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Nigel Stewart Robson

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Thermal and Photochemical Routes to Compounds Containing
the Tricyclo[3.3.1. $\text{0}^{2,7}$]nonane Skeleton using Polyfluoro-
aryl and heteroaryl Prop-2-enyl Ethers

By

Nigel Stewart Robson
(Van Mildert College)

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A Thesis Submitted to the University of Durham for the
Degree of Master of Science



13. AUG. 1984

ABSTRACT

This work is concerned with the synthesis of fluorine containing derivatives of the novel tricyclo[3.3.1.0^{2,7}]nonane skeleton by both thermal and photochemical routes from Claisen rearrangement products obtained from polyfluoroaryl and heteroaryl prop-2-enyl ethers. Fluorine is used as a blocking group to prevent an intermediate dienone from rearranging to a tautomeric phenol.

Thermal rearrangement of 2,3,5,6-tetrafluoro-4-pyridyl prop-2-enyl ether 41 in the vapour phase gives (via an intramolecular Diels-Alder addition reaction of the intermediate dienone) 2,4,5,7-tetrafluoro-3-aza-tricyclo[3.3.1.0^{2,7}]non-3-en-6-one 42. The structure of this product was confirmed by complete hydrolysis with 50% sulphuric acid to give 4-hydroxybenzoic acid. Hydrolysis and hydration of the Diels-Alder adduct with water gave 2,5,7-trifluoro-6,6-dihydroxy-3-aza-tricyclo[3.3.1.0^{2,7}]nonan-4-one 43. This compound was readily dehydrated by sublimation under high vacuum to give 2,5,7-trifluoro-3-aza-tricyclo[3.3.1.0^{2,7}]nonan-4,6-dione 44.

1,3,5,6,7,8-Heptafluoro-2-naphthyl prop-2-enyl ether 77 readily underwent Claisen rearrangement in xylene at reflux to give 1,3,4,5,6,7,8-heptafluoro-1-(prop-2-enyl)-naphthalen-2-one 80. Irradiation of the naphthalenone in solution at 366nm gave rise to two isomeric tricyclic compounds 2,5,7-trifluoro-3,4-(tetrafluorobenzo)-tricyclo

[3.3.1.0^{2,7}]non-3-en-6-one 95 and 1,2,7-trifluoro-3,4-(tetrafluorobenzo)-tricyclo[3.3.1.0^{2,7}]non-3-en-6-one 103. Compound 103 is formed by an initial [3,5] sigmatropic shift, followed by a [2+2] cycloaddition and then a [1,3] sigmatropic shift. This compound was easily hydrated to give the corresponding gem-diol 1,2,7-trifluoro-3,4-(tetrafluorobenzo)-tricyclo[3.3.1.0^{2,7}]non-3-en-8,8-diol 104. The structure of the second compound 95, formed by a direct [2+2] cycloaddition reaction was shown by hydrolysis and methylation to give 1 β ,4 β ,5,6,7,8,8b β -heptafluoro-1 α -methoxycarbonyl-8b,2a,3,4-tetrahydro-8b α ,2a α -ethanonaphthalene 96c which was identified by ¹⁹F nmr and i.r. spectroscopy.

Pyrolysis of compound 95 at 450°C gave the naphthalenone 80 whilst at higher temperatures (490°C) a new compound 1-fluorovinyl-4,5,6,7,8-pentafluoro-1-naphthyl ketone 105 was formed.

Pyrolysis of 1,3,4,5,6,7,8-heptafluoro-1-(prop-2-enyl)-naphthalen-2-one 80 at 455°C gave the the compound 95 in very low yield. At higher temperatures (490°C) the 1-fluorovinyl ketone 105 was formed.

DECLARATION

This work was carried out in the Chemistry Department of the University of Durham between 1-10-77 and 30-9-79 and is the original work of the author except where acknowledged by reference. This work has not been submitted for any other degree. The work described in this thesis has been published in two papers and a short communication:-

G.M. Brooke, R.S. Matthews & N.S. Robson, J. Chem. Soc. Chem. Comm. (1980) 194

G.M. Brooke, R.S. Matthews & N.S. Robson, J. Chem. Soc. Perkin 1 (1980) 102

G.M. Brooke, R.S. Matthews & N.S. Robson. J. Fluorine Chem. 16 (1980) 461

The work from chapter 2 also formed part of a poster presented at the 9th International Fluorine Symposium, September 3-7th 1979, Avignon, France.

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To Mr T. Holmes and his staff for technical support.

My thanks are also due to the members of lab 25 for their helpful (?) suggestions.

To Mrs Pat Maxwell and Mrs Julia Hearn for the typing and word processing they did for me, and for putting up with my handwriting!! Having finished off the thesis on the word processor myself, I now realise what I subjected them to.

Thanks are also due to Dr. Jon and Wanda Dickens for proof reading the manuscript for me.

Notes to the Reader

1. Abbreviations

The following abbreviations have been used in this thesis:-

tlc	thin layer chromatography
i.r.	infra-red spectroscopy
nmr	nuclear magnetic resonance spectroscopy
THF	Tetrahydrofuran

2. Nomenclature

In J. Chem. Soc Chem. Comm. (1980) 194 the two compounds 95 and 103 were named as 2,4,5,6,7,9,11-heptafluorotetracyclo[7.3.1.0^{2,11}.0^{3,8}]trideca-3(8),4,6-trien-10-one and 1,2,4,5,6,7,11-heptafluorotetracyclo[7.3.1.0^{2,11}.0^{3,8}]trideca-3(8),4,6-trien-12-one respectively. However in J. Fluorine Chem. 16 (1980) 461 95 and 103 were named as 2,5,7-trifluoro-3,4-(tetrafluorobenzo)tricyclo[3.3.1.0^{2,7}]non-3-en-6-one and 1,2,7-trifluoro-3,4-(tetrafluorobenzo)tricyclo[3.3.1.0^{2,7}]non-3-en-8-one respectively. The latter nomenclature is used in this thesis.

The names prop-2-enyl and allyl are synonyms for the -CH₂CH:CH₂ group and both are used in this thesis although the former predominates.

The notation 'F' in a ring indicates that all unmarked bonds are to fluorine e.g. hexafluorobenzene can be drawn as:



What is accomplished by fire is alchemy,
whether in the furnace or kitchen stove.

Paracelcus 1493 - 1541

To My Parents

CONTENTS

Abstract	i
Declaration	iii
Acknowledgements	iv
Notes to the Reader	v
Quotation	vi
Dedication	vii
Contents	viii

CHAPTER 1

1.1	Introduction	1
1.2a	The Claisen Rearrangement	1
1.2b	Mechanism of the Claisen Rearrangement	2
1.3	Sigmatropic Rearrangements	5
1.4	The Ortho-Ortho Claisen Rearrangement	9
1.5	Cycloaddition Reactions	11
1.5a	The Diels-Alder Reaction	13
1.5a.1	Mechanism of the Diels-Alder Reaction	14
1.5a.2	Photochemical [4 + 2] Cycloadditions	15
1.5b	[2 + 2] Cycloadditions	16
1.5b.1	[2 + 2] Cycloadditions via Ionic Intermediates	16
1.5b.2	[2 + 2] Cycloadditions via Radical Intermediates	17
1.5b.3	Photochemical [2 + 2] Cycloadditions	19
1.6a	Intramolecular Diels-Alder Adducts ..	20
1.6b	Orientation of the Intramolecular Diels-Alder Addition	21

1.7 Thermal Rearrangements of Perfluoroaryl
Allyl Ethers 24

CHAPTER 2

2.1 The Pyridine Claisen Rearrangement..... 29
2.2 Pyrolysis of 2,3,5,6-Tetrafluoro-4-
pyridyl Prop-2-enyl Ether 41 31
2.3 Experimental 41

CHAPTER 3

3.1 Thermal Rearrangements of Naphthyl
Prop-2-enyl and Prop-2-ynyl Ethers..... 45
3.2 Preparation of 1,3,4,5,6,7,8-Heptafluoro
-2-naphthyl Prop-2-enyl Ether 77 49
3.3 Pyrolysis of 1,3,4,5,6,7,8-Heptafluoro-
2-naphthyl Prop-2-enyl Ether 77 52
3.4 Photochemical [2 + 2] Cycloadditions in
Cyclic Enones 52
3.5 Orientation of the Intramolecular Photo-
chemical Cycloaddition Reaction 55
3.6 Photolysis of the Naphthalenone 80 56
3.6a Identification of the Major Photoadduct 56
3.6b Identification of the Minor Photoadduct 62
3.7 Mechanism for the Formation of 10365
3.8 Experimental 67

CHAPTER 4

4.1	Introduction	74
4.2	Pyrolysis of the Photoproduct <u>95</u>	74
4.3	Pyrolysis of the Naphthalenone <u>80</u>	77
4.3	Experimental	78

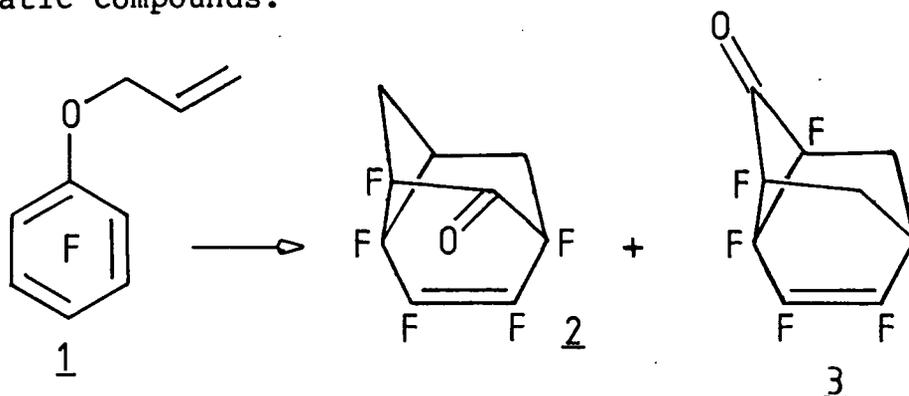
APPENDICES

Appendix A	Apparatus and Instruments	81
Appendix B	I.R. Spectra	83
Appendix C	References	87

CHAPTER ONE

1.1 Introduction

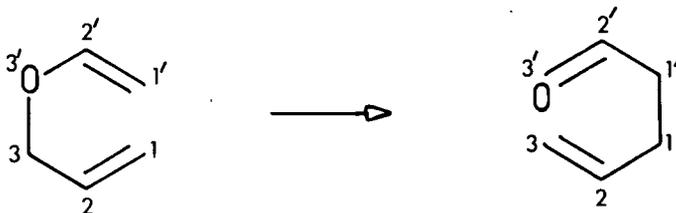
This work is concerned with the synthesis of compounds containing the tricyclo[3.3.1.0^{2,7}]nonane skeleton via the Claisen rearrangement and cycloaddition reactions. This follows work by Hall¹ who prepared the tricyclic compounds 2 and 3 by thermal rearrangement of pentafluorophenyl prop-2-enyl ether 1 (Scheme 1). This work concerns the extension of the reactions to polynuclear and heterocyclic aromatic compounds.



Scheme 1

1.2a The Claisen Rearrangement

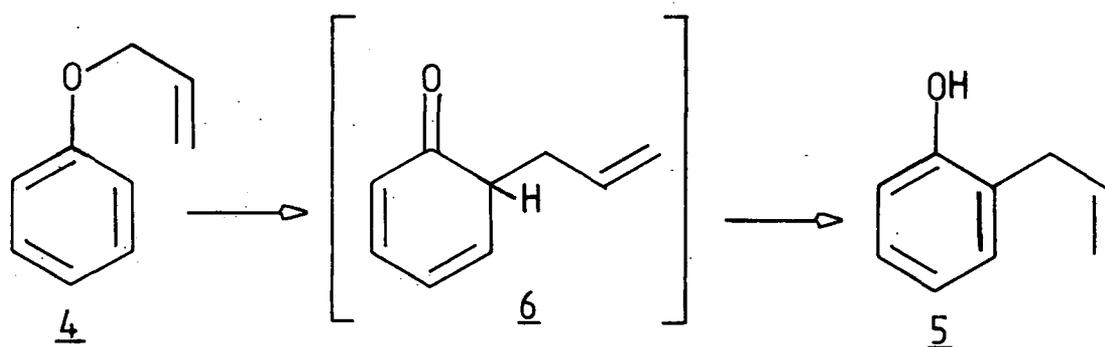
The Claisen rearrangement involves the thermal rearrangement of an allyl vinyl ether into a homoallylic carbonyl compound by a concerted intramolecular pathway (Scheme 2).



Scheme 2



The best known examples of the Claisen rearrangement occur in allyl phenyl ethers and have been extensively studied². The reaction was discovered when Claisen was attempting to prepare prop-2-enyl aryl ethers³. Claisen found that on distillation the ethers rearranged to give an ortho prop-2-enyl phenol (Scheme 3) if the distillation temperature rose too high. Claisen suggested that the ortho prop-2-enyl phenol was formed from the ortho-dienone 6⁴.



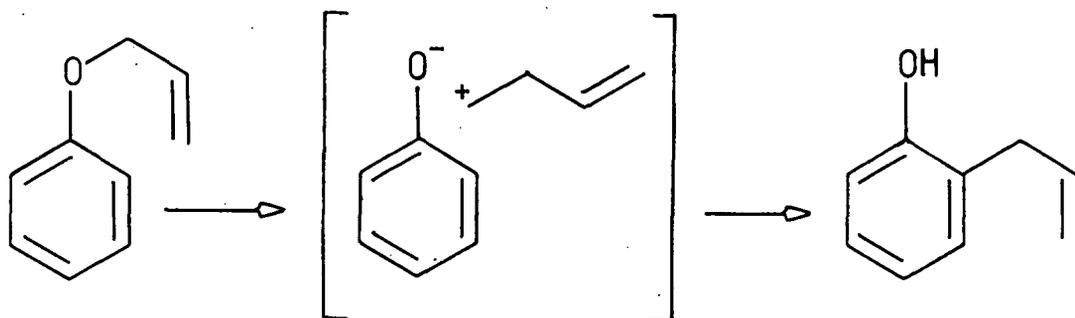
Scheme 3

It was found that if both the ortho positions were substituted, the para-phenol was formed⁵. Conversion of an independently prepared ortho-dienone to both the para-dienone and the prop-2-enyl ether showed that the ortho-dienone was the intermediate and that the reaction was reversible⁶. This was confirmed by trapping the ortho-dienone in a Claisen rearrangement with maleic anhydride⁷.

1.2b Mechanism of the Claisen Rearrangement

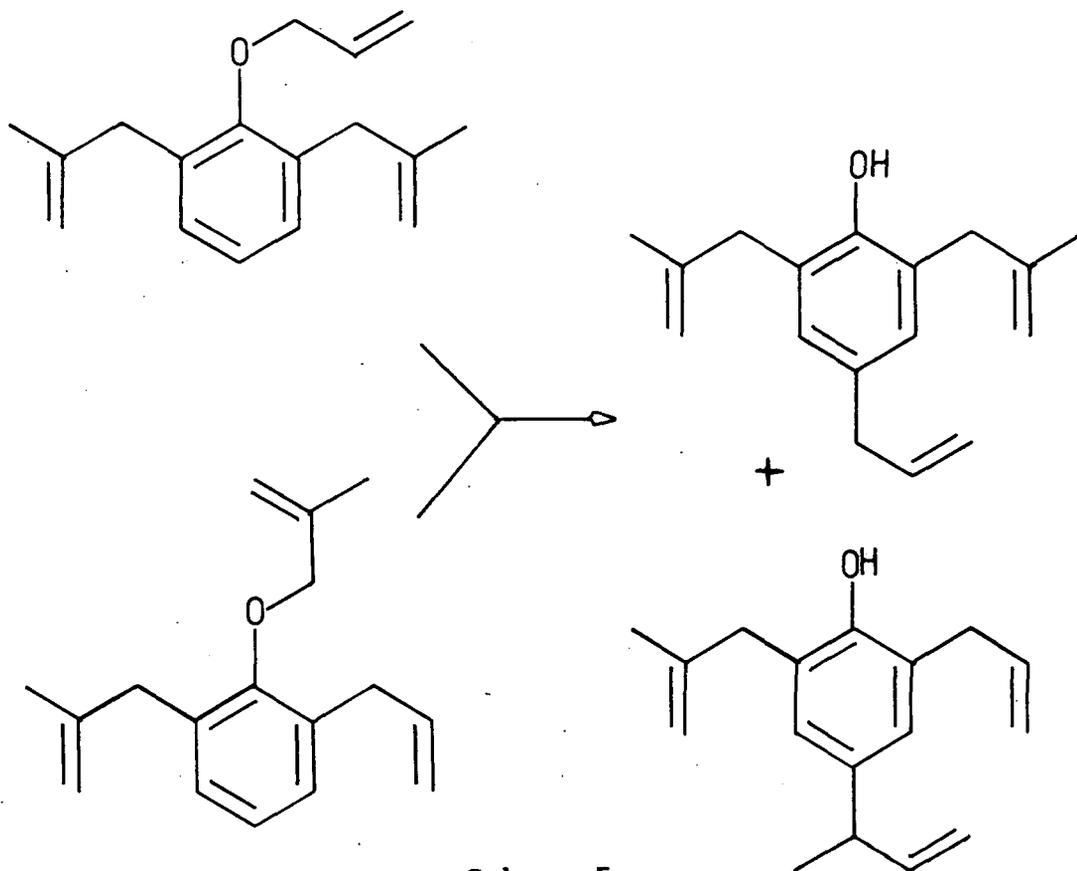
Claisen had postulated a radical mechanism for the reaction. However the reaction was shown to be intramolecular by the lack of any crossover products when 2-naphthyl prop-2-enyl ether and phenyl (3-phenyl

prop-2-enyl) ether were heated together⁸. Since a radical reaction is unlikely to be intramolecular the idea was abandoned. Dewar proposed an ionic mechanism (Scheme 4) with an intermediate complex which collapsed to give the product⁹.



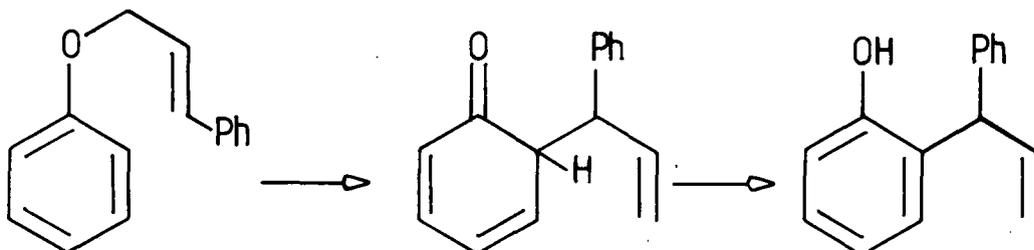
Scheme 4

This theory was disproved by using two isomeric allyl ethers which gave the same products in the same ratio (Scheme 5) which was only possible if they had a common intermediate¹⁰.



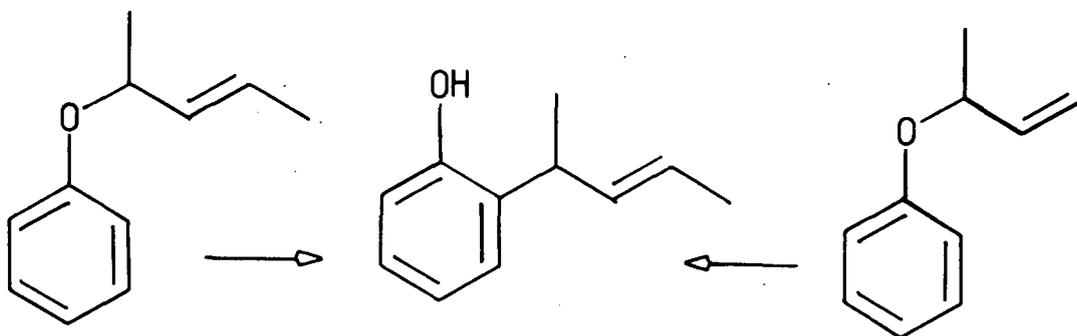
Scheme 5

The currently accepted mechanism, a concerted electron transfer, was first proposed by Hurd and Pollack¹¹. This mechanism requires an inversion of the prop-2-enyl group and this has been shown by using a substituted prop-2-enyl phenyl ether⁸ (Scheme 6).



Scheme 6

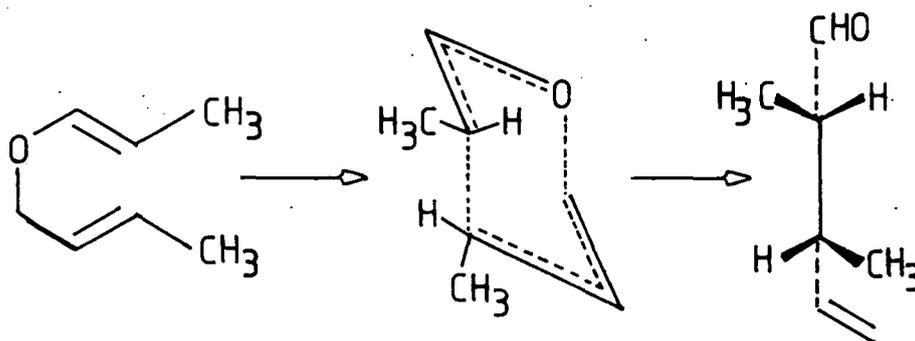
The Claisen rearrangement is highly stereoselective, the transition state being able to adopt either a chair or boat-like conformation. Consideration of the possible chair and boat-like transition states for the rearrangement of cis and trans 1-methylbut-2-enyl phenyl ether shows that the transition states with the lowest activation energy all give rise to trans 1-methyl but-2-enyl phenol (Scheme 7)¹².



Scheme 7

However, these results do not show whether a chair or boat-like transition state is preferred. The preferred

conformation of the transition state has been shown by the thermal rearrangement of trans, trans crotyl prop-2-enyl ether which gives (+)threo 2,3,dimethylpent-4-enal (Scheme 8)¹³. This product can only be formed via a chair-like transition state. Rearrangement of optically active prop-2-enyl phenyl ethers has been shown to give retention of optical activity¹⁴.



Scheme 8

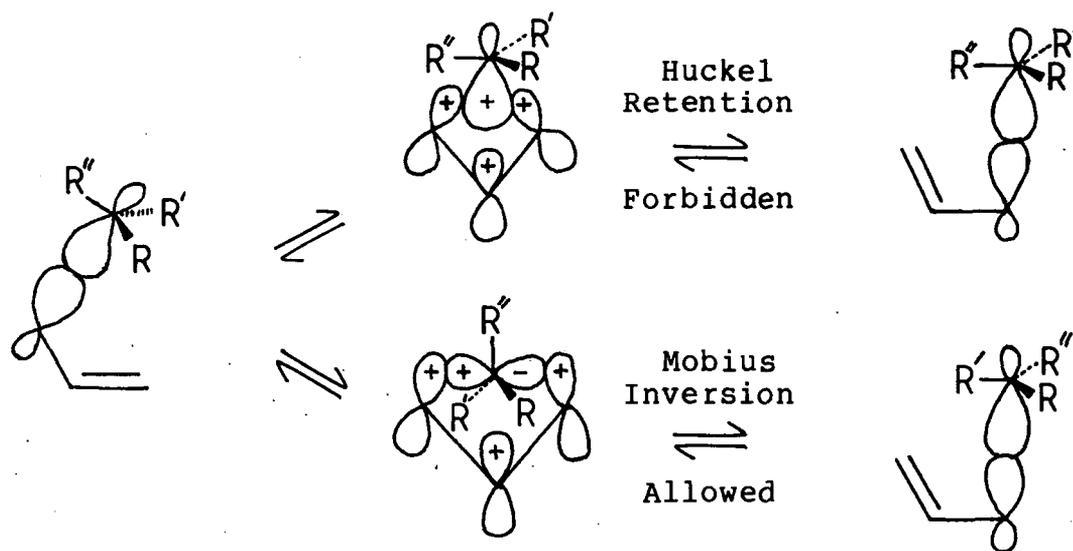
1.3 Sigmatropic Rearrangements

The Claisen rearrangement belongs to a group of reactions known as sigmatropic rearrangements. A sigmatropic rearrangement is defined as a reaction in which a sigma bond (i.e. a substituent or group) moves across a conjugated system to a new site. Examples of sigmatropic rearrangements have been known for many years. The unifying features of these rearrangements are that they are concerted, uncatalysed, and the bond migration occurs in a cyclic transition state in which the migrating atom or group is simultaneously joined to both ends of the n electron system.

Sigmatropic rearrangements are defined by their order $[i,j]$ where $(i-1)$ is the number of bonds moved through the migrating group and $(j-1)$ is the number of bonds moved

through the π system. The numbering must go through the π system even if an alternative route would give a lower value of j . The simplest sigmatropic rearrangements are those with an order of $[1,j]$ where a hydrogen atom moves across the π system. By considering the migration of a hydrogen atom across a polyene it can be shown that a concerted suprafacial thermal rearrangement has a Huckel type transition state and is allowed for systems where $(4n + 2)$ electrons participate. Similarly a concerted antarafacial thermal rearrangement has a Mobius type transition state and is allowed for systems where $4n$ electrons participate¹⁵.

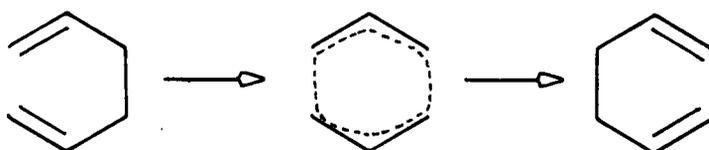
When an alkyl group undergoes a sigmatropic rearrangement the selection rules are the same as for the hydrogen atom. However, the ability to use the back of the alkyl bonding orbital means that suprafacial (or antarafacial) rearrangements previously forbidden for hydrogen are now permitted, and result in inversion of configuration in the migrating group. Scheme 9 shows the case for a suprafacial $[1,3]$ rearrangement.



Scheme 9

However, the selection rules only predict the preferred stereochemistry of the permitted concerted process and do not rule out lower energy stepwise mechanisms.

The Claisen rearrangement is an example of a [3,3] sigmatropic rearrangement. These form an important group of thermal rearrangements involving a six membered cyclic transition state which can be considered as two interacting allyl systems (Scheme 10).



Scheme 10

This Huckel aromatic system is thermally allowed with either suprafacial-suprafacial or antarafacial-antarafacial migration of the allyl group. However, the antarafacial-antarafacial migration is very unlikely due to the high strain imposed to obtain efficient overlap.

Using the phase relationships of the HOMO's of the migrating group and the π system, it can be shown that thermal rearrangements are permitted for $(i + j) = (4n + 2)$ whilst photochemical rearrangements are permitted for $(i + j) = 4n$. The system of the allyl radical can be described by three molecular orbitals using Huckel theory (Diagram 1).

The +ve and -ve signs refer to the phase of the wave front. The HOMO for the allyl system is ψ_2 . The phenoxy radical has seven molecular orbitals ψ_4 being the HOMO (Diagram 2)^{2f}.

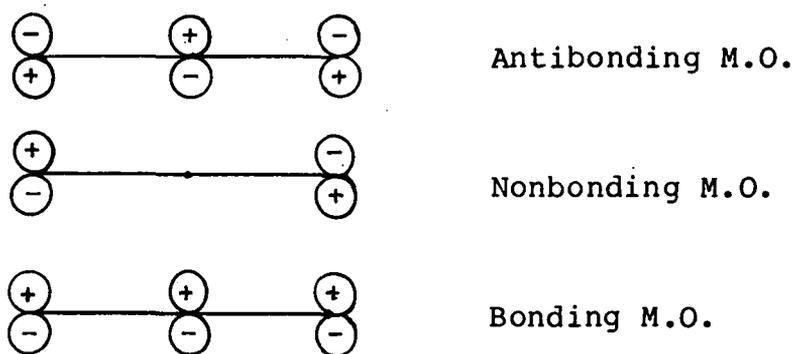


Diagram 1

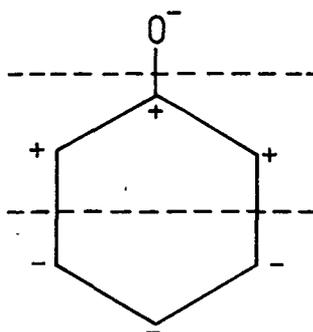


Diagram 2

Since the coefficients of the oxygen and ortho and para carbon atoms are the only ones of interest a simplified form of ψ_4 , ψ'_4 can be used (Diagram 3).

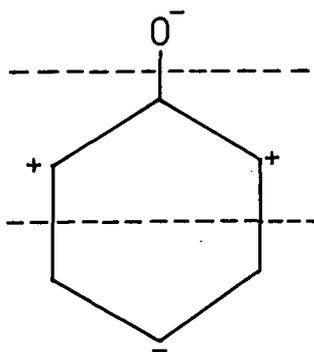


Diagram 3

The stereochemical requirements of the allyl group call for a suprafacial reaction on both components. The allyl radical has a phase change between C1 and C3 whilst the phenoxy has two phase changes, one between the oxygen and the ortho carbon and the other between the ortho and para carbons. The molecular orbitals must be of the same

phase for bonding and assuming suprafacial migration on both components: diagram 4 shows a [3,3] shift is allowed whilst a [1,3] shift is not.

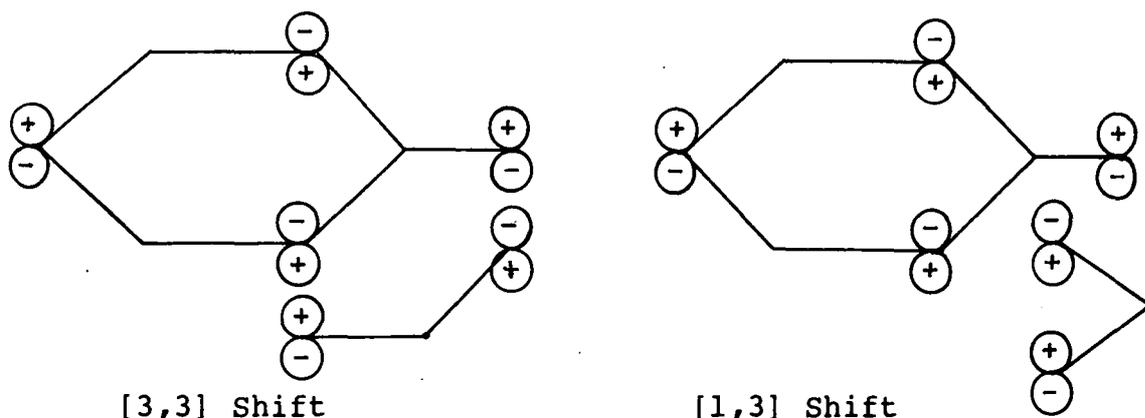
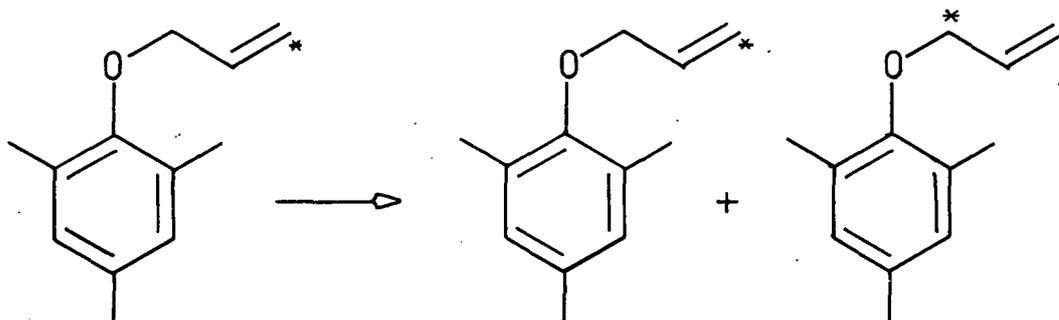


Diagram 4

1.4 The Ortho-Ortho Claisen Rearrangement

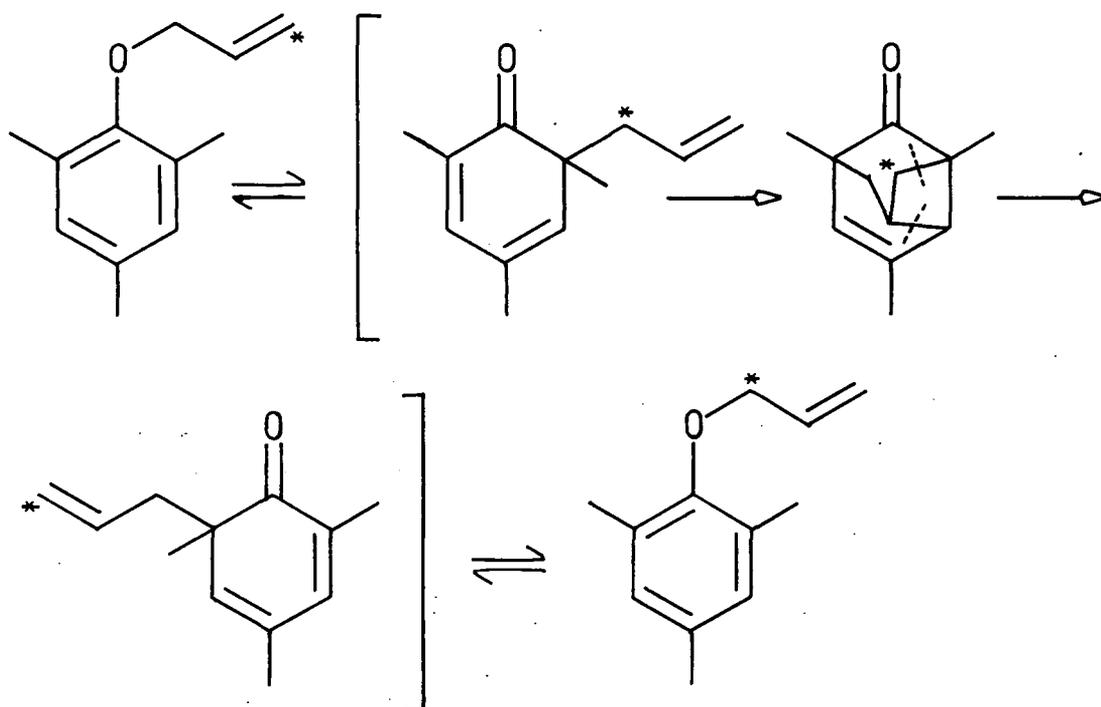
In 1959 Schmid reported that when the prop-2-enyl group of 2,4,6-trimethyl phenyl prop-2-enyl ether was labelled with ^{14}C at C-3 the label became scrambled between C-1 and C-3 (Scheme 11).



Scheme 11

Isomerisation of the allyl group in the allyl ether, which would give both isomers, can be ruled out as it would involve a suprafacial [1,3] shift which is a thermally forbidden process. A non-concerted isomerisation can also be discounted as the Claisen

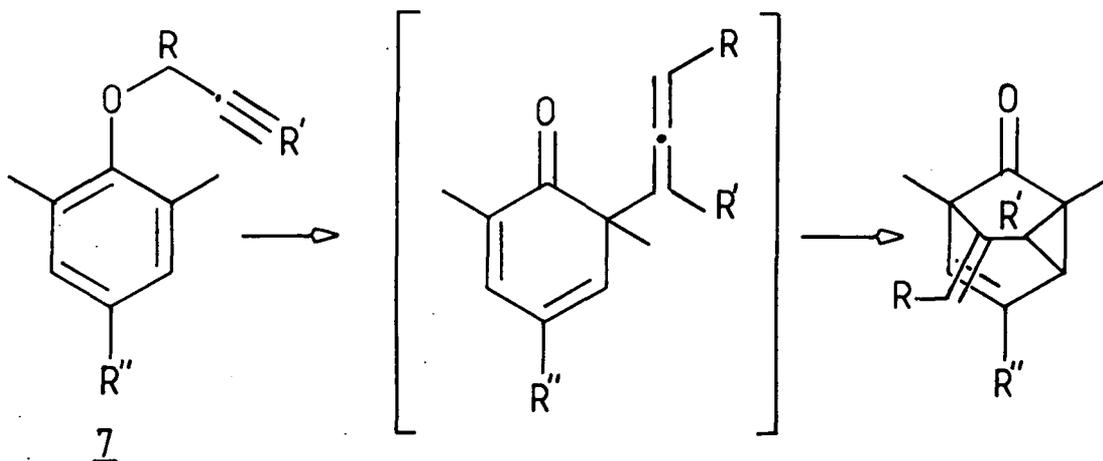
rearrangement is a well established concerted reaction. Another alternative was a reversible ortho-ortho migration of the allyl group in the dienone. This migration would be a thermal [3,5] shift and is only permitted by suprafacial-antarafacial mechanism which would involve a highly strained transition state, making this route very unlikely. The most likely route is stepwise and involves an intramolecular Diels-Alder adduct. The ortho-dienone has all the requirements for an intramolecular Diels-Alder reaction. The resulting adduct can then break down by cleavage of the four membered ring (an established non-concerted process¹⁵) to give the new dienone (Scheme 12).



Scheme 12

This mechanism was suggested by Schmid¹⁶. However attempts to isolate the Diels-Alder adduct from the rearrangement of allyl phenyl ethers were unsuccessful although Diels-Alder adducts have been isolated from the rearrangement of aryl propargyl ethers.

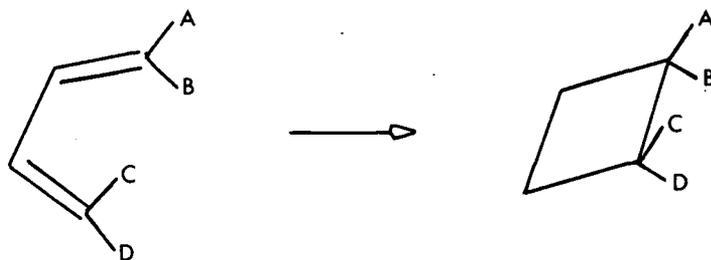
Using the para substituted 2,6-dimethylphenyl propargyl ether **7** Schmid succeeded in isolating intramolecular Diels-Alder adducts¹⁷ in good yields (50-80%) (Scheme 13).



Scheme 13

1.5 Cycloaddition Reactions

A cycloaddition is defined as a process in which two or more reactants combine to form a stable cyclic molecule, in which no fragments are eliminated and sigma bonds are formed but not broken (this definition does not include reactions such as the Dieckmann condensation). In the majority of cycloadditions two sigma bonds are formed, the exception is the electrocyclic reaction where only one sigma bond is formed (Scheme 14).



Scheme 14

In the concerted addition of a diene to a monoene bond formation must occur to some extent in the transition

state and so orbital overlap must occur at both termini simultaneously. This requires the overlap to be not only geometrically feasible but also bonding on both of the components. Suprafacial addition on both components is sterically favourable and gives good orbital overlap. However, the interaction is only energetically favourable if the orbitals' interaction is bonding.

The total number of electrons involved in the cycloaddition is fundamentally important in determining whether the reaction is thermally allowed or not, as this determines whether the reaction goes through a Huckel or a Mobius type transition state. Using the aromatic transition state approach it can be shown that only systems with a Huckel aromatic transition state and $(4n + 2)\pi$ electrons, can undergo concerted thermal suprafacial suprafacial cycloadditions. Systems with a Mobius aromatic transition state and $(4n)\pi$ electrons are symmetry forbidden.

Similar selection rules can be drawn up for other modes of approach. Suprafacial-antarafacial reactions are allowed for $(4n)\pi$ electrons but disallowed for $(4n + 2)\pi$ electrons. However, suprafacial-antarafacial overlap is sterically less favourable than suprafacial-suprafacial overlap and so thermal reactions involving $(4n)\pi$ electrons are unlikely. Antarafacial-antarafacial processes are also allowed for $(4n + 2)\pi$ electrons but are unlikely because of the problems of getting good orbital overlap.

Since the thermal $[2s + 2s]$ process is forbidden and the $[2s + 2a]$ process is sterically unfavourable $[2 + 2]$ additions nearly always go through stepwise mechanisms.

[4 + 2] reactions on the other hand are nearly always concerted in thermal reactions.

1.5a The Diels-Alder Reaction

The reaction of a conjugated diene with a monoene (the dienophile) to give a six-membered ring is the best known [4 + 2] cycloaddition reaction. The usefulness of the reaction was first recognised and the mechanism investigated by Diels and Alder in the late 1920's and has been extensively reviewed¹⁸. The dienophile can be almost any π bond whilst the diene system is generally all carbon but may contain heteroatoms. The structural variation is limited. The diene must be in the cisoid configuration to react, if the diene is fused in the transoid configuration it will not react. The rate of reaction of open chain dienes depends on the equilibrium proportion of the cisoid conformer and on the diene substituents which can affect the rate by electronic and steric effects. Cis fused cyclic dienes are the most reactive but the ring size is important as it governs how far apart the ends of the diene are.

Increasing aromaticity decreases the reactivity of the diene e.g. furan is more reactive than pyrrole which is more reactive than thiophene. Benzene only reacts with arynes and reactive acetylenes. Polycyclic aromatic compounds are more reactive than benzene whilst cyclopentadienones are highly reactive and normally dimerise spontaneously.

Dienes are normally electron rich and are further activated by electron releasing groups (e.g. MeO, Me,

NMe₂ etc.) whilst the dienophile is activated by electron withdrawing groups. Electron deficient dienes have an "inverse" electron demand¹⁹ and as a result require electron rich dienophiles.

It has been suggested that the rate of reaction depends upon the energy difference between the interacting orbitals²⁰. The presence of electron releasing groups on the diene raise the energy of the diene orbitals thereby lowering the energy difference between the diene orbitals and the dienophile orbitals and increasing the rate of reaction. Similarly electron withdrawing substituents on the dienophile lower the energy of the reacting orbitals also increasing the rate of reaction²¹. For a diene with "inverse" electron demand the position is reversed: electron withdrawing substituents activate the diene and electron donating substituents activate the dienophile.

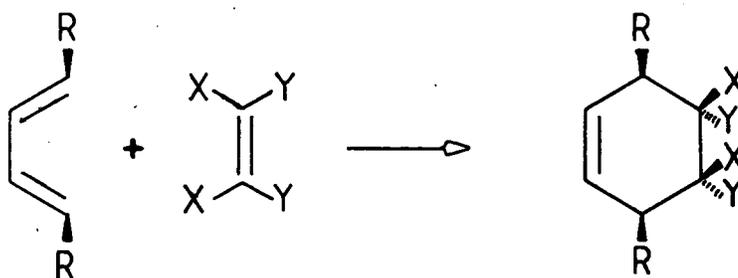
1.5a.1 Mechanism of the Diels-Alder Reaction

The currently accepted mechanism for the Diels-Alder reaction involves a cyclic six centred transition state. The reaction is concerted: that is both new bonds are formed at the same time although not necessarily to the same extent. This mechanism is consistent with the observed stereochemistry and rate of reaction in various solvents.

The similarity of the rates of reaction of dienes and dienophiles in the gas phase and solvents of differing polarity is inconsistent with a stepwise reaction going through an ionic intermediate. Although the rate of reaction shows some substituent effects a process

involving a zwitterionic intermediate would be expected to show a much greater effect. A diradical intermediate can also be ruled out as this would not be dependent on the conformation (cisoid or transoid) of the diene and evidence suggests the intermediate from the transoid form of the diene would lead to a four membered ring system¹⁵.

The Diels-Alder reaction is highly stereoselective with respect to the diene and dienophile, the relative orientation of substituents on both reactants being unchanged in the product, a result which would be very unlikely with an ionic or diradical transition state (Scheme 15).



Scheme 15

1.5a.2 Photochemical [4 + 2] Cycloadditions

A concerted photochemical $4\pi + 2\pi$ reaction²² proceeding suprafacially on one component and antarafacially on the other is symmetry allowed by Woodward-Hoffmann rules, but there are no authenticated [4a + 2s] or [4s + 2a] photochemical cycloadditions. When dienes and monoenes are irradiated some six membered ring products are formed as minor components, the major products being [2 + 2] adducts²³.

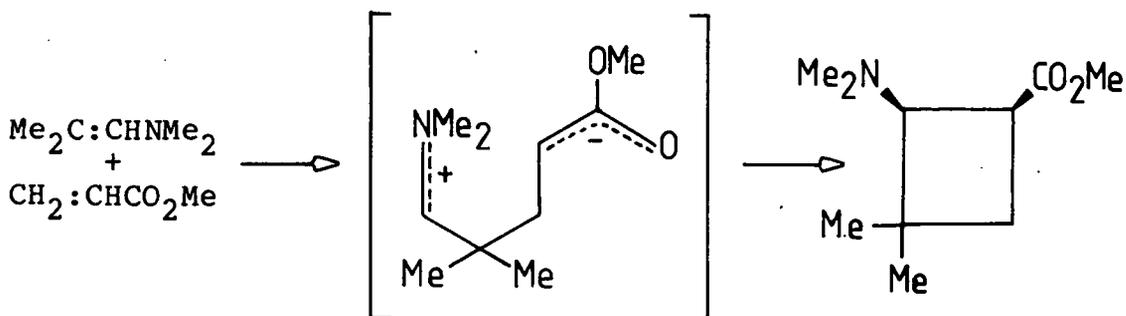
1.5b [2 + 2] Cycloadditions

After the six π electron cycloaddition the next most common is the four π electron cycloaddition. A concerted thermal [2s + 2s] cycloaddition is forbidden by orbital symmetry rules but the [2s + 2a] reaction is allowed. Suprafacial-antarafacial reactions involve inefficient overlap and produces a strained transition state as the π bonds have to twist to try and achieve good overlap. The approach of the reactants is also hindered by steric interactions between the substituents. As a result the concerted [2a + 2s] reaction is unfavourable and [2 + 2] cycloadditions normally follow stepwise mechanisms. These are energy demanding and require forcing conditions unless the intermediate is stabilised by substituents. No example of a concerted [2a + 2s] cycloaddition has been established yet. Since the π bonds must be twisted in the transition state the system most likely to undergo a concerted thermal [2 + 2] reaction will have a π system which is twisted to begin with.

1.5b.1 [2 + 2] Cycloadditions via Ionic Intermediates

Zwitterionic intermediates are found in [2 + 2] cycloadditions²⁴ when one component has strong electron releasing groups and the other has strong withdrawing groups as these substituents stabilise the charged intermediate. These reactions often give high yields under mild conditions and the reaction is reversible in some cases. The orientation of addition depends upon the stabilisation in the intermediate (Scheme 16).

These reactions show the normal characteristics of



Scheme 16

stepwise reactions with ionic intermediates, being solvent dependent²⁵ (polar solvents favour the reaction) and sensitive to substituent effects^{24d}. Possible competing reactions are proton transfer and reaction with a second mole of the electron deficient component.

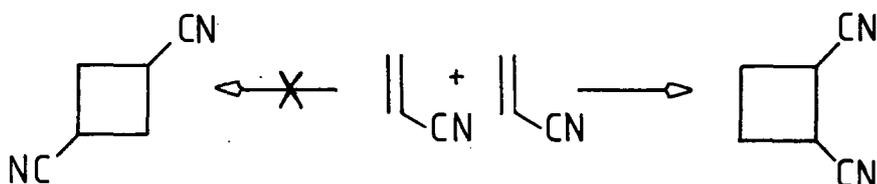
The low stereospecificity observed in some ionic [2 + 2] cycloadditions²⁶ is consistent with an intermediate in which bond rotation can occur. Generally however, these additions are highly stereoselective due to electrostatic attractions between the ends of the 1,4 dipole intermediate which allows the second bond to be formed without rotation of the other bonds. Increasing the solvent polarity causes a loss of stereo-selectivity.

1.5b.2 [2 + 2] Cycloadditions via Radical Intermediates

Alkenes and alkynes which have substituents capable of stabilising a radical intermediate also undergo [2 + 2] cycloadditions²⁷. Normally these reactions require forcing conditions i.e. temperatures of 100-200°C and pressures above atmospheric. Polyfluoro-olefins are exceptionally reactive either dimerising or reacting with

activated olefins²⁸. They also undergo almost exclusive [2 + 2] additions with dienes rather than the more usual Diels-Alder addition.

Evidence for diradical intermediates in [2 + 2] cycloadditions comes from the orientation of the addition, the products being those arising from the most stable diradical intermediate (e g. cyanoethylene dimerises to give 1,2-dicyanobutane and not 1,3-dicyanobutane^{27a} (Scheme 17)).



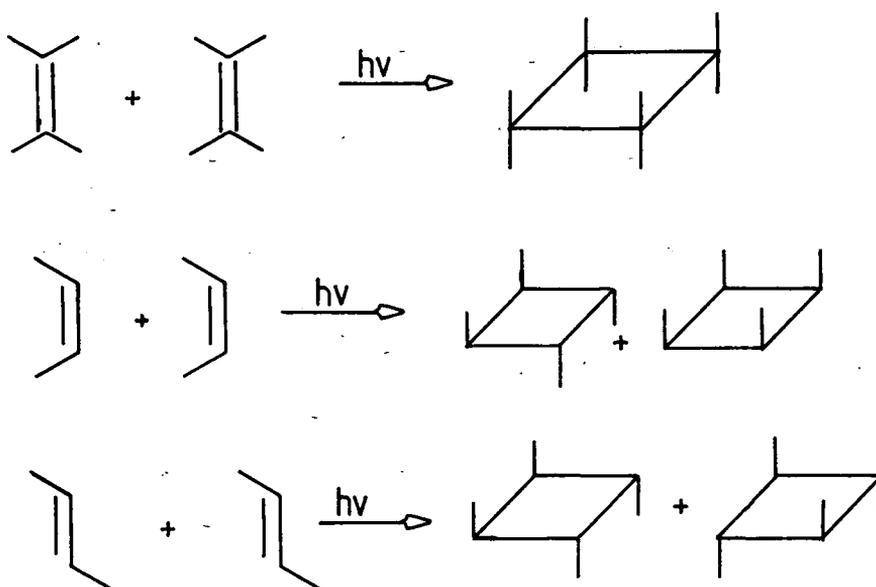
Scheme 17

The rate of these radical [2 + 2] cycloadditions is independent of solvent polarity and the reactions often go well even in the gas phase. As these are not chain reactions they are not affected by the usual free radical inhibitors or initiators. Radical [2 + 2] cycloadditions show the expected lack of stereospecificity due to the occurrence of free rotation in the intermediate.

Diradicals are also formed in photochemical cycloadditions but these are normally triplet diradicals which provide the additional barrier to ring closure of spin inversion. Evidence suggests that triplet diradicals are longer lived and so photochemical cycloadditions involving triplet diradicals lead to greater loss of configuration^{24d}.

1.5b.3 Photochemical [2 + 2] Cycloadditions

Although the concerted photochemical [2s + 2s] cycloaddition is an allowed process few reactions actually go by this route. In most cases triplet excited species are involved especially when photo-sensitisers are used. The singlet state can collapse to a triplet state by intersystem crossing and as a result many photochemical cycloadditions are stepwise radical processes. Cycloadditions thought to involve a genuinely concerted [2s + 2s] addition include the dimerisation of tetramethylethylene²⁹ and of cis and trans but-2-ene³⁰ (Scheme 18).



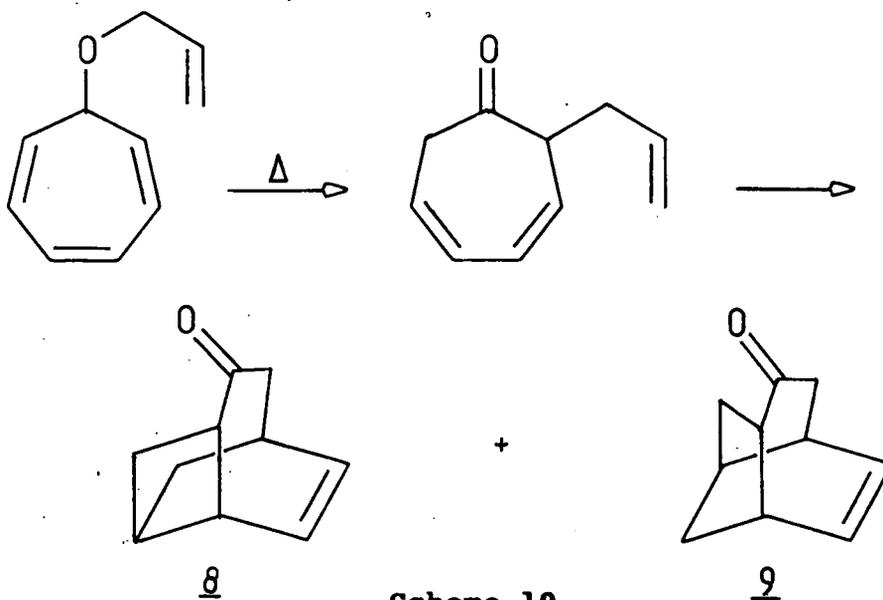
Scheme 18

The triplet sensitised photodimerisation of dienes and the photochemical addition of a diene to a monoene generally leads to [2 + 2] cycloaddition products with some [4 + 2] products^{22b}. The irradiation of cyclopentenones and cyclohexenones leads to dimerisation, but when irradiated in the presence of olefins, acetylenes or allenes addition occurs³¹. These reactions are

believed to be stepwise reactions proceeding via triplet excited enones and appear to be limited to cyclic enones.

1.6a Intramolecular Diels-Alder Adducts

Several examples of intramolecular Diels-Alder adducts have been isolated from the thermal rearrangements of cycloheptatriene alkenyl ethers and related compounds³². 7-Cycloheptatrienyl prop-2-enyl ether undergoes a Claisen rearrangement to 1-prop-2-enyl cycloheptadi-2,4-en-7-one which undergoes an intra-molecular Diels-Alder addition to give two isomeric tricyclic ketones^{32a} 8 & 9 (Scheme 19).

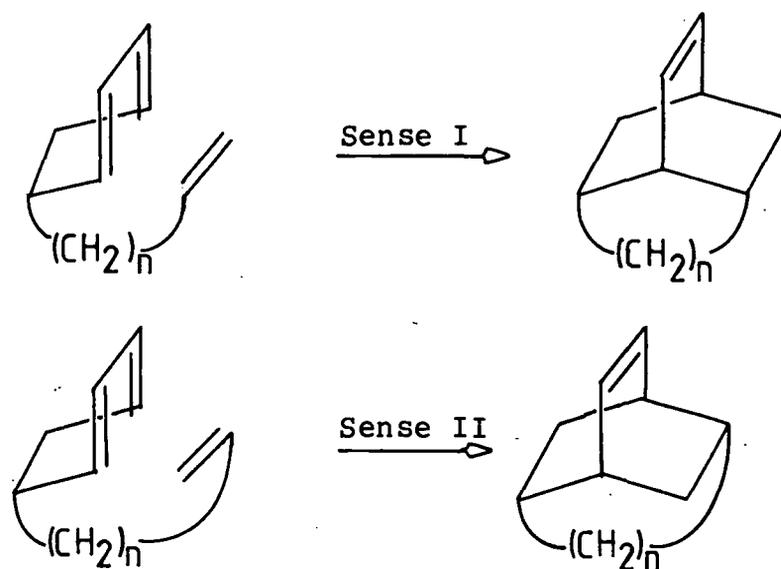


Scheme 19

Similar reactions are observed with 7-cycloheptatriene but-3-enyl ether^{32b} and 7-cycloheptatriene pent-4-enyl ether^{32c} and also with the 2-prop-2-enyl and 2-prop-2-ynyl ethers of 3,5,7 trimethyl tropone giving Claisen rearrangement products and intramolecular Diels-Alder adducts^{32d-f}. Diels-Alder adducts have also been isolated from the thermal rearrangements products of all carbon systems³³.

1.6b Orientation of the Intramolecular Diels-Alder Addition

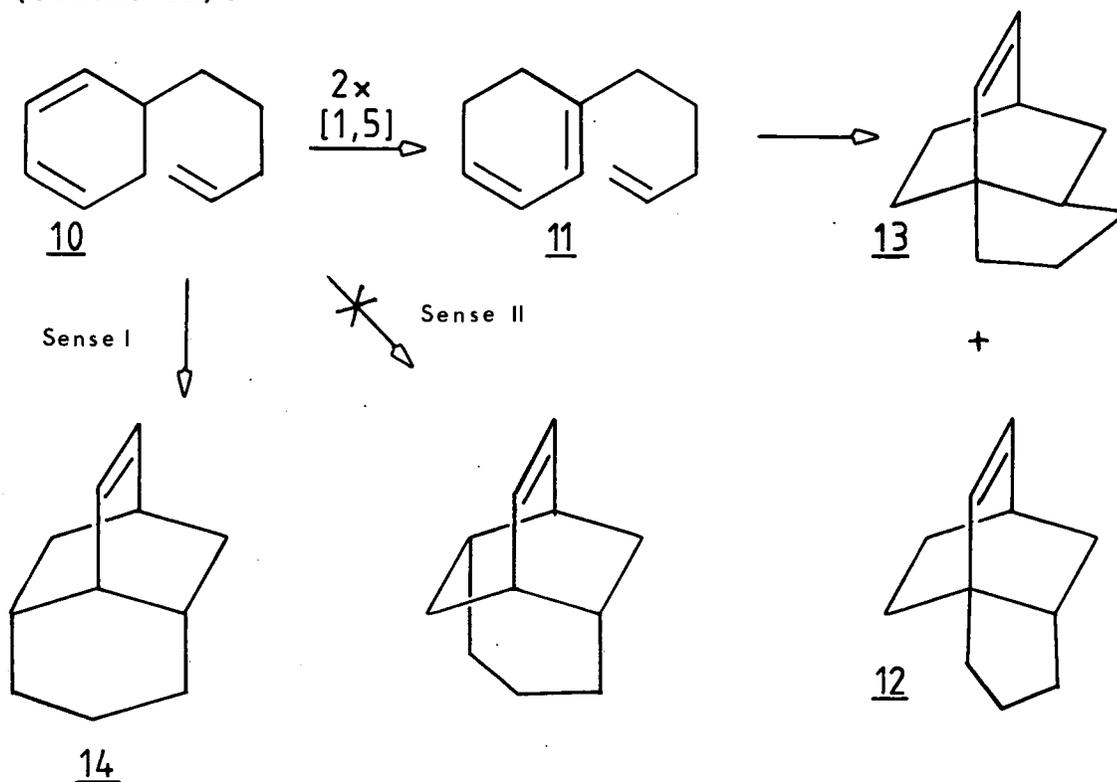
In these internal Diels-Alder cycloadditions there are two possible orientations for the dienophile side chain giving two isomeric products. The orientation of the dienophile depends upon several factors but the most important is the flexibility of the alkenyl side chain as this will affect the side chain's ability to adopt each orientation without producing excess strain. Obviously the longer the side chain the more flexible it will be. For the alkenyl cyclohexa-1,3-dienes (Scheme 20) only Sense I addition has been observed for values of $n = 0, 1, 2$ ³⁴.



Scheme 20

The absence of any Sense II product is due to the limited flexibility of these short chains preventing this orientation being adopted. Krantz³⁴ concluded, from examination of molecular models, that a value of $n = 3$ would allow the side chain to adopt either orientation without significant strain. This would allow him to

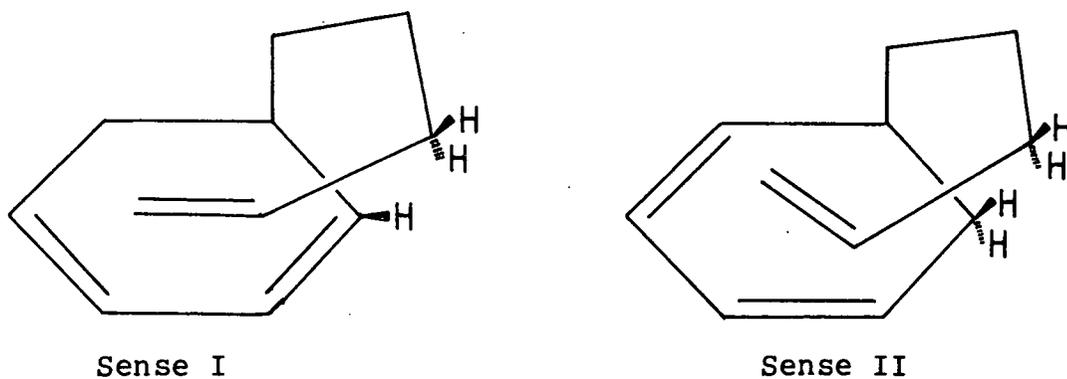
observe the ratio of products from Sense I and Sense II addition and so find the preferred orientation of the side chain. Only three products were observed from the pyrolysis of 5-(pent-4-enyl) cyclohexa-1,3-diene 10 (Scheme 21).



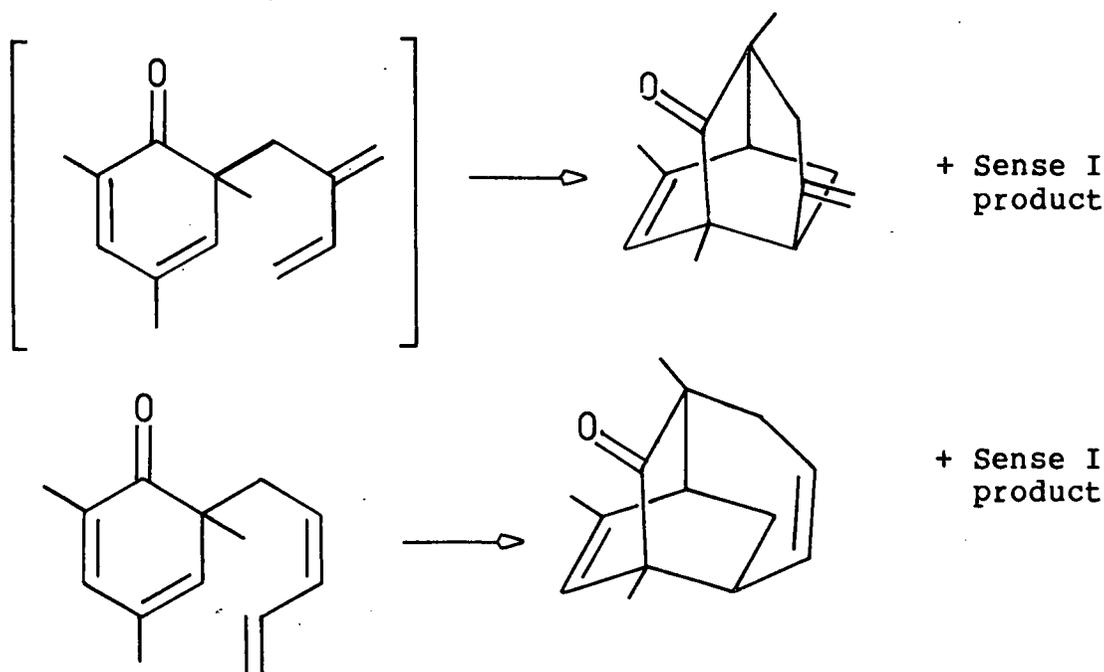
Scheme 21

Two of these were the exo 12 and the endo 13 Diels-Alder adducts formed from the 1-(pent-4-enyl) cyclohexa-1,3-diene 11 which is formed from 10 by two [1,5] hydrogen shifts. The third Diels-Alder adduct 14 was formed by a Sense I addition of the pentenyl chain to the 1,3 diene. The lack of any Sense II product was explained in terms of steric interactions between the allylic protons on the side chain and the ring protons which prevent the molecule adopting the best orientation for maximum overlap (Scheme 22).

Sense II additions have been observed in more complex alkenyl cyclohexadienones³⁵ (Scheme 23). In these cases

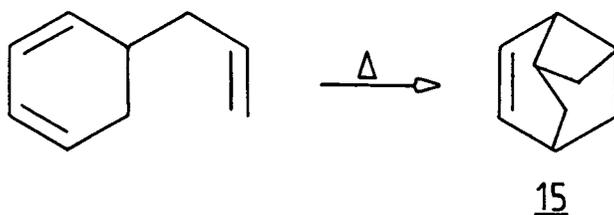
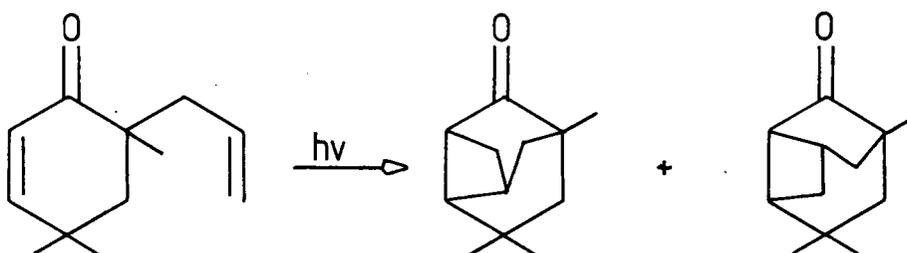
**Scheme 22**

the reaction is thought to proceed by a two step diradical mechanism³⁶.

**Scheme 23**

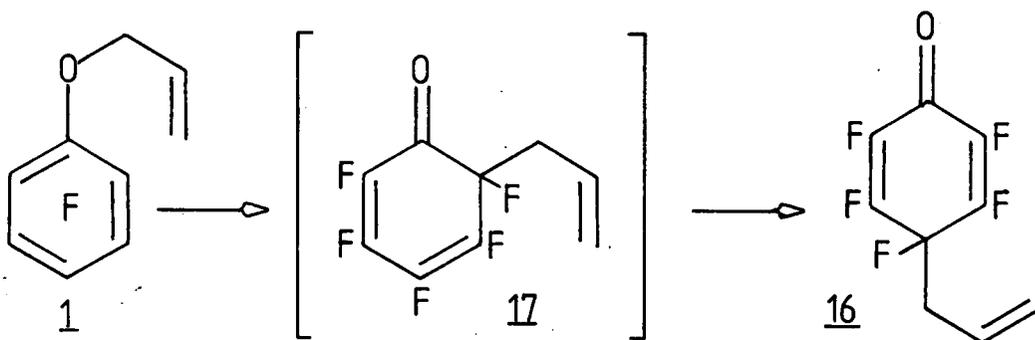
When $n = 1$ the Diels-Alder adduct from the Sense I addition has the same skeletal structure as the proposed intermediate in the ortho-ortho Claisen rearrangement, and this adduct 15 has been isolated by Krantz³⁷ (Scheme 24).

The same skeleton has been prepared photochemically³⁸ (Scheme 25), and has also been prepared via a multi-step synthesis from 3-endocarboxy-bicyclo(3.3.1)non-6-ene³⁹.

**Scheme 24****Scheme 25**

1.7 Thermal Rearrangements of Perfluoroaryl Allyl Ethers

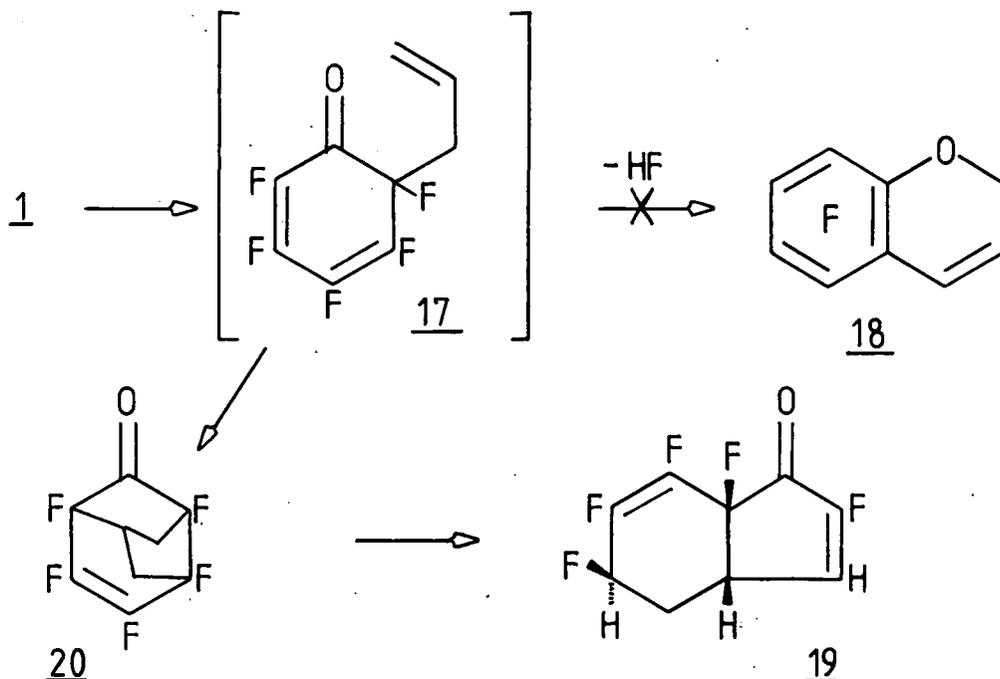
The flow pyrolysis of 2,3,4,5,6-pentafluorophenyl prop-2-enyl ether **1** at 365°C gives a stable para-dienone **16** as the major product (Scheme 26)⁴⁰.

**Scheme 26**

The intermediate ortho-dienone **17** was not isolated. The presence of fluorine atoms instead of hydrogen prevents the dienone tautomerising to the allyl phenol by hydrogen transfer. The presence of fluorine also renders the diene **17** electron deficient and consequently it has an "inverse" electron demand.

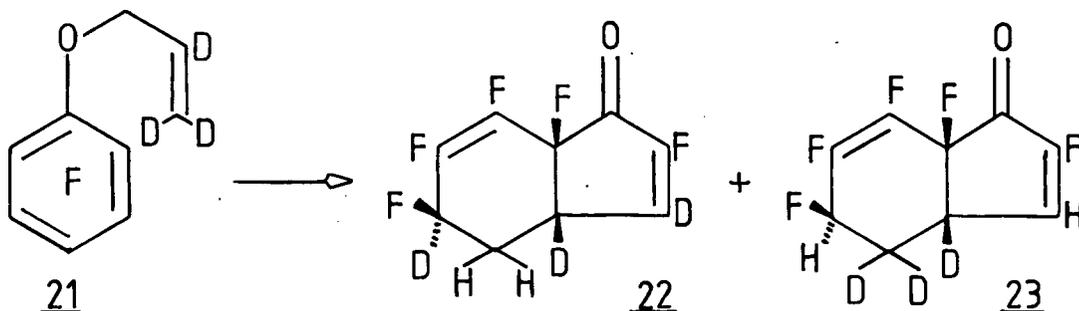
During a series of experiments designed to produce the tetrafluorochromen **18** (Scheme 27) the penta-fluoro

tetrahydroindenone 19 was isolated¹. The formation of this compound 19 was rationalised by the breakdown of the Sene II Diels-Alder adduct 20 by the cleavage of a C-C bond and a hydrogen migration. Pyrolysis of the dienone 16 also gave the indenone 19 as the major product¹.



Scheme 27

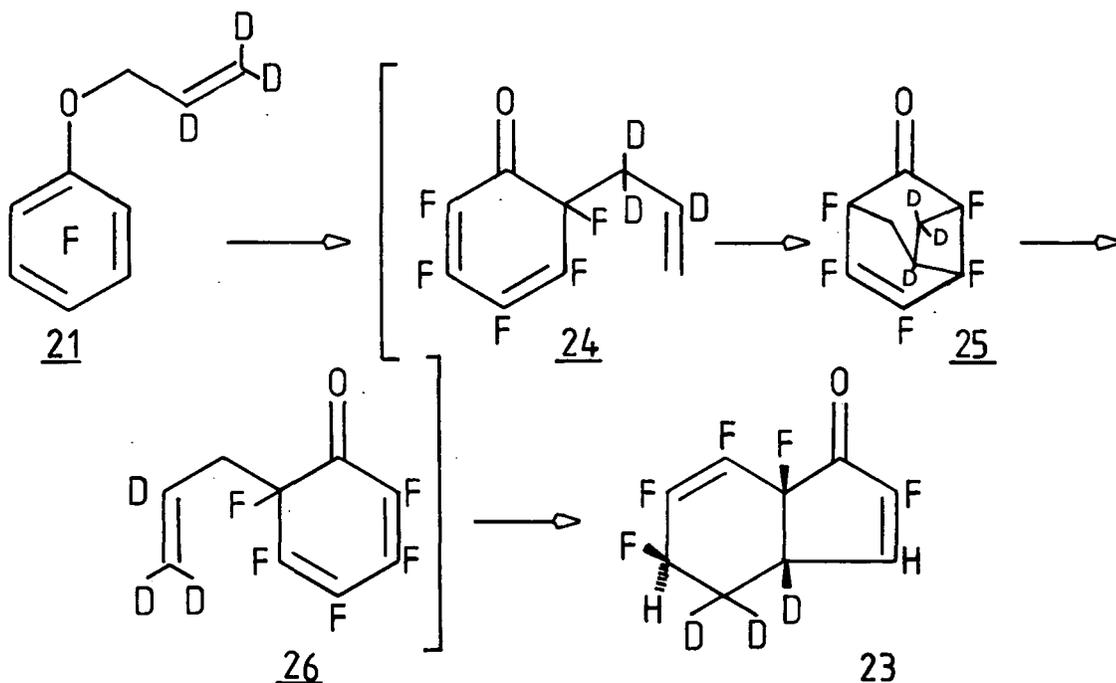
When the experiment was repeated using the deuterium labelled allyl ether 21 (Scheme 28) not only was the expected indenone 22 formed but also the indenone 23 was formed in a ratio of 9:10.



Scheme 28

The formation of 23 requires the inversion of the allyl group in the ortho-dienone 24 (i.e. an ortho-ortho

shift). The formation of 23 was rationalised by the formation of a Sense I Diels-Alder adduct 25, which then breaks down by cleavage of the four membered ring to give the isomeric dienone 26 which in turn gives 23 via a Sense II Diels-Alder addition (Scheme 29).

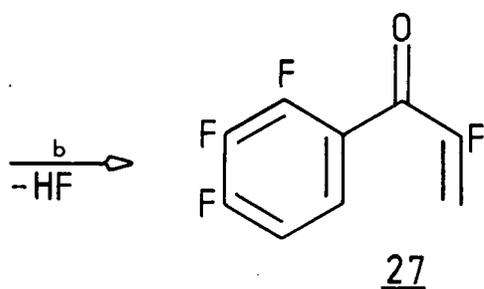
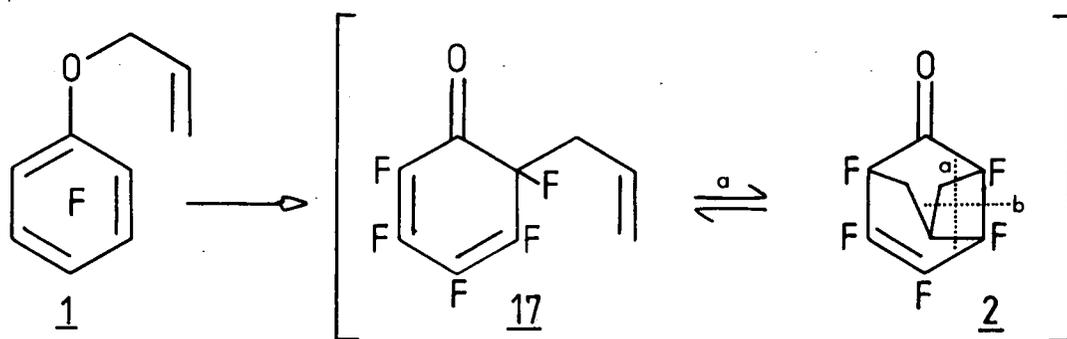


Scheme 29

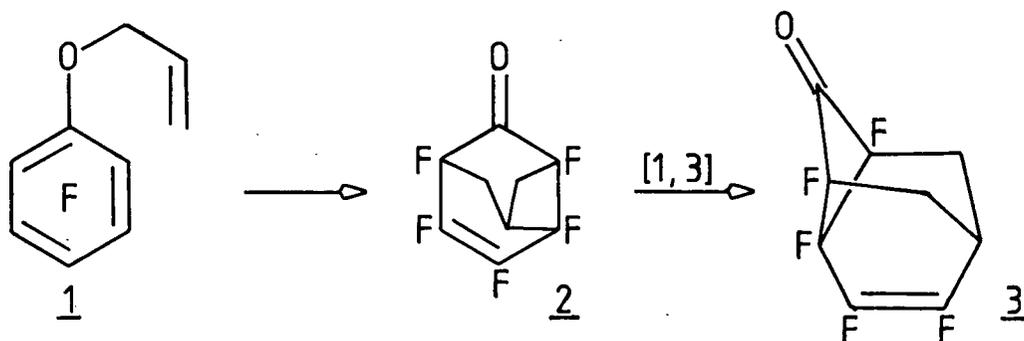
Further investigation of this reaction by Hall showed the presence of the vinyl ketone 27 which is formed by breaking the four membered ring in the Sense I Diels-Alder adduct 2 (Scheme 30).

The symmetric tricyclic ketone 3 was also isolated from the pyrolysis reaction in low yields. This ketone is formed from the Sense I Diels-Alder adduct 2 by a rearrangement equivalent to a [1,3] shift (Scheme 31). A compound thought to be the Diels-Alder adduct 2 was isolated and the structure has now been proved conclusively^{1f}.

Recently the thermal rearrangement of pentafluorophenyl prop-2-ynyl ether 28 has been reported⁴¹. Vapour

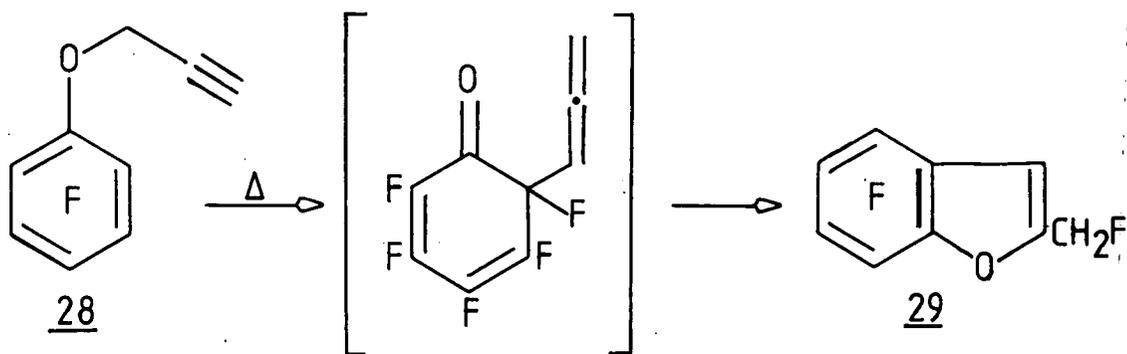


Scheme 30



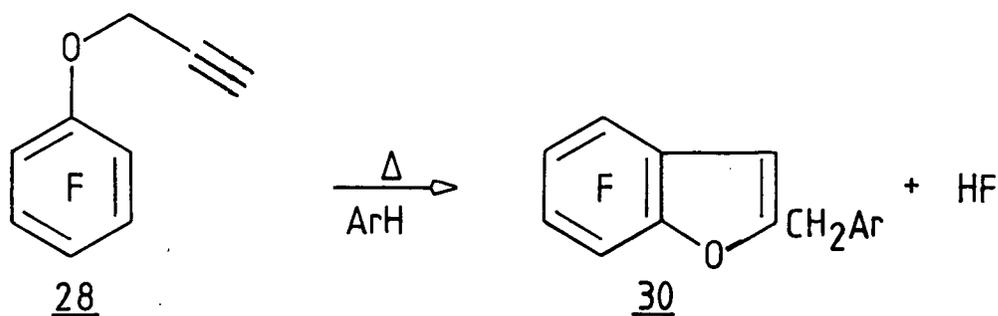
Scheme 31

phase pyrolysis of 28 at 370°C gave a complex mixture from which the major product 29 was isolated (Scheme 32).



Scheme 32

However, when heated in benzene in a sealed tube at 140°C the major product was 30a. Similarly heating in p-xylene at reflux gave 30b (Scheme 33).



a) Ar = C₆H₅

b) Ar = 2,5-Me₂C₆H₃

Scheme 33

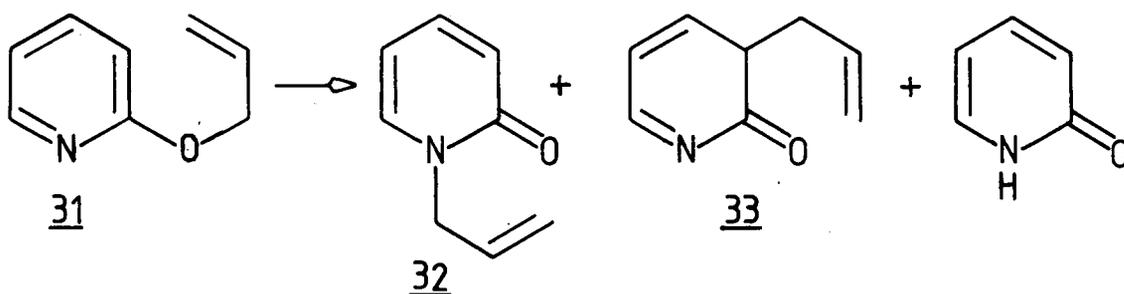
Free radical or ionic pathways could account for the formation of these products. It is interesting to note that the analogous hydrocarbon prop-2-ynyl ethers can give chromenes under the conditions used for the Claisen rearrangement⁴².

CHAPTER II

2.1 The Pyridine Claisen Rearrangement

The Claisen rearrangement in pyridyl alkenyl ethers is much less extensive than with aryl systems. Until recently there was no synthetic route to 3-pyridyl alkenyl ethers⁴³ and attempts to rearrange 4-pyridyl-prop-2-enyl ethers failed, producing mainly tar with no isolatable rearrangement products⁴⁴. As a result very little work has been done on the Claisen rearrangement in pyridine derivatives.

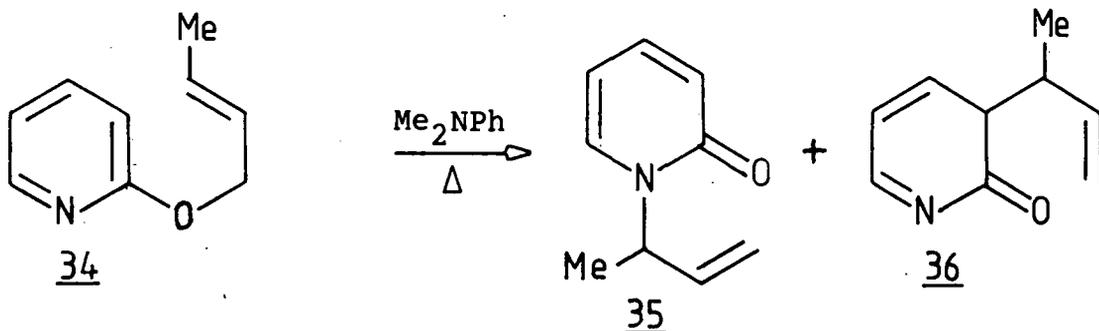
2-Pyridyl prop-2-enyl ether 31 rearranges in *N,N*-diethylaniline to give two pyridones 32 & 33 in approximately equal proportions as well as 2-pyridone and tar (Scheme 34). Heating the ether 31 without a solvent or at temperatures above 250°C gave only tar⁴⁴.



Scheme 34

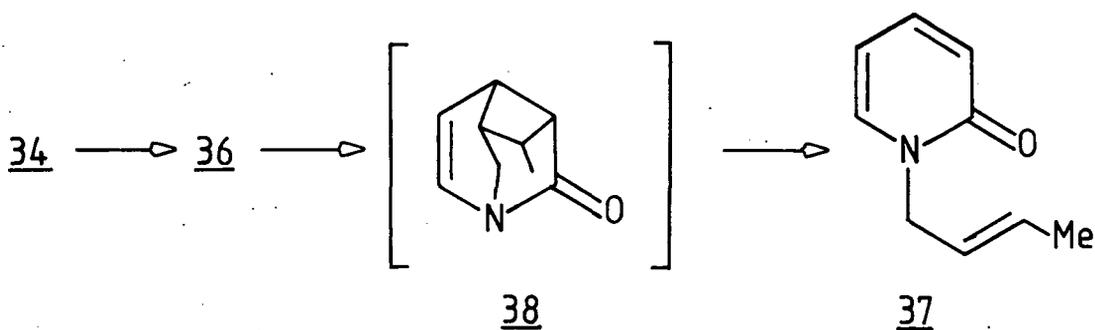
When two dissimilar positions are available for the Claisen rearrangement, the rearrangement takes place to the position of higher electron density⁴⁵. This means that in the pyridyl alkenyl ethers the prop-2-enyl group should preferentially migrate towards the nitrogen.

2-Pyridyl but-2-enyl ether 34 rearranges as expected⁴⁵ in dimethylaniline to give the two pyridones 35 & 36 (Scheme 35).



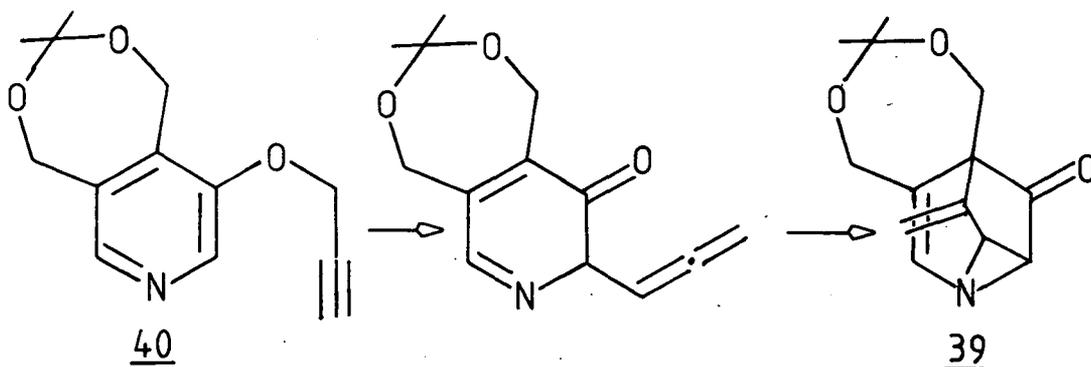
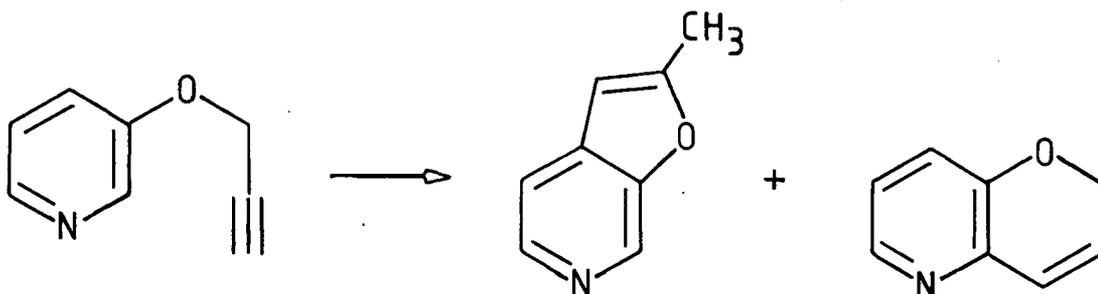
Scheme 35

However, when 34 was heated neat large amounts of 37 (up to 60%) were formed (Scheme 36). There is no inversion of the side chain in 37 (cf. 35) and its formation can be rationalised by invoking an ortho-ortho rearrangement proceeding via an internal Diels-Alder adduct 38, followed by cleavage of the four membered ring to give 37. The internal Diels-Alder adduct 38 was not isolated.



Scheme 36

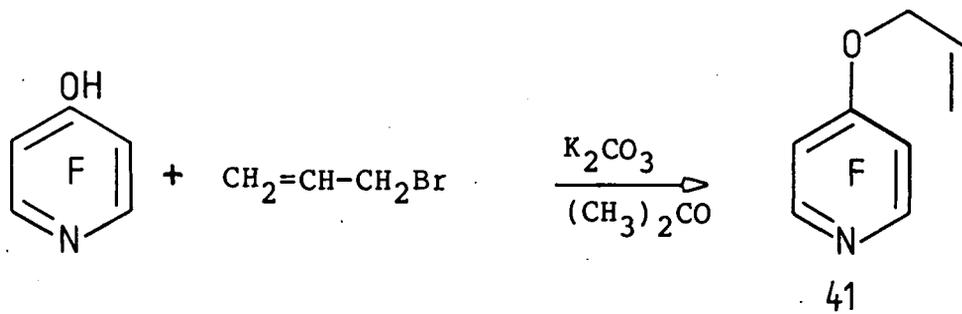
A Diels-Alder adduct 39 has been isolated from the rearrangement of the substituted 3-pyridyl prop-2-ynyl ether 40 (Scheme 37)⁴⁴. Without the blocking groups on C-4 and C-5 the rearrangement gives cyclisation products (Scheme 38).

**Scheme 37****Scheme 38**

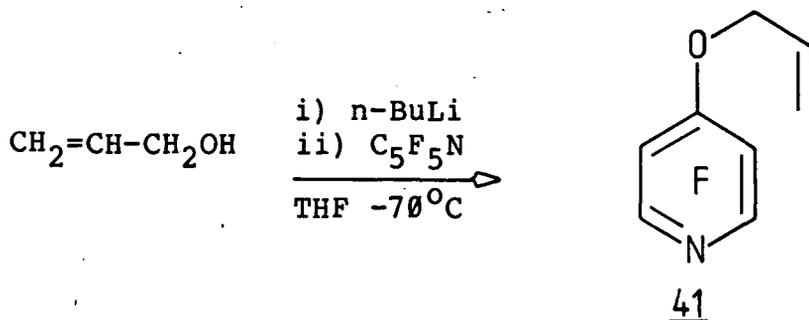
2.2 Pyrolysis of 2,3,5,6-Tetrafluoro-4-pyridyl Prop-2-enyl Ether 41.

In chapter 1 section 1.8, the thermal rearrangement of pentafluorophenyl prop-2-enyl ether 1 was described. As an extension to this work the pyrolysis of 2,3,5,6-tetrafluoro-4-pyridyl prop-2-enyl ether 41 was investigated. The 2,3,5,6-tetrafluoro-4-pyridyl prop-2-enyl ether 41 was readily prepared by heating tetrafluoro-4-hydroxy pyridine⁴⁶ and prop-2-enyl bromide with anhydrous potassium carbonate in dry acetone under reflux (Scheme 39).

After filtration and distillation of the solvent the residue was distilled under reduced pressure to give the ether 41. The i.r. spectrum showed the presence of a C=C at 1645 cm^{-1} and the ^{19}F nmr showed two peaks of equal

**Scheme 39**

intensity at 92.19 ppm (F-2 and F-6) and 159.78 ppm (F-3 and F-5) upfield from CFCl_3 . The ether was also prepared from prop-2-en-1-ol and pentafluoropyridine in THF using n-butyl lithium (Scheme 40).

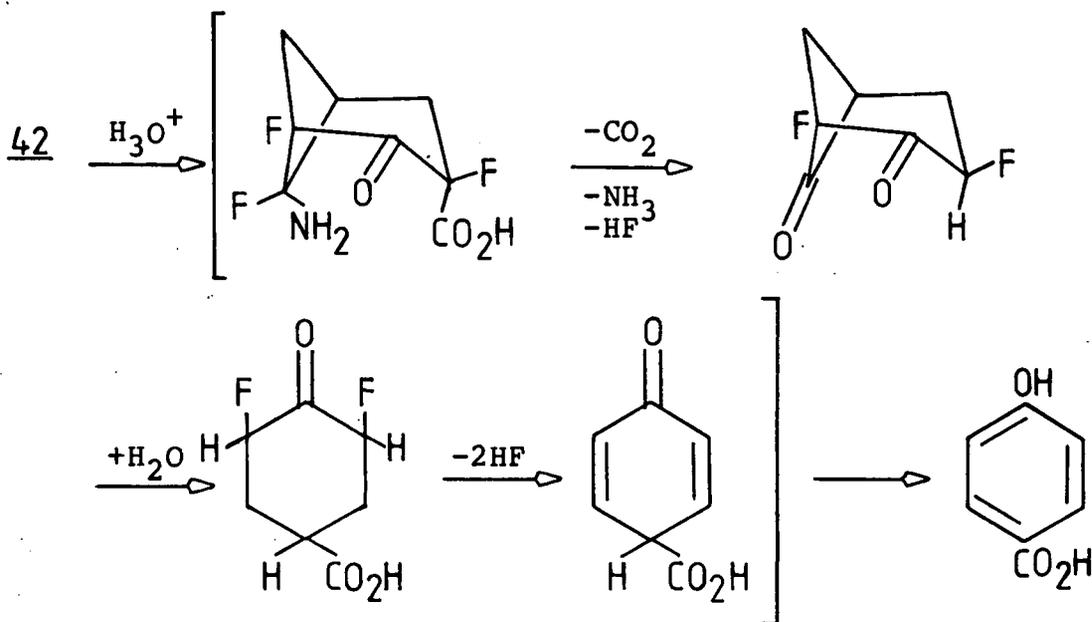
**Scheme 40**

A series of small scale exploratory static thermolyses showed that the products were susceptible to hydrolysis by atmospheric moisture. This problem was easily overcome by thoroughly drying the apparatus and reagents and by careful handling of the products to prevent hydrolysis. These exploratory reactions showed the best conditions to be $138-140^\circ\text{C}$ for ten days. Similar exploratory small scale flow pyrolyses were tried but abandoned as static thermolysis gave a cleaner reaction.

A large scale thermolysis reaction was carried out over ten days at 138°C . The volatile materials were removed in vacuo and were identified as starting material (15%) by i.r. spectroscopy. The non-volatile products were washed from the bulb with dry acetone leaving a

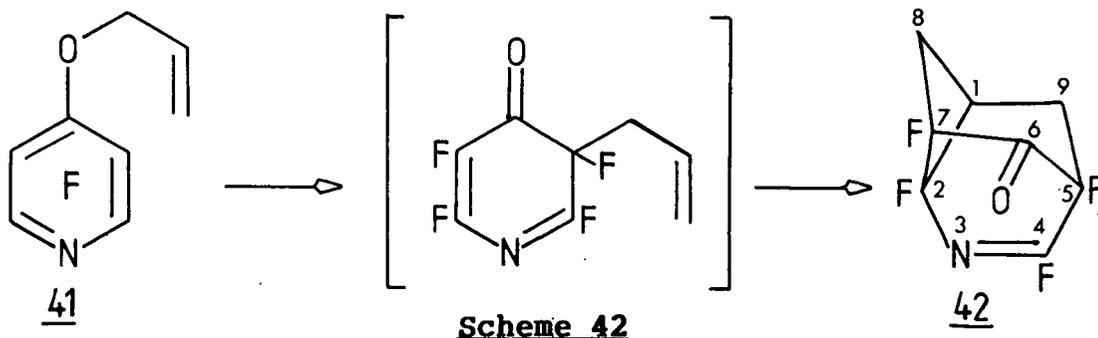
polymeric residue (54%). The washings were evaporated in vacuo to give a white solid, sublimation of which gave the major product (16%) the structure of which was consistent with it being an internal Diels-Alder adduct on the basis of i.r. and ^{19}F nmr spectroscopy. The i.r. spectrum showed the presence of a carbonyl group at 1778 cm^{-1} and a C=N group at 1702 cm^{-1} . The ^{19}F nmr recorded in D_6 acetone showed four absorptions of equal intensity: one at low field (61.5 ppm upfield of CFCl_3) and three at high field (163.5, 176.2, & 192.2 ppm upfield of CFCl_3).

The overall structure of the adduct was established by degradation to 4-hydroxybenzoic acid using 50% (v/v) sulphuric acid (Scheme 41). This confirmed the structure of the adduct as the Sense I Diels-Alder adduct 42. Scheme 42 shows the formation of 42 from the ether 41.



Scheme 41

The individual peaks of the ^{19}F nmr spectrum of 42 were too complex to examine without broadband decoupling of the protons, which simplified the peaks and allowed the F-F couplings to be measured. The peak at lowest field

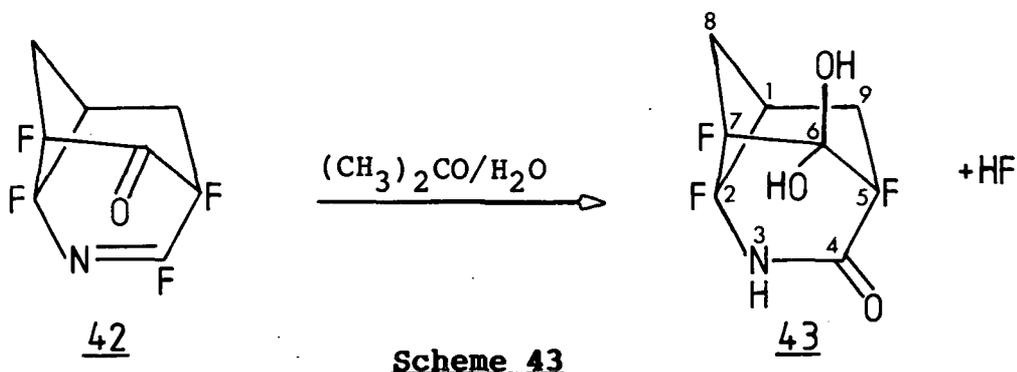


(61.5 ppm) was assigned as F-4. This peak showed considerable broadening due to the proximity of the nitrogen atom and so it was not possible to measure the coupling constants accurately. However, a large coupling of about 20 Hz was observed. The only other peak which showed a coupling of this magnitude was the high field peak at 192.2 ppm. The coupling was found to be 20.4 Hz and the peak was assigned to F-5. F-5 also showed a coupling at 7.0 Hz with the peak at 176.2 ppm which was assigned as F-7. The remaining peak at 163.3 ppm was assigned to F-2. Other small (2-5 Hz) through-space F-F couplings were observed.

The ^1H nmr spectrum showed three groups of peaks, the first at 3.156 ppm (intensity = 1) was a triplet of multiplets and must be H-1. The second peak was a triplet of doublets at 2.64 ppm (intensity = 2) and the third peak was a doublet (intensity = 2) centred at 2.40 ppm.

The presence of the nitrogen atom in the $-\text{N}=\text{C}-$ group causes the nearby fluorines to be shifted downfield. F-4 is at 61.5 ppm as compared with 139.6 ppm in the all carbon system 2¹. F-2 also shows a large downfield shift. A tertiary fluorine in a highly strained four membered ring would be expected to be at very high field (216 ppm in 2¹) but comes at 163.5 ppm in 42.

The residue from the sublimation (10%) was identified by i.r., ^1H nmr, and ^{19}F nmr spectroscopy as the hydrolysed and hydrated material 43. The ketone 42 was easily converted to compound 43 by dissolving it in aqueous acetone and allowing the solvent to evaporate off (Scheme 43).

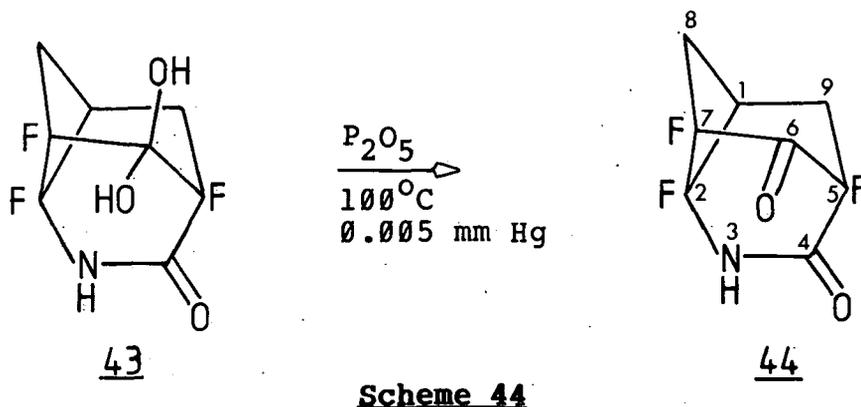


The resulting diol 43 was recrystallised from butan-2-one/petroleum ether. The i.r. spectrum showed strong absorptions in the regions $3170\text{--}3420\text{ cm}^{-1}$ due to the O-H and N-H groups. A strong absorption due to the carbonyl at C-4 was observed at 1723 cm^{-1} .

As expected the ^{19}F nmr of 43 only showed three absorptions due to F-2, F-5 and F-7. The conversion of the $-\text{N}=\text{C}-\text{F}$ group to the $-\text{NH}-\text{C}=\text{O}$ group caused F-2 to shift upfield to 176.6 ppm which is still much further downfield than in 2¹. F-7 remained almost unchanged at 177.0 ppm as did F-5 at 191.6 ppm. As with 42 broad band decoupling of the protons was necessary to simplify the spectrum so that the coupling constants could be measured. The large 20 Hz coupling observed in 42 between F-4 and F-5 had gone but F-5 still showed the coupling of 7.0 Hz to F-7. Some small 1-5 Hz through-space F-F couplings were also observed. The ^1H spectrum showed five absorptions: a broad singlet at 8.47 ppm due to the N-H proton; a singlet

at 6.05 ppm due to the O-H protons; a singlet at 2.94 ppm; a multiplet at 2.34 ppm and a triplet at 2.05 ppm due to the CH and the two CH₂ groups respectively.

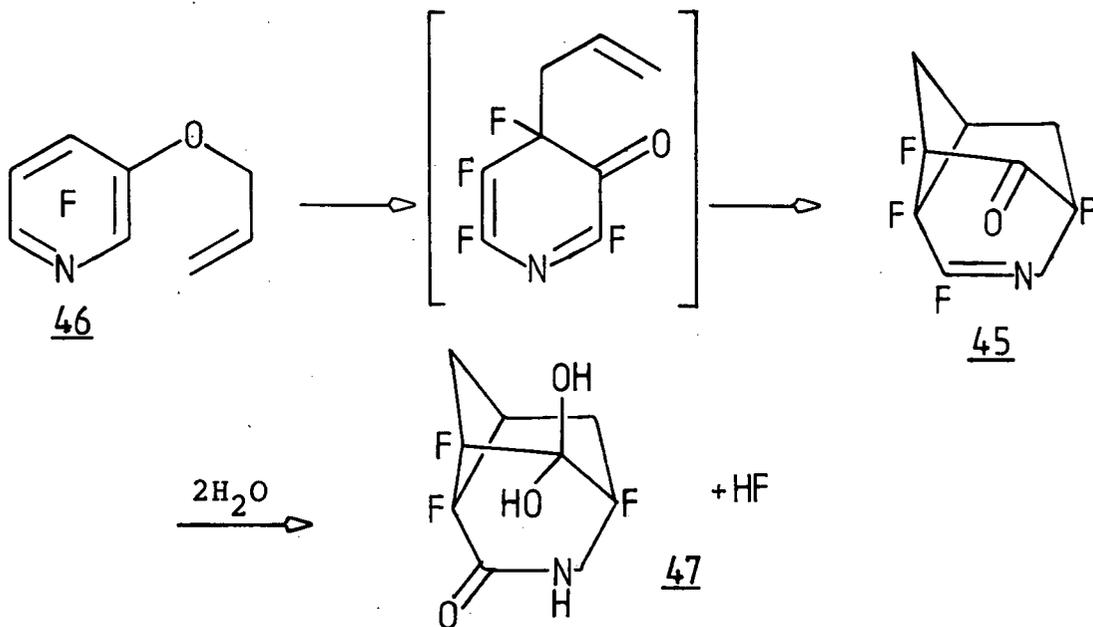
The gem diol 43 was easily dehydrated by sublimation from P₂O₅ at 100°C in vacuo to give the dione 44 (Scheme 44).



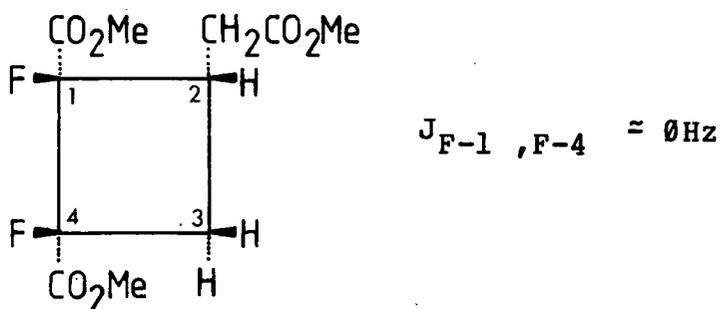
The i.r. spectrum showed two absorptions at 3100 and 3200 cm⁻¹ due to the N-H group; and two carbonyl absorptions: one at 1735 cm⁻¹ due to the amide carbonyl (-NH-CO-) and one at 1780 cm⁻¹ (C=O). The ¹⁹F nmr showed that F-2 had moved upfield to 179.9 ppm whilst F-5 was moved downfield by about 5 ppm to 186.6 ppm, and F-7 remained almost unaffected at 176.4 ppm. Broad band decoupling of the protons revealed the 7.0 Hz coupling between F-7 and F-5 and some small 2-3 Hz through-space F-F couplings.

The isomeric tricyclic ketone 45 has been prepared from 2,4,5,6-tetrafluoro-3-pyridyl prop-2-enyl ether 46 in very high yield (80%) by Brooke (Scheme 45)⁴⁷. This compound was not as susceptible to hydrolysis as 39 but was readily converted into the hydrated gem diol 47.

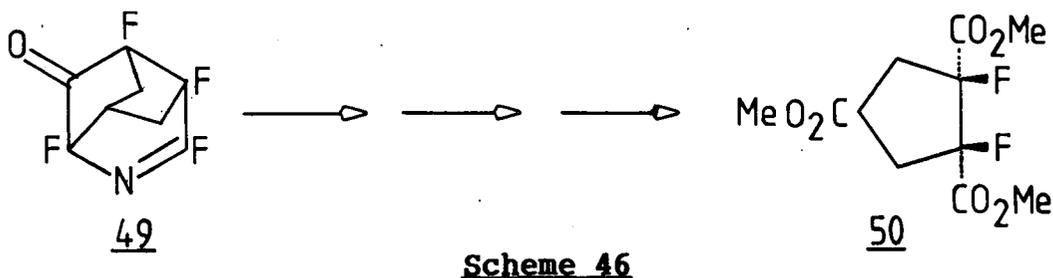
The skeletal structure was determined by cleaving two of the rings by acid hydrolysis and periodic oxidation followed by esterification with diazomethane to give a



cyclobutane derivative 48 (Diagram 5) which showed two absorptions in the ^{19}F nmr and no coupling between the fluorines.

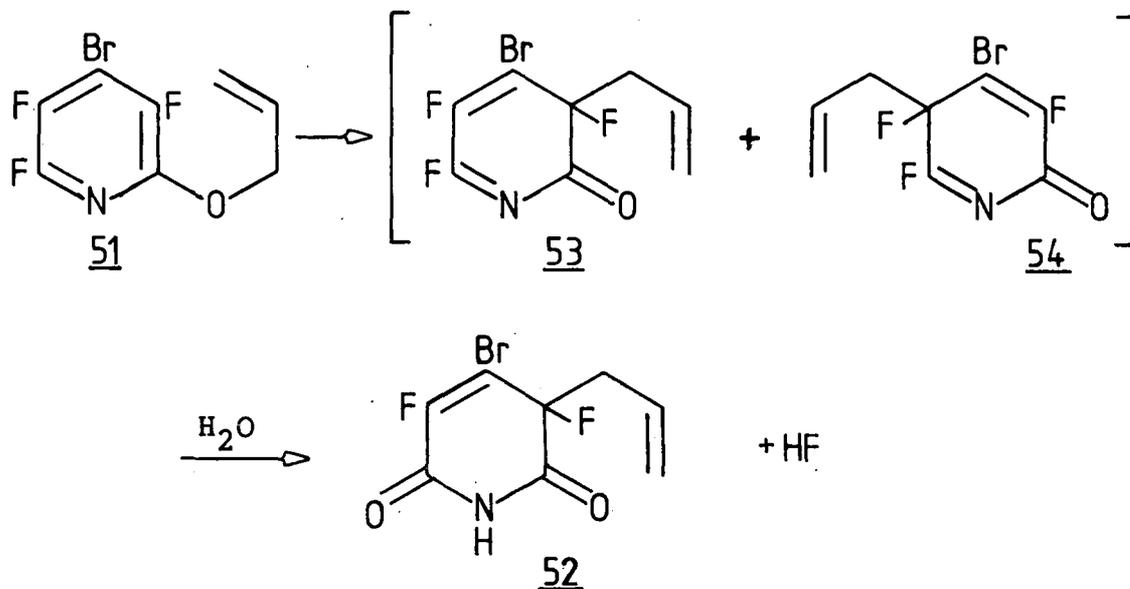


The Sense II Diels-Alder adduct 49 would have given a symmetrical cyclopentane derivative 50 (Scheme 46) which would have had only one signal in the ^{19}F nmr spectrum.



Brooke also showed that the 4-bromo-3,5,6-trifluoropyridyl-2-prop-2-enyl ether 51 gave no intra-molecular

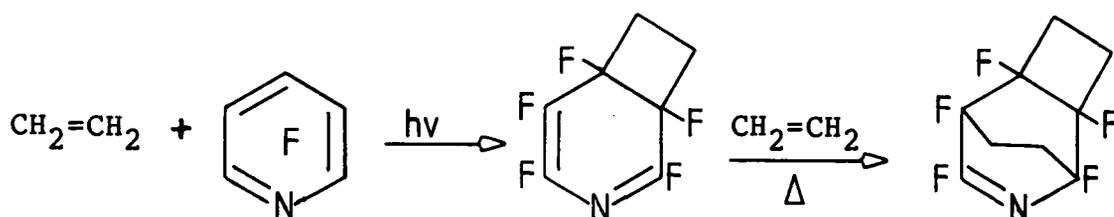
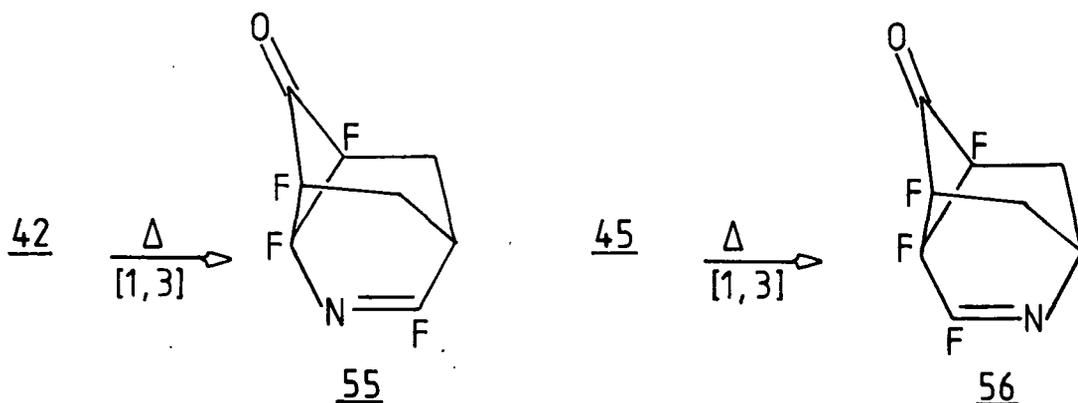
Diels-Alder adducts (Scheme 47), the majority of the recovered material being starting material. Some imide 52 was isolated from the residue and is formed by hydrolysis of either of the intermediate dienones 53 & 54⁴⁷.



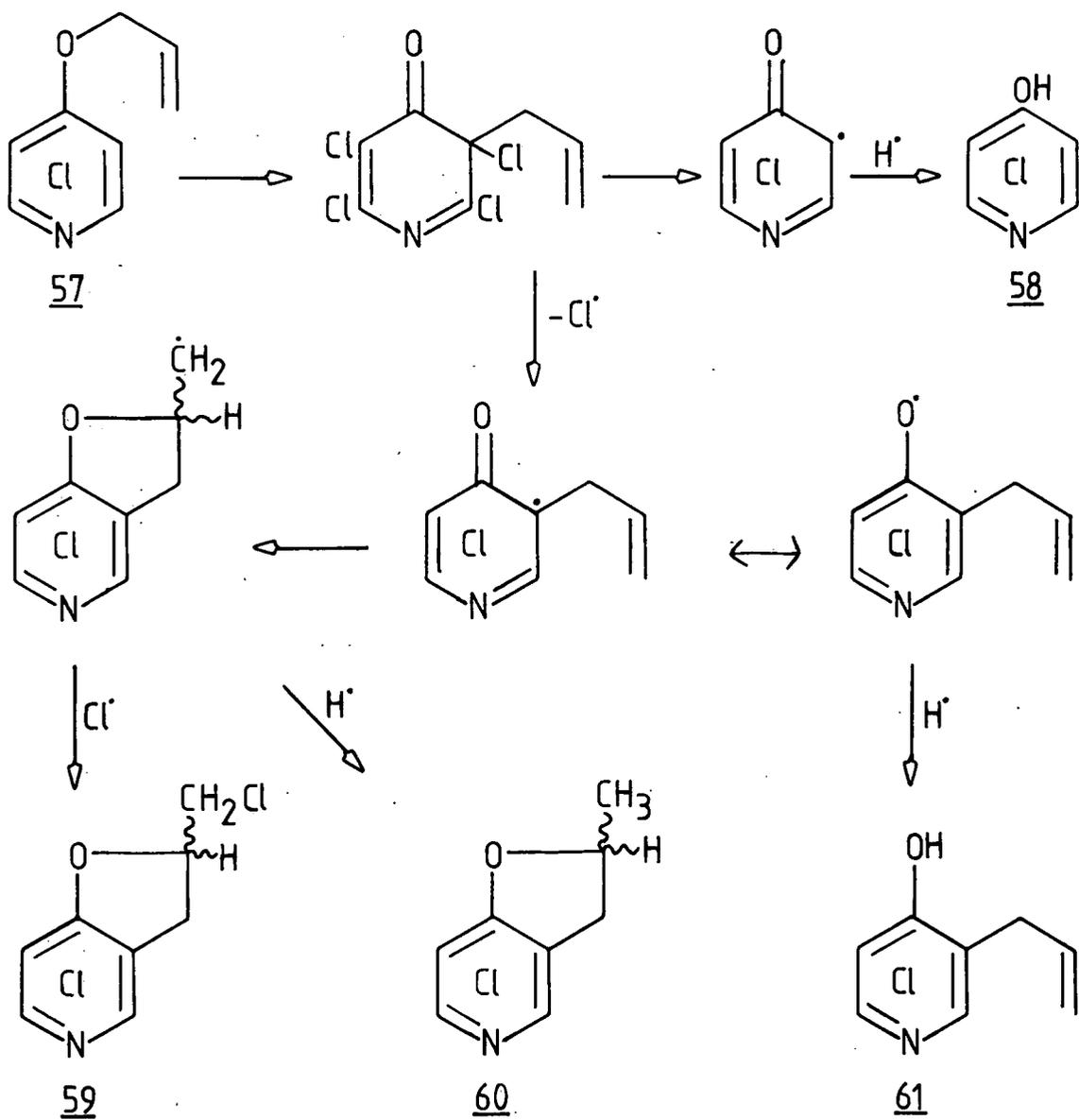
In both compounds 46 and 51 the allyl group only migrates away from the nitrogen unlike the hydrocarbon analogues systems where migration towards the nitrogen is preferred⁴⁵.

Attempts to isolate analogues of 3 by rearranging 42 and 45 failed. The rearrangement is equivalent to a [1,3] shift and would have given the symmetric ketones 55 and 56 (Scheme 48) which would probably hydrate to give gem diols as the all carbon system 3 does¹.

There is only one report in the literature of a Diels-Alder adduct in fluorinated pyridines: the addition of ethene to the product of a photochemical addition of ethene to the 3,4 positions of pentafluoropyridine (Scheme 49)⁴⁸.



Recent work⁴⁹ on the pyrolysis of tetrachloro-4-pyridyl allyl ether 57 shows its behaviour is quite different from the tetrafluoro compound 41. Heating the allyl ether 57 at 190°C gave a complex mixture of products (Scheme 50). Although a Claisen rearrangement was observed, the ortho-dienone was not isolated. Instead this broke down by two different routes: one giving tetrachloro-4-hydroxypyridine 58 by the loss of an allyl radical and the other by the homolytic fission of a C-Cl bond giving two furan derivatives 59 & 60 and 2,5,6-trichloro-3-allyl-4-hydroxypyridine 61. No intramolecular Diels-Alder adducts were isolated. Using tetrachloro-4-pyridyl propargyl ether, only the starting material and tetrachloro-4-hydroxy pyridine were isolated.



Scheme 50

2.3 Experimental

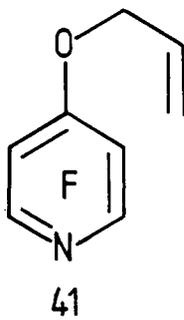
2,3,5,6-Tetrafluoro-4-pyridyl Prop-2-enyl ether 41

1. 2,3,5,6-tetrafluoro-4-hydroxypyridine (22g) and prop-2-enyl bromide (25ml) were heated under reflux with anhydrous potassium carbonate (50g) in dry acetone (200ml) for 16 hours. The mixture was filtered through a short column of anhydrous $MgSO_4$, the solvent removed by distillation, and the residue distilled under reduced pressure to give 2,3,5,6-tetrafluoro-4-pyridyl prop-2-enyl ether 41 (24g, 87%) b.p. $80^\circ C$ at 16mm Hg. [Found: C, 46.5; H, 2.8; N, 7.0%; M^+ , 207 $C_8H_5F_4NO$ requires C, 46.4; H, 2.4; N, 6.8%; M, 207]

$\delta_F[(CD_3)_2CO]$, 92.19 (F-2 and F-6); 159.78 ppm (F-3 and F-5) upfield from internal CFC_3

ν_{max} : 1645 (CH=CH2) cm^{-1} .

2. Prop-2-en-1-ol (8.1g) in dry THF was cooled under dry nitrogen to $-70^\circ C$ (CO_2 /acetone) and treated with n-butyllithium in n-hexane (101ml, 0.125 moles) while stirring. Pentafluoropyridine (21.45g) was added and stirring continued whilst the mixture warmed to room temperature. The products were poured into water, acidified and extracted with ether (3 x 75ml). The extracts were dried ($MgSO_4$), filtered, and the solvent evaporated. The residue was distilled under reduced pressure to give the ether 41 (19.4g, 74%).



Thermolysis reactions

2,4,5,7-Tetrafluoro-3-azatricyclo[3.3.1.0^{2,7}]non-3-en-6-one 42

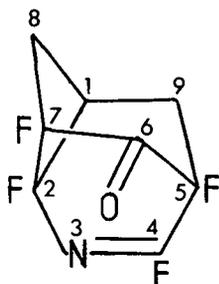
The ether 41 (2.8g) was sealed under vacuum (0.005mm Hg) in a 10 dm³ bulb fitted with a side arm, and heated at 138-140°C for ten days. The products were condensed into the side arm by cooling in liquid air. After opening the bulb, volatile material was removed by pumping through a trap cooled in liquid air and was identified as the starting material 41 (0.44g, 17%) by its i.r. spectrum. The solid remaining in the side arm was washed out using dry acetone. The acetone was then evaporated off and the products sublimed under vacuum (0.005mm Hg) at room temperature to give the crude tricyclic product (0.45g, 19%) leaving the hydrolysed product (0.28g, 12%) behind along with polymeric material (1.52g, 69%). The crude tricyclic product was recrystallised from benzene-petroleum ether (b.p. 60-80°C) followed by sublimation to give 2,4,5,7-tetrafluoro-3-azatricyclo[3.3.1.0^{2,7}]non-3-en-6-one 42 m.p. 81.5-83°C. [Found: C, 46.7; H, 2.4; N, 7.1%; M⁺, 207. C₈H₅F₄NO requires C, 46.4; H, 2.4; N, 6.8%; M, 207].

δ_F [(CD₃)₂CO], 61.5 (F-4); 163.5 (F-2); 176.2 (F-7); and 192.2 ppm (F-5) upfield from CFC1₃.

δ_H [(CD₃)₂CO], 3.15 (H-1); 2.64 and 2.40 ppm (both I=2, H-8, H-9) with intensities 1:2:2 respectively, downfield from internal TMS.

$J_{(F-4, F-5)}$ 20.4 Hz; $J_{(F-5, F-7)}$ 7.0 Hz;

ν_{max} : 1702 (N=CF), and 1778 (C=O) cm⁻¹.



2,5,7-Trifluoro-6,6-dihydroxy-3-azatricyclo[3.3.1.0^{2,7}]nonan-4-one 43

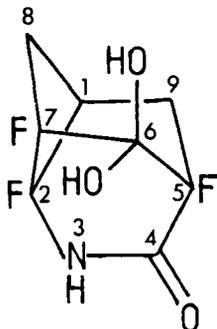
The tricyclic ketone 42 (0.45g) was dissolved in 'wet' acetone and the solvent allowed to evaporate in air. The crude hydrolysed tricyclic material (0.48g) was recrystallised from 2-butanone petroleum ether (b.p.60-80°C) to give 2,5,7-trifluoro-6,6-dihydroxy-3-azatricyclo[3.3.1.0^{2,7}]nonan-4-one 43 m.p. 167-168°C. [Found: C,43.2; H,4.0; N,6.4%. C₈H₈F₃NO₃ requires C,43.1; H,3.6; N,6.3%].

δ_F [(CD₃)₂CO], 13.6 (F-2, doublet of doublets); 14.0 (F-7, doublet of doublets) and 28.6ppm (F-5, doublet of doublets) upfield from internal C₆F₆.

δ_H [(CD₃)₂CO], 8.47 (N-H, singlet, I = 1); 6.05 (O-H, singlet, I=1); 2.94, 2.34 and 2.05ppm (singlet, triplet, multiplet, H-1, H-8 and H-9)

$J_{(F-5, F-7)}$ 7.5Hz; $J_{(F-2, F-5)}$ 4.5Hz; $J_{(F-2, F-7)}$ 1.2Hz.

ν_{max} : 1725 (C=O); 3170, 3280 and 3420 cm⁻¹ (O-H, N-H region).



43

2,5,7-Trifluoro-3-azatricyclo[3.3.1.0^{2,7}]nonan-4,6-dione44

The gem diol 43 was sublimed from P₂O₅ at 100°C and 0.005mm Hg causing it to dehydrate and give the 2,5,7-trifluoro-3-azatricyclo[3.3.1.0^{2,7}]nonan-4,6-dione 44

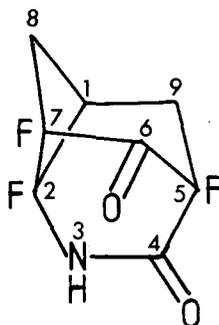
m.p. 172-174°C. [Found: C, 47.1; H, 2.7; N, 7.2%; M⁺, 205.

C₈H₆F₃NO₂ requires C, 46.8; H, 2.9; N, 6.8%; M, 205].

δ_F [(CD₃)₂CO], 13.4 (F-7, doublet of doublets); 16.9 (F-2, doublet of doublets); 23.6ppm (F-5, doublet of doublets) upfield from internal C₆F₆

J_(F-5, F-7) 7.0Hz; J_(F-2, F-7) 2.8Hz; J_(F-2, F-5) 2.2Hz

ν_{\max} : 1735 (HN-C=O); 1780 (C=O); 3100 and 3200 cm⁻¹ (N-H region).

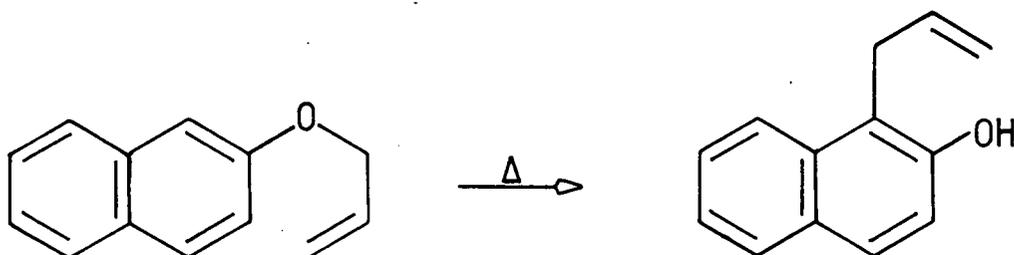
44Hydrolysis of the Gem Diol 43

The tricyclic diol 43 (95 mg) was heated under reflux in sulphuric acid (10 ml, 50% v/v) for five minutes. The solution was diluted with water, extracted with ether, and the dried (MgSO₄) extracts evaporated to give a solid (59 mg) the i.r. spectrum of which was identical with an authentic sample of 4-hydroxybenzoic acid.

CHAPTER 3

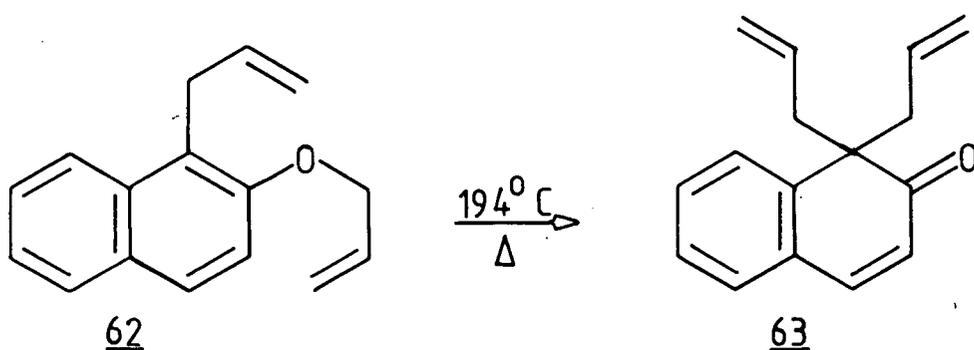
3.1 Thermal Rearrangements of Naphthyl Prop-2-enyl and Prop-2-ynyl Ethers

The thermal rearrangement of 2-naphthyl prop-2-enyl ether to 1-(prop-2-enyl)-naphth-2-ol was first observed by Claisen (Scheme 51)⁵⁰.



Scheme 51

1-Prop-2-enyl-2-naphthyl prop-2-enyl ether 62 heated either neat or in *N,N*-dimethylamine at 194°C gives the dienone 63 in 55% yield (Scheme 52)⁵¹.

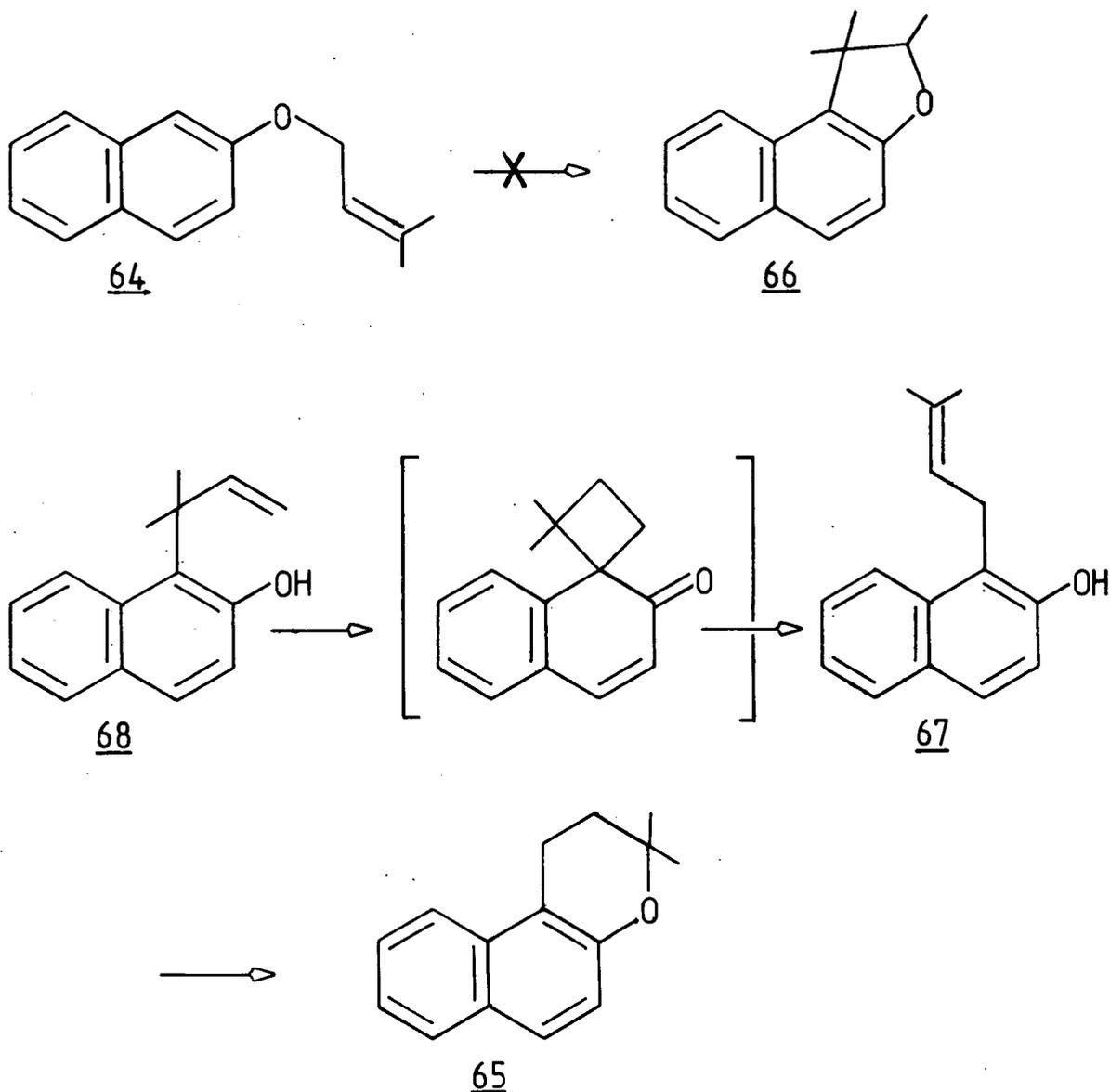


Scheme 52

Compound 63 is stable at room temperature but on heating to 194°C reverts to 1-prop-2-enyl-2-naphthyl prop-2-enyl ether and 1-prop-2-enyl-2-naphthol. The stability of the dienone was attributed to the fact that a para Claisen rearrangement is impossible and the formation

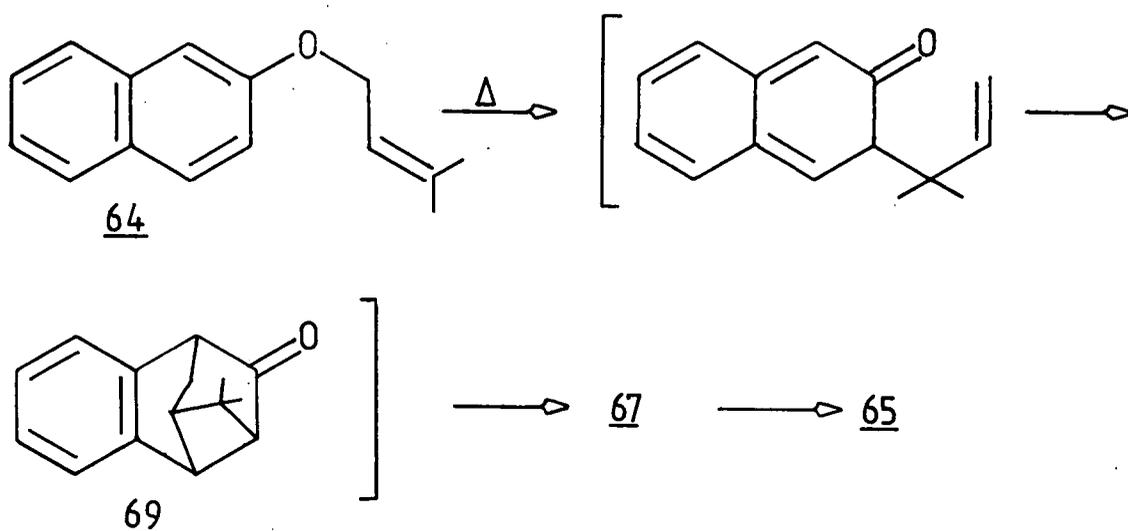
of an intramolecular Diels-Alder adduct would lead to an unreasonable loss of resonance energy.

Pyrolysis of 2-naphthyl (3-methylbut-2-enyl) ether 64 (Scheme 53) in vacuo gave the cyclised material 65 instead of the expected product 66⁵². Compound 65 was also obtained by pyrolysis of the naphthol 67. The suggested mechanism for this reaction was a Claisen rearrangement of the butenyl ether 64 to give the naphthol 68 followed by rearrangement of the butenyl group via a spirocyclobutane to give 67 which cyclised to give the product 65.

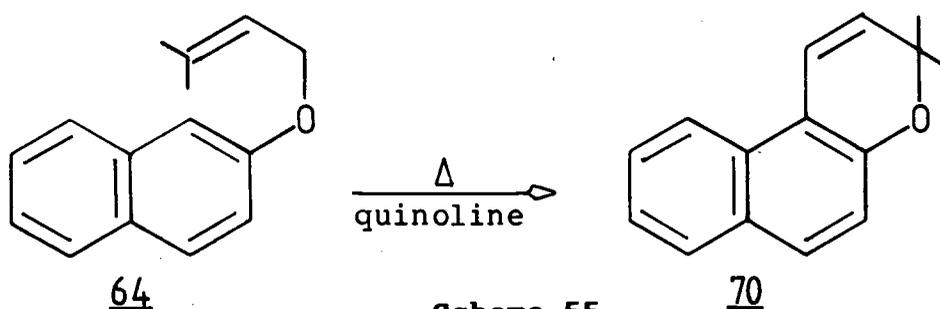


Scheme 53

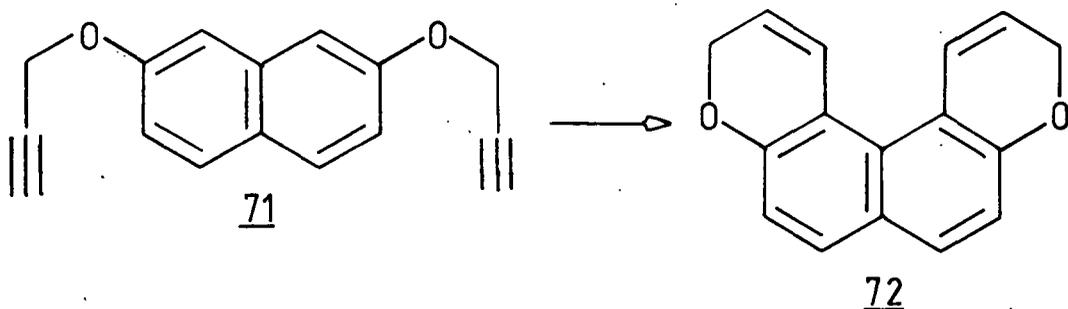
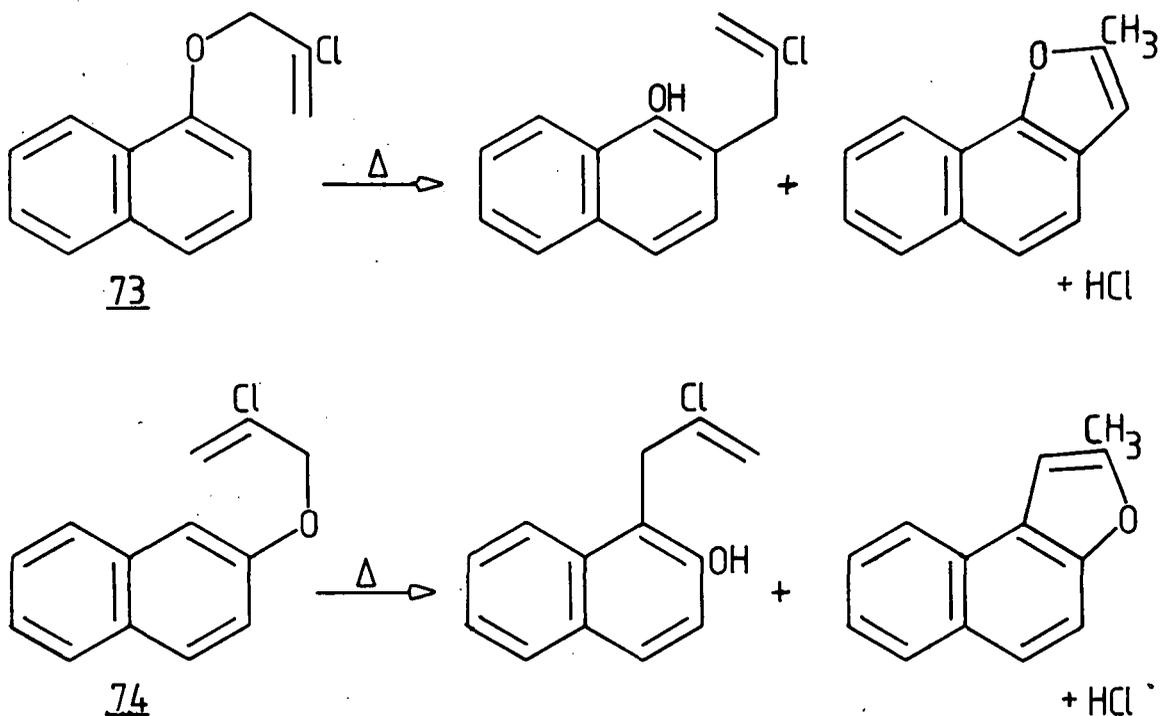
An alternative rationalisation of this rearrangement would be a Claisen rearrangement to C3 on the naphthalene followed by an ortho-ortho shift via the Diels-Alder adduct 69 (Scheme 54). However, this is unlikely since no rearrangements of 2-substituted naphthalenes to 3-substituted naphthalenes have been reported.



When the butenyl ether 64 was heated in quinoline surprisingly the dehydro analogue of compound 65 namely compound 70 was obtained (Scheme 55).

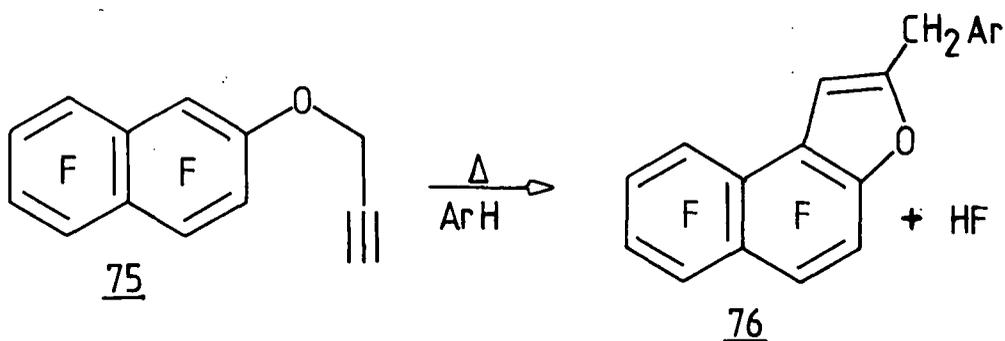


Like the propargyl phenyl ethers, the dipropargyl naphthyl ether 71 also gives a cyclisation product 72 on heating in diethylaniline (Scheme 56)⁵³, as do the 1-(2-chloro-prop-2-enyl) naphthyl ether 73 and the 2-(2-chloro-prop-2-enyl) naphthyl ether 74 (Scheme 57)⁵⁴.

**Scheme 56****Scheme 57**

A recent paper describes the thermal rearrangement of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether **75** in benzene and p-xylene⁴¹. When heated with benzene in a sealed tube at 140°C or in p-xylene at reflux the major products were **76a** and **76b** respectively (Scheme 58).

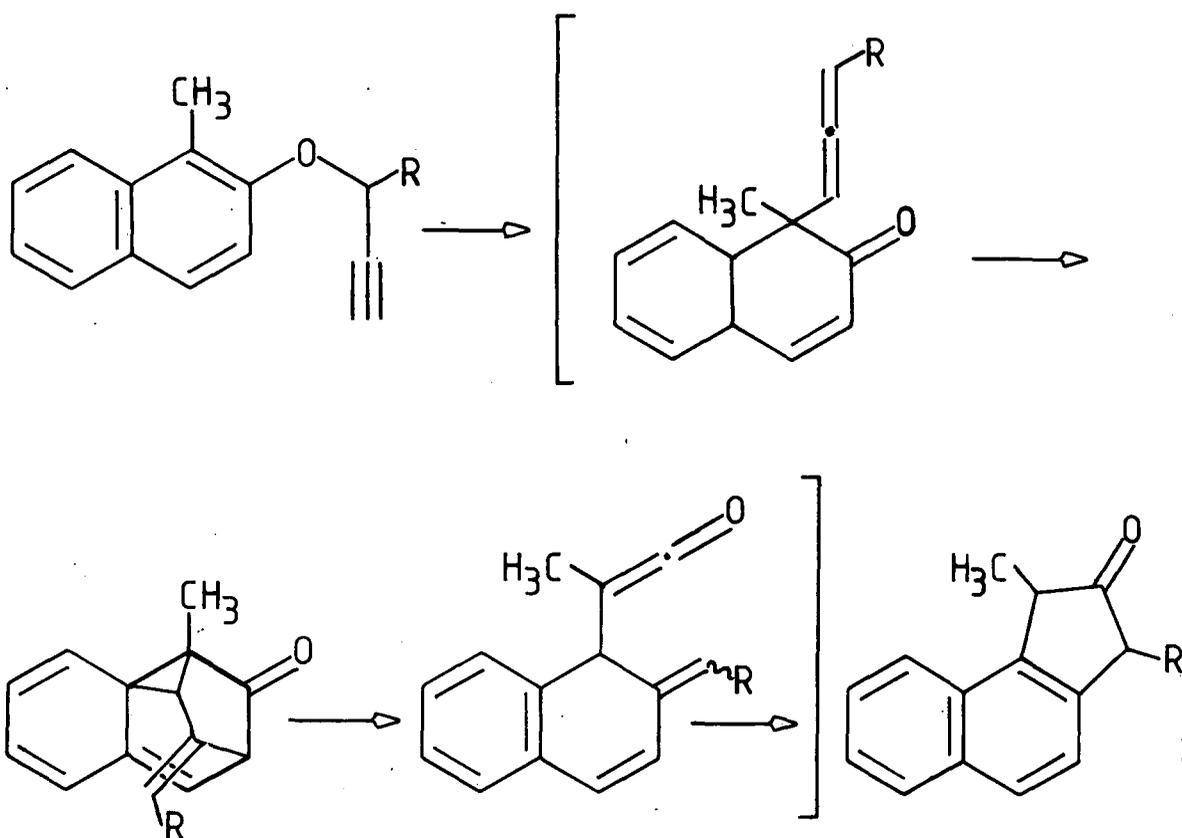
Schmid has suggested that intramolecular Diels-Alder adducts are involved in the thermal rearrangements of 1-substituted propargyl 2-naphthyl ethers⁵⁵ (Scheme 59), although no Diels-Alder adducts were isolated.



a) Ar = C₆H₅

b) Ar = 2,5-Me₂C₆H₃

Scheme 58

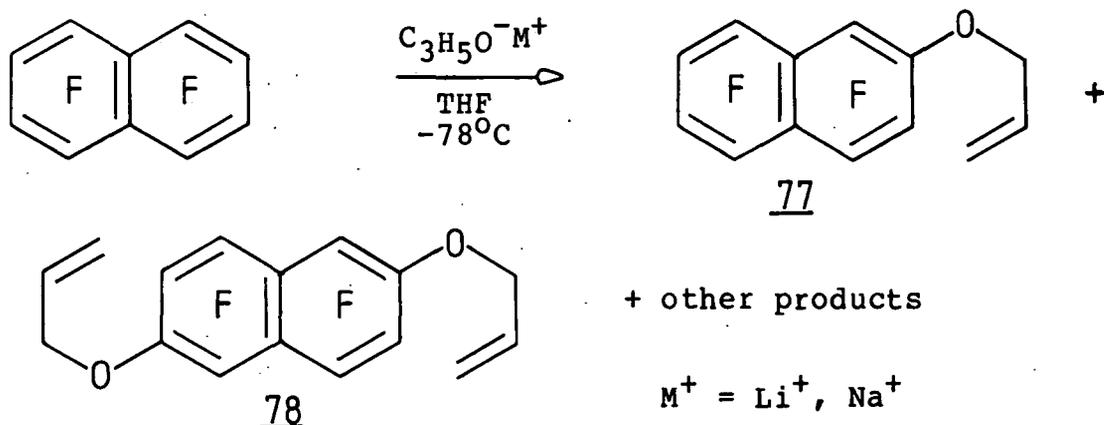


Scheme 59

3.2 Preparation of 1,3,4,5,6,7,8-Heptafluoronaphthyl-2-Prop-2-enyl Ether 77

The pyrolysis of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-enyl ether **77** was chosen for study because the higher double bond character of the ether **77** means that thermal rearrangements should be more facile than in the

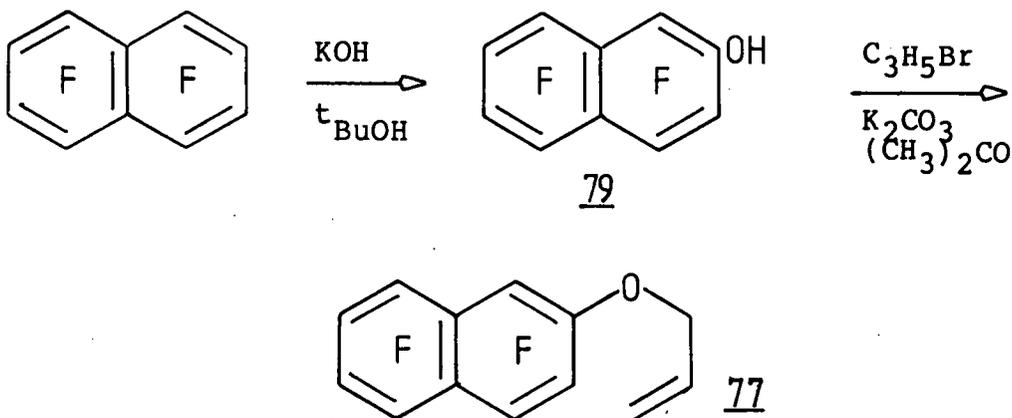
corresponding pentafluorophenyl prop-2-enyl ether 1. Attempts to produce the prop-2-enyl ether 77 directly from octafluoronaphthalene and the lithium or sodium salt of prop-2-enyl alcohol produced a mixture of compounds including the prop-2-enyl ether 77 and the 2,6 diprop-2-enyl ether 78 (Scheme 60). A mass spectrum of the mixture suggested the presence of the n-butyl ether and a butyl prop-2-enyl ether as well.



Scheme 60

The symmetrical diprop-2-enyl ether 78 was readily identified by its mass spectrum ($m/e = 348$), and the ^{19}F nmr which showed only three absorptions. Since this route gave mixtures, the prop-2-enyl ether was synthesised from the naphthol 79 which was readily made by heating octafluoronaphthalene and potassium hydroxide in t-butanol under reflux⁵⁶. The prop-2-enyl ether 77 was prepared by heating the heptafluoro-2-naphthol with allyl bromide and anhydrous potassium carbonate under reflux in dry acetone (Scheme 61).

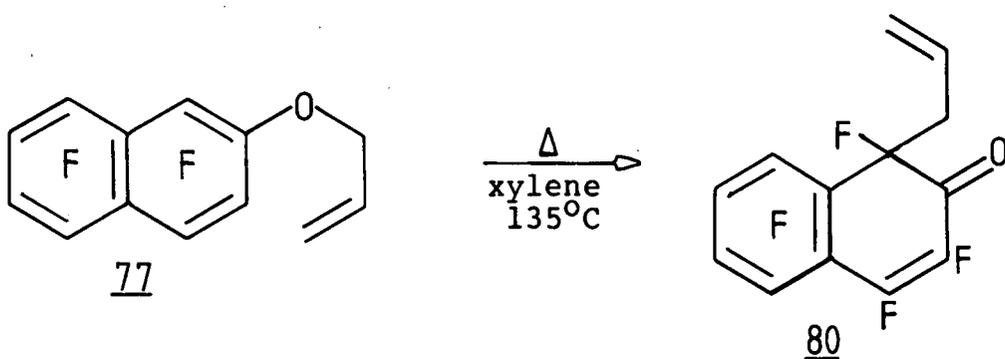
The product was purified by distillation in vacuo to give a pale yellow oil (64%). If the distillation temperature was allowed to rise above about $125^\circ C$ a white crystalline solid was formed. This material was



Scheme 61

identified as the naphthalenone 80 by its i.r. spectrum and ^{19}F nmr spectrum. The i.r. spectrum showed strong absorptions at 1708 cm^{-1} ($\text{C}=\text{O}$) and 1670 cm^{-1} ($-\text{CF}=\text{CF}-$). The ^{19}F nmr showed seven absorptions. Two fluorines showed a large peri coupling of 75.5 Hz whilst a smaller peri coupling of 25.5 Hz was also observed. This confirmed the structure as the 1-prop-2-enyl naphthalenone rather than the alternative Claisen rearrangement product, the 3-prop-2-enyl naphthalenone, which would be expected to show two large peri couplings involving four fluorines.

The prop-2-enyl ether 77 was readily converted to the naphthalenone 80 (Scheme 62) by heating it in xylene at 135°C for two and a half hours. The crude naphthalenone was purified by sublimation in vacuo and then recrystallisation from petroleum ether (64%).



Scheme 62

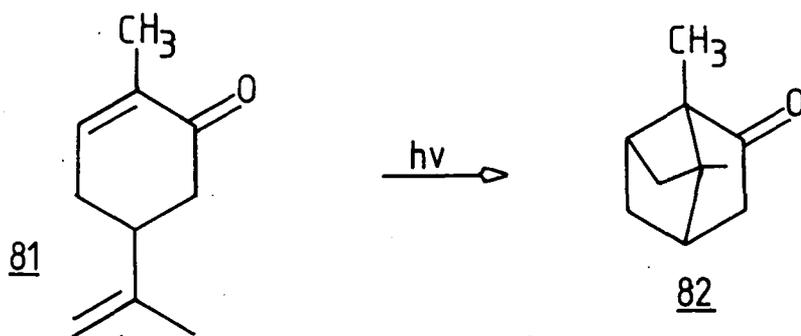
3.3 Pyrolysis of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-enyl ether 77

Pyrolysis of the prop-2-enyl ether 77 in vacuo (480°C, 0.005 mm Hg) through a quartz tube packed with quartz wool produced a complex mixture of products which were separated by preparative thick-layer chromatography. The three major products were isolated and identified as the prop-2-enyl ether 77 the naphthalenone 80 and naphthol 79 by i.r. and ^{19}F nmr spectroscopy. The minor products were not identified. The large amounts of naphthol formed caused problems by obscuring the baseline on tlc preventing slow-running products being seen. Since tricyclic products could not be formed successfully by the thermal route the pyrolysis reactions were abandoned and photolysis tried instead.

3.4 Photochemical [2 + 2] Cycloadditions in Cyclic Enones

The photochemical cycloaddition between an olefin and an α, β unsaturated ketone is known as the Eaton-de Mayo reaction and is quite well known⁵⁷.

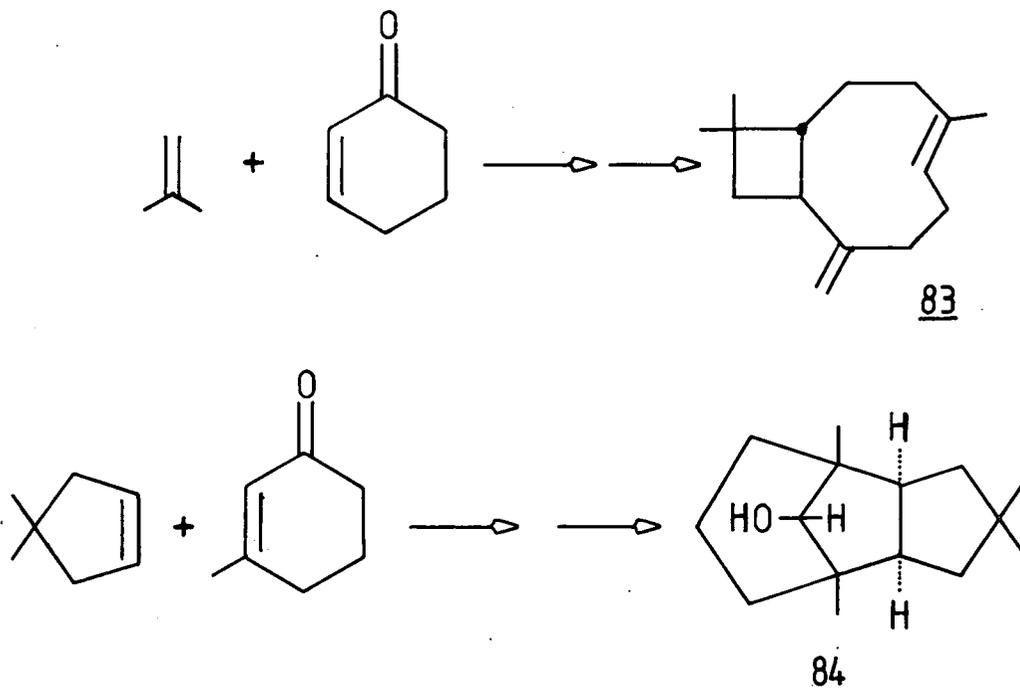
The reaction was first reported by Ciamician⁵⁸ who found that when carvone 81 was irradiated, a new compound was formed, for which Ciamician proposed the tricyclic structure 82 (Scheme 63).



Scheme 63

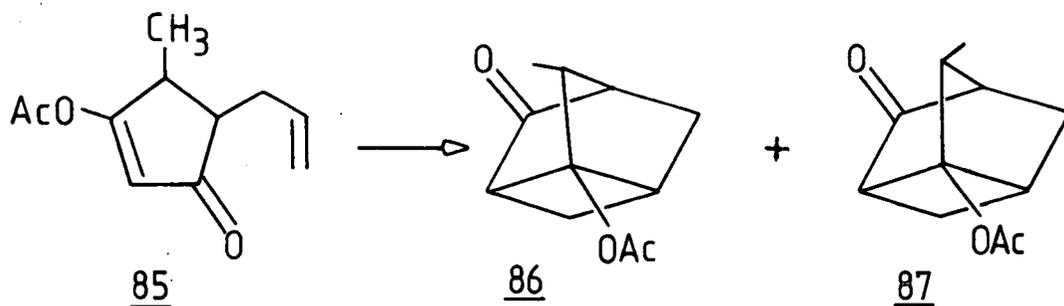
Ciamician was unable to verify the structure though the structure was later confirmed by Buchi and Goldman⁵⁹.

The reaction has become important in the synthesis of multicyclic compounds. The reaction is used in the synthesis of the cubane skeleton⁶⁰. The reaction was also used by Corey in the synthesis of caryophyllene 83⁶¹ and α -caryophyllene alcohol 84⁶² (Scheme 64).



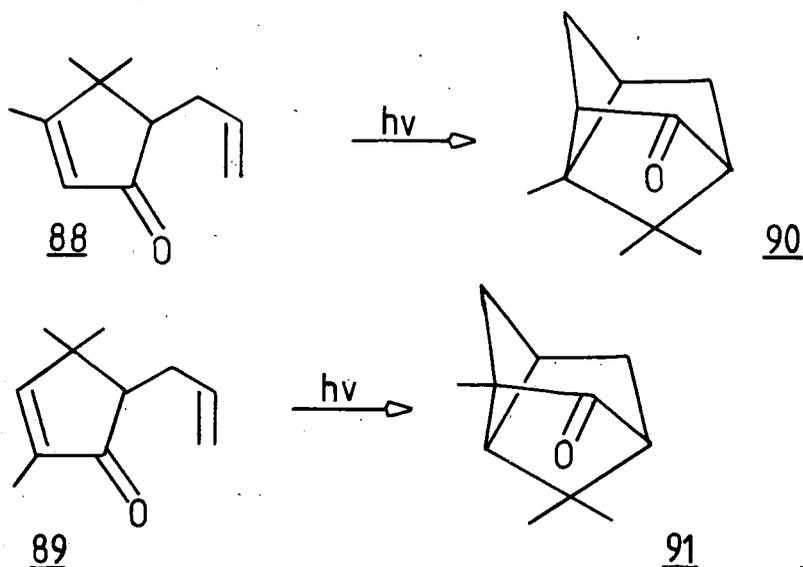
Scheme 64

Recently the reaction has been used in the synthesis of compounds with structures closely related to the tricyclo[3.3.1.0^{2,7}]nonane skeleton. Irradiation of 3-acetoxy-4-methyl-5-prop-2-enyl cyclopentenone 85 gives the two tricyclic compounds 86 & 87 (Scheme 65)⁶³.



Scheme 65

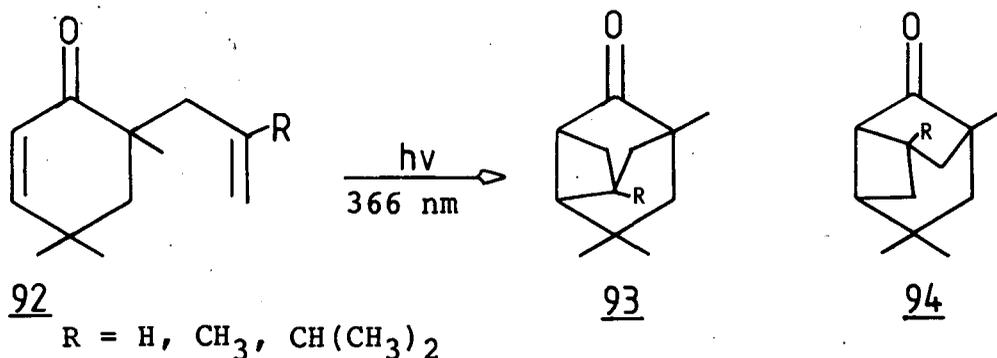
Photolysis of 5-prop-2-enyl-3,4,4- and 5-prop-2-enyl-2,4,4-trimethylcyclopentenone 88 & 89 (Scheme 66) give rise to the corresponding trimethyl tricyclo[3.2.1.0^{3,6}] octan-2-one 90 & 91⁶⁴.



Scheme 66

These four tricyclic compounds have a skeleton which differs by only one carbon atom from the tricyclo [3.3.1.0^{2,7}]nonane skeleton.

There is only one reference in the literature to the formation of a tricyclo [3.3.1.0^{2,7}] nonane skeleton by a photochemical route³⁸. Irradiation of the substituted allyl cyclohexenone 92 in either cyclohexane or acetonitrile gives a mixture of two isomeric photoadducts 93 & 94 (Scheme 67).



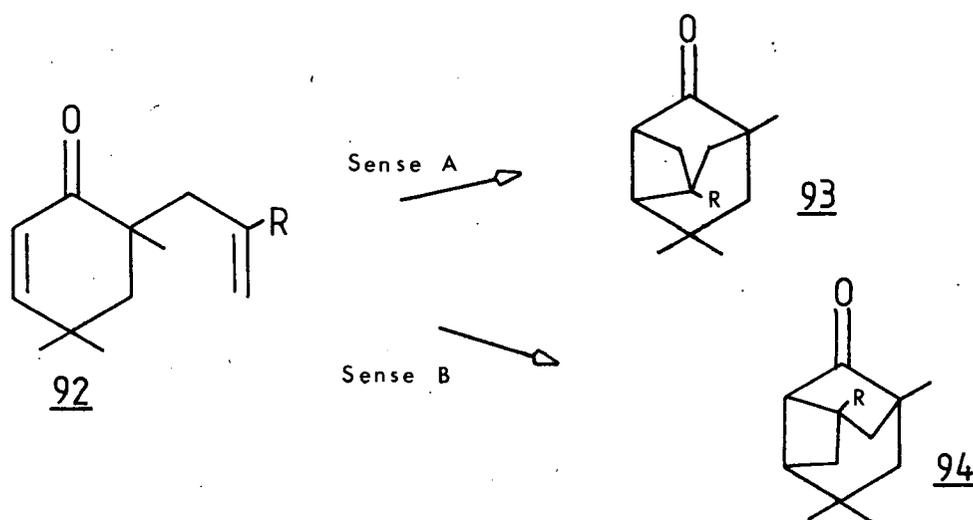
Scheme 67

3.5 Orientation of the Intramolecular Photochemical Cycloaddition Reaction

The structure of the products formed in the [2 + 2] photochemical reaction depends upon the orientation of the prop-2-enyl group. As in the case of the intramolecular Diels-Alder cycloaddition (Chapter 1, Section 1.8b) the prop-2-enyl chain can adopt two different orientations leading to two isomeric photoadducts.

The main factor governing which orientation is preferred is the flexibility of the side chain, as this will affect its ability to adopt a position for good orbital overlap in the transition state. While the reaction could be concerted it could also proceed by a diradical mechanism in which one orientation may be stabilised more than the other in the transition state.

4-Methyl-4-(prop-2-enyl)-6,6-dimethyl cyclohexen-3-one 92 gave two isomeric photoadducts 93 & 94 due to the two possible orientations of the side chain (Scheme 68)³⁸.



Scheme 68

The relative proportions of the Sense A (cf. Sense 1) adduct and the Sense B (cf. Sense 2) adduct were governed by the side chain substituent R and by the polarity of the

solvent the reaction was done in. Increasing the size of the substituent R (H, CH₃, CH(CH₃)₂) increased the proportion of the Sense B adduct 94 formed. Increasing the polarity of the solvent (using CH₃CN instead of C₆H₁₂) had the opposite effect: increasing the proportion of the Sense A adduct formed. When there was no substituent on the side chain (i.e. R = H) then only compound 93 was formed irrespective of which solvent was used.

3.6 Photolysis of the Naphthalenone 80

A series of small scale photolyses using cyclohexane or acetonitrile as the solvent were carried out in a pyrex tube (9cm x 20cm) to establish the best conditions for the reaction. The naphthalenone 80 was dissolved and the solution then purged with dry nitrogen before irradiation. Upon irradiation of the naphthalenone in cyclohexane the products crystallised upon the walls of the photolysis tube. These exploratory photolyses indicated that using a filter solution (with a cut off at 340 nm) around the photolysis tube helped prevent unwanted side reactions. Photolysis in acetonitrile gave two new products in the ratio 3:1 (by ¹⁹F nmr).

3.6a Identification of the Major Photoadduct

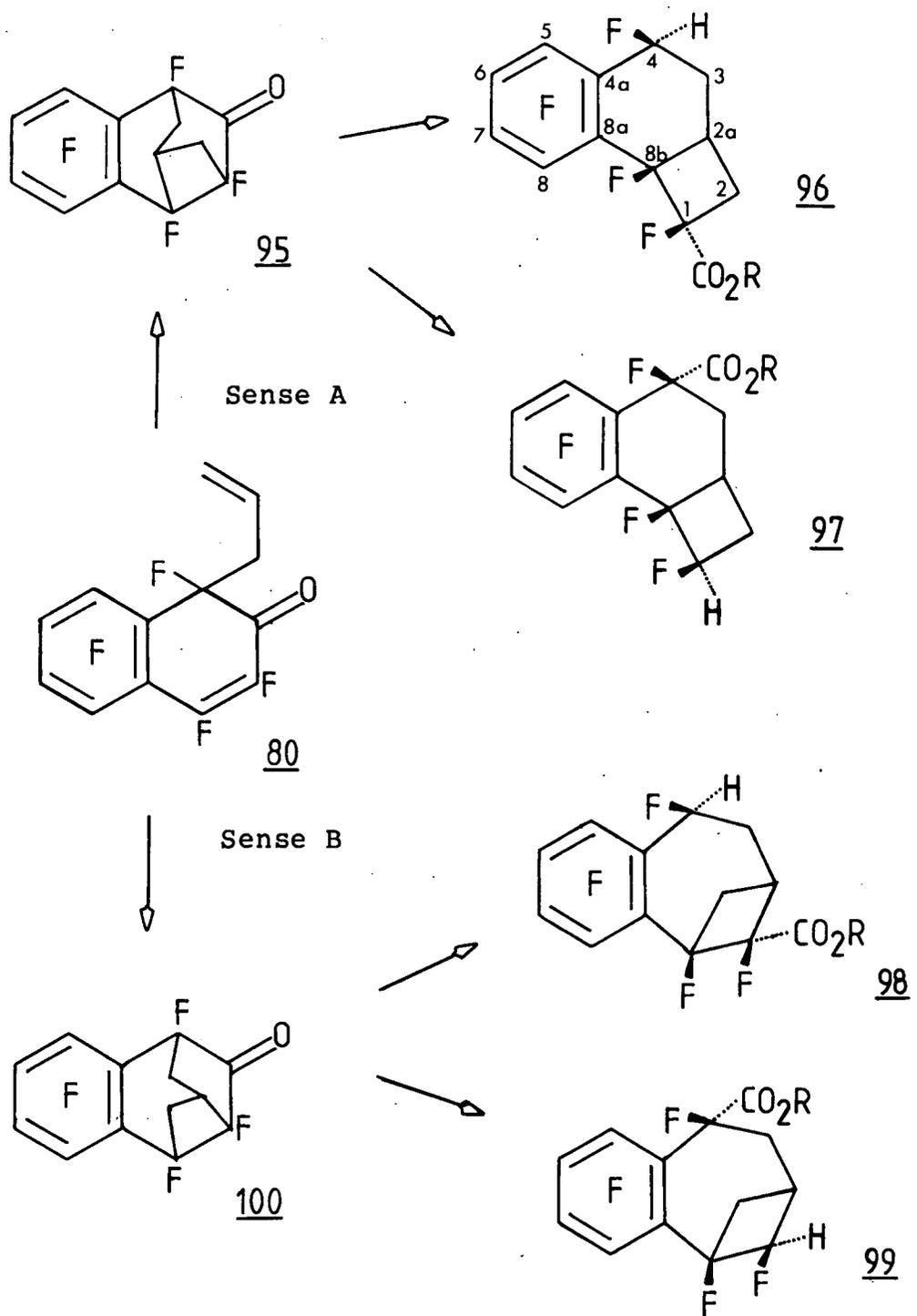
The major component, one of the expected [2 + 2] adducts, was obtained from photolysis in cyclohexane where it crystallised out on the walls of the photolysis tube. This solid was filtered off and recrystallised from benzene/petroleum-ether (b.p.60-80°) and sublimed in vacuo to give a white crystalline solid (43%). The

elemental analysis and mass spectrum showed it to be isomeric with starting material whilst the i.r. spectrum showed a strong absorption at 1780 cm^{-1} (C=O). The ^{19}F nmr spectrum showed six absorptions five of intensity=1 and one of intensity=2. These were due to four aromatic fluorines at low field (145-156ppm) and three non-overlapping non-aromatic fluorines at high field (175-199ppm). Two of the non-aromatic fluorines at high field showed large peri couplings (45 & 46 Hz) with two of the aromatic fluorines. The highest field fluorine also showed $J_{(\text{H-F})}$ 14 Hz.

The identity of the major product was determined by a hydrolysis reaction using one equivalent of caustic soda in a halo-form type cleavage and then, after acidifying, converted to the methyl ester. Each of the two photoadducts can give a pair of esters: 96c and 97c from 95 (the product of a Sense A addition) and 98c and 99c from 100 (the product of a Sense B addition) (Scheme 69).

Attempts to remove HF from the hydrolysis products by using excess base failed. A series of reactions on small amounts of the photoproduct were carried out under reflux and in sealed tubes at temperatures between $120\text{-}160^\circ\text{C}$ in an attempt to eliminate HF from the hydrolysis products. However, these reactions only gave the hydrolysis products i.e the carboxylic acid, or decomposition of the photoproduct.

The hydrolysis products were acidified and converted to the methyl ester before purification by column chromatography to give a viscous oil (6%). Attempts to distill this oil under vacuum only resulted in



a) R = H b) R = Na c) R = Me

Scheme 69

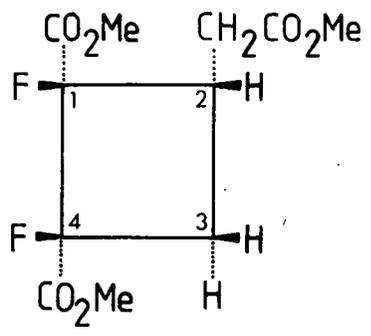
decomposition of the products.

The mass spectrum of the ester showed a parent ion at $m/e = 342$ whilst the i.r. showed a strong carbonyl absorption at 1710 cm^{-1} . The ^1H nmr showed three absorptions: a doublet at 6.13 ppm with a large gem H-F

coupling ($J_{(H-F)}$ 50 Hz) a singlet at 3.68 ppm ($-CO_2CH_3$) and a complex multiplet centred at 2.6 ppm ($2 \times CH_2, CH$).

The ^{19}F nmr showed seven absorptions of equal intensity due to four aromatic and three non-aromatic fluorines. Broad band decoupling of all the protons except the gem HF distinguished the non-aromatic fluorines. The absorption at 180.8 ppm, a triplet, ($J_{(H-F)}$ 25 Hz) collapsed to a singlet whilst the broad "triplet of doublets" ($J_{(H-F)}$ 50; 42; 20 Hz) at 161.9 ppm collapsed to a doublet ($J_{(H-F \text{ gem})}$ 50 Hz). Decoupling the gem HF proton only affected this peak, causing it to collapse to a doublet of doublets ($J_{(H-F)}$ 42; 20 Hz). The remaining triplet peak at 140.3 ppm collapsed to a doublet showing that it contained a peri coupling ($J_{(F-F)}$ 20 Hz) with the aromatic fluorine at 137.8 ppm which is a quartet due to the extra coupling. To produce the large triplet of doublets at 161.9 ppm the hydrolysis product must have a gem HF with an adjacent CH_2 group. This requirement eliminated 99c as the structure as it only has a gem HF with an adjacent CH group. Compound 98c can be eliminated because the only fluorine which can give a peri coupling with an aromatic fluorine is adjacent to a CH_2 whilst the splitting pattern of the ^{19}F nmr requires that the peri-coupling aromatic fluorine is coupled to only one proton. Furthermore the third non-aromatic fluorine is adjacent to a CH in 98c whereas the data shows this fluorine is adjacent to a CH_2 .

To distinguish between structures 96c and 97c the compound 48 (Diagram 6)⁴⁷ was used for a model of the four membered ring in 96c.



$$J_{F-4\beta, H-3\beta} = J_{F-4\beta, H-3\alpha} = 26 \text{ Hz}$$

$$J_{F-1\beta, F-4\beta} \approx 0 \text{ Hz}$$

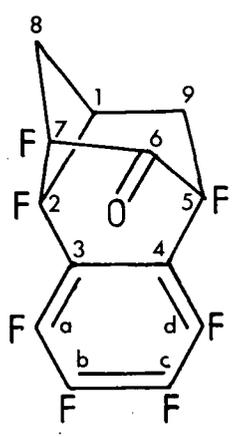
48

Diagram 6

Comparison of the coupling constants: $J_{(F-1\beta, H-2\alpha)} = J_{(F-1\beta, H-2\beta)} = 25\text{Hz}$ with those for 48 leads to 96c as the structure of the hydrolysis product. This confirms the structure of the major photoadduct as the Sense A product 95.

The large value of $J_{(F-4\beta, H-3\beta)}$ 42Hz and the absence any peri coupling to F-4 in 96c can be explained by rigid conformation. Theoretical calculations for coupling constant in substituted ethanes predict values for trans vicinial HF couplings of between 37 and 62Hz⁶⁵.

The large peri couplings observed in 95 (Diagram 7) are between F-2 and F-a and F-5 and F-d whilst F-2 shows an H-F coupling with H-1 (14Hz).



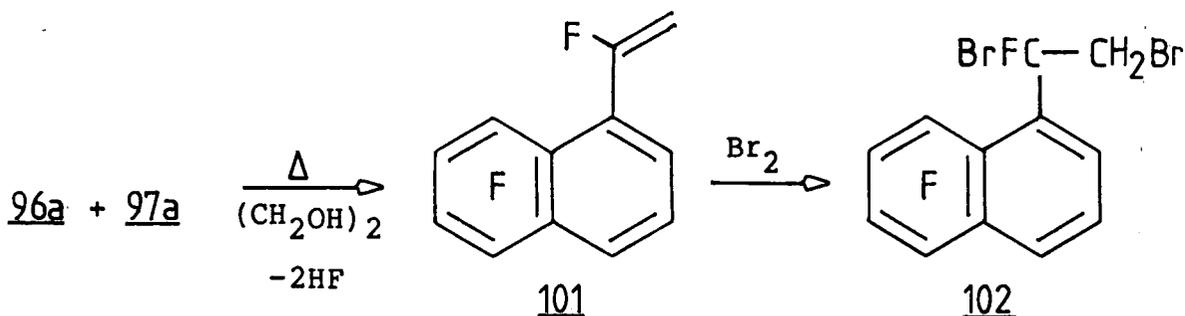
95

Diagram 7

Attempts to convert 95 to a gemdiol (cf 39 & 42) were unsuccessful. Although the diol was formed in solution and could be distinguished from the ketone by ^{19}F nmr spectroscopy, it could not be isolated.

Recently the other possible isomer from the hydrolysis and esterification of 95, namely 97c, has been isolated by Brooke⁶⁶. Although the mass spectrum of this compound is very similar to that of 96c, the ^{19}F nmr is completely different and only one of the non-aromatic fluorines can be assigned unambiguously. This is a broad triplet at 170.1 ppm which was assigned to F-1 with a gem HF coupling of 47Hz and a coupling of 39Hz to one of the vicinial protons. The other vicinial proton did not show any coupling.

Brooke effected the decarboxylation of a mixture of 96a and 97a by heating at reflux in ethylene glycol which lead to one isolatable product in very low yield (<0.5%) which was identified as 1-(1-fluorovinyl)-5,6,7,8-tetrafluoronaphthalene 101 by mass spectroscopy and ^{19}F nmr. Bromination of 101 using bromine in carbon tetrachloride at room temperature gave the dibromo compound 102 (Scheme 70). Compound 101 can only be formed from precursors with the structures 96a and 97a.



Scheme 70

3.6b Identificatin of the Minor Photoadduct

The second photoproduct, obtained in 25% yield from the naphthalenone 80, shown to be isomeric with starting material by its elemental analysis and mass spectroscopy was initially thought to be the product of the Sense B addition. However, the frequency of the carbonyl absorption (1840 cm^{-1}) was far higher than that which would have been expected and the ^{19}F nmr was not consistent with the Sense B product. The presence of a doublet (intensity = 2) at 185.1 ppm ($J_{(\text{H-F})}$ 14 Hz) whose separation was unaffected when the spectrum was run at 56.4 MHz and 84.67 MHz showed the molecule contained two magnetically equivalent fluorine atoms and that it must be 103 (Diagram 8) the analogue of the symmetrical tricyclic ketone 3.

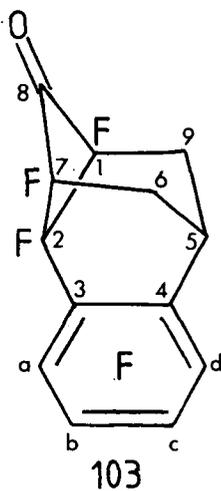
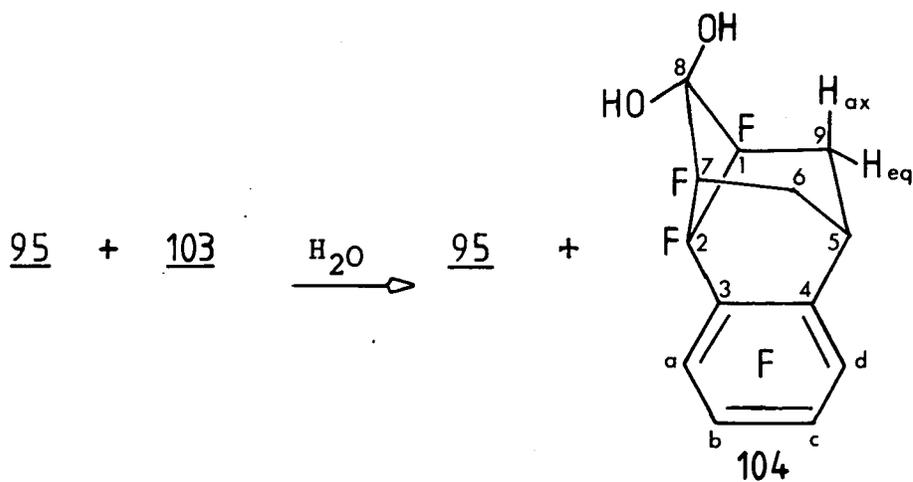


Diagram 8

The material was isolated from the filtrate from the photolysis reaction after the solvent had been evaporated off. The mixture of 95 and 103 was recrystallised to remove other impurities and then boiled with water and filtered. Compound 103 was converted to a stable gem diol 104 whilst 95 remained as the ketone. Boiling this

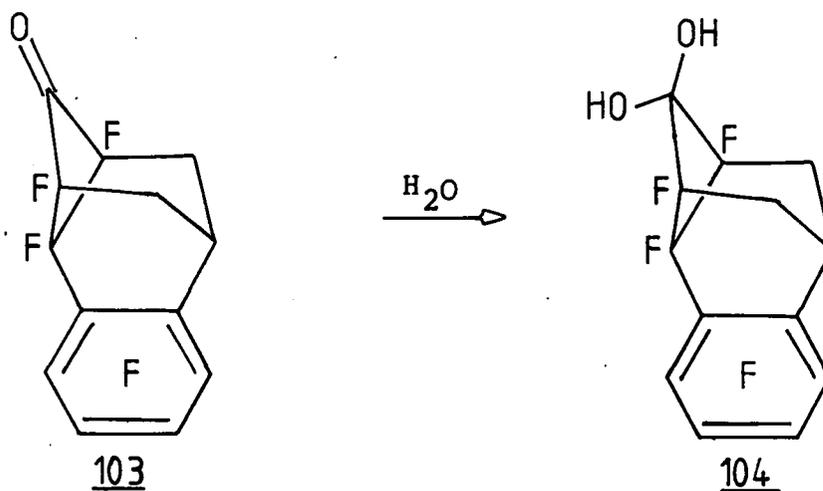
mixture in CCl_4 dissolved 95 leaving the gem diol 104 behind to be filtered off (Scheme 71).



Scheme 71

The diol was recrystallised twice and sublimed from P_2O_5 in vacuo at 100°C to give the ketone 1,2,7-trifluoro-3,4-(tetrafluorobenzene)-tricyclo[3.3.1.0^{2,7}]non-3-en-8-one 103 (7%). The i.r. spectrum showed a sharp absorption at 1840 cm^{-1} due to the carbonyl in the four membered ring. The ^{19}F nmr showed four aromatic fluorines and three non-aromatic fluorines. The highest field fluorine F-2 at 208.7 ppm was a doublet ($J_{(\text{F}-\text{F})}$ 46.6 Hz) due to peri coupling with F-a. No coupling between F-2 and F-1 (or F-7) was observed. The doublet at 185.1 ppm due to F-1 (and F-7) showed an H-F coupling of 14Hz which remained constant when the spectrum was run at 56.4 and 84.67 MHz. F-1 (and F-7) also showed an HF coupling of 4Hz with the axial protons on C-6 and C-9 as well as the 14Hz coupling with the equatorial protons. The ^1H nmr showed three absorptions; a singlet (H-5) at 3.92 ppm, a doublet of doublets ($J_{(\text{Hax}-\text{Heq})}$ 14Hz, $J_{(\text{Hax}-\text{F1})}$ 4Hz) due to the axial protons on C-6 and C-9 at 3.08 ppm and a triplet ($J_{(\text{Heq}-\text{F1})}$ 14Hz, $J_{(\text{Heq}-\text{Hax})}$ 14Hz) at 2.05 ppm. The

ketone 103 was easily hydrated by atmospheric moisture to give the gem diol 104 (Scheme 72).

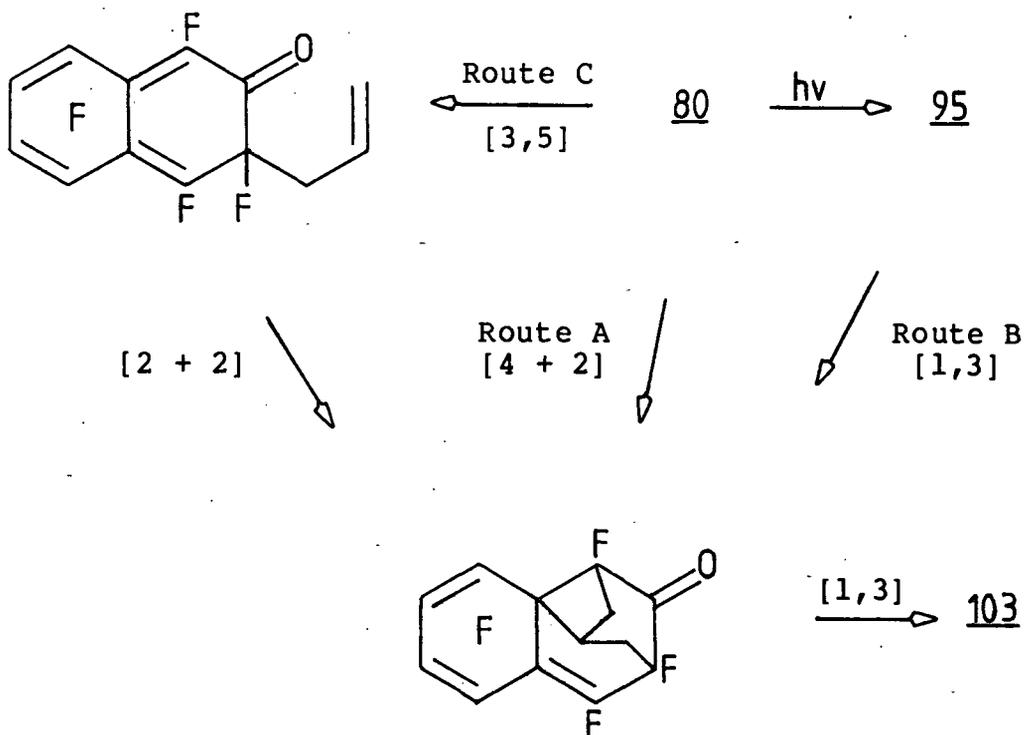


Scheme 72

The stability of the gem diol is probably due to the release of the high strain in the keto compound 103. In the keto form the carbon atom of the carbonyl group (C-8) is sp^2 hybridised and has an optimum bond angle of 120° . In the four membered ring in 103 the bond angles will be about 90° and so the system will be under considerable strain. Hydration of the ketone to a gem diol changes the hybridisation at C-8 from sp^2 to sp^3 where the optimum bond angle is $109^\circ 28'$. As this is much closer to the bond angles in the four membered ring, the strain in the system will be reduced. An analytically pure sample of the gem diol was prepared by successive recrystallisation of 103 from water. The diol showed no absorption in the $1800-1900\text{ cm}^{-1}$ region of the i.r. spectrum. On sublimation from P_2O_5 in vacuo at 100°C the ketone 103 was formed, which was confirmed by the return of the band at 1840 cm^{-1} in the i.r. spectrum.

3.7 Mechanism for the Formation of 103

There are three possible routes to 103 (Scheme 73).

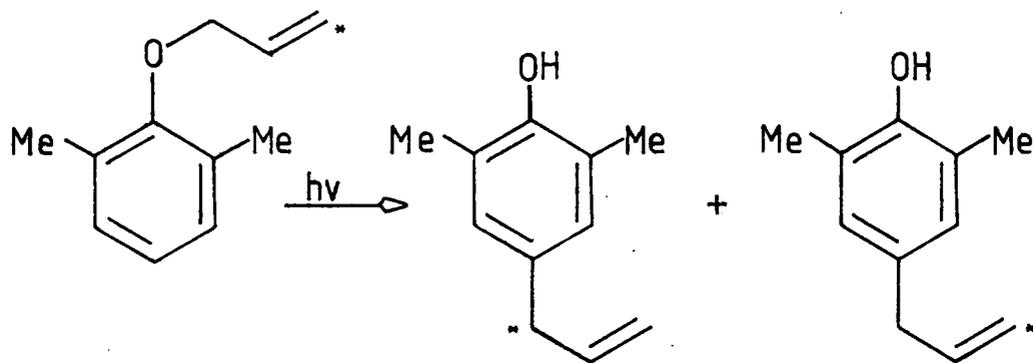


Scheme 73

The [4 + 2] photochemical cycloaddition (Route A) is very unlikely. Although a concerted [4a + 2s] addition is permitted photochemically it is sterically unfavourable. Normally when mixtures of dienes and monoenes are irradiated the [2 + 2] addition is favoured and only small amounts of [4 + 2] addition products are observed²³. In this case the high yield of 103 (25%) rules out this route.

Irradiation of the photoproduct 95 in acetonitrile for over 70 hours failed to give any of compound 103 only unchanged 95 was recovered, thus ruling out route B, leaving only route C : a photochemical [3,5] shift followed by a [2 + 2] cycloaddition and a [1,3] shift to give the symmetric ketone 103. A photochemically induced

concerted [3,5] sigmatropic shift proceeding suprafacially on both components is allowed by orbital symmetry rules;²¹ there is only one example recorded in the literature (Scheme 74)⁶⁷.



Scheme 74

3.8 Experimental

1,3,4,5,6,7,8-Heptafluoro-2-naphthol 79⁵⁶

Octafluoronaphthalene (100g) and potassium hydroxide (50g) were heated under reflux with stirring in t-butanol for 17 hrs. The reaction mixture was steam distilled to remove the solvent, unreacted octafluoronaphthalene and any t-butyl ether which may have been formed. The residue was acidified, ether extracted (1 x 500ml, 2 x 250ml) and dried (MgSO_4). The extracts were filtered and the solvent removed by distillation. The residue was sublimed under high vacuum (0.005mm Hg) at 110°C to give the crude naphthol (90g, 89%). A small quantity of the crude material was recrystallised from petroleum ether (b.p. $100 - 120^\circ\text{C}$) to give pure 1,3,4,5,6,7,8-heptafluoro-2-naphthol 79 m.p. $120 - 121^\circ\text{C}$ (Litt: $120-121^\circ\text{C}$). [Found: C, 44.6%; M^+ , 270. $\text{C}_{10}\text{HF}_7\text{O}$ requires C, 44.4%; M, 270.]

ν_{max} : 3380 (O-H); 1660cm^{-1} .

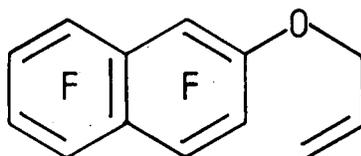
1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-enyl ether 77

The heptafluoro-2-naphthol (90g), prop-2-enyl bromide (60ml) and anhydrous potassium carbonate (90g) in dry acetone (900ml) were heated under reflux with stirring for 18 hours. The mixture was filtered and the solvent distilled from the filtrate. The residue was steam distilled to give a mixture of the ether and water (7dm^3). The organic layer was separated and the aqueous layer extracted with ether (3 x 300ml). The combined extracts were dried (MgSO_4) and the solvent evaporated to give 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-enyl

ether 77 (66g, 64%) b.p. 83.5°C at 0.01mm Hg [Found: C, 50.5; H, 1.6%; M⁺, 310. C₁₃H₅F₇O requires C, 50.3; H, 1.6%; M, 310.]

δ_F [CDCl₃] 140.3; 147.1; 148.8; 149.8; 159.2 ppm upfield from external CFC₃.

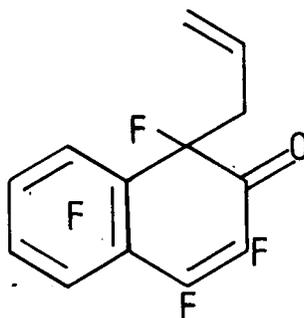
ν_{\max} : 1650 cm⁻¹ (CH=CH₂).



77

1,3,4,5,6,7,8-Heptafluoro-1-(prop-2-enyl)-naphthalen-2-one
80

The ether 77 (25.0g) was heated in xylene (60ml) at 130-135°C for 2.5 hours and the solvent removed by distillation under high vacuum. The residue was washed once with petroleum ether (b.p. 40-60°C) (20ml) and the crude naphthalenone was sublimed (0.005mm Hg, 48-50°C) and recrystallised three times from petroleum ether (b.p. 40-60°C) to give pure 1,3,4,5,6,7,8-heptafluoro-1-(prop-2-enyl)-naphthalen-2-one 80 (16g, 64%) m.p. 57-59°C. [Found: C, 50.0; H, 1.4%; M⁺, 310. C₁₃H₅F₇O requires C, 50.3; H, 1.6%; M, 310]



80

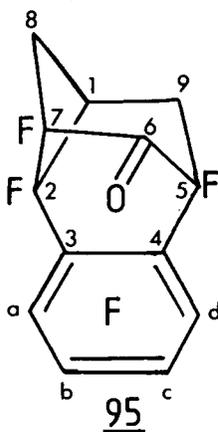
δ_F [CDCl₃], 122.6 (F-4); 135.0 (F-8); 138.9 (F-5); 148.8 (F-7); 150.4 (F-6); 155.4 (F-1); 157.0 ppm (F-3) upfield from external CFC1₃.

$J_{(F-1, F-8 \text{ peri})}$ 25 Hz; $J_{(F-4, F-5, \text{ peri})}$ 75.7 Hz.

ν_{max} : 1708 (C=O) and 1670 cm⁻¹ (CF=CF).

Photolysis of 1,3,4,5,6,7,8-heptafluoro-1-(prop-2-enyl)-naphthalen-2-one 80

The naphthalenone 80 (20.0g) dissolved in spectrophotometric grade cyclohexane (600ml) in a pyrex tube (4.6 x 4.5cm) was immersed in a 340nm filter solution (66g NaBr, 0.3g Pb(NO₃)₂ in 100ml water) and irradiated for 68 hours using a 350 nm lamp. The crystalline solid which precipitated was filtered off, recrystallised three times from benzene/petroleum ether (b.p. 40-60°C) and sublimed to give 2,5,7-trifluoro-3,4-(tetrafluorobenzo)-tricyclo [3.3.1.0^{2,7}]non-3-en-6-one 95 (8.5g, 43%) m.p. 137-139°C. [Found: C, 50.0; H, 1.3%; M⁺, 310. C₁₃H₅F₇O requires C, 50.3; H, 1.6%; M, 310]

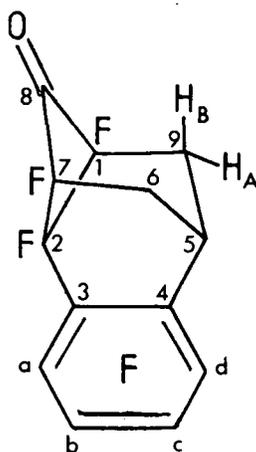


δ_F [CDCl₃], overlapping multiplets centered at 145.7 (F-a and F-d); 152.9, 153.9 (F-b and F-c both triplets); 174.0 (F-7, multiplet); 185.7 (F-5, doublet); 199.3 ppm (F-2, doublet of doublets);

$J_{(F-a, F-2, \text{peri})}$ 46Hz; $J_{(F-d, F-5, \text{peri})}$ 45Hz; $J_{(H-1, F-2)}$ 14Hz

ν_{max} : 1775 (C=O) cm^{-1} .

The solvent was evaporated from the filtrate from the photolysis reaction and a ^{19}F nmr analysis of the residue (8.5g) showed that in addition to 95 there was present a second photoproduct 103 to the extent of 50% (20% in the overall product). Compound 103 was isolated from the mixture by the following procedure. The mixture was recrystallised from benzene/petroleum ether (b.p. 40-60°C) and the solid was then boiled with water and filtered. By this treatment 95 is thought to be unchanged while 103 is hydrated to the 8,8-diol. This product was boiled with CCl_4 to dissolve 95 and the undissolved solid (crude hydrated 103) was filtered off. This material was recrystallised twice from benzene/petroleum ether (b.p. 40-60°C) and finally sublimed in vacuo at 100°, 0.005mm Hg to give 1,2,7-trifluoro-3,4-(tetrafluorobenzoyl)-tricyclo[3.3.1.0^{2,7}]non-3-en-8-one 103 (1.3g, 7%) m.p. 122-123°. [Found: C, 50.3; H, 1.4%; M^+ , 310. $\text{C}_{13}\text{H}_5\text{F}_7\text{O}$ requires C, 50.3; H, 1.6%; M , 310].



103

$\delta_F[(CD_3)_2CO]$, overlapping multiplets centered at 147.0 (F-a and F-d); 155.9, 157.6 (F-b and F-c, both triplets); 185.1 (F-1 and F-7, doublet unchanged using a 56.4 MHz ^{19}F spectrometer) intensity 2; 208.7 ppm (F-2, doublet) intensity 1.

$\delta_H[(CD_3)_2CO]$, 2.05(H-6A and H-9A showing splitting of 14 and 17 Hz); 3.08 ppm (H-6B and H-9B showing a splitting of 14Hz); 3.92ppm (H-5, broad singlet)

$J(F-a, F-2)$ 45Hz.

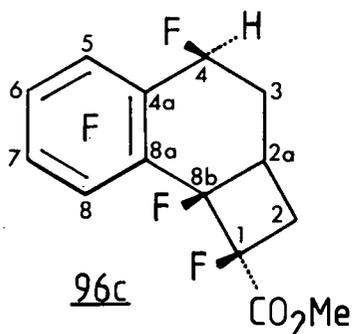
ν_{max} : 1840 cm^{-1} (C=O).

Photolysis of the naphthalenone 80 (0.48g) in spectroscopic grade acetonitrile (10ml) for 21 hours as before and analysis of the product by ^{19}F nmr showed the presence of only compound 95 (75%) and the symmetrical ketone 103 (25%).

Hydrolysis of 2,5,7-trifluoro-3,4-(tetrafluorobenzotricyclo[3,3,1,0^{2,7}])non-3-en-6-one 95

The photoproduct 95 (3.2g) was heated under reflux in caustic soda (57ml; 0.20M) for 1.5 hours. The solution was cooled, extracted with ether (3 x 100ml), dried ($MgSO_4$), filtered and evaporated in vacuo to give unreacted starting material 95, identified by i.r. spectroscopy. The aqueous alkaline layer was acidified (4M HCl), extracted with ether, the extracts combined and dried ($MgSO_4$). After filtration the solution was treated with an excess of ethereal diazomethane (Ca 6g), and the excess diazomethane and solvent distilled to leave a viscous yellow oil. Chromatography of the products (2.4 x

90cm, silica, $\text{CHCl}_3/\text{CCl}_4$ 3:2 v/v) gave two major products: an unidentified solid (1.4g) and an impure ester (1.4g). Rechromatography of the crude ester gave pure 1 β ,4 β ,5,6,7,8,8b β -heptafluoro-1 α -methoxycarbonyl-8b,2 α ,3,4-tetrahydro-8b α ,2 α -ethanonaphthalene 96c as a viscous oil 188mg, 5.8%. [Found: C,48.8; H,2.9%; M^+ , 342. $\text{C}_{14}\text{H}_9\text{F}_7\text{O}_2$ requires C,49.1; H,2.6%; M,342].



δ_{F} [(CD_3) $_2\text{CO}$], 137.8 (F-8, quartet); 140.3 (F-8b β , triplet); 142.6 (F-5, triplet); 153.3 and 154.5 (unassigned F-6, F-7, both triplets); 161.9 (F-4 β , broad "triplet of doublets"); 180.8 ppm (F-1 β , triplet).

δ_{H} [(CD_3) $_2\text{CO}$], multiplet centred on 2.6 (2 x CH_2 , CH); 3.68 (CH_3 , singlet); 6.13 ppm (H-4, doublet).

J (F-8, F-8b β , peri) 20Hz; J (F-8b β , H-2a β) 20Hz;
 J (F-4 β , H-4 α) 50Hz; J (F-4 β , H-3 α) 42Hz;
 J (F-4 β , H-3 β) 20Hz; J (F-1 β , H-2 α) = J (F-1 β , H-2 β) 25Hz.

Attempted Photolysis of Photoproduct 95

The photoproduct 95 (0.49g) in spectroscopic grade acetonitrile (10ml) was irradiated in a 340nm filter solution using a 350nm lamp for 70 hours. The solvent was evaporated and the residue dissolved in (CD_3) $_2\text{CO}$. Examination by ^{19}F nmr spectroscopy showed only unreacted starting material.

Hydration of the Symmetrical Tricyclic ketone 103

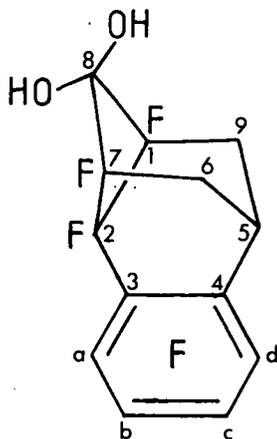
The tricyclic ketone 103 (0.3g) was dissolved in boiling water and allowed to crystallise. The crystalline material was filtered and dried in vacuo to give

1,2,7-trifluoro-3,4-(tetrafluorobenzo)-tricyclo

[3.3.1.0^{2,7}]non-3-en-8,8-diol 104 m.p.117-119°C. [Found:

C,47.4; H,2.3%. C₁₃H₇F₇O₂ requires C,47.5; H,2.1%]

ν_{\max} : 3400cm⁻¹ (O-H).

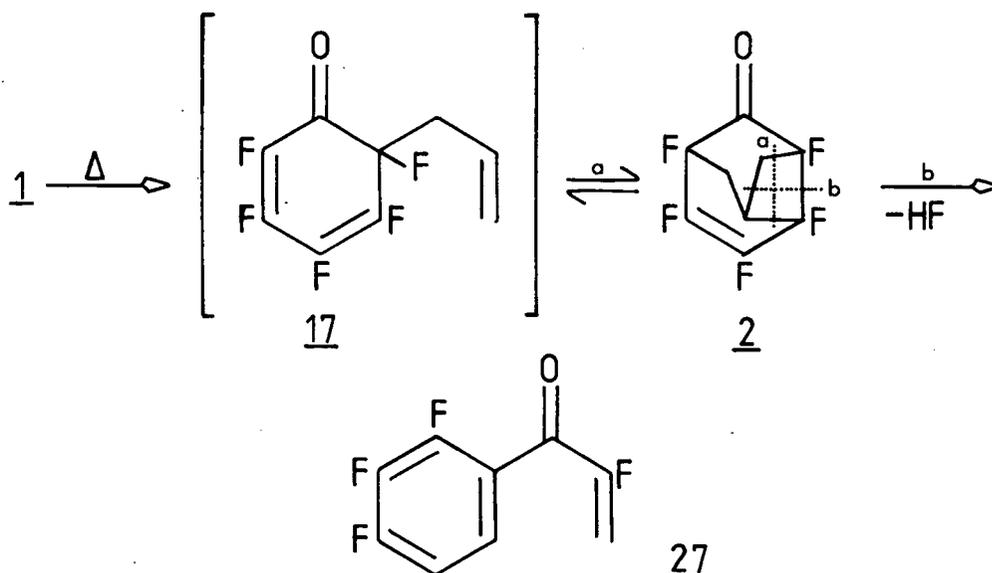


Sublimation of 104 at 110° and 0.005mm Hg over P₂O₅ gave the ketone 103 identified by i.r. spectroscopy.

CHAPTER 4

4.1 Introduction

Pyrolysis of pentafluorophenyl prop-2-enyl ether **1** at 410°C gave rise to the tricyclic ketone **2** and the vinyl ketone **27** (Scheme 75). The ketone **27** is one of the possible cleavage products of the four membered ring in the tricyclic ketone **2**¹



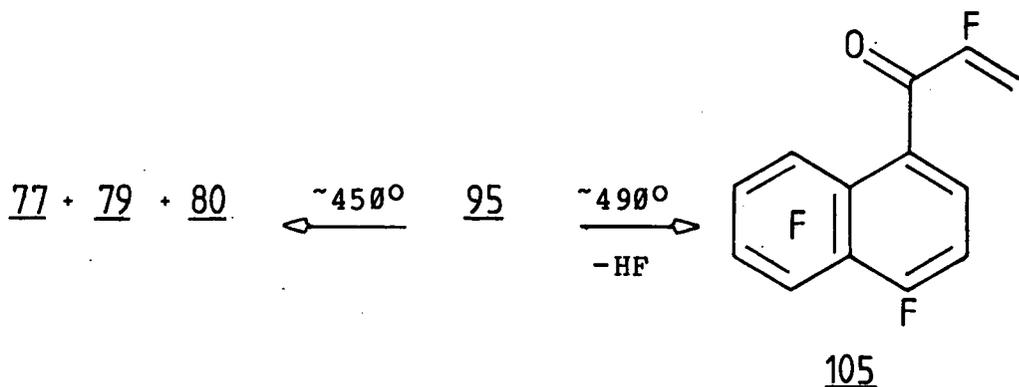
Scheme 75

The products from the early pyrolysis experiments on the naphthalenone **80** were not examined for the vinyl ketone formed from **95**. Neither were any tricyclic [2 + 2] adducts observed during these pyrolysis experiments. However, these may have been masked by the naphthol **79** which was formed.

4.2 Pyrolysis of the Photoproduct 95

Exploratory pyrolysis experiments on the photoproduct showed that below 450°C the only products were naphthol **79**, naphthalenone **80**, and the naphthyl prop-2-enyl ether

77, all of which were identified by their i.r. spectra after separation by preparative thick layer chromatography. Above 490°C the major product was 1,3,4,5,6,7,8-heptafluoronaphth-2-ol 79. However, at temperatures between 450°C and 490°C a new material 105 was formed in increasing amounts (Scheme 76).



Scheme 76

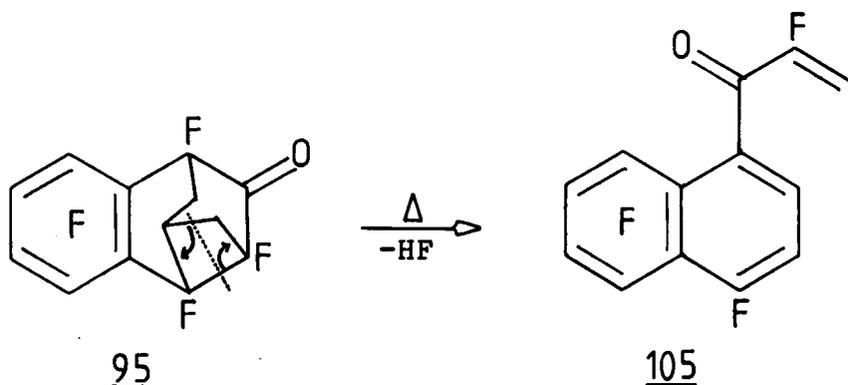
The photoproduct 95 was distilled through a quartz tube packed with quartz wool at 490°C in vacuo. The products were collected and separated by column chromatography and purified by preparative thick layer chromatography to give a viscous oil which was sublimed in vacuo to give a white crystalline solid. This was readily identified as the vinyl ketone 105 (17%) by spectroscopy. The mass spectrum gave a parent peak at $m/e = 290$ which is correct for starting material -HF. The i.r. spectrum showed strong absorptions in the region 1600-1700 cm^{-1} due to C=O and CF=C.

The ^{19}F nmr showed six absorptions of equal intensity. The lowest field absorption at 112.7 ppm, a doublet of multiplets, collapsed to a doublet ($J_{\text{F-F}} 6.6\text{Hz}$) on broadband decoupling of the protons. This peak was assigned as F-4

with a large peri coupling to F-5 (144.3 ppm, doublet of triplets). The next absorption at 115.8 ppm was a doublet of doublets (J_{H-F} 46Hz; 14Hz) which collapsed to a singlet on broadband decoupling. This peak was assigned as F-1'. The two HF couplings were to the cis proton ($J_{(H-F_{cis})}$ 14Hz), and the trans proton ($J_{(H-F_{trans})}$ 46Hz). The remaining three peaks were aromatic fluorines and showed a triplet structure (J_{F-F} 20Hz; 20Hz).

The 1H nmr spectrum showed two absorptions of equal intensity. The aromatic protons (7.2 - 7.5 ppm) showed a complex multiplet structure. The vinylic protons (5.3 - 5.4 ppm) showed the two HF couplings and an H-H coupling ($J_{(H-A, H-B)}$ 3Hz)

The vinyl ketone 105 is formed from the tricyclic ketone 95 by cleavage of the four membered ring (Scheme 77). The reaction proceeds via a stepwise mechanism, probably through a 1,4 diradical intermediate. A concerted retro [2 + 2] cycloaddition would involve a suprafacial-antarafacial mechanism which requires severe twisting of the four membered ring and consequently the reaction is thermodynamically unfavourable.

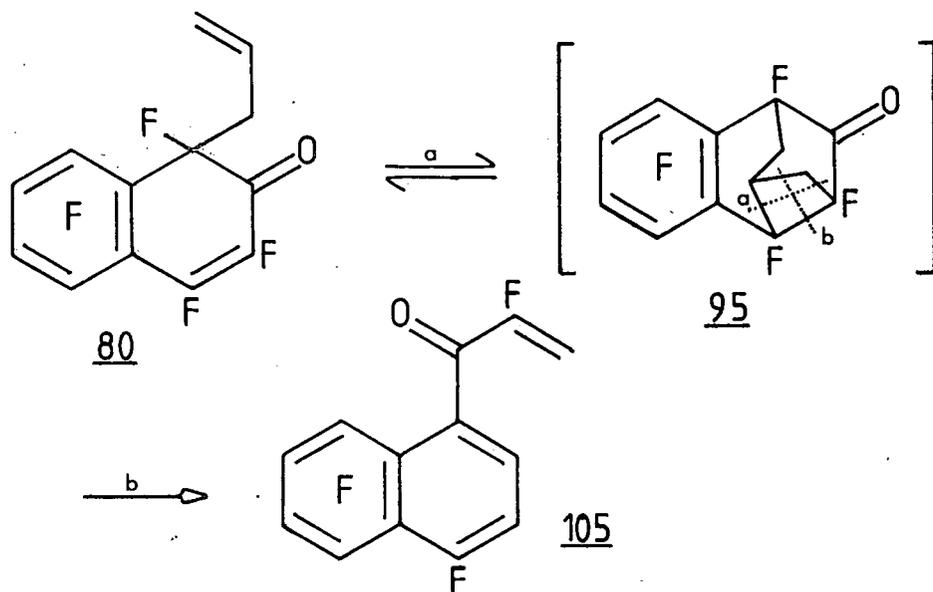


Scheme 77

4.3 Pyrolysis of the Naphthalenone 80

Pyrolysis of the naphthalenone 80 at 490°C in the same apparatus as before (page 75) gave products which were separated by column chromatography. The major component was purified by preparative thick layer chromatography to give a viscous oil (2.6%) whose ^{19}F nmr and i.r. spectra were identical with the previously prepared vinyl ketone 105.

The most plausible mechanism for the formation of the vinyl ketone 105 from compound 80 involves the formation and break up of the [2 + 2] adduct 95 (Scheme 78)



Scheme 78

Pyrolysis of the naphthalenone 80 at 455°C in the same apparatus as before (page 75) actually enabled the [2 + 2] adduct to be isolated in low yield (1.6%) accompanied by the naphthol 79. The [2 + 2] adduct was identified as the tricyclic ketone 95 by i.r. spectroscopy. The formation of 95 in a thermal reaction requires a non concerted [2 + 2] cycloaddition which probably involves a diradical transition state.

4.3 Experimental

Pyrolysis of Photoproduct 95

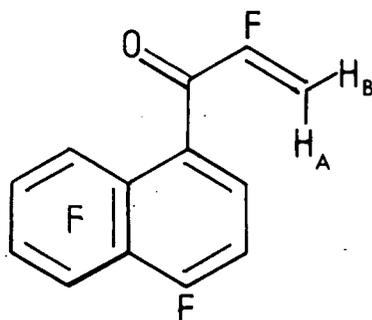
Compound 95 (1.5g) was sublimed under high vacuum (0.005mm Hg) at 490°C through a silica tube loosely packed with quartz wool and the products collected in a trap cooled in liquid air. The products were separated by column chromatography (2.4 x 90 cm, silica, CHCl₃/CCl₄, 1:1 v/v) and the crude vinyl ketone 105 (977mg) was further purified by preparative thick layer chromatography (Silica, CHCl₃/CCl₄ 1:1 v/v) to give an oily liquid which was sublimed at room temperature in vacuo (0.005mm Hg) to give a white solid. This was recrystallised three times from petroleum ether (b.p. 40-60°C) to give 1-fluorovinyl 4,5,6,7,8-pentafluoro-1-naphthyl ketone 105 (263mg, 17%) m.p.70-71°C. [Found: C,54.0; H,1.0%; M⁺, 290. C₁₃H₄F₆O requires C,53.8; H,1.4%; M, 290].

δ_F [(CD₃)₂CO], 112.7 (F-4, doublet of multiplets); 115.8 (F-A, doublet of doublets); 137.1 (F-8, triplet); 144.3 (F-5, doublet of triplets); 155.2 and 157.0 ppm (F-6 and F-7, both triplets).

δ_H [(CD₃)₂CO], 5.45(H-A); 5.77(H-B); 7.46 - 7.88 ppm (H-2 and H-3).

$J_{(F-4, F-5, \text{peri})}$ 68Hz; $J_{(F-A, H-A)}$ 46Hz; $J_{(F-A, H-B)}$ 14Hz; $J_{(H-A, H-B)}$ 4.5Hz.

ν_{max} : 1700 (C=O) cm⁻¹.



105

Pyrolysis of the Naphthalenone 80

1) Isolation of the Vinyl Ketone 105

The naphthalenone 80 (2.45g) was pyrolysed under vacuum (0.005mm Hg) at 490°C in the apparatus previously described. Separation of the mixture of products by column chromatography (2.4 x 90cm, silica, CHCl₃/CCl₄ 1:1 v/v) gave a fraction containing the crude vinyl ketone 105 (157mg) which was further purified by preparative thick layer chromatography (silica, CHCl₃/CCl₄ 1:1 v/v) to give the pure vinyl ketone (63mg, 2.5%) identified by ¹⁹F nmr and i.r. spectroscopy.

2) Isolation of Photoproduct 95

The naphthalenone 80 (1.8g) was pyrolysed under vacuum (0.005mm Hg) at 455°C and the complex mixture of products separated by column chromatography (2.4 x 90cm, silica, CHCl₃/CCl₄ 1:1 v/v). The slowest eluting fraction contained a mixture of the naphthol 79 and compound 95 (568mg); sublimation of this mixture at 0.005mm Hg gave two fractions : (i) (257mg) (25-90°C) comprising mainly naphthol 79 and (ii) (92mg) (90-110°C) comprising mainly compound 95. The second fraction was resublimed and leached with petroleum ether (b.p. 60-80°C) to give a

solid (36mg, 1.6%) identified by i.r. spectroscopy as compound 25. A further sample of the photoproduct (63mg) was obtained from the first fraction by washing with Na_2CO_3 solution to remove the naphthol 79 and then leeching with petroleum ether (b.p. 60-80°C).

APPENDIX A

Apparatus and Instruments

Vacuum System A standard glass vacuum line fitted with liquid air traps, an Edwards vacustat vacuum gauge and a rotary oil pump capable of attaining 0.005 mm Hg was used for high vacuum operations.

Static Thermolysis Static thermolyses were carried out in sealed glass bulbs fitted with a side arm into which the product could be condensed. Two sizes of bulb were used: 2 dm³ for amounts upto 0.5g and 10 dm³ for amounts up to 2.5g. Preweighed samples were placed in the side arm by pipette and after attachment to the vacuum system and cooling in liquid air the flask was evacuated and sealed.

Flow Pyrolysis Flow pyrolyses were carried out by distilling the sample under high vacuum through a silica tube (1.5 cm x 60 cm) packed with quartz wool. The tube was heated by an electric oven controlled by a variac. The temperature was measured by a thermocouple. The products were collected in a trap cooled in liquid air.

Photolysis Reactions Photolysis reactions were carried out in a Rayonet 204 U.V. reactor using four 366.0nm U.V. lamps. The samples were dissolved in Spectrosol grade cyclohexane or acetonitrile in a pyrex tube and purged with nitrogen before irradiation. Three

sizes of tube were used: 1 cm x 15 cm (upto 0.5g material in 10 ml solvent), 3.5 cm x 12 cm (upto 2.0g in 80 ml), and 5 cm x 45 cm (upto 20g in 750 ml). The tubes were immersed in a filter solution with a cut-off at 340nm. The filter solution was made up from NaBr (56g) and $\text{Pb}(\text{NO}_3)_2$ (0.3g) in water (100 ml).

I.R. Spectra Infra-red spectra were recorded on a Perkin-Elmer model 197 Infra-red spectrometer as either nujol mulls or KBr discs for solids and as thin films for liquids.

N.M.R. Spectra ^1H nmr spectra were recorded on a Bruker HX-90E spectrometer operating at 90 MHz. Chemical shifts δ_{H} are measured downfield from an internal TMS reference. ^{19}F nmr spectra were recorded on the same instrument operating at 84.67 MHz or on a Varian A 56/60D operating at 56.4 MHz. Chemical shifts δ_{F} are measured upfield from internal CFCl_3 unless otherwise stated.

Elemental Analyses Elemental analyses were obtained on a Perkin-Elmer model 240 CHN analyser.

Mass Spectra Mass spectra were recorded on an AEI MS9 mass spectrometer with an ion beam energy of 70 eV.

-85-

APPENDIX B

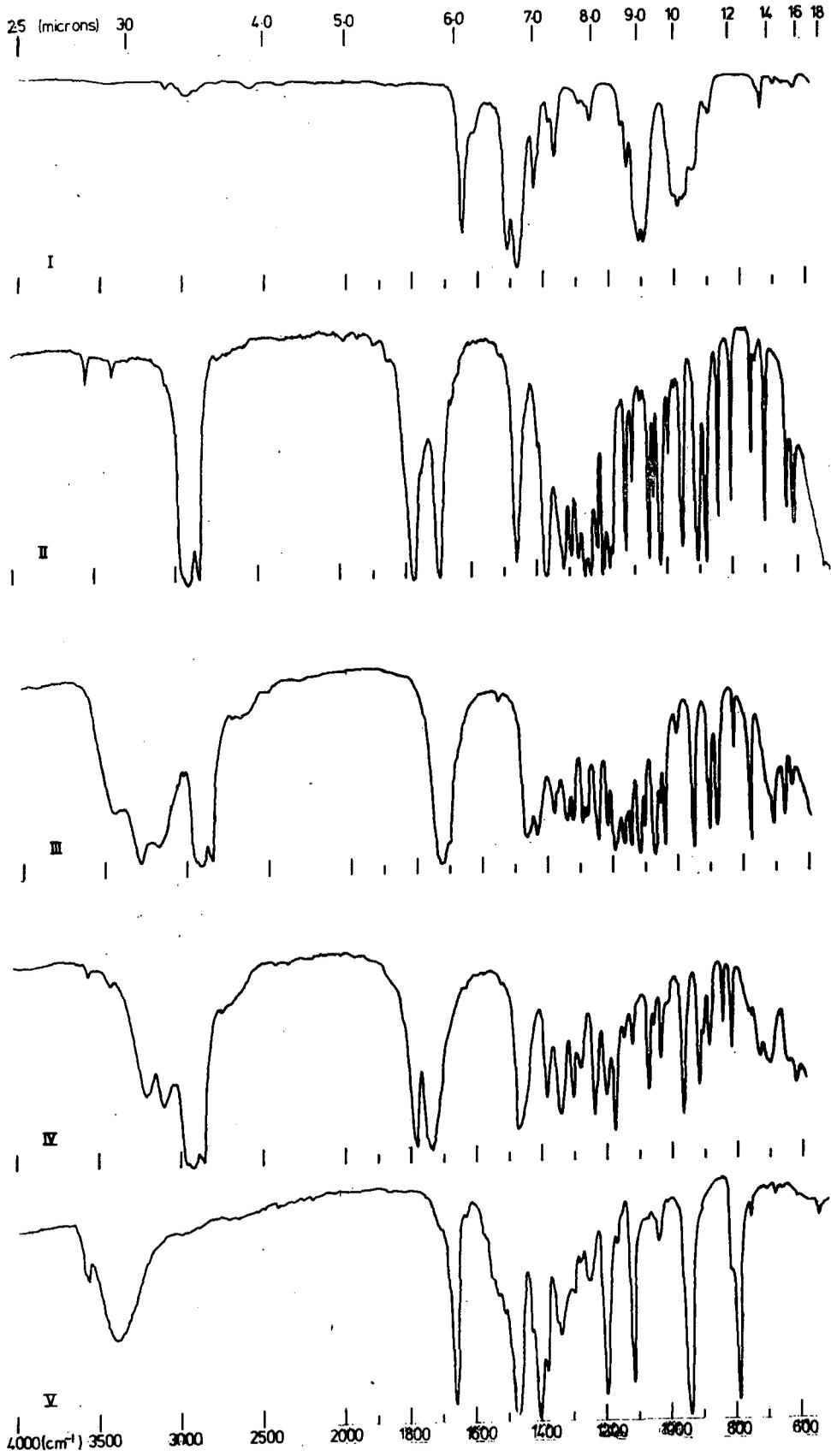
I.R. Spectra

- I. 2,3,5,6-Tetrafluoro-4-pyridyl Prop-2-enyl Ether (F)
- II. 2,4,5,7-Tetrafluoro-3-aza-tricyclo[3.3.1.0^{2,7}]non-3-en-6-one
- III. 2,5,7-Trifluoro-3-aza-tricyclo[3.3.1.0^{2,7}]non-4-one-6,6-diol
- IV. 2,5,7-Trifluoro-3-aza-tricyclo[3.3.1.0^{2,7}]non-4,6-dione
- V. 1,3,4,5,6,7,8-Heptafluoro-2-naphthol (K)
- VI. 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl prop-2-enyl ether (F)
- VII. 1,3,4,5,6,7,8-Heptafluoro-1-(prop-2-enyl)-naphthalen-2-one (K)
- VIII. 2,5,7-Trifluoro-3,4-(tetrafluorobenzo)-tricyclo[3.3.1.0^{2,7}]non-3-en-6-one
- IX. 1 β ,4 β ,5,6,7,8,8b β -Heptafluoro-1 α -methoxycarbonyl-8b,2a,3,4-tetrahydro-8b α ,2a α ethanonaphthalene (F)
- X. 1,2,7-Trifluoro-3,4-(tetrafluorobenzo)-tricyclo[3.3.1.0^{2,7}]non-3-en-8-one
- XI. 1,2,7-Trifluoro-3,4-(tetrafluorobenzo)-tricyclo[3.3.1.0^{2,7}]non-3-en-8,8-diol
- XII. 1-Fluorovinyl 4,5,6,7,8-pentafluoro-1-naphthyl ketone

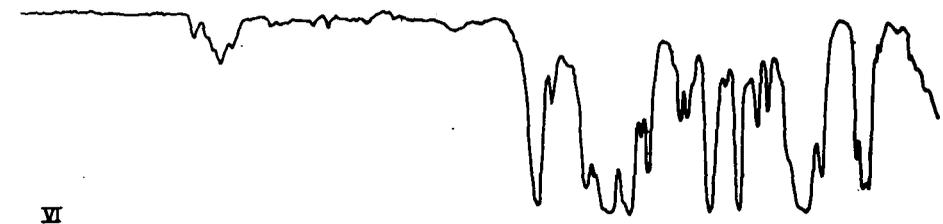
All spectra recorded as nujol mulls using NaCl discs unless otherwise indicated:-

(F) Recorded as a liquid film

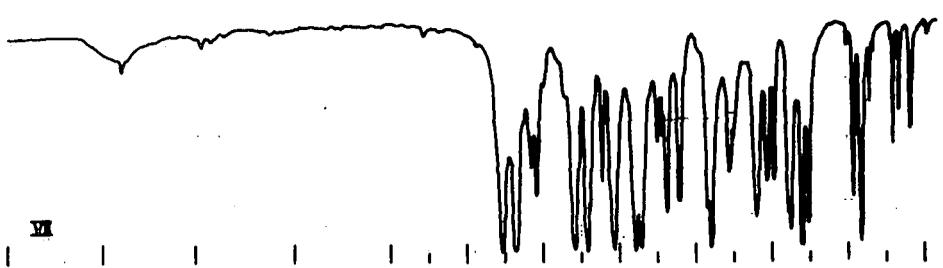
(K) Recorded as a KBr disc



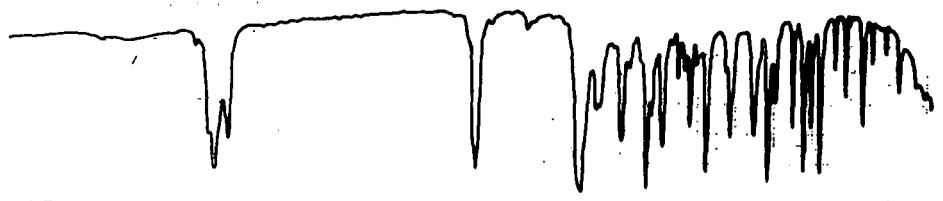
25 (microns) 30 40 50 60 70 80 90 10 12 14 16 18



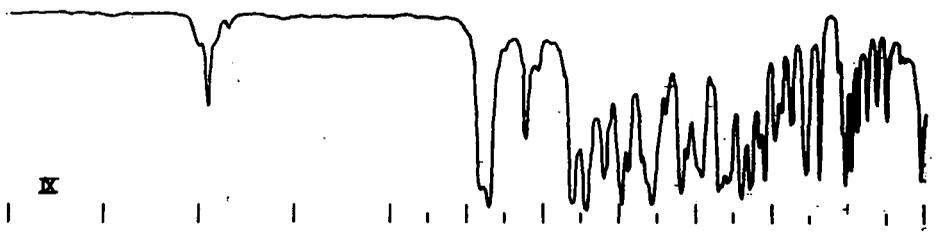
VI



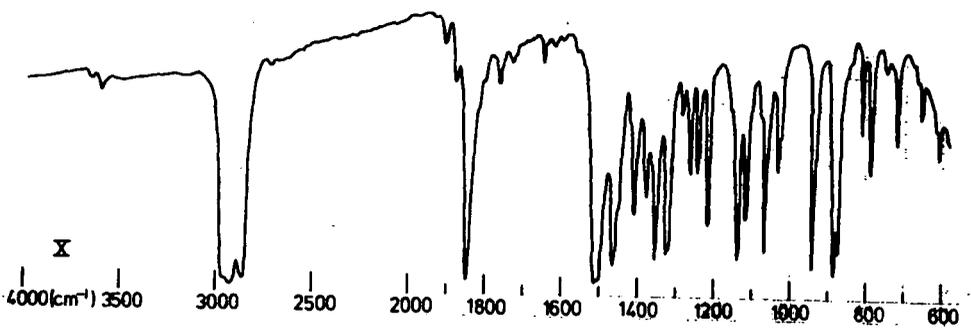
VII



VIII

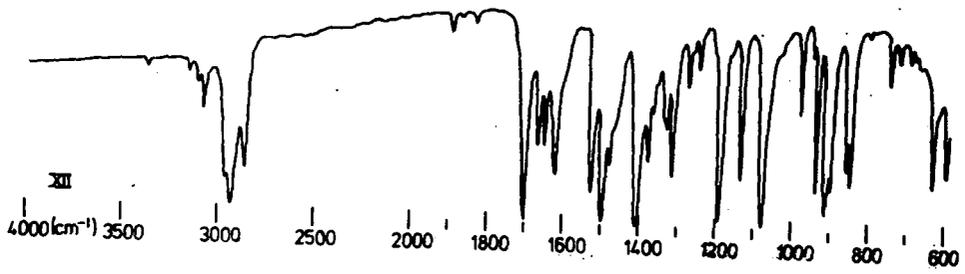
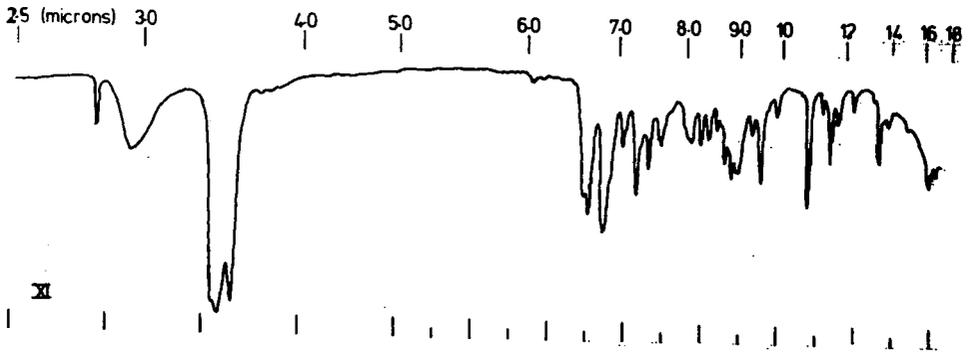


IX



X

4000 (cm⁻¹) 3500 3000 2500 2000 1800 1600 1400 1200 1000 800 600



-87-

APPENDIX C

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