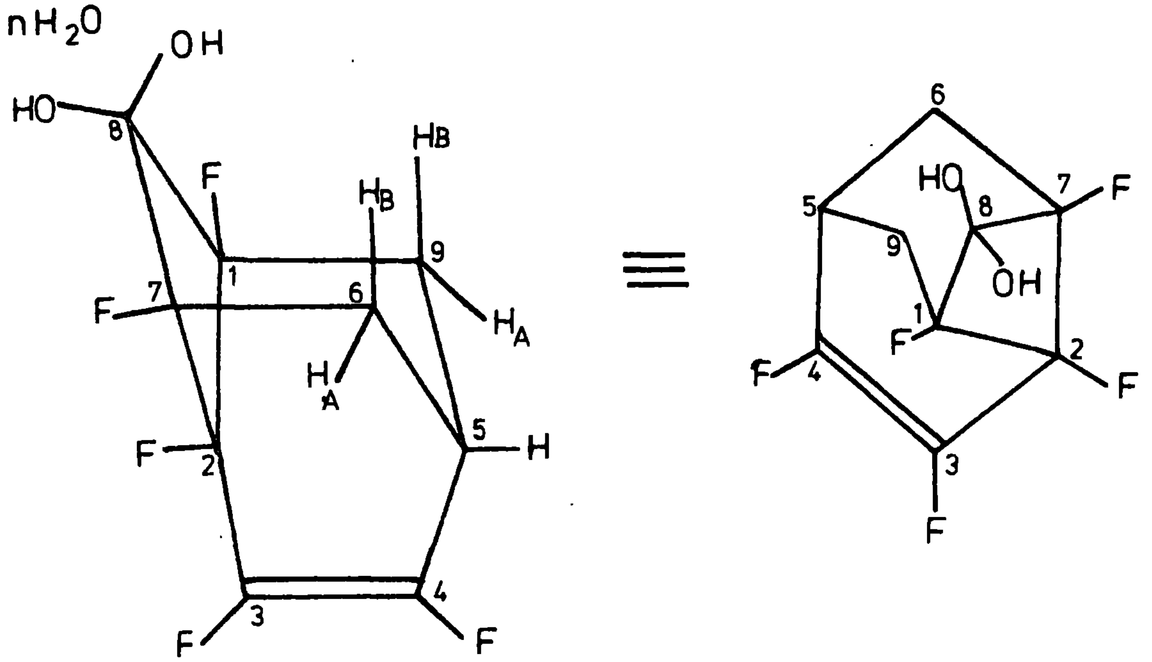
(107)

3.3 Characterisation of the Hydroxy-compound (104)

The highest peak in the mass spectrum of (104) was 224. However, elemental analysis did not give results consistent with a mass of 224 and indeed suggested a mass greater than 224. This was verified by molecular weight determinations by vapour phase osmometry which gave $M_{av} = 257 \pm 8$. The mass spectrum degradation pattern inferred that mass 224 probably corresponded to a ketone species. However, i.r. analysis showed only the presence of a fluorinated double bond (1758 cm^{-1}) and hydroxyl groups. The above data could be rationalised if (104) was a hydrated gem-diol, capable of rapid dehydration in a mass spectrometer. Compound (104) was heated with P_2O_5 to produce a ketone, identified by i.r. spectroscopy, which was stable in a moisture-free nitrogen atmosphere but reverted to (104) rapidly in air.

The ^{19}F n.m.r. spectrum of (104) significantly showed only four absorptions at 138.8, 164.5, 193.5 and 218.0 p.p.m. upfield from $CFCl_3$, present in the ratio (1:1:2:1). The absorption at 193.5 p.p.m. contained a large separation, 18.0 Hz, which was not a function of the applied field frequency (spectrum run at 84.67 and 56.7 MHz field frequency) and thus must be a coupling constant rather than a chemical shift. It was clear that (104) contained two fluorine atoms in positions that were magnetically equivalent to n.m.r. analysis. To explain this observation, in the absence of any CF_2 function, the two magnetically equivalent fluorine atoms must be in positions related through a plane of symmetry. The ^1H n.m.r. spectrum showed τ 6.13, 7.40 and 8.40, in the ratio 1:2:2, in addition to a broad absorption at τ 4.58 which could not be integrated to give an integral number of OH groups. Matching up coupling constants derived from a detailed ^{19}F and ^1H n.m.r. analysis, it was found that: the magnetically equivalent fluorine atoms were coupled to a proton at τ 7.40 (18.0 Hz) and a fluorine at 218.0 p.p.m. (5.0 Hz); the ^{19}F absorption at 138.8 p.p.m. was coupled to the single hydrogen at τ 6.13 (14.0 Hz); and the two protons at τ 7.40 and τ 8.40 were also coupled (12.0 Hz). The above assertions were substantiated by hetero nuclear n.m.r. decoupling experiments which eliminated the effect of one atom.

Noting that mass, i.r. and ^{19}F n.m.r. spectroscopy showed the presence of a hydrated gem-diol linkage, a fluorinated double bond, and a plane of symmetry respectively, the product was assigned the structure 1,2,3,4,7-pentafluorotricyclo[3.3.1.$0^{2,7}$]non-3-en-8,8-diol hydrate (104).



(104)

^{19}F		^{1}H	
p.p.m.	Assignment	τ	Assignment
138.8	F-4	6.13	H-5
164.5	F-3	7.40	H-6A H-9A
193.5	F-1 F-7	8.40	H-6B H-9B
218.0	F-2		

Numerous examples of solvated gem-diols are documented in the literature.[43] The stability of these gem-diols is thought to be dependent on the presence of the small solvent molecule which interacts strongly with the hydroxyl groups.[44]

Elemental analysis of (104) was consistent with the formula $C_9H_7F_5O_2.\frac{1}{2}H_2O$. The hemihydrate structure was also suggested by the ^{1}H n.m.r. spectrum which integrated to give three OH groups.

X-ray crystal structure of (104), Fig. 10, confirmed that one molecule of water was associated with two organic molecules, and that the structural

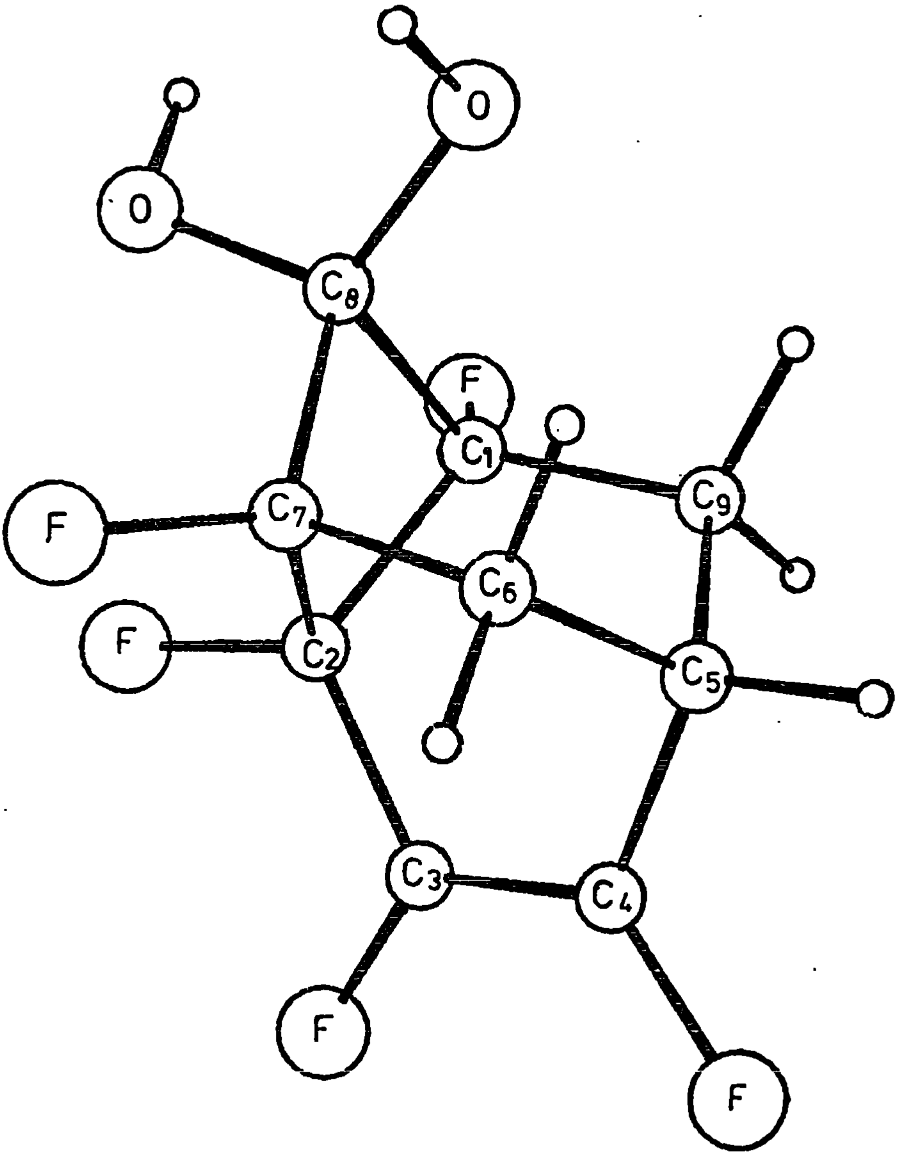
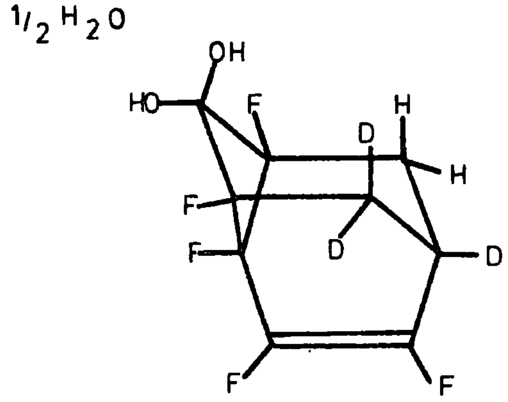


Fig. 10

assignment of (104) was indeed correct.

The ^{1}H n.m.r. assignment of (104) was verified by isolation of the hemihydrate formed in the static thermolysis of pentafluorophenyl [2,3,3-$^{2}H_{3}$]prop-2-enyl ether (86). 1,2,3,4,7-Pentafluoro[5,6,6-$^{2}H_{3}$] tricyclo[3.3.1.0^{2,7}]non-3-ene-8,8-diol hemihydrate (108) has a ^{1}H n.m.r. spectrum with five absorptions: τ 3.62 (OH), 3.84 (OH), 6.80 (OH + 43% H-5, exchanged deuterium), 7.28 (H-9B) and 8.32 (H-9A).

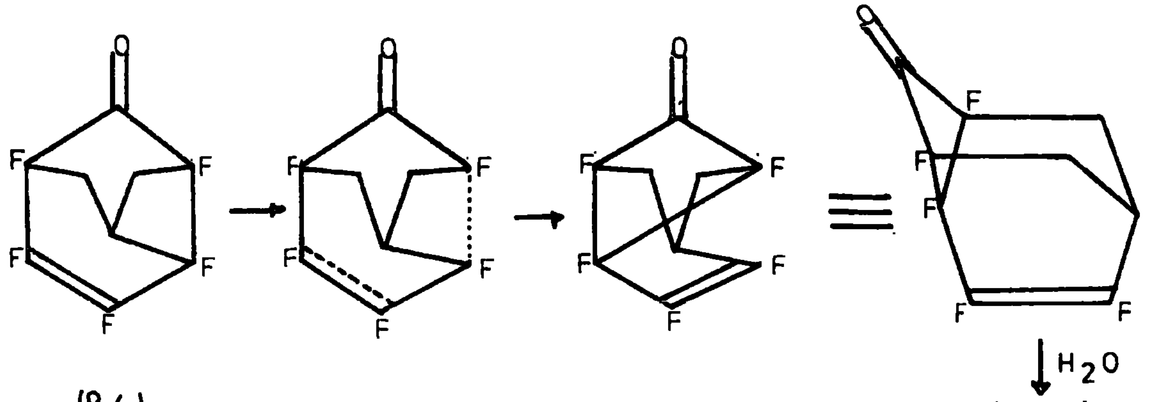


(108)

The acidity of H-5 could be due in part to an inductive or field effect associated with F-2.^{45,46}

3.4 The mechanism for the formation of 1,2,3,4,7-pentafluorotricyclo[3.3.1.0^{2,7}] non-3-ene-8,8-diol hemihydrate (104)

The gem-diol (104) could be formed from the Diels-Alder adduct (84), by a rearrangement approximating to a 1,3- shift followed by hydration (Scheme 22).



(84)

Scheme 22

(104)

Orbital considerations imply that a concerted 1,3-suprafacial shift must occur with inversion of stereochemistry[47] (Fig. 11), a widely quoted example being shown in Scheme 23.[48] However ring strain or steric blockage may hinder or even preclude an allowed concerted process and if the reaction occurs it does so by either a stepwise mechanism, probably involving a diradical.[49] Berson and Holder found that (109) rearranged to give both the allowed and forbidden products by concerted and stepwise processes respectively, the former predominating only by a small degree.[50]

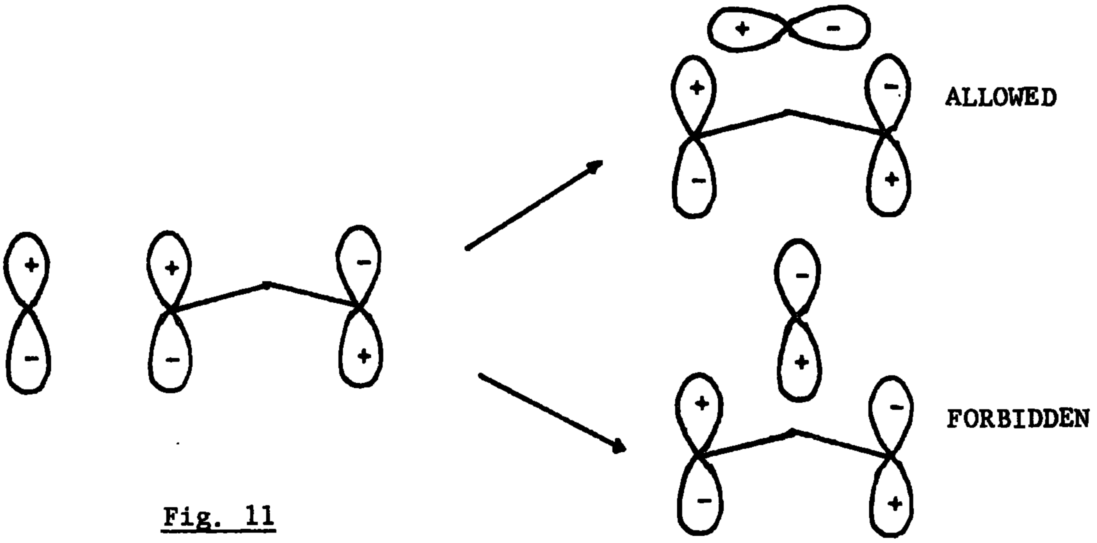
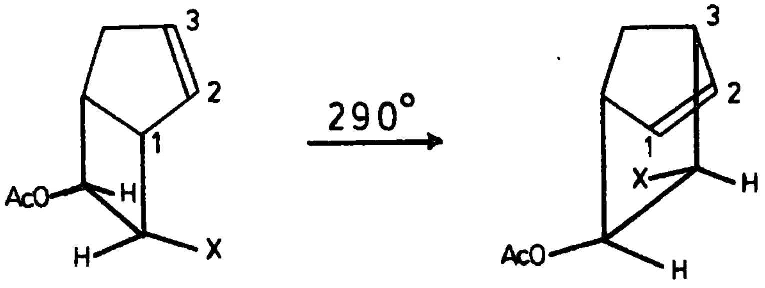
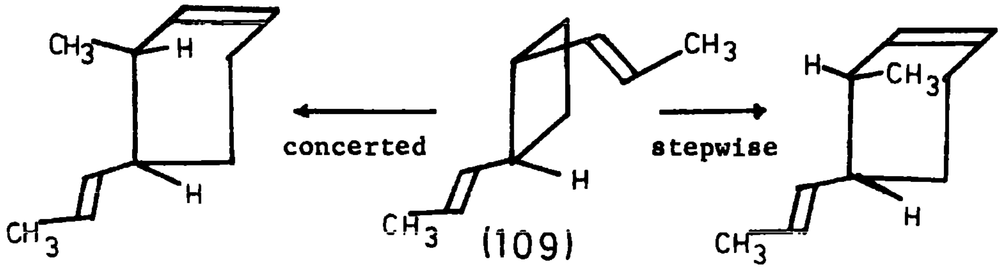


Fig. 11



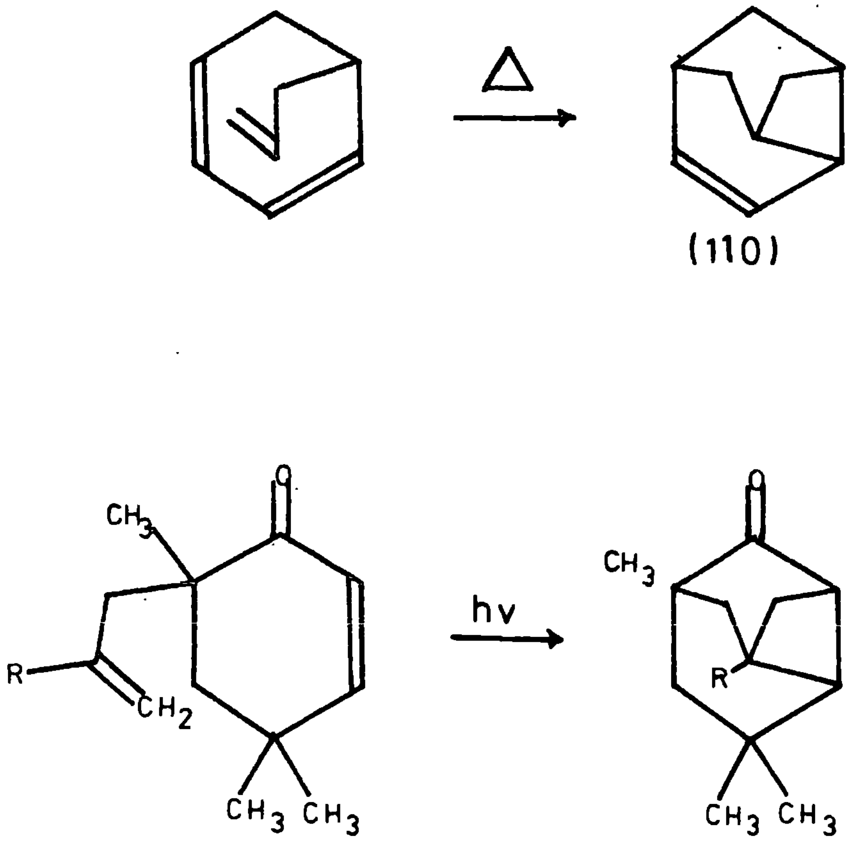
Scheme 23



(109)

Clearly in the process under consideration, (84) → (104), only a suprafacial mechanism is feasible in the tricyclic compound. Ring strain would preclude a concerted process occurring with inversion, and thus a stepwise mechanism must be operating. A diradical process is envisaged in which transition state would be stabilised by delocalisation involving the carbonyl and olefinic groups present.

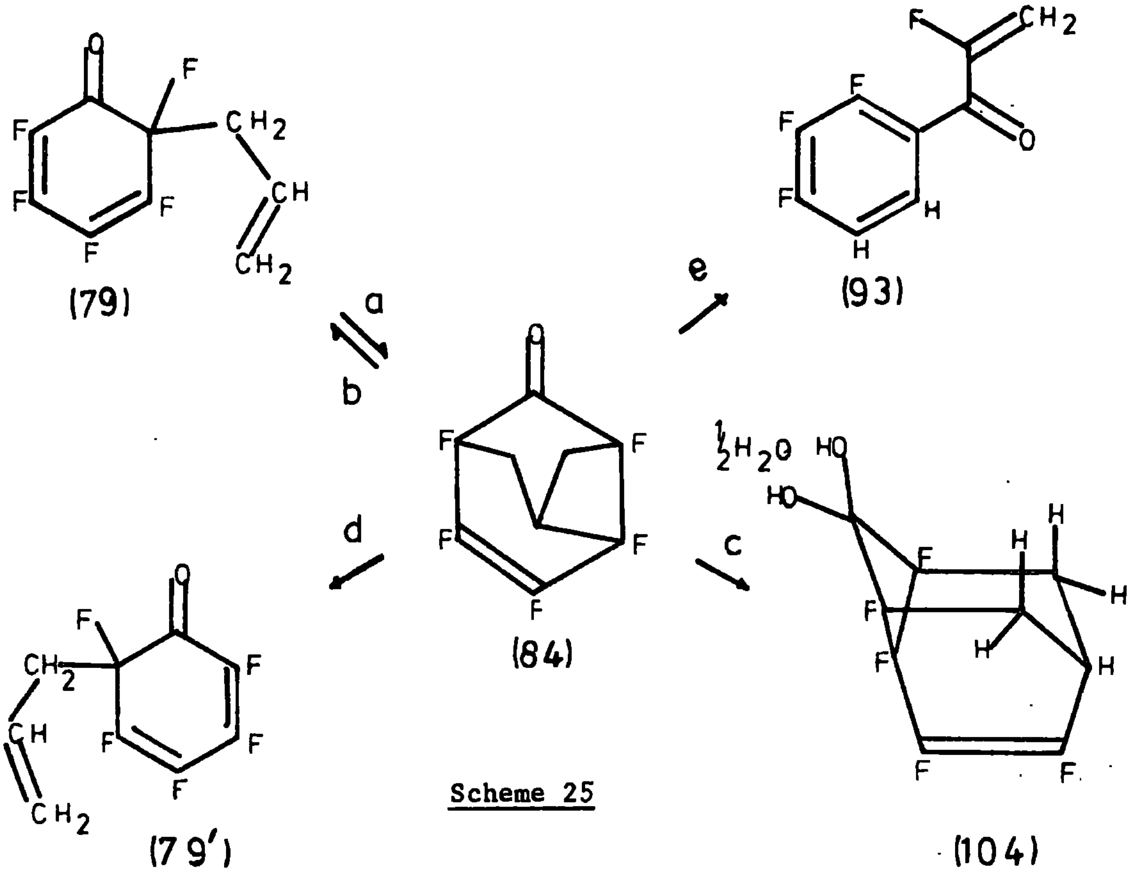
The ring system of (104) is a rare example of the [3.3.1.$0^{2,7}$]tricyclononane skeleton, and only two syntheses of this skeleton have been described: (a) compound (110) is produced by a Diels-Alder reaction,[42] and (b) compound (111) is a product from a photochemical reaction[51] (Scheme 24).



(110)

(111)

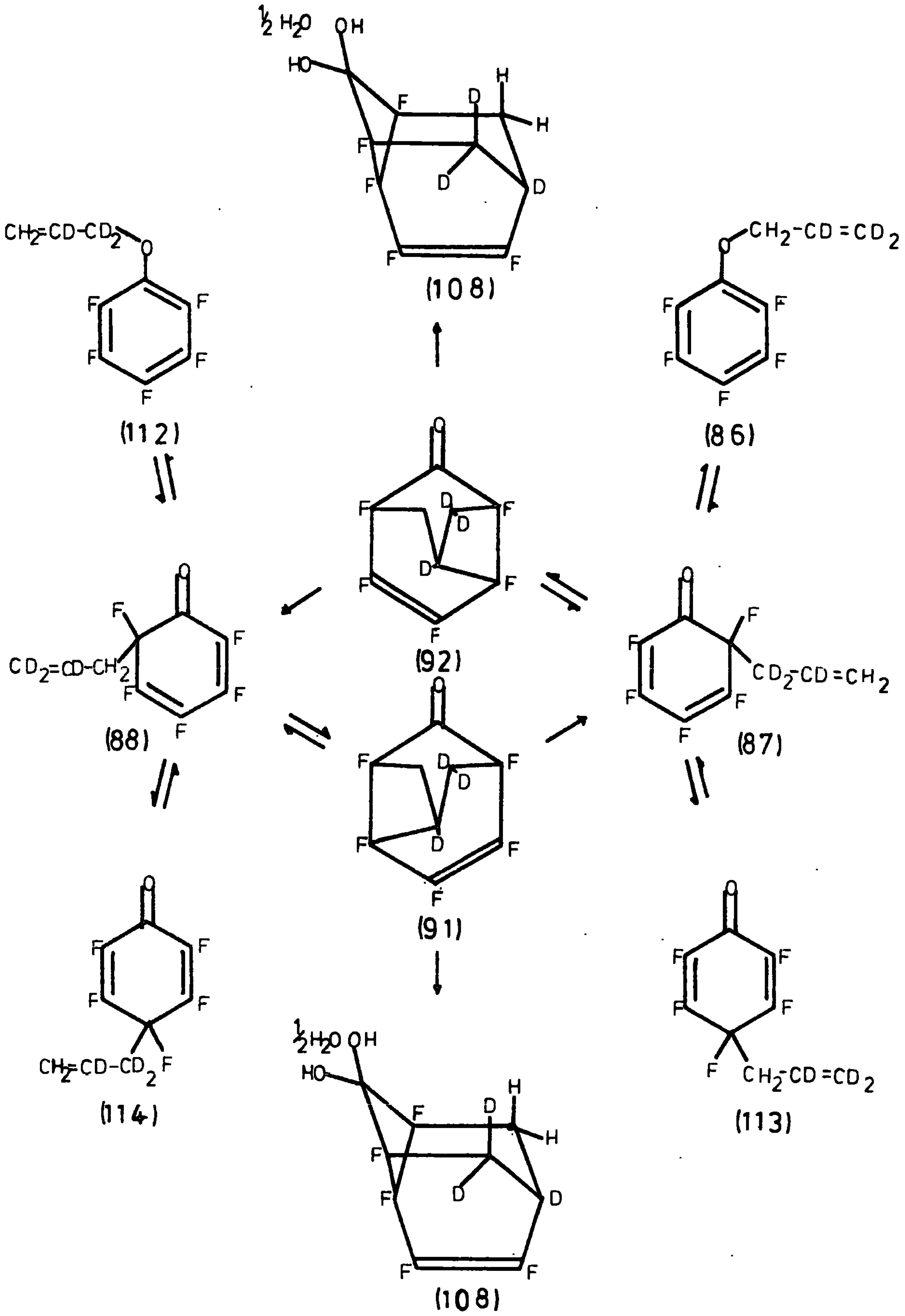
Scheme 24



Scheme 25

There are four possible reactions with the Diels-Alder adduct (84): b, a retro-Diels-Alder reaction generating the original dienone (79); c, formation of the ketone (115) - the hemihydrate precursor; d, cleavage of the four membered ring to form the ortho-ortho′ rearrangement product (79′); e, cleavage of the four membered ring to form the ketone (93) (Scheme 25).

At temperatures less than 165°C the ketone (93) was not observed. In order to investigate the relative rates of the processes b, c and d, the static thermolysis was repeated using pentafluorophenyl[2,3,3-$^{2}H_{3}$]prop-2-enyl ether (86). The products were separated into three components: volatiles (86, 112, 113 and 114) (55%); room temperature sublimate (91 and 92) (4%); solid residue (108) (41%) (Scheme 26). The ^{19}F n.m.r. analysis of the volatile component revealed that the composition was: 86 (53%), 112 (7%), 113 (35%), 114 (5%) (Scheme 26).



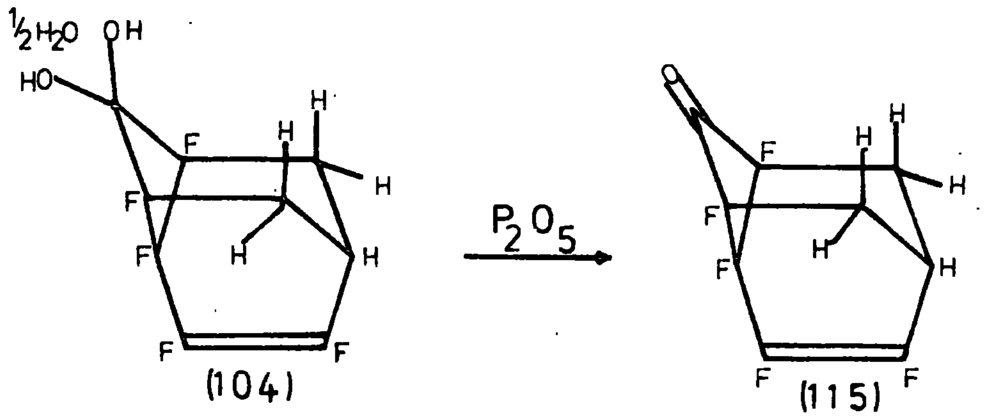
Scheme 26

Clearly then process b must occur much more rapidly than d (Scheme 25), since only 12% of the volatiles had a rearranged structure.

3.5 Reactions of 1,2,3,4,7-Pentafluorotricyclo[3.3.1.$0^{2,7}$]non-3-ene-8,8-diol hemihydrate (104)

Preparation of 1,2,3,4,7-Pentafluorotricyclo[3.3.1.$0^{2,7}$]non-3-en-8-one (115)

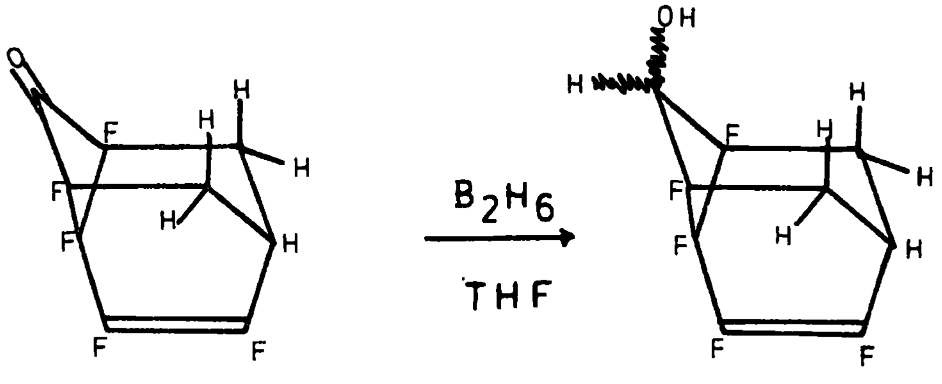
The gem-diol (104) was dehydrated with P_2O_5 and the product (115) was sublimed and handled in a moisture free nitrogen atmosphere. Infra red analysis showed the presence of a carbonyl group in a highly strained environment. ^{19}F N.m.r. spectroscopy again indicated the plane of symmetry observed previously in the gem-diol (104).



Preparation of 1,2,3,4,7-Pentafluorotricyclo[3.3.1.$0^{2,7}$]non-3-en-8-ol (116)

The gem-diol (104) was dehydrated with P_2O_5 to generate the ketone (115), which was reduced with diborane, the electrophilic nature of the reducing agent ensuring that the fluorinated double bond remained in the product (116).

N.m.r. analysis showed the presence of two magnetically equivalent fluorine atoms, and the absence of any associated water molecules. Attempts to determine the stereochemistry of the OH group using a lanthanide shift

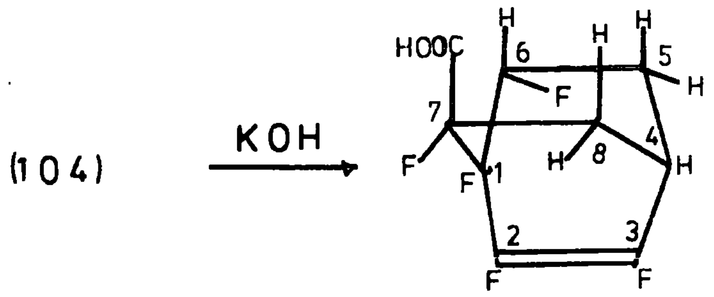


(115) (116)

reagent in ^{19}F n.m.r. spectroscopy were frustrated due to the inability to find a suitable solvent.

Preparation of 1,2,3,6,7-Pentafluoro-7-carboxybicyclo[2.2.2.]oct-2-ene (117)

The gem-diol (104) was treated with potassium hydroxide to give the haloform cleavage product (117).

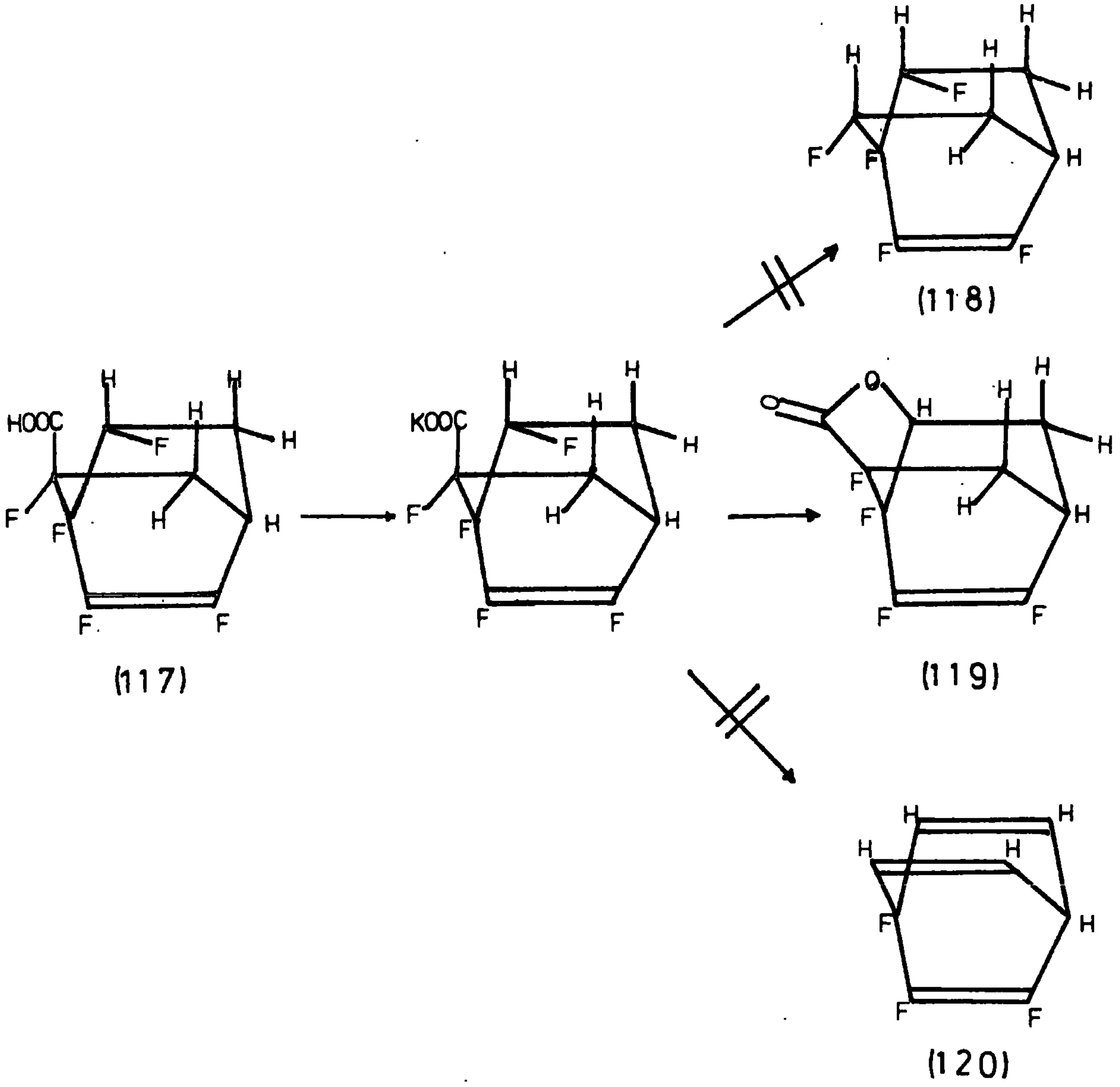


(117)

The ^{19}F n.m.r. spectrum showed a characteristic geminal H-F interaction ($J_{gem}HF=56.0$ Hz) and long range coupling between F-6 and F-7 (37.5 Hz). The formation of (117) under mild conditions gives an indication of the high ring strain present in the gem-diol (104).

Preparation of 2,3,4,7-Tetrafluoro-8-keto-9 -oxytricyclo[3.4.1.$0^{2,7}$]non-3-ene (119)

An equivalent amount of Potassium Hydroxide solution was added to the acid (117) and the solution was sealed in a tube under vacuum and heated, the intention being to decarboxylate the salt and generate the symmetrical compound (118). However, the product isolated was the lactone (119), formed by a nucleophilic substitution. The reaction was repeated using three equivalents of potassium hydroxide, when it was expected that (120) would

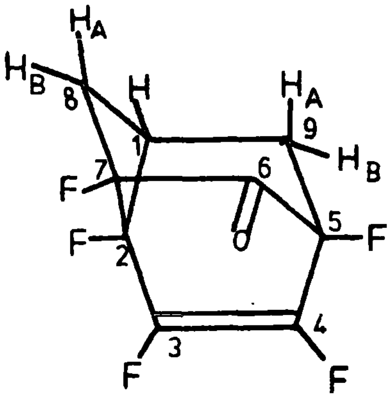


be formed. However , the lactone (119) was isolated again. In this reaction a poor nucleophile replaces a very poor leaving group, and is a classical example of neighbouring group participation. A fluorine atom (leaving group) and the carboxylate group (nucleophile) are ideally positioned for a nucleophilic substitution reaction, which is thus favoured by entropy factors.

Chapter 3 Experimental

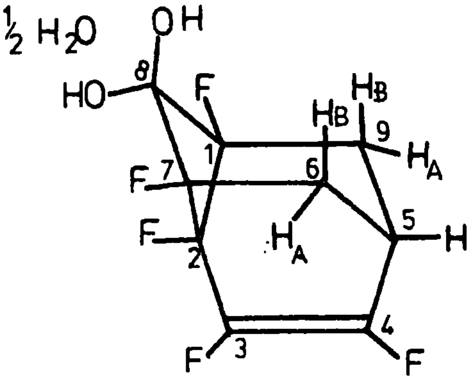
3.6 Static thermolysis of Pentafluorophenyl Prop-2-enyl Ether (78)

The ether (78) (2.72g) was sealed in a 10 litre vessel evacuated to low pressure (0.001 mm Hg), and heated at 137-141°C for 13 days. The products were condensed into a side-arm using liquid air, the vessel was opened and the mixture was washed out using diethyl ether. Water (1 ml) was added to ensure maximum yield of the hemihydrate, the ether solution was then dried ($MgSO_4$) and the solvent evaporated. The residue was sucked at room temperature at high vacuum (0.001 mm Hg) past a cold finger into a trap surrounded by liquid air, which condensed a mixture of pentafluorophenyl prop-2-enyl ether (78) and 4-allyl-2,3,4,5,6-pentafluoro-2,5-cyclohexadienone (80), (0.87g), present in the ratio of 2:1 (by ^{1}H n.m.r. spectroscopy). The solid on the cold finger was recrystallised from toluene-petroleum (b.p. 80-100°C) to give suspected 2,3,4,5,7-pentafluorotricyclo[3.3.1.0^{2,7}]non-3-en-6-one (84) (0.51g) m.p. 93.5 - 94.0°C. (Found: C, 48.2; H, 2.0%; M^+, 224. $C_9H_5F_5O$ requires C, 48.2; H, 2.2%; M, 224). The ^{19}F n.m.r. spectrum [$(CD_3)_2CO$] showed five signals: 151.4 and 155.8 (olefinic), 175.7 (F-5), 193.2 (F-2) and 212.4 (F-7) p.p.m. upfield from external $CFCl_3$. The ^{1}H n.m.r. spectrum [$(CD_3)_2CO$] showed τ 6.72 (CH_2-8), 7.45 (CH_2-9) and 7.65 (H-1). [J(F-2, H-8B) 18.5, J(F-7, H-8B) 16.0 Hz]; V_{max} 1760 (CF=CF), 1700 cm^{-1} (C=O).



(84)

Sublimation of the residue at 60°C and .001 mm Hg and recrystallisation from water gave 1,2,3,4,7-pentafluorotricyclo[3.3.1.0^{2,7}]non-3-ene-8,8-diolhemi-hydrate (104) (0.81g) m.p. 117.0 - 118.0°C. (Found: C, 43.05; H, 3.41%; M (average) 257 ± 8 (by vapour phase osmometry); highest peak in mass spectrum, M^+, 224. $C_9H_7F_5O_2.\frac{1}{2}H_2O$ requires C, 43.07; H, 3.21%; M-1$\frac{1}{2}H_2O$, 224). The ^{19}F n.m.r. spectrum [$(CD_3)_2CO$] showed signals at 138.8 (F-4), 164.5 (F-3), 193.5 (F-1 and F-7) and 218.0 (F-2) p.p.m. upfield from external $CFCl_3$. [J(F-4, H-5) 14.0, J(F-1, H-9A and F-7, H-6A) 18.0, J(F-1, H-9B and F-7, H-6B) 5.0, J(F-1, F-2 and F-7, F-2) 5.0, Hz]. The ^1H n.m.r. spectrum [$(CD_3)_2CO$] showed τ6.13 (H-5), 7.40 (H-6B and H-9B) and 8.40 (H-6A and H-9A). [J(H-5, F-4) 14.0, J(H-6A, H-6B and H-9A, H-9B) 12.0 Hz]; τ4.58 [C-8$(OH)_2$ plus $\frac{1}{2}H_2O$] (half height line width: 120 Hz). V_{max} 3550, 3480, 3350 (3 OH frequencies), 2998 and 2980 (Aliphatic H), 1758 (CF=CF) and 1650 cm^{-1} (overtone of OH stretch).

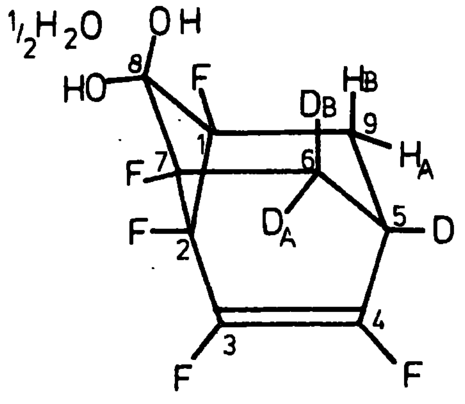


(104)

3.7 Static thermolysis of Pentafluorophenyl[2,3,3-$^2H_3$] prop-2-enyl ether (86)

The ether (86) (0.55g) was heated at 142-143°C for 11 days 16 hours. The mixture was separated as in the previous experiment into three components: volatile material (0.30g); solid on the cold finger (0.02g); and solid residue (0.23g). The solid residue was recrystallised from water to give 1,2,3,4,7-pentafluoro[5,6,6-$^2H_3$]tricyclo[3.3.1.0^{2,7}] non-3-ene-8,8-diol hemihydrate (108) (0.10g) m.p. 115-118°C. (Found:

highest peak in mass spectrum 227. $C_9H_4D_3F_5O_2.\frac{1}{2}H_2O - 1\frac{1}{2}H_2O$ requires M, 227). The ^{19}F n.m.r. spectrum $[(CD_3)_2CO]$ showed signals at 139.6 (F-4), 159.7 (F-3), 192.4 (F-1), 192.6 (F-7) and 217.0 (F-2) p.p.m. upfield from internal $CFCl_3$. [J(F-1, H-9A) 18.5 Hz]. The ^1H n.m.r. spectrum $[(CD_3)_2CO]$ showed τ7.28 (H-9B) and 8.32 (H-9A) [J(H-9A, H-9B) 12.0, J(H-9B, F-1) 4.5Hz]; τ3.62 and 3.84 $[C\text{-}8(OH)_2]$; τ6.8 ($\frac{1}{2}H_2O$ + 43% H-5). ν_{max} ca. 2950 (aliphatic C-H), ca. 2200 (aliphatic C-D), 1752 (CF=CF), 3530, 3380 and 3250 (OH stretching frequencies), 1648 cm^{-1} (overtone of OH stretching frequency).



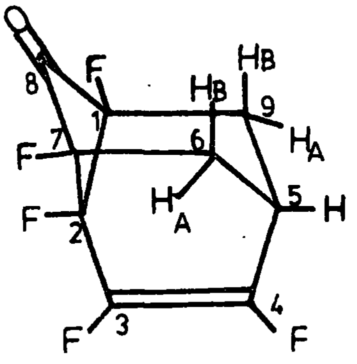
(108)

The ^1H n.m.r. spectrum of the volatile components showed the mixture contained pentafluorophenyl[2,3,3-$^2H_3$]allyl ether (86) (52.8%), pentafluorophenyl[1,1,2-$^2H_3$]allyl ether (112) (7.2%), 4[2,3,3-$^2H_3$]allyl-2,3,4,5,6-pentafluoro-2,5-cyclohexadienone (113) (35.2%) and 4[1,1,2-$^2H_3$] allyl-2,3,4,5,6-pentafluoro-2,5-cyclohexadienone (114) (4.8%).

3.8 1,2,3,4,7-Pentafluorotricyclo[3.3.1.0^{2,7}]non-3-en-8-one (115)

The diol hemihydrate (104) (0.10g) mixed with P_2O_5 (0.33g) in a sublimation apparatus, was connected to a high vacuum system (0.01-0.05 mm Hg). On gentle warming to 40°C, a white crystalline solid sublimed onto the cold finger. The apparatus was opened up in a moisture-free N_2 atmosphere to give the ketone (115) (0.09g), m.p. 84-86°C, which was analysed without delay. (Found: C, 48.0; H, 2.1%; M^+, 224. $C_9H_5F_5O$ requires

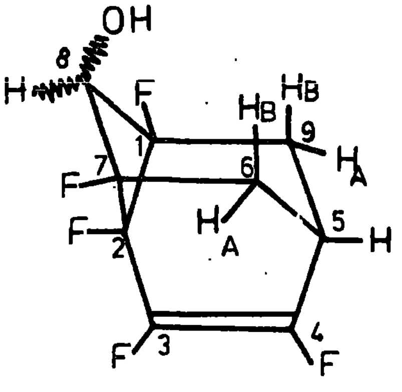
C, 48.2; H, 2.2%; M, 224). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed signals at 131.7 (F-4), 161.0 (F-3), 186.6 (F-7 and F-1) and 216.1 (F-2) p.p.m. upfield from external $CFCl_3$. [J(F-1, H-9A and F-7, H-6A) 15.0 Hz]. The ^1H n.m.r. spectrum ($CDCl_3$) showed τ6.63 (H-5), 6.93 (H-6B and H-9B) and 7.54 (H-6A and H-9A), [J(H-9A, F-1 and H-6A, F-7) 15.0, J(H-6B, H-6A and H-9B, H-9A) 14.0 Hz]; V_{max} 1840 (C=O) and 1760 cm^{-1} (CF=CF).



(115)

3.9 1,2,3,4,7-Pentafluorotricyclo[3.3.1.$0^{2,7}$]non-3-en-8-ol (116)

Diborane in tetrahydrofuran (10mls, 1M) was added to the ketone (115) (0.10g) under nitrogen at room temperature. The mixture was diluted and made alkaline with $NaHCO_3$, and the product was ether extracted. The extracts were dried ($MgSO_4$), filtered, and the solvent evaporated to give a non-3-en-8-ol (116) (0.09g), m.p. 140.5-141.5°C [from toluene-petroleum (bp. 80-100°C)]. (Found: C, 47.6; H, 3.5%; M^+, 226. $C_9H_7F_5O$ required C, 47.8; H, 3.1%; M, 226). The ^{19}F n.m.r. spectrum [$(CD_3)_2CO$] showed signals at 138.4 (F-4), 163.3 (F-3), 193.9 (F-1 and F-7) and 217.5 (F-2) p.p.m. upfield from external $CFCl_3$. [J(F-4, H-5) 16.0, J(F-1, H-9A and F-7, H-6A) 18.0, J(F-1, F-2 and F-7, F-2) 5.0, J(F-1, H-9B and F-7, H-6B) 5.0 Hz]. The ^1H n.m.r.

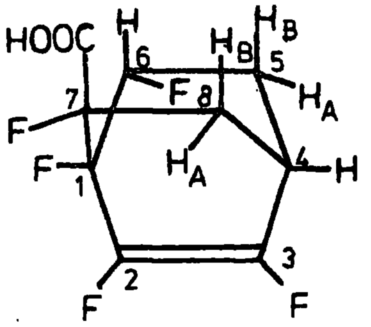


(116)

spectrum showed τ4.69 (OH), 5.80 (H-8), 7.02 (H-5), 7.73 (H-6B and H-9B) and 8.20 (H-6A and H-9A). [J(H-5, F-4) 16.0, J(H-6A, H-6B and H-9A, H-9B) 12.0 Hz]; V_{max} 1754 cm^{-1} (CF=CF).

3.10 1,2,3,6,7-Pentafluoro-7-carboxybicyclo[2.2.2]oct-2-ene (117)

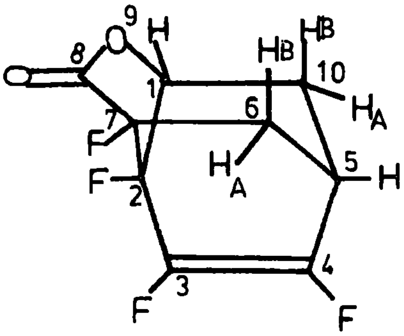
Potassium hydroxide solution (27 mls, 0.61N) was added to the diol-hemihydrate (104) (1.28g) and the mixture was boiled for 3 minutes. The solution was acidified with 2M HCl and the product was extracted with ether. Solvent was evaporated from the dried ($MgSO_4$) extracts to give the acid (117) (0.96g), m.p. 147-148°C (from benzene). (Found: C, 44.4; H, 3.2%; M^+, 242. $C_9H_7F_5O_2$ requires C, 44.4; H, 3.2%; M, 242). The ^{19}F n.m.r. spectrum [$(CD_3)_2CO$] showed signals at 141.4 (F-3), 155.8 (F-7), 158.6 (F-2), 184.4 (F-6) and 204.6 (F-1) p.p.m. upfield from external $CFCl_3$. [J(F-6, H-6) 56.0, J(F-6, F-7) 37.5, J(F-6, H-5A) 20.0, J(F-6, H-5B) 13.0, J(F-3, H-4) 16.0 Hz]. The ^1H n.m.r. spectrum [$(CD_3)_2CO$] showed τ4.62 (H-6), 6.87 (H-4) and τ7.18-8.85 (complex multiplet H-5A, H-5B, H-8A, H-8B); V_{max} 1750 (CF=CF), 1715 cm^{-1} (C=O).



(117)

3.11 2,3,4,7-Tetrafluoro-8-keto-9-oxytricyclo[3.4.1.0^{2,7}]dec-3-ene (119)

Potassium Hydroxide (3.35 ml, 0.296M; 9.9 x 10^{-4} mole) was added to the acid (117) (0.24g; 9.9 x 10^{-4} mole) and the solution was sealed in a 50ml tube under reduced pressure (0.001 mm Hg). The tube was heated at 160°C for 19 hours and then cooled to produce a white suspension. The solution was ether extracted, dried ($MgSO_4$) and the solvent evaporated. The residue was sublimed (40°C, 0.001 mm Hg) and recrystallised (toluene) to give 2,3,4,7-tetrafluoro-8-keto-9-oxytricyclo[3.4.1.$0^{2,7}$]dec-3-ene (119) (0.07g) m.p. 149-150°C. (Found: C, 48.4; H, 2.6%; M^+, 222. $C_9H_6F_4O_2$ requires C, 48.7; H, 2.7%; M, 222). The ^{19}F n.m.r. spectrum [$(CD_3)_2CO$] showed signals at 135.3 (F-4), 161.3 (F-3), 184.7 (F-7) and 205.1 (F-2) p.p.m. upfield from internal $CFCl_3$. [J(F-4, H-5) 16.0, J(F-7, H-6A) 27.0, Hz]. The ^1H n.m.r. spectrum [$(CD_3)_2CO$] showed τ4.75 (H-1) 6.68 (H-5) and 6.99 to 8.00 (complex multiplet incorporating H-6A, H-6B, H-10A, H-10B); ν_{max} 1808 (C=O), 1755 cm^{-1} (CF=CF).



(119)

Chapter 4

Flow pyrolysis and static thermolysis of Pentafluorophenyl 2-methyl-prop-2-enyl ether (121)

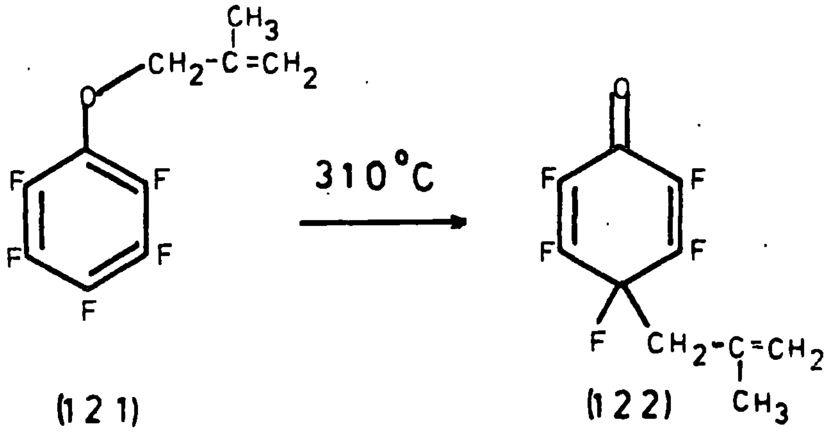
4.1 Introduction

It has been recognised that the rate of a Diels-Alder reaction with inverse electron demand is increased by electron donating substituents in the dienophile and by electron attracting substituents in the diene.[52] On this basis it was considered that the substitution of hydrogen atoms in the dienophile with methyl groups would enhance the yield of Diels-Alder adducts and related species.

4.2 Flow pyrolysis of Pentafluorophenyl 2-methyl-prop-2-enyl ether (121)

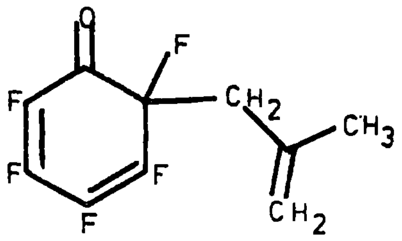
The ether (121) was prepared from pentafluorophenol and 2-methyl-prop-2-en-1 chloride in the presence of base. Mass spectroscopy, elemental analysis, infrared and n.m.r. spectroscopy conclusively showed that the ether was pentafluorophenyl 2-methylprop-2-enyl ether (121).

Flow pyrolysis at 310°. The ether (121) was distilled from a vessel at 75°C through a silica tube packed with silica fibre and heated to 310° into a trap cooled with liquid air connected to a high vacuum system. Two components were separated from the mixture by preparative t.l.c. on Kiesel gel (carbon tetrachloride as eluant). The faster moving component was shown by i.r. and n.m.r. spectroscopy to be ether (121), returned to the extent of 60%. The slower moving component was sublimed and recrystallised to give a material (122), produced in 17% yield. Mass spectroscopy and elemental analysis showed that the material was isomeric with the ether (121). The ^{19}F n.m.r. spectrum showed three absorptions at 137.6, 157.4 and 159.3 p.p.m. upfield from $CFCl_3$, present in the ratio 2:2:1. The resonance at 159.3 p.p.m. contained a triplet of triplets splitting pattern and was coupled to the two magnetically equivalent fluorine atoms at 137.6 p.p.m. and to the methylene group in the hydrocarbon side chain, and on this basis the compound was assigned the structure 4-[2-methylprop-2-enyl]-2,3,4,5,6-pentafluoro-2,5-cyclohexadienone (122).



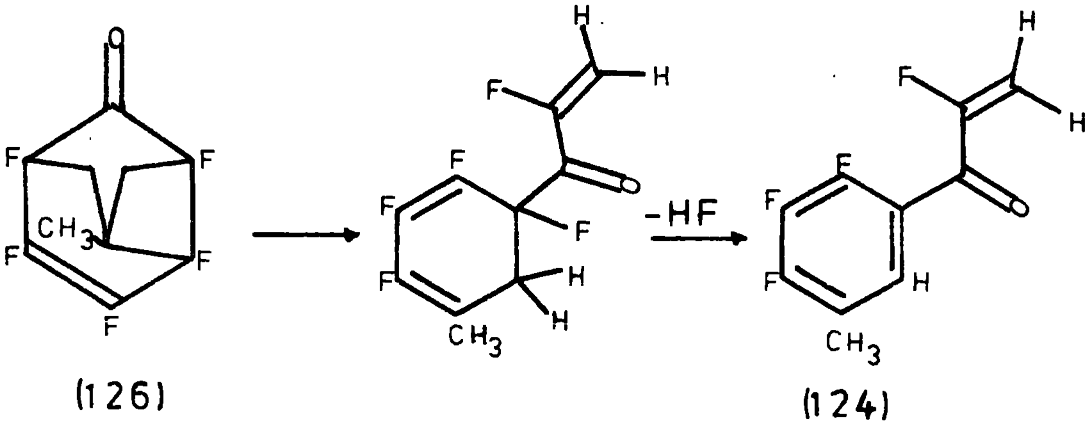
(121) (122)

The para-substituted dienone (122) was produced from the ether (121) by two consecutive [3,3] migrations, the first one being a Claisen rearrangement generating the ortho-substituted dienone (123), the second being a Cope rearrangement transforming (123) into (122). The predominance of (122) in the equilibrium mixture illustrated that (122) has a higher relative stability than (123), and parallels the behaviour found in the dienones (79) and (80) derived from pentafluorophenyl prop-2-enyl ether (78).



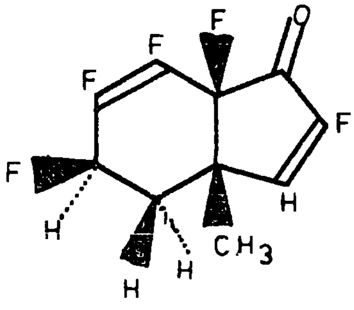
(123)

4.3 Flow pyrolysis at 420°. The ether (121) was distilled through a silica packed tube as before, heated to 420°. A yellow oil was separated by preparative t.l.c. (carbon tetrachloride as eluant) and distilled in vacuo to give a material (124), isolated in 27% yield. Elemental analysis and mass spectroscopy showed M, 218, equivalent to starting material (121) having lost HF. The ^{19}F n.m.r. showed four absorptions at 116.5, 132.8, 139.6 and 162.1 p.p.m. upfield from CFCl$_3$. The lowest resonance at 116.5 p.p.m., contained a large characteristic J(vinylic F, anti-H) coupling constant (45.0 Hz). Examination of the magnitude of the coupling constants derived from the remaining absorptions showed that the three remaining fluorines lay in adjacent positions on a benzene ring. The ^{1}H n.m.r. analysis indicated the presence of only one aromatic hydrogen in a meta position to two of the aromatic fluorines, by comparison of the coupling constants observed with those in the literature. Compound (124) was oxidised to give an acid, unambiguously identified as 2,3,4-trifluoro-5-methylbenzoic acid. On the basis of these observations (124) was assigned the structure 1-fluorovinyl 2,3,4-trifluoro-5-methyl-phenyl ketone, formed from the internal Diels-Alder adduct (126) analogous to the formation of the vinyl ketone (93) from the ether (78). The position of the methyl group in (124) further substantiates the proposed mechanism for vinylic ketone-formation (Scheme 27).



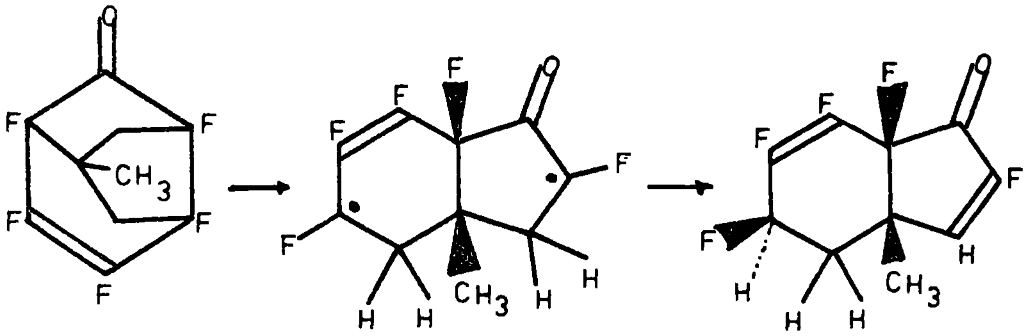
Scheme 27

The material remaining after the vinylic ketone (124) had been separated was distilled in vacuo to give pentafluorophenol, identified by i.r. spectroscopy, in 3% yield. The involatile residue was separated by chromatography on silica to give a solid (125) produced in a 22% yield. Mass spectroscopy and elemental analysis indicated that (125) was isomeric with the starting material (121) The i.r. spectrum showed characteristic absorptions at3080 (vinylic C-H), 2950 (aliphatic C-H), 1759 (C=O conjugated with C=C), 1739 (CF=CF) and 1652 cm^{-1} (CH=CF conjugated with C=O). Five resonances were present in the ^{19}F n.m.r. spectrum, at 139.7, 143.4, 153.8, 177.5 and 193.4 p.p.m. The absorption at 193.4 p.p.m. contained a characteristic J_{gem} HF coupling (52.0 Hz) and was also coupled to the absorption at 143.4 p.p.m. (24.0 Hz). There was also a prominent interaction between the resonances at 153.8 and 177.5 p.p.m. (29.0 Hz), whereas the absorption at 139.7 showed very little coupling and was assigned to be CF=CH in a position isolated from the remaining four fluorine atoms. The ^{1}H n.m.r. spectrum showed absorptions at τ 2.55 (CH=CF), 4.57 (containing J_{gem} HF), 7.12-7.85 (complex multiplet containing two hydrogen atoms) and 8.45 (CH_3). On the basis of these observations (125) was assigned the structure 2,5β,6,7,7aβ-pentafluoro-3-aβ-methyl-3aβ,4,5,7 -tetrahydroinden-1-one, the spectral properties of which were entirely consistent with the replacement of the hydrogen in the 3aβ position in (81) by a CH_3 group. By analogy with (81), the formation of (125) is also consistent with the intermediacy of the internal Diels-Alder adduct (127) (Scheme 28).



(125)

Thus the intermediacy of the two Diels-Alder adducts (126) and (127), derived from the ortho-substituted dienone (123) has to be invoked to account for the formation of the vinylic ketone (124) and inden-1-one (125) respectively.

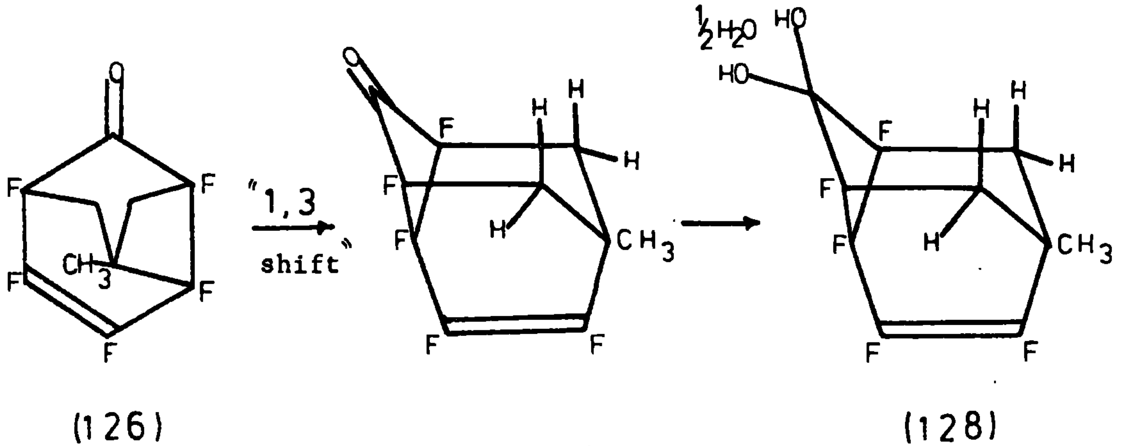


(127) (125)

Scheme 28

4.4 Static Thermolysis of Pentafluorophenyl 2-methylprop-2-enyl ether (121)

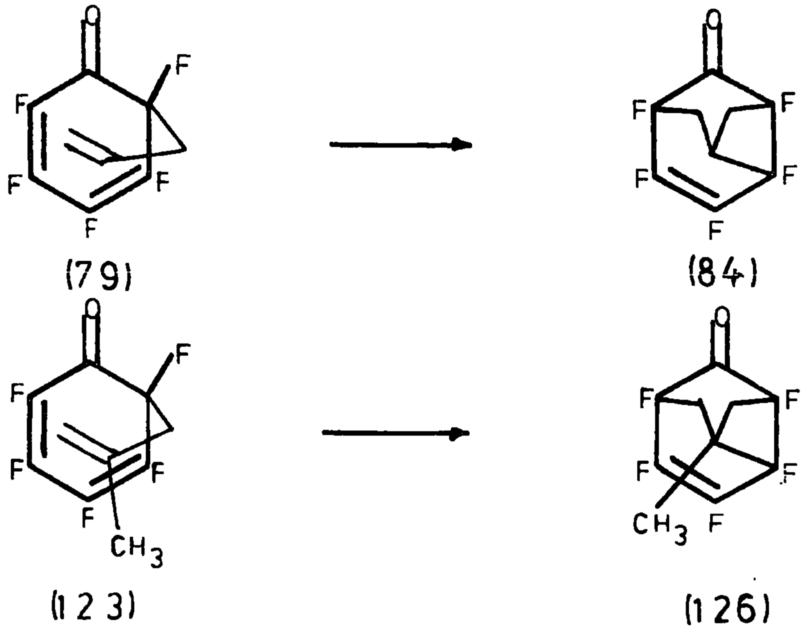
The ether (121) was heated at 160°C for 15 days in a 10 litre bulb. The product was washed from the bulb with diethyl ether and the volatile components were removed by prolonged suction with a high vaccum system (0.001mm Hg). A small quantity of boiling water was added to the residue, the aqueous layer was separated and allowed to cool, and a product (128) (4% yield) crystallised from solution. The i.r. spectrum indicated that (128) was probably the methyl analogue of the hemi-hydrate (104). The ^{19}F n.m.r. spectrum showed four absorptions at 155.7, 163.4, 192.4 and 215.6 p.p.m. in the ratio 1:1:2:1 respectively. The resonance at 192.4 p.p.m. contained two magnetically equivalent fluorine atoms which showed that the molecule had a plane of symmetry and had coupling constants analogous to those found in the hemi-hydrate (104). The ^{1}H n.m.r. spectrum showed absorptions at τ 3.80, 6.63, 7.50, 8.35 and 8.62, in the ratio 2:1:2:2:3. On the basis of the spectroscopic observations (128) was assigned the structure 1,2,3,4,7-pentafluoro-5-methyltricyclo $[3.3.1.0^{2,7}]$non-3-ene-8,8-diol hemi-hydrate, formed from the Diels-Alder adduct (126) (Scheme 29).



Scheme 29

The mechanism is substantiated by the position of the methyl at C-5 on the ring skeleton. Elemental anslysis gave results consistent with a hemi-hydrate structure.

Comparing the conditions used in the production of the hemi-hydrates (104) and (128), the high temperature requirement and low yield in the latter could be explained in part by the relative ease of formation of the corresponding Diels-Alder adducts (84) and (126).



The inductive effect associated with a methyl group was expected to enrich the electron density of the dienophile and thus increase the yield of the Diels-Alder adduct. However, a low yield was observed and clearly the steric interactions between the methyl group and the fluorine atoms in the ring must inhibit the approach of the dienophile towards the diene.

Chapter 4 Experimental

4.5 Pentafluorophenyl 2-methyl-prop-2-enyl ether (121)

A mixture of pentafluorophenol (50g), 2-methyl-2-propen-1-chloride (37g), and anhydrous potassium carbonate (50g) in dry acetone (150 mls.) was heated under reflux for 168 hours and filtered through anhydrous $MgSO_4$. The filtrate was distilled in vacuo to give the pentafluorophenyl 2-methyl-prop-2-enyl ether (51.2g) b.p. 76° at 14 mm Hg. (Found: C, 50.1; H, 3.1%; M^+, 238. $C_{10}H_7F_5O$ requires C, 50.4; H, 2.9%; M, 238). The ^{19}F n.m.r. spectrum $[(CD_3)_2CO]$ showed signals at 159.7 and 167.8 p.p.m. upfield from external $CFCl_3$ in the ratio of 2:3 respectively. The ^1H n.m.r. spectrum $[(CD_3)_2CO]$ showed τ4.98 (H syn + H anti), 5.45 (CH_2), 8.20 (CH_3).

4.6 Flow pyrolysis of Pentafluorophenyl 2-methyl-prop-2-enyl ether (121) at 310°C

The ether (121) (3.0g) was distilled over 6h from a vessel at 75°C through a silica tube (20 cm x 1.5 cm diam.) packed with silica fibre and heated to 310°C, into a trap cooled with liquid air connected to a high vacuum system (0.05-0.1 mm Hg). Two components were separated from the complex product by preparative t.l.c. on kieselgel GF_{254} (carbon tetrachloride as eluant). The fast moving component was the ether (121) (1.9g). Sublimation of the slower moving component at 40°C and 0.05 mm Hg and recrystallisation from petroleum (b.p. 30-40°C) gave 4[2-methyl-prop-2-enyl] 2,3,4,5,6-pentafluoro-2,5-cyclohexadienone (.5g) m.p. 32.5-32.8°C. (Found: C, 50.7; H, 2.5%; M^+, 238. $C_{10}H_7F_5O$ requires C, 50.4; H, 2.9%; M, 238). The ^{19}F n.m.r. spectrum $[(CD_3)_2CO]$ showed signals at 137.6 (F-3 and F-5), 157.4 (F-2 and F-6) and 159.3 (F-4) p.p.m. upfield from external $CFCl_3$. [J(F-4, F-3) 31.0, J(F-4, F-5) 31.0, J(F-4, CH_2) 11.0 Hz]. The ^1H n.m.r. spectrum $[(CD_3)_2CO]$ showed signals at τ5.02 (H-anti), 5.14 (H-syn), 6.93 (CH_2) and 8.35 (CH_3). [J(CH_2, F-4) 11 Hz].

4.7 Flow pyrolysis of Pentafluorophenyl 2-methyl-prop-2-enyl ether (121) at 420°C

The ether (121) (4.8g) was distilled over 8 hours from a vessel at 75°C through a silica tube (20 cm x 1.5 cm diam.) packed with silica fibre and heated to 420°C, into a trap cooled with liquid air connected to a high vacuum system (0.05 - 0.1 mm Hg). A yellow oil, separated from the complex product by preparative t.l.c. on kieselgel GF_{254} (carbon tetrachloride as eluant), was distilled in vacuo to give 1-fluoro-vinyl 2,3,4-trifluoro-5-methyl-phenyl ketone (124) (1.3g) b.p. 33°C at .001 mm Hg. (Found: C, 55.3; H, 3.0%; M^+, 218. $C_{10}H_6F_4O$ requires C, 55.1; H, 2.8%; M, 218). The ^{19}F n.m.r. spectrum $[(CD_3)_2CO]$ showed signals at 116.5 (vinylic F), 132.8 (F-4), 139.6 (F-2) and 162.1 (F-3) p.p.m. upfield from external $CFCl_3$. [J vinylic F, anti-H) 45.0, J (vinylic F, syn-H) 13.0, J(vinylic F, F-2) 13.0, J(F-2, F-3) 19.0, J(F-2, H-6) 7.0, J(F-3, H-6) 2.5, J(F-4, H-6) 7.0, J(F-3, F-4) 19.0 Hz]. The ^1H n.m.r. spectrum $[(CD_3)_2CO]$ showed τ, 2.84 (H), 4.54 (syn-H), 4.57 (anti-H), and 7.84 (CH_3); V_{max} 1690 cm^{-1} (C=O).

The vessel containing the material (3.2g) remaining after the ketone (124) had been separated was connected to a trap, cooled with liquid air, and the system evacuated (0.05-0.1 mm Hg). The volatile material which collected in the trap was distilled in vacuo to give pentafluorophenol (0.2g) (b.p. 41-42°C 4 mm Hg) identified by i.r. spectroscopy. The involatile residue (2.9g) remaining was separated by chromatography on silica (40 cm x 3.5 cm diam.) (chloroform as eluant) to give 2,5β,6,7,7aβ-pentafluoro-3aβ methyl-3aβ,4,5,7a-tetrahydroinden-1-one (125) (1.07g) m.p. 77-78°C [from toluene-petroleum (b.p. 80-100°C)]. (Found: C, 50.2; H, 3.2%; M^+, 238. $C_{10}H_7F_5O$ requires, C, 50.4; H, 3.0%; M, 238). The ^{19}F n.m.r. spectrum $[(CD_3)_2CO]$ showed signals at 139.7 (F-2), 143.4 (F-6), 153.8 (F-7), 177.5 (F-7a) and 193.4 (F-5) p.p.m. upfield from external $CFCl_3$. [J(F-5, H-5) 52.0, J(F-5, F-6) 24.0, J(F-7, F-7a) 29.0, J(F-7a, CH_3) 6.0 Hz]. The ^1H n.m.r. [$(CD_3)_2CO$] showed τ, 2.55 (H-3), 4.57 (H-5α), 7.12-7.85 (complex multiplet CH_2) and 8.45 (CH_3). [J(H-5, F-5) 52.0, J(CH_3, F-7a) 6.0 Hz]; V_{max} 3080 (vinylic C-H), 2950 (aliphatic C-H), 1759 (C=O conjugated with C=C), 1739 (CF=CF) and 1652 cm^{-1} (CH=CF conjugated with C=O).

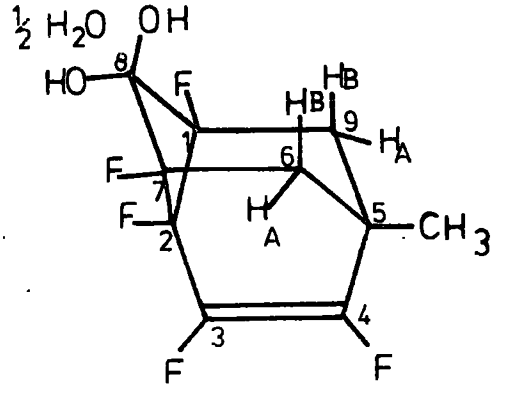
4.8 2,3,4-Trifluoro-5-methylbenzoic Acid

The crude vinyl ketone (124) (1.3g) was heated under reflux with nitric acid (50 cm^3; 70% w/w) for 1hour. The mixture was diluted with water, ether extracted and the dried ($MgSO_4$) extracts were evaporated. Sublimation of the residue at 130°C and 0.05 mm Hg and recrystallisation from toluene-petroleum (b.p. 80-100°C) gave 2,3,4-trifluoro-5-methylbenzoic acid (.29g) m.p. 135-136°C. (Found: C, 50.2; H, 2.8%; M^+, 190. $C_8H_5F_3O_2$ requires C, 50.5; H, 2.6%; M, 190). The ^{19}F n.m.r. spectrum [$(CD_3)_2CO$] showed signals at 132.4 (F-4), 136.2 (F-2), 162.6 (F-3) upfield from external $CFCl_3$. [J(F-2, F-3) 19.0, J(F-2, F-4) 12.0, J(F-3, F-4) 19.0, J(F-3, H-6) 3.0, J(F-2, H-6) 8.0, J(F-4, H-6) 8.0, J(F-4, CH_3) 2.0 Hz]. The ^1H n.m.r. spectrum [$(CD_3)_2CO$] showed τ 2.45 (H-6) and 7.83 (CH_3) (external Me_4Si standard); V_{max} 1700 cm^{-1} (C=O)

4.9 Static Thermolysis of Pentafluorophenyl 2-methyl-prop-2-enyl ether (121)

Static thermolysis of pentafluorophenyl 2-methyl-prop-2-enyl ether (121) (2.48g) for 15 days at 160°C produced a complex mixture. 1,2,3,4,7-Pentafluoro-5-methyltricyclo[3.3.1.$0^{2,7}$]non-3-ene-8,8-diol hemihydrate (128) (0.10g), m.p. 112-113°C (recrystallised from water), was separated using the same technique used in the isolation of (104). (Found: C, 45.4; H, 4.16%; Highest peak in mass spectrum M^+, 238. $C_{10}H_9F_5O_2.\frac{1}{2}H_2O$ requires

C, 45.29; H, 4.18%; M-1½H_2O, 238). The ^{19}F n.m.r. spectrum [$(CD_3)_2CO$] showed signals at 155.7 (F-4), 163.4 (F-3), 192.4 (F-1 and F-7) and 215.6 (F-2) p.p.m. upfield from external $CFCl_3$. [J(F-1, H-9A, and F-7, H-6A) 18.0, J(F-1, F-2 and F-7, F-2) 5.0, J(F-2, F-4) 8.0 Hz]. The ^1H n.m.r. spectrum [$(CD_3)_2CO$] showed τ 3.80 [C-8$(OH)_2$], 6.63 (½H_2O), 7.50 (H-6B and H-9B), 8.35 (H-6A and H-9A) 8.62 (CH_3-5) [J(H-6A, H-6B and H-9A, H-9B) 12.0 Hz]; V_{max} 3580, 3420, 3190 (3 OH Frequencies), 3000 and 2940 (Aliphatic H), 1748 (CF=CF) and 1641 cm^{-1} (overtone of OH stretch).



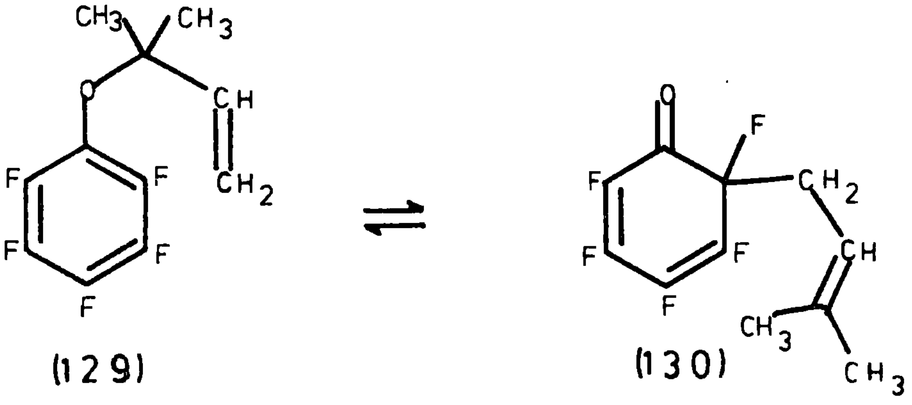
(128)

Chapter 5

Reactions of Pentafluorophenyl 2-methylbut-3-en-2-yl ether (129)

5.1 Introduction

The Claisen rearrangement product of the ether (129) would be the ortho-substituted dienone (130). It was envisaged that the inductive effect of two methyl groups would counteract any associated steric interactions and that Diels-Alder adduct formation in (130) would be favoured.[52]



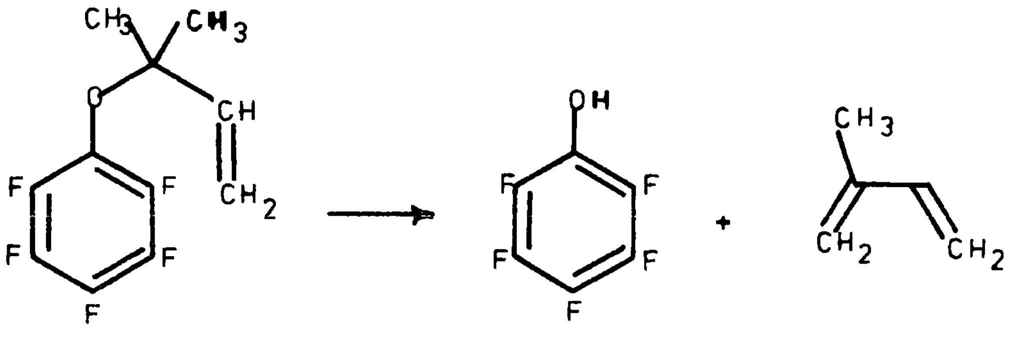
(129) (130)

5.2 Thermolysis of Pentafluorophenyl 2-methylbut-3-en-2-yl ether (129)

The ether (129) was prepared from 2-methylbut-3-en-2-ol and hexafluorobenzene and separated from the mixture by distillation in vacuo. Consistent mass spectrometry and elemental analysis data could not be obtained but n.m.r. spectroscopy showed that the product had a structure consistent with (129). The ^{19}F n.m.r. showed three absorptions at 153.4, 165.7 and 167.8 p.p.m. in the ratio 2:1:2. The absorption at 165.7 p.p.m. was split into a triplet of triplets pattern (containing 20.0 and 3.0 Hz coupling constants), whereas the major structure of the resonance at 167.8 was a triplet (constant 20.0 Hz). The ^{1}H n.m.r. spectrum showed τ 3.80, 4.73, 4.80 and 8.43 in the ratio 1:1:1:6. The absorptions at 4.73 and 4.80 were from the H-3 anti and H-3 syn hydrogen atoms respectively, with major couplings to H-2 [J(H-2, H-3 $_{anti}$) 18.0, J(H-2, H-3 $_{syn}$) 12.0 Hz].

In an attempt to obtain consistent elemental analysis data the ether (129) was distilled using a concentric tube fractionating column. However, a pure sample of (129) was not obtained, the ether (129) decomposing to give a mixture which was separated into three components: a gas, trapped by liquid air; pentafluorophenol, identified by i.r. spectroscopy (26% yield); and a higher boiling residue.

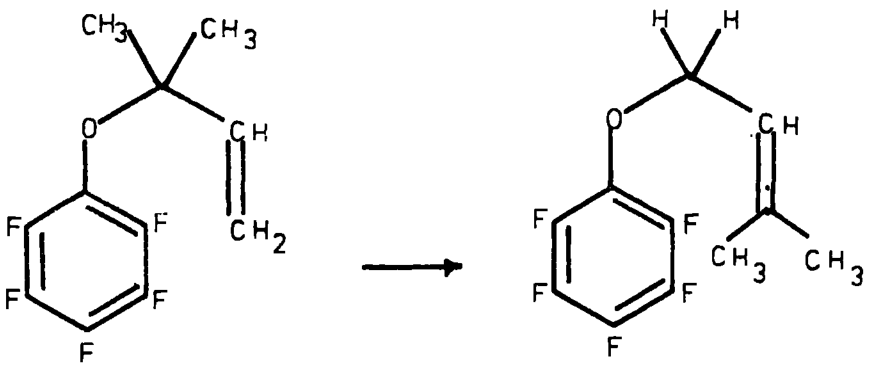
The gas was analysed by mass spectroscopy and was found to have M, 132. This data is consistent with a dimer of 2-methyl-1,3-butadiene (131) produced in the phenolic cleavage of (129) (Scheme 30).



(129) (131)

Scheme 30

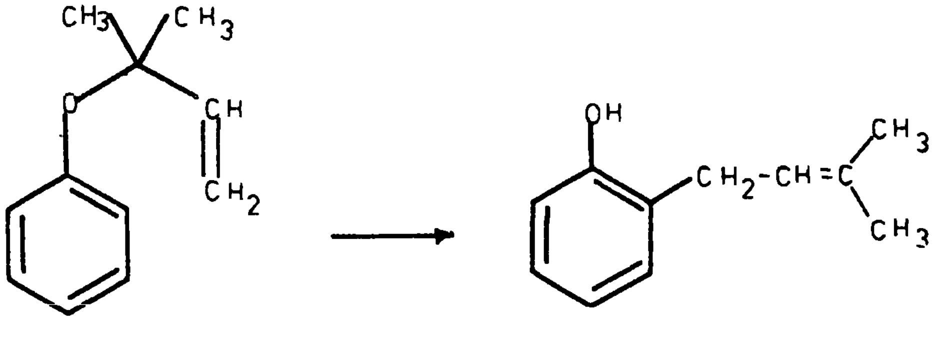
The higher boiling residue was separated by preparative g.l.c. into two components: the starting material (129) (44% yield) and a product (132) (20% yield) which was found to be isomeric with the ether (129). Compound (132) was shown to be very similar in structure to (129) by a comparison of their respective i.r. spectra. The ^{19}F n.m.r. spectrum contained two resonances at 158.4 and 167.0 p.p.m., present in the ratio 2:3 respectively. The ^{1}H n.m.r. spectrum showed τ 4.72, 5.48, 8.43 and 8.48 in the ratio 1:2:3:3, and it was clear that the methyl groups were no longer equivalent. On the basis of the spectroscopic data the product (132) was assigned the structure pentafluorophenyl 3-methylbut-2-en-1-yl ether.



(129) (132)

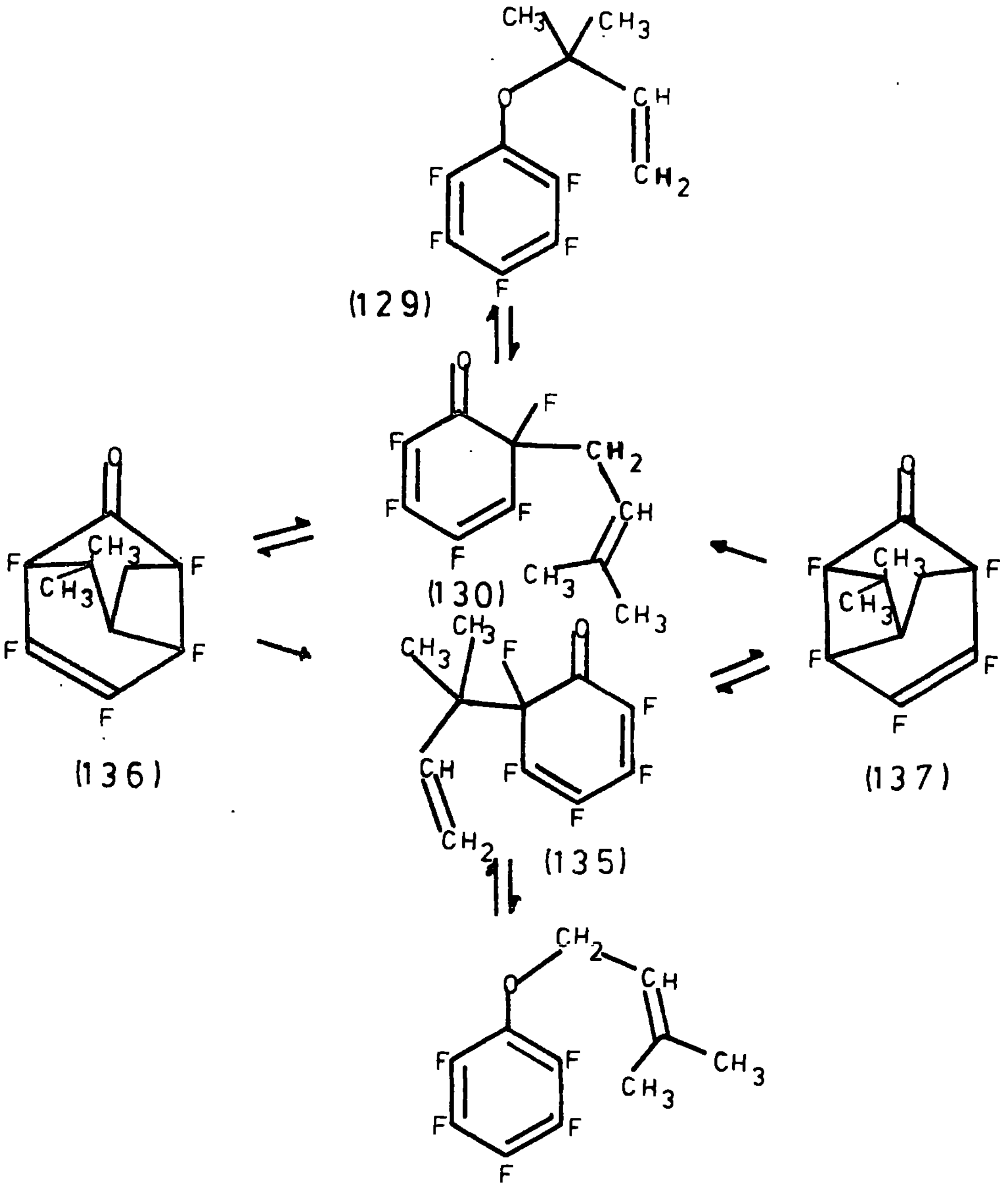
This structural assignment was confirmed by an alternative synthesis from 3-methylbut-2-en-1-ol and hexafluorobenzene.

The ether (129) was heated in refluxing toluene for three days, and g.l.c analysis showed (132) to be the only volatile component present. When (132) was subjected to identical conditions the ether remained unchanged. The slow transformation of (129) into (132) at room temperature was followed by ^{1}H n.m.r. spectroscopy. The behaviour of (129) is in complete contrast to the hydrocarbon analogue (133) which rearranged in refluxing NN-diethyl aniline to the ortho-substituted phenol (134).^{53}



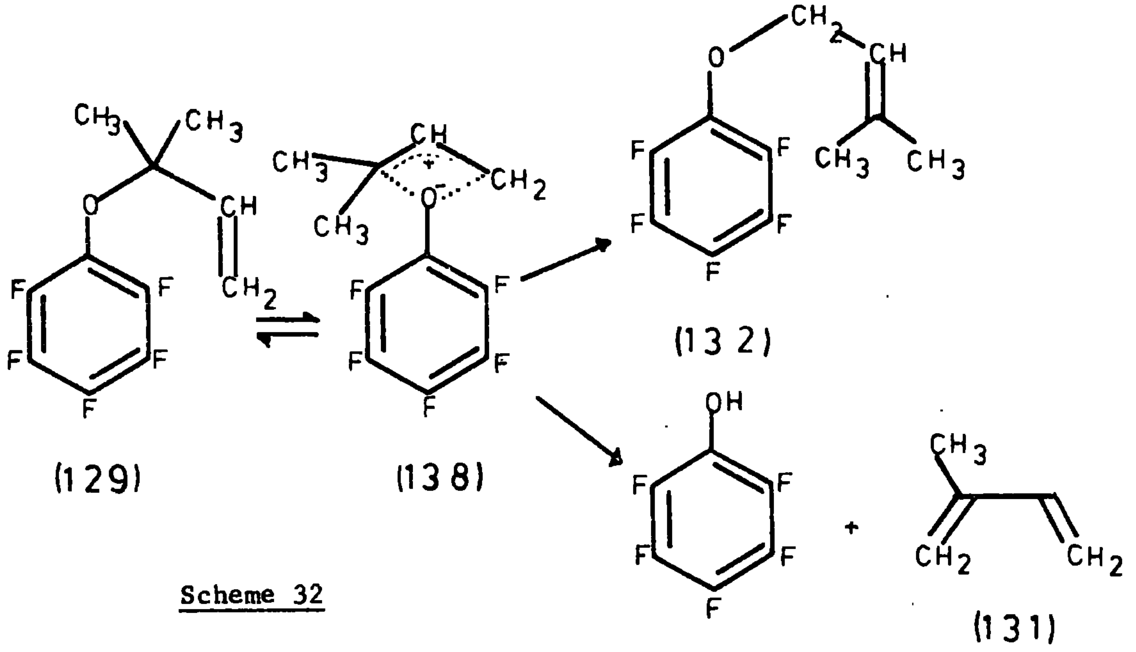
(133) (134)

The transformation of (129) into (132) could proceed by a series of 3,3 migrations and an ortho-ortho′ rearrangement (Scheme 31). However, the reaction proceeds rapidly at temperatures low enough to preclude 3,3 migrations. The inability to isolate dienones (130) and (135), and the absence of high field absorptions when the reaction was followed by ^{19}F n.m.r. analysis exclude this mechanism (Scheme 31).

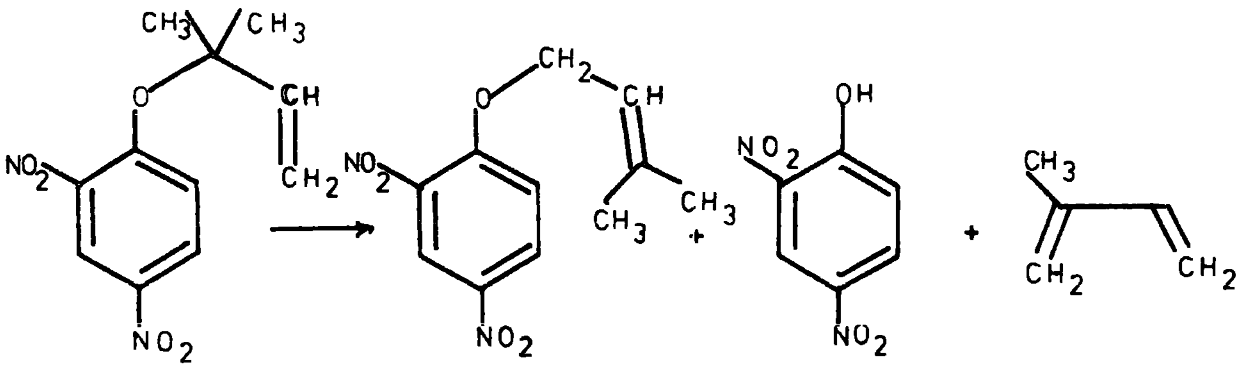


Scheme 31

An ionic mechanism could explain both the transformation to (132) and phenolic cleavage (Scheme 32). The intermediacy of ionic complexes analogous to (138) has been well documented.[54,55,56] It was reported recently that the solvolysis of 2,4-dinitrophenyl 2-methylbut-3-en-2-yl ether (139) in acetic acid produced 2,4-dinitrophenyl 3-methylbut-2-en-1-yl ether (140), 2,4-dinitrophenol and 2-methyl-1,3-butadiene.[57] The


(129) (138) (132) (131)

Scheme 32


(139) (140)

ethers (129) and (139) are similar in that they both have in the leaving group electron attracting groups at the 2- and 4-positions capable of stabilising the charge which develops on the oxygen atom.

Due to the instability of (129), the proposed formation of Diels-Alder adducts from the ortho-substituted dienone (130) could not be investigated.

5.3 Pentafluorophenyl 2-methylbut-3-en-2-yl ether (129)

2-Methyl-3-buten-2-ol (4 ml) in dry tetrahydrofuran (30 ml) was treated with sodium hydride (1.6g). Hexafluorobenzene (12.7g) in dry tetrahydrofuran (20 ml) was added to the mixture over 20 min. The solution was heated under reflux for 3 min., diluted with ether and washed with water. The organic phase was dried ($MgSO_4$), the solvent evaporated and the residue distilled in vacuo to give pentafluorophenyl 2-methylbut-3-en-2-yl ether (129) (8.48g), b.p. 82-83°C at 11 mm Hg. Consistent mass spectroscopy and elemental analysis data was impossible to obtain. The ^{19}F n.m.r. spectrum (neat) showed signals at 153.4 (F ortho) 165.7 (F para) and 167.8 (F meta) ppm upfield from external $CFCl_3$ [J(F ortho, F meta) 20.0, J(F meta, F para) 20.0, J(F ortho, F para) 3.0 Hz]. The ^1H n.m.r. spectrum (neat) showed τ 3.80 (H-2), 4.73 (H-3 anti), 4.80 (H-3 syn) and 8.43 (2 x CH_3). [J(H-2, H-3 anti) 18.0, J(H-2, H-3 syn) 12.0, J(H-3 anti, H-3 syn) 3.0 Hz].

5.4 Pentafluorophenyl 3-methylbut-2-en-1-yl ether (132)

3-Methyl-2-buten-1-ol (0.5g) in dry tetrahydrofuran (30 ml) was treated with sodium hydride (1.6g). Hexafluorobenzene (10.2g) in dry tetrahydrofuran (50 ml) was added to the mixture over 30 min. The solution was heated under reflux for 3 min., diluted with ether and washed with water. The organic layer was dried ($MgSO_4$), the solvent evaporated and the residue distilled in vacuo to give pentafluorophenyl 3-methylbut-2-en-1-yl ether (132) (5.9g), b.p. 81-82°C at 8 mm Hg. (Found: C, 52.2; H, 3.8%; M^+, 252. $C_{11}H_9F_5O$ requires C, 52.4; H, 3.6%; M, 252). The ^{19}F n.m.r. spectrum (neat liquid) showed signals at 158.4 and 167.0 ppm upfield from external $CFCl_3$ in the ratio of 2:3 respectively. The ^1H n.m.r. spectrum (neat) showed τ 4.72 (H-2), 5.48 (CH_2), 8.43 (CH_3) and 8.48 (CH_3) [J(H-2, CH_2) 7.5 Hz].

Reactions of Pentafluorophenyl 2-methylbut-3-en-2-yl ether (129)

(a) The ether (129) (2.5g) was heated under reflux, 70°C at reduced pressure (8 mm Hg), for 8 hr. A gas which evolved was collected in a trap surrounded by liquid air and was shown to be 2-methyl 1,3 butadiene (mass spect: 132, Dimer of 66. C_5H_8 requires 66). The complex mixture was distilled in vacuo to give pentafluorophenyl b.p. 41°C at 7 mm Hg pressure. The higher boiling residue was separated using preparative g.l.c. (silicone gum rubber at 140°C) into two components: the ether (129) (1.1g) and pentafluorophenyl 3-methylbut-2-en-1-yl ether (132) (0.5g).

(b) The ether (129) (0.1g) in toluene (0.5 mls) was heated under reflux (110°C) for 3 days to give pentafluorophenyl 3-methylbut-2-en-1-yl ether (132) as the exclusive volatile product.

When pentafluorophenyl 3-methylbut-2-en-1-yl ether (132) was subjected to the conditions above, g.l.c. analysis showed that it remained unchanged.

APPENDIX A

Apparatus and Instruments

Vacuum System

Volatile compounds were handled in a conventional vacuum system incorporating a mercury diffusion pump and a rotary oil pump.

Mass Spectra were measured with an A.E.I. spectrometer at an ionisation beam energy of 70 eV.

Combined g.l.c./mass spectra - V.G. micromass 12B coupled to a Pye 104 gas chromatograph.

Infrared Spectra were recorded with either a Perkin-Elmer 457 or 577 Grating Infrared Spectrophotometer.

Ultraviolet Spectra were recorded with a Unican SP800 spectrophotometer.

N.M.R. Spectra were measured with either a Bruker Spectrospin HX 90E High Resolution N.M.R. Spectrometer (operating at 84.67 MHz for ^{19}F and 90.0 MHz for ^{1}H spectra), or a Varian A56/60 spectrometer (operating at 56.40 MHz for ^{19}F and 60.0 MHz ^{1}H).

Analytical Gas Liquid Chromatography (g.l.c.)

The following instruments were used:-

a) Perkin-Elmer 452 gas chromatograph, using hydrogen as carrier gas, with a hot wire detector.

b) Griffin Gas Density Balance (GDB) chromatograph, using nitrogen as carrier gas, with a gas density balance detector.

c) Pye 104 Chromatograph, using nitrogen as carrier gas, with a flame ionisation detector.

Columns used were:-

a) 452 Column A; 2.2m x 7mm diameter, with a stationary phase of di-iso-decyl phthalate/Celite 1:2.

b) GDB Column A; 2.0m x 5mm diameter, with a stationary phase of di-iso-decyl phthalate/Celite 1:2.

c) Pye 104 Column O; 2.0m x 5mm diameter, with a stationary phase of silicone oil (30%)/Chromosorb P.

Preparative g.l.c. A varian autoprep was used with di-iso-decyl phthalate and silicone oil (30%)/Chromosorb P columns were used [H_2 carrier gas, 7m x 5mm diameter, hot wire detector].

Carbon and Hydrogen Analysis were carried out with a Perkin-Elmer 240 CHN Analyser.

Vapour phase osmometry molecular weight determinations were carried out on a Perkin Elmer Model 115 molecular weight apparatus using chloroform as the solvent and benzil as the standard.

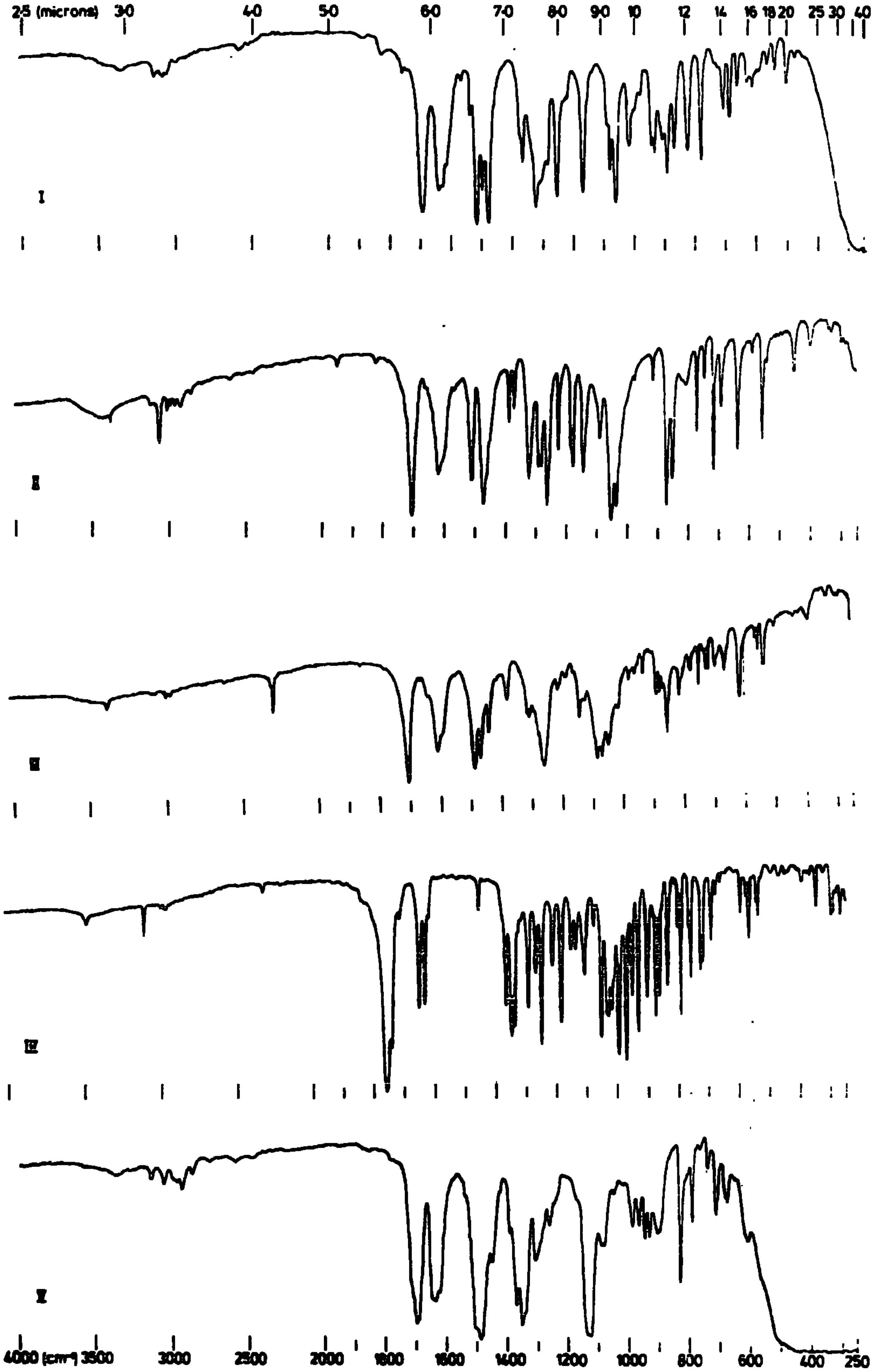
APPENDIX B

Infra-red Spectra

The spectra were obtained using KBr cells and were run as liquids, unless denoted by (D) which designates that the spectrum was obtained from a KBr disc. [The exception being compound (XX) whose spectrum was obtained as a Nujol mull].

Compound Number	Name of Compound
I	1-Fluorovinyl 2,3,4-trifluorophenyl Ketone
II	1-Fluoroethyl 2,3,4-trifluorophenyl Ketone (D)
III	1-Fluoro [1,2,2,2-$^{2}H_{4}$] ethyl 2,3,4-trifluoro [5-$^{2}H_{1}$] phenyl Ketone and 1-fluoro [1,2-$^{2}H_{2}$] ethyl 2,3,4-trifluoro [5,6-$^{2}H_{2}$] phenyl Ketone (D)
IV	[3,3 aβ, 5α-$^{2}H_{3}$]-2,5β,6,7,7aβ-pentafluoro-3a,4,5,7a-tetrahydroinden-1-one and [3aβ,4,4-$^{2}H_{3}$]-2,5β,6,7,7aβ-pentafluoro-3a,4,5,7a-tetrahydroinden-1-one (D)
V	1-Fluorovinyl 2,3,4-trifluoro-5-methyl-phenyl Ketone
VI	2,3,4-Trifluorobenzoic Acid (D)
VII	2,3,4-Trifluoro-5-methyl benzoic Acid (D)
VIII	Pentafluorophenyl 2-methyl-prop-2-enyl ether
IX	Pentafluorophenyl 3-methyl-but-2-en-1-yl ether
X	Pentafluorophenyl 2-methyl-but-3-en-2-yl ether
XI	4[2-methyl-prop-2-enyl] 2,3,4,5,6-pentafluoro-2,5-cyclohexadienone

XII	1,2,3,4,7-Pentafluorotricyclo $[3.3.1.0^{2,7}]$ non-3-ene-8,8-diol hemihydrate (D)
XIII	1,2,3,4,7-Pentafluoro $[5,6,6-{}^{2}H_{3}]$ tricyclo $[3.3.1.0^{2,7}]$ non-3-ene-8,8-diol hemihydrate (D)
XIV	1,2,3,4,7-Pentafluoro-5 methyltricyclo $[3.3.1.0^{2,7}]$ non-3-ene-8,8-diol hemihydrate (D)
XV	2,3,4,5,7-Pentafluorotricyclo $[3.3.1.0^{2,7}]$ non-3-en-6-one (D)
XVI	2,5β,6,7,7aβ-Pentafluoro-3aβ methyl-3aβ,4,5,7a-tetrahydroinden-1-one (D)
XVII	1,2,3,4,7-Pentafluorotricyclo $[3.3.1.0^{2,7}]$ non-3-en-8-ol (D)
XVIII	1,2,3,6,7-Pentafluoro - 7-carboxytricyclo [2.2.2] oct-2-ene (D)
XIX	2,3,4,7-Tetrafluoro-8-keto-9-oxytricyclo $[3.4.1.0^{2,7}]$ dec-3-ene (D)
XX	1,2,3,4,7-Pentafluorotricyclo $[3.3.1.0^{2,7}]$ non-3-en-8-one (D)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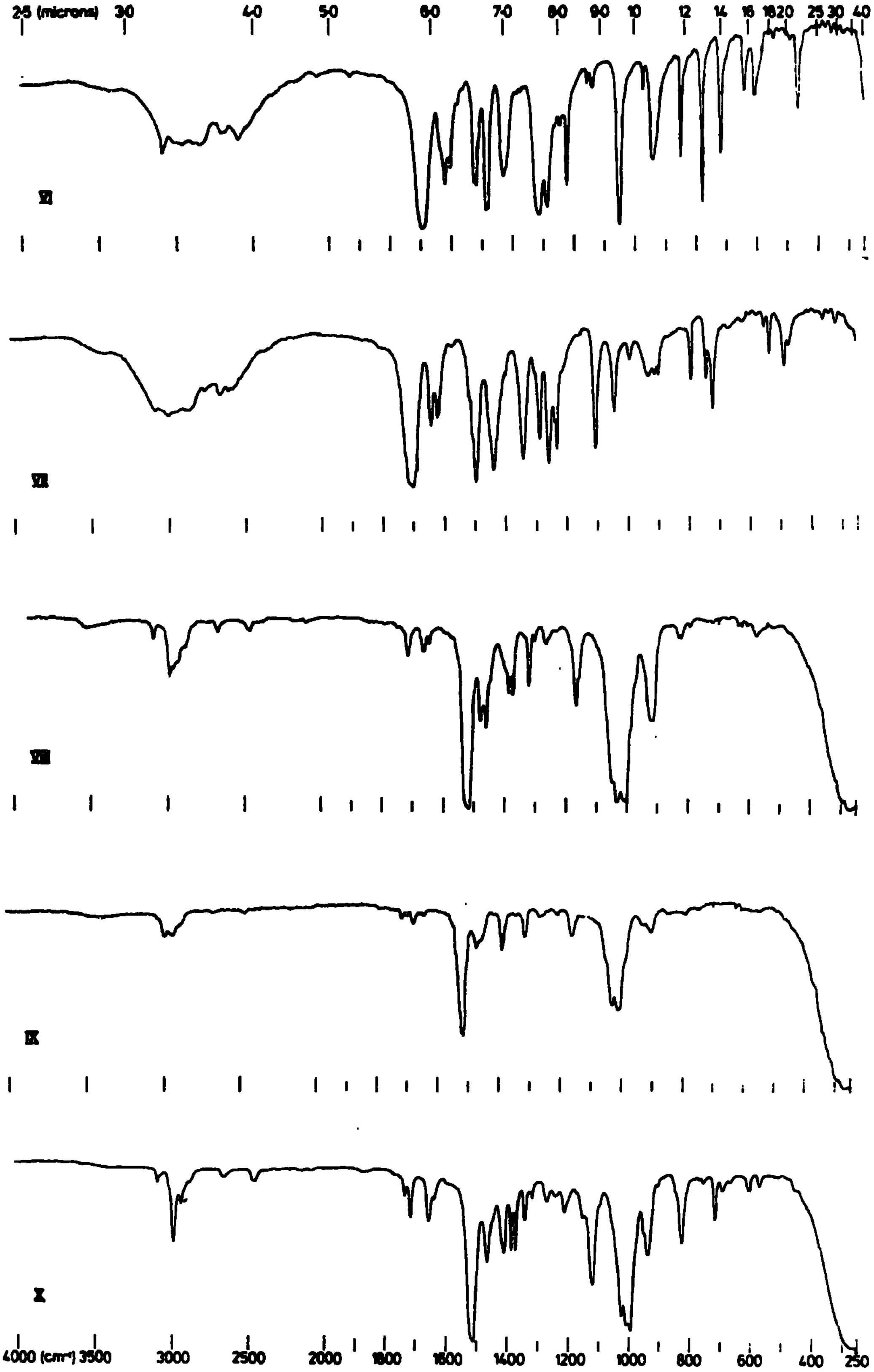
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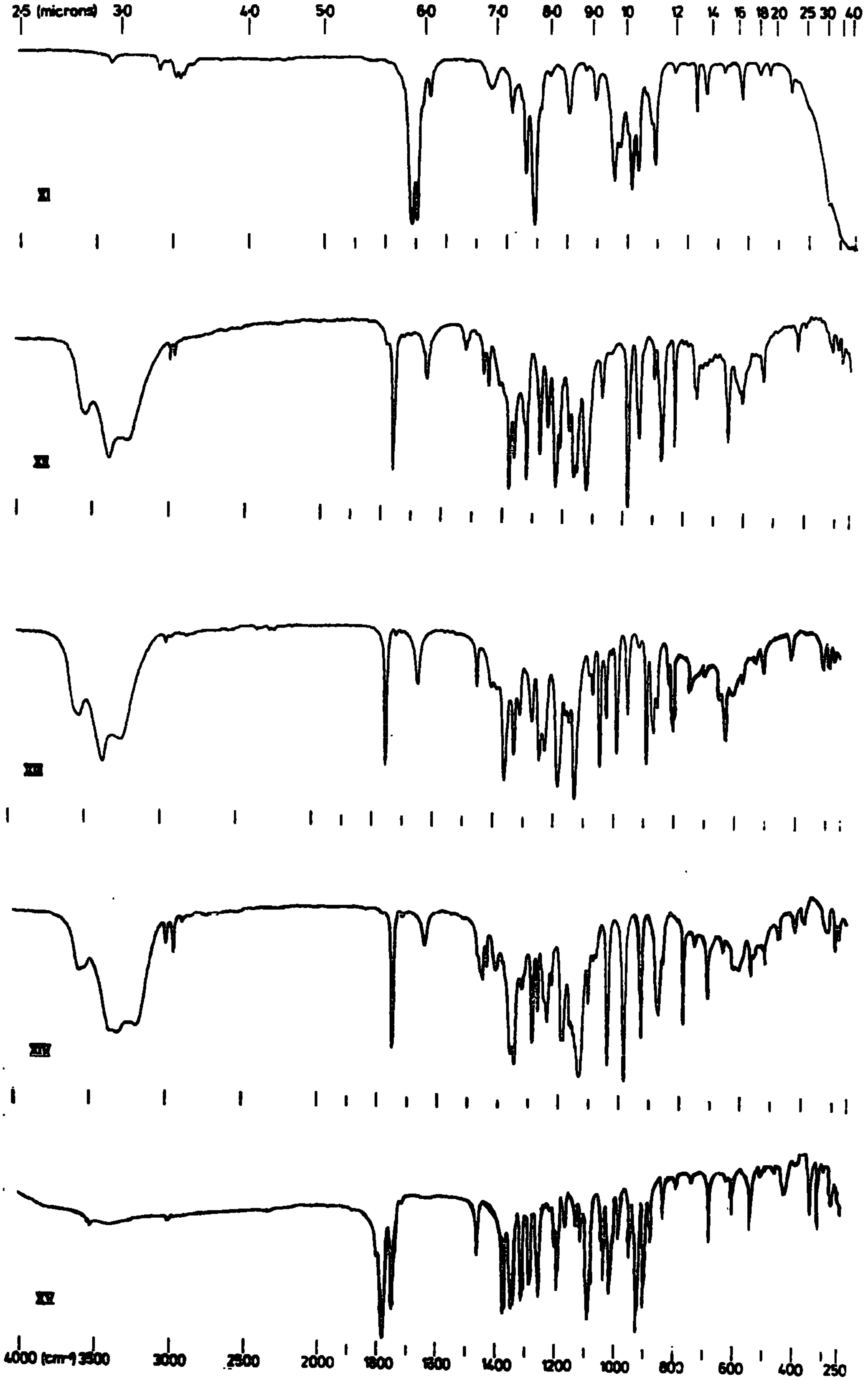
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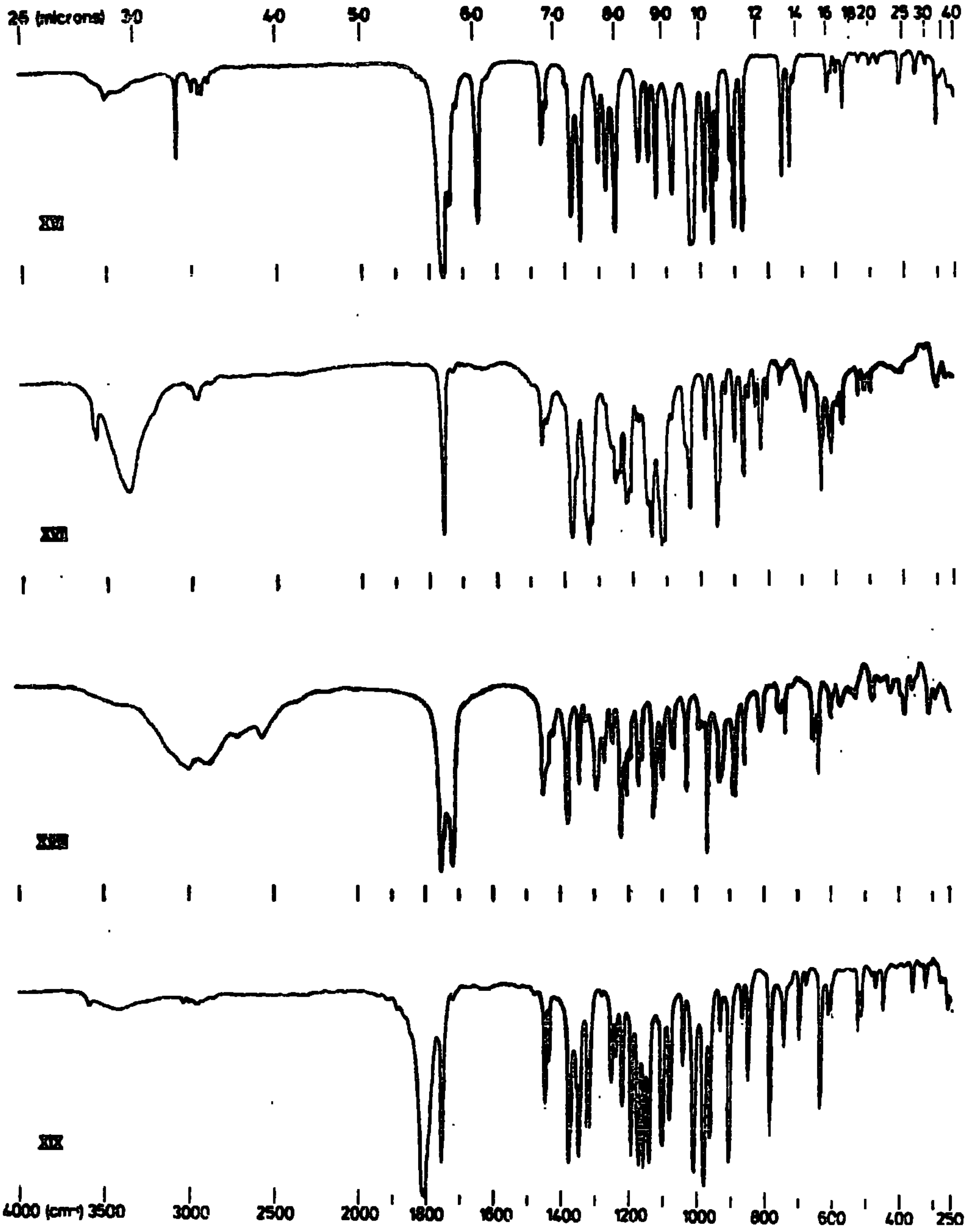
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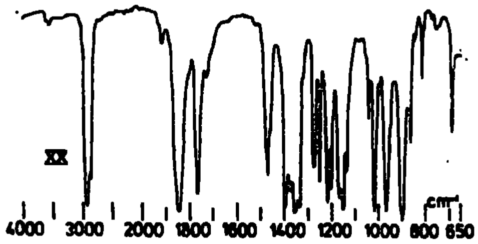
XX
cm⁻¹
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1400
1200
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650

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