# *An investigation into the thermolysts reactions of polyfluoroaromatic prop-2-ynyl ethers and thioethers*

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# AN INVESTIGATION INTO THE THERMOLYSIS REACTIONS OF POLYFLUOROAROMATIC PROP-2-YNYL ETHERS AND THIOETHERS.

BY

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(St. Cuthbert's Society)

Submitted to the University of Durham
to obtain an M.Sc. Degree.

Dedicated to my parents for
their endless support and
encouragement.

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# ABSTRACT

This work investigates the thermal behaviour of polyfluoroaryl prop-2-ynyl ethers and thioethers in the vapour phase and solution phase. It also reports the thermolyses of 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) in the presence of 2,3-dimethylbut-2-ene and 3,3-dimethylbut-1-ene respectively.

Chapter 1 discusses the history, mechanism and stereochemistry of the Claisen and thio-Claisen rearrangements of aromatic prop-2-enyl and prop-2-ynyl systems. While Chapter 2, reports on the various cyclisation reactions that may follow an initial Claisen rearrangement. Chapter 3 deals with the literature on the Claisen and thio-Claisen rearrangements of polyfluoroaryl systems which are directly related to those under study in this thesis.

Chapters 4 and 5 describe the isomerisation reactions of pentafluorophenyl prop-2-ynyl thioether (167) and 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl thioether (171). Chapter 4 is concerned with the reaction of compound (167) with p-xylene and benzene at 180°C and in the presence of $BF_3$-etherate, at 25°C. Chapter 5 reports upon the reactions of the thioether (171) with benzene and p-xylene at 140°C and 160°C. At 160°C, in nickel apparatus the isomerisation product 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (173) is shown to be an intermediate in the conversion of the thioether (171) to the substitution product, 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (177) with p-xylene. This chapter also highlights the differing courses of reactions of the thioether (171) in glass and nickel apparatus.

Chapter 6 reports the isomerisation reactions of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156) in both the liquid phase and vapour phase. The glass surface of the reaction vessel was shown to act as a Lewis-acid catalyst at elevated temperatures, in the reaction of the naphthyl ether (156) with p-xylene and isopropylbenzene to give the aromatic substitution products (159) and (160) respectively. Whereas in nickel apparatus, the 2-fluoromethyl compound (161) was the main product in both reactions.

Chapter 7 discusses the mechanism of the isomerisation reactions of the polyfluoroaryl prop-2-ynyl ethers and thioethers studied in this thesis. It also incorporates a critical experiment in which compound (161) is reacted with N,N-diethylaniline at 140°C only to be recovered unchanged. (The thermolysis of (161) in p-xylene at the same temperature gives the substitution product (159) exclusively). The charge-separated species (197) and (195) are proposed as intermediates in the reactions of the ether (156) and thioether (171) via the heterolytic fission of the $sp^3$ C-F bond in the Claisen rearrangement intermediates (157) and (172) respectively. It is concluded that the isomerisation reactions of (156) and (171), which require a 1,4-fluorine shift, proceed via an ionic mechanism.

The final chapter describes the thermolysis reactions of the naphthyl ether (156) and the 2-fluoromethyl compound (161) with 2,3-dimethylbut-2-ene and 3,3-dimethylbut-1-ene. Compounds (156) and (161) react with 2,3-dimethylbut-2-ene at 150°C to give 2-(2,2,3-trimethylbut-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (186) and a small amount of 2-(2,3,3-trimethylbut-1-enyl)-4,5,6,7,8,9-hexafluoronaphtho(2,1-b)furan (187). Compound(161) reacts with 3,3-dimethylbut-1-ene at 25°C in the presence of $BF_3$-etherate to give the Markovnikov addition-elimination product, 2-(3,4-dimethylpent-3-enyl)-4,5,6,7,8,9-hexafluoro-naphtho (2,1-b) furan (194) and a small amount of (186). Thermolysis of both (156) and (161) with 3,3-dimethylbut-1-ene gave (186) as the major product accompanied by smaller amounts of (187) and (194). It is proposed that compounds (186) and (187) arise via reaction with 2,3-dimethylbut-2-ene formed by isomerisation of the terminal alkene. 2-Chloromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161a) has been prepared; it reacts with 3,3-dimethylbut-1-ene in the presence of $ZnCl_2$ to give (186), (194) and (196).

## Declaration

The work in this thesis was undertaken in the Chemistry Laboratories of the University of Durham between October 1983 and September 1984. It is the Author's own work except where acknowledged and has not been submitted for any other degree.

JR Cooperwaite

J.R. Cooperwaite

# Memorandum

## Notes to the Reader

Throughout this thesis a number of abbreviations have been used regularly, these are:-

n.m.r. : Nuclear magnetic resonance spectroscopy

I.R. : Infra-Red spectroscopy

T.L.C. : Thin layer Chromatography

G.L.C. : Gas-liquid Chromatography

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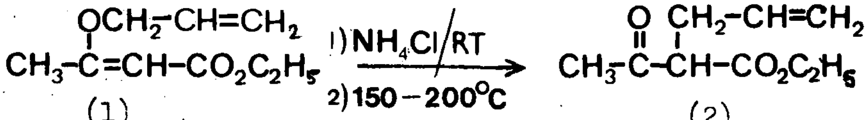
# Chapter 1 The Aromatic Claisen and Thio-Claisen Rearrangement

## 1.1. Introduction

The Claisen Rearrangement is one of the best known examples of a sigmatropic rearrangement in which a σ-bond migrates three positions along two unsaturated systems. Its scope and utility have led to a large number of reviews in the chemical literature. In the following sections, the more important aspects of the Claisen rearrangement reaction and also the closely related Cope rearrangements of aromatic prop-2-enyl and prop-2-ynyl systems are reviewed.

## 1.2. Development of the Claisen Rearrangement.

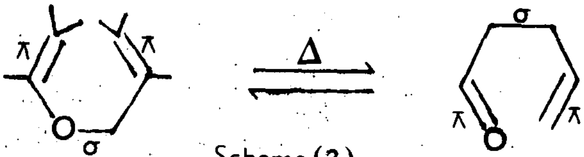
The original rearrangement reaction associated with the discoverer's name involved the thermally induced conversion of the prop-2-enyl vinyl ether (1) to the ethyl acetoacetate derivative (2) in the presence of ammonium chloride;[1] later this rearrangement was shown to occur in absence of a Lewis-acid at 150-200°C although at a significantly reduced rate[2]. Scheme (1)



$$\underset{(1)}{CH_3\text{-}\overset{OCH_2\text{-}CH=CH_2}{\overset{|}{C}}=CH\text{-}CO_2C_2H_5} \xrightarrow[2)\,150-200^{\circ}C]{1)\,NH_4Cl/RT} \underset{(2)}{CH_3\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{CH_2\text{-}CH=CH_2}{\overset{|}{C}H}\text{-}CO_2C_2H_5}$$

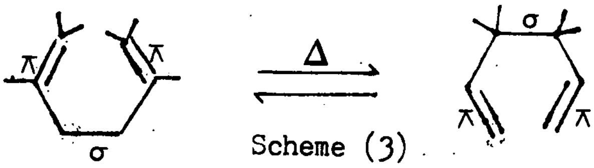
Scheme (1)

This first report led to an extensive study of the thermal rearrangements of open chain vinyl allyl ethers[3]. However, it is the rearrangement of aryl allyl ethers with which the Claisen rearrangement is more commonly associated. Claisen found that the allyl ethers of phenols rearranged smoothly at 200°C in the absence of a Lewis acid catalyst[4]. From these initial discoveries there evolved the recognition of a general rearrangement which can be applied to numerous systems which have an arrangement of six atoms, with unsaturated terminal linkages; Scheme (2).



Scheme (2)

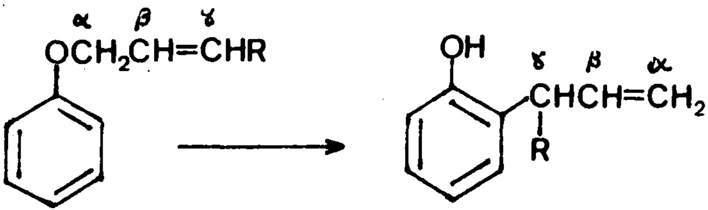
Cope, later identified the analogous bond reorganisation in a series of substituted 1,5-hexadienes$^{5}$. Scheme (3)



Scheme (3)

## The Ortho-Claisen Rearrangement.

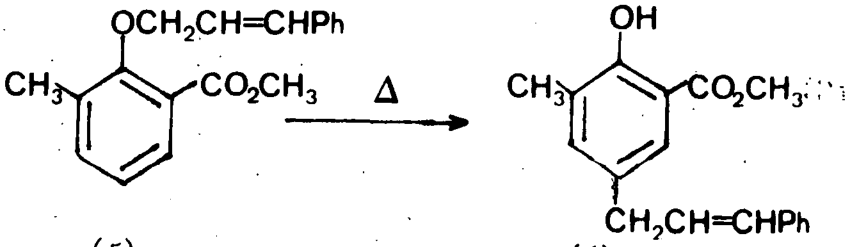
Distillation of an aryl prop-2-enyl ether (3)$^{6}$ with an unsubstituted ortho-position gave an ortho-(prop-2-enyl) derivative (4) as the product. Using $\alpha$-and $\gamma$-substituted prop-2-enyl phenyl ethers it was found that these groups become attached to the ortho-position relative to the oxygen and the carbon atom which becomes bonded to the aromatic nucleus is not the same as the one attached to the oxygen atom of the ether, but rather the one in the $\gamma$-position$^{7}$. Scheme (4)



(3) Scheme (4) (4)

## The Para-Claisen Rearrangement

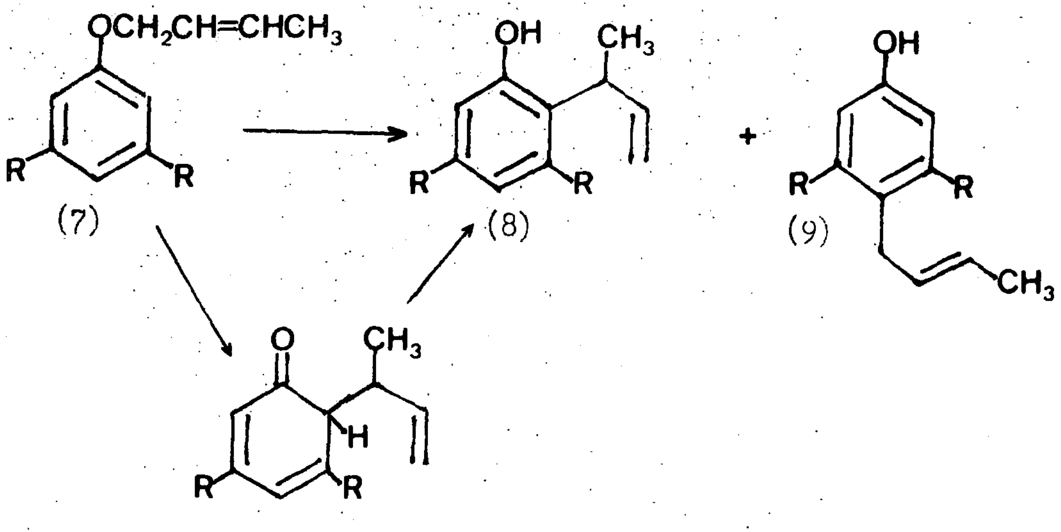
Thermal studies of ortho -disubstituted phenyl prop-2-enyl ethers gave the para-prop-2-enyl phenolic compounds$^{8}$. As was observed in the ortho-rearrangement, placing specific groups in the rearranging group led to further elucidation of the reaction process$^{9}$. Thus in the thermal rearrangement of the ether(5) Scheme (5), it was noted that the allyl group in the para-position was not inverted$^{10-11}$.



(5) (6)

Scheme (5)

As the scope of the Claisen rearrangment reaction was extended, examples were found where migrations to both ortho- <u>and</u> para-positions occured. Several detailed investigations have confirmed the competitive nature of such rearrangement[12-14]. The resulting ortho/para ratio was shown to depend on the bulk of the substituents in the migrating allyl group and the number, size and location of the other ring substituents[15-17]. More importantly these studies confirmed the conclusions drawn very early in the development of the Claisen rearrangement, namely that the products are dependent upon the experimental conditions adopted. A solvent effect was demonstrated in the rearrangement of (7) by using solvents of different polarity[12], Scheme (6)

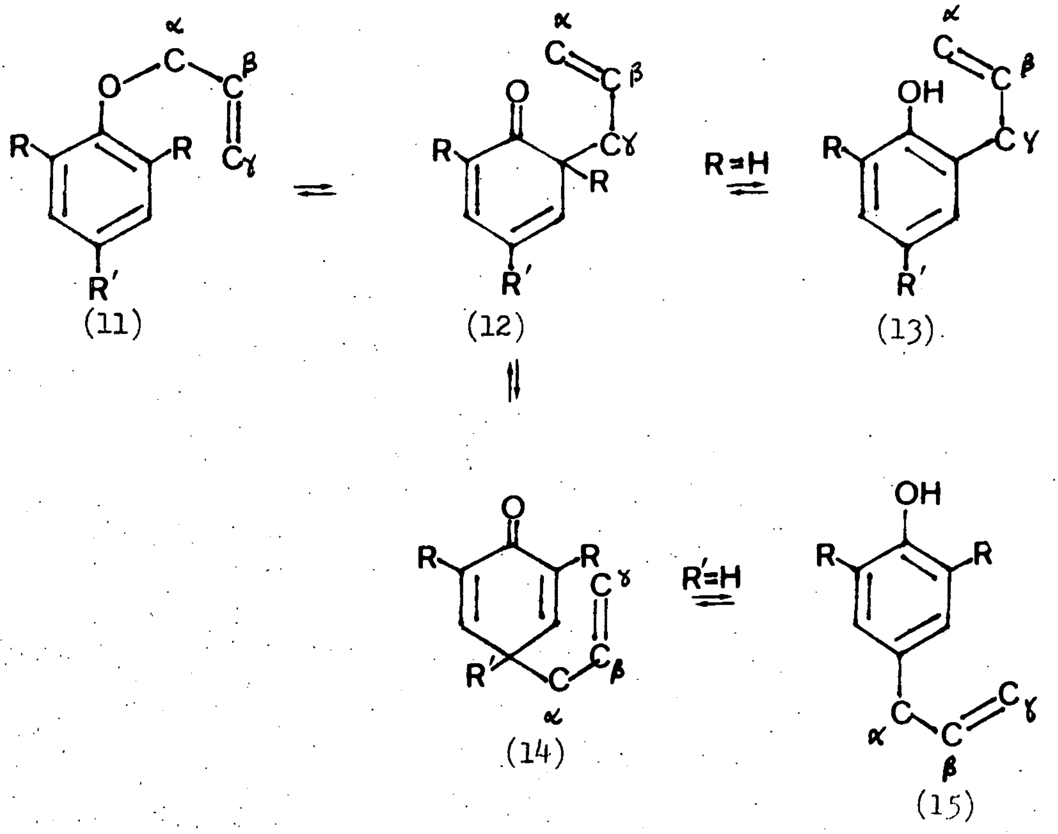


| Solvent | Products<br>Ortho | Para |
|---|---|---|
| Decalin | 38 | 42 |
| Diethylaniline | 79 | 21 |
| Dimethylformamide | 91 | 1.5 |

Scheme (6)

The more polar solvents were thought to facilitate the enolisation and restore the preference to the ortho rearrangement when steric effects in the initial ortho-dienone (10) prevented the usual rapid enolisation.

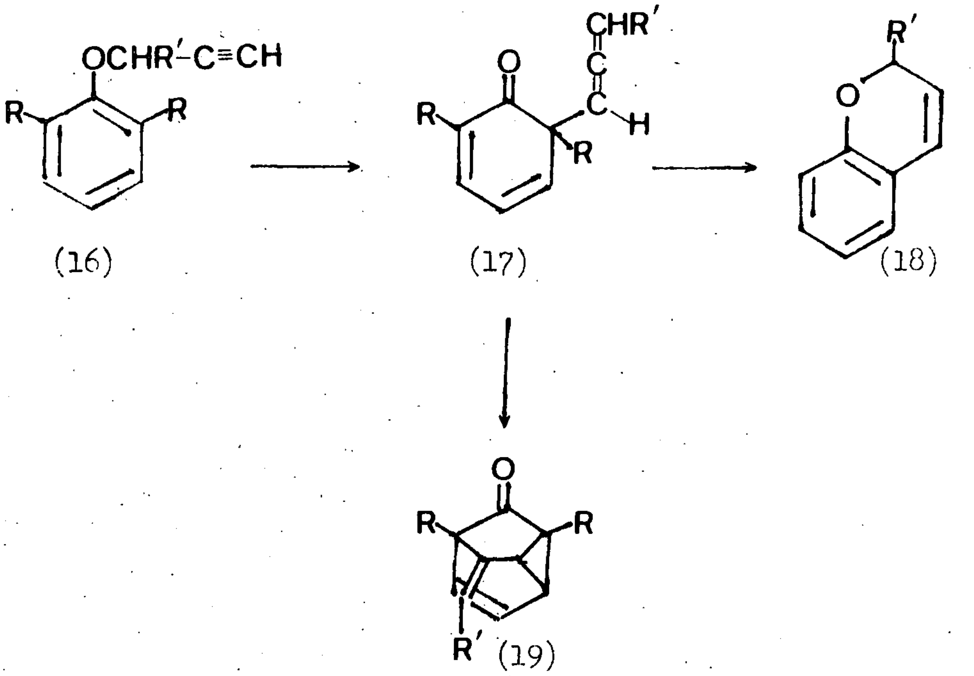
It is possible to summarize the thermal behaviour of allylic phenyl ethers (11) in the general scheme(7), which shows the γ-carbon atom of the allyl group first bonding to the ortho-carbon atom of the aromatic ring to give the ortho dienone (12), which results in an inversion of the migrating group. The ortho-dienone (12) may then undergo enolisation, if the ortho-substitutent R is hydrogen, to give the ortho allyl phenol (13), to complete the ortho-Claisen rearrangement. Alternatively the ortho-dienone (12) may, after realignment of the allyl group, undergo a Cope rearrangement (Sec 1.2). With this second inversion of the allyl group, the α-carbon becomes attached to the para-position on the aromatic ring, restoring the original structure of the allylic side chain. When the para substituent, R', is hydrogen, then rapid enolisation occurs, to give (15), and so completes the para-Claisen rearrangement.



Scheme (7)

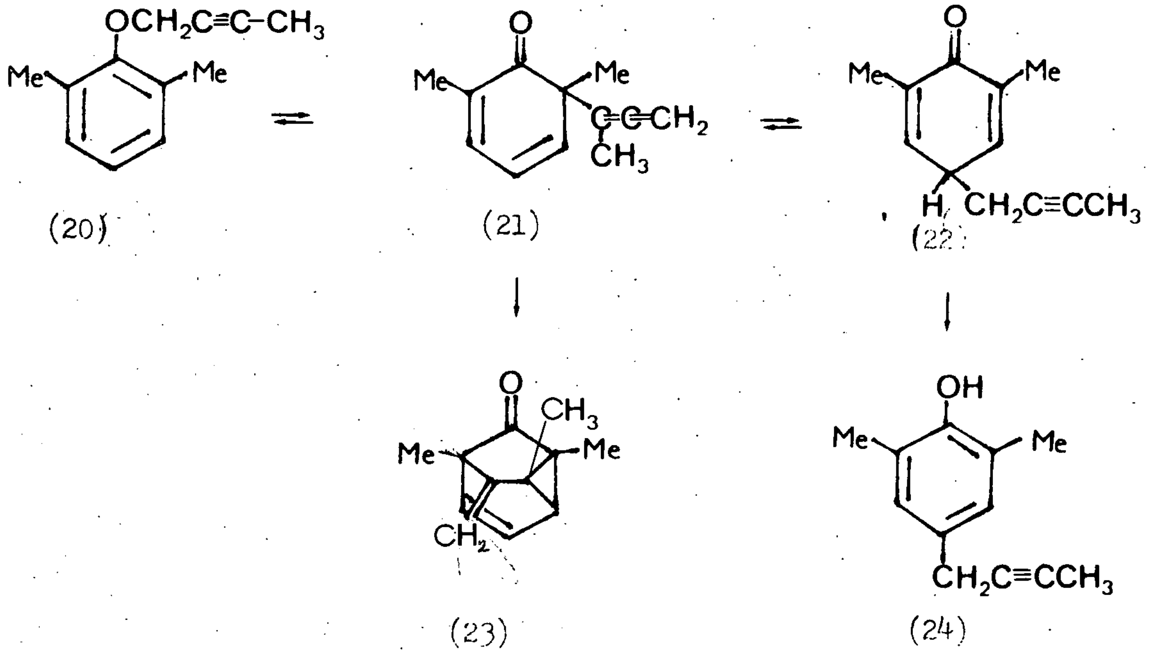
## 1.3. The Claisen Rearrangement of Aryl Prop-2-ynyl Ethers

While the Claisen rearrangment is more commonly associated with a prop-2-enyl rearranging group, many analogous reactions have been observed with prop-2-ynyl ether compounds. The prop-2-ynyl ethers (16) and (20) have been shown to rearrange smoothly in boiling diethylaniline to either 2H-chromenes (18) or tricyclic ketones (19)[18-20], both of which are derived from an intermediate o-propa-1,2-dienyl derivative, Scheme (8).



Scheme (8)

There appears to be only one recorded example of a para-Claisen rearrangement involving a prop-2-ynyl derivative. But-2-ynyl 2,6-dimethyl-phenyl ether (20) rearranged to give the internal Diels-Alder adduct (23) as the major product but was accompanied by 4-(but-2-ynyl)-2,6-dimethyl phenol (24) in small quantities Scheme (9)[19].

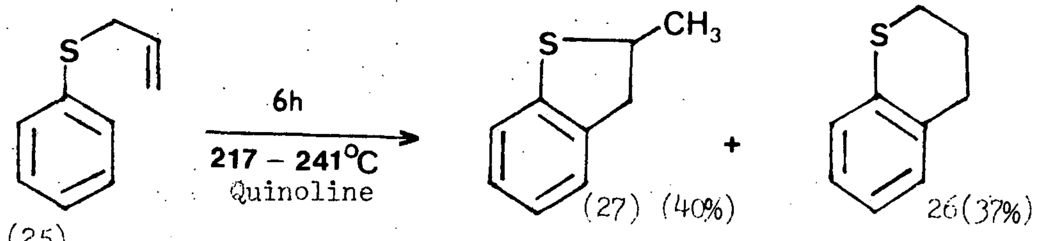


Scheme (9)

## 1.4. The Thio-Claisen Rearrangement of Aryl Prop-2-enyl and Prop-2-ynyl Thioethers

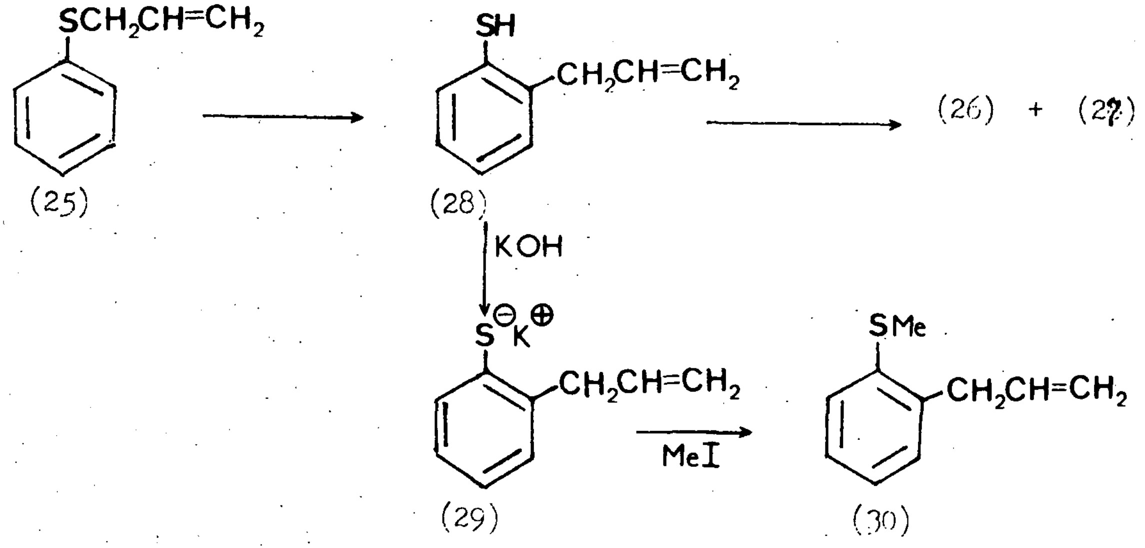
The majority of the work reported on the Claisen rearrangement is concentrated on aryl prop-2-enyl ethers. However, replacement of the O-ether linkage with an S-ether linkage results in a reduced but still observable tendency to rearrange[21]. Generally, the thermal behaviour of the phenyl prop-2-enyl thioethers has been shown to depart from that pattern observed in analogous oxygen systems (Sec 1.2). Attempts to promote a thio-Claisen rearrangement of prop-2-enyl thioethers, under the same reaction conditions which brought about rearrangement of the corresponding prop-2-enyl ethers, failed to produce any cyclisation products[22].

The sulphur analogues exhibit a higher thermal stability but undergo cleavage when heated to ca.300°C[23]. However, as ethers and thioethers of high boiling point frequently undergo undesirable side reactions at such temperatures, the thermolyses were conducted in a high boiling amine solvent which accelerated the rate of rearrangement of the thioethers but had a negligible influence upon the corresponding ethers.[23] The solvents most commonly used were dimethylaniline (bp 193°C) and diethylaniline (b.p. 215°C)[24]. Heating the prop-2-enyl thioether (25) for 6h in boiling quinoline gave an equal ratio of thiachroman (26) and 2H, 3H-2-methylbenzo (b) thiophen (27)[25]. Scheme (10).



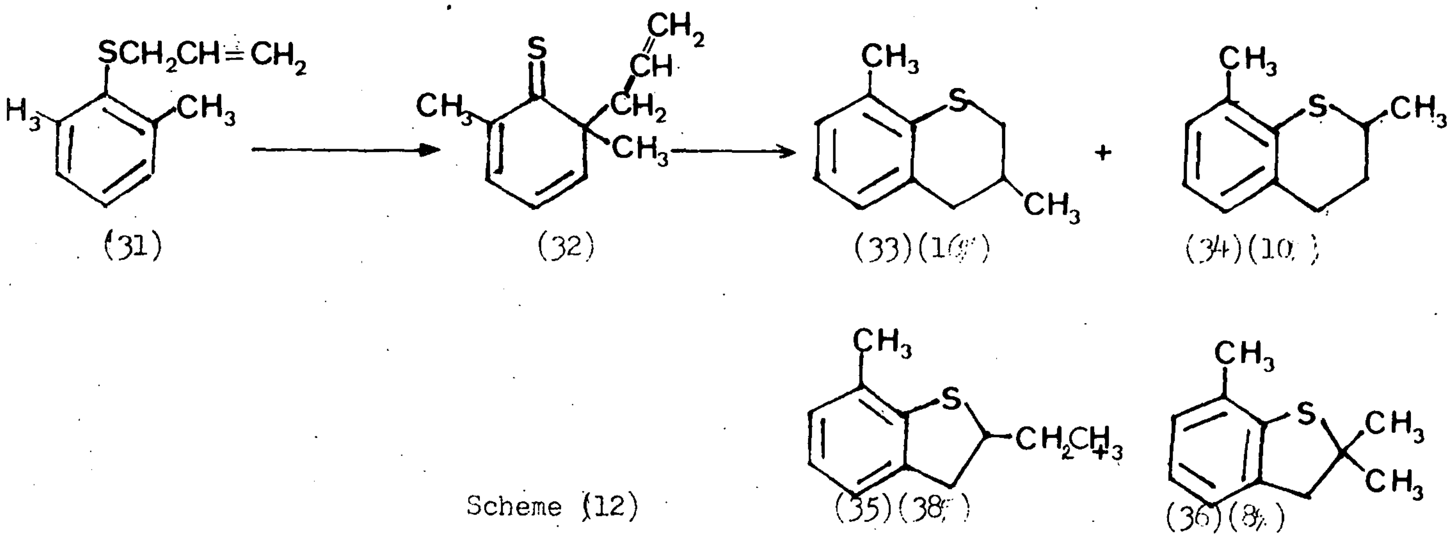
Scheme (10)

Despite earlier conflicting data, the formation of the ortho-prop-2-enyl thiophenol (28) was established as the initial product of the rearrangement,[26] but under the rearrangement conditions adopted, it cyclizes rapidly to the observed products[27]. The intermediacy of (28) was confirmed with the aid of trapping experiments using potassium hydroxide and methyl iodide.[26] The base was added prior to reaction being completed and the thiol was converted to the thiophenate (29). Methyl iodide was then added and the methyl thioether (30) was isolated. Moreover, refluxing the authentic thiophenol (28) in quinoline gave the same product distribution of cyclised products (26) and (27). Scheme (11).



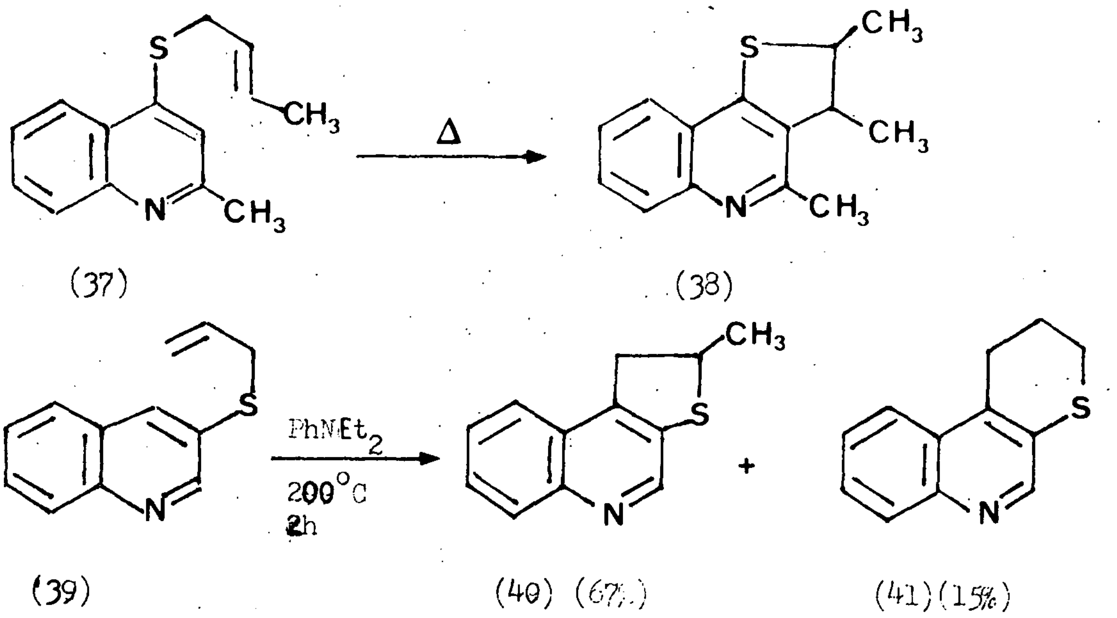
Scheme (11)

In an attempt to observe a para-Claisen rearrangement, 2,6-dimethylphenyl prop-2-enyl thioether (31) was refluxed in quinoline[28]. The reaction failed to yield the expected para-substituted thiophenol: the bicyclic products (33)(34)(35) and (36) were isolated which could only arise via an initial (3,3) sigmatropic shift. Scheme (12).



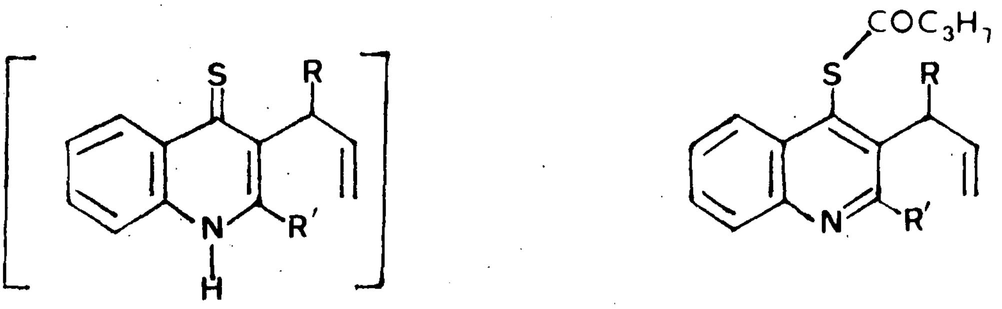
Scheme (12)

The rearrangements of allyl thioethers of heterocyclic compounds (Scheme 13) proceeded more readily and with fewer complications than the corresponding carbocyclic systems.



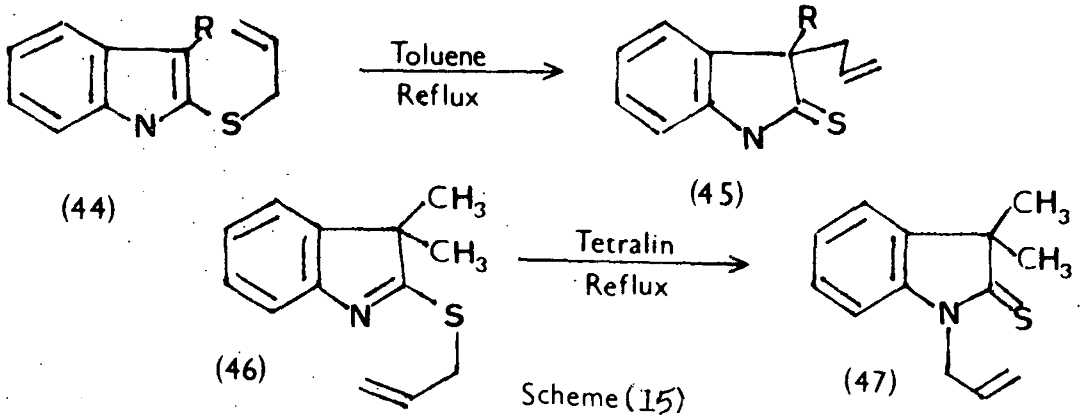
Scheme (13)

Although the thione (42) was not detected in the above reactions, the thermolysis of (37) in the presence of butyric anhydride yielded the corresponding ester (43)[29]. (Scheme 14)



(42) Scheme (14) (43)

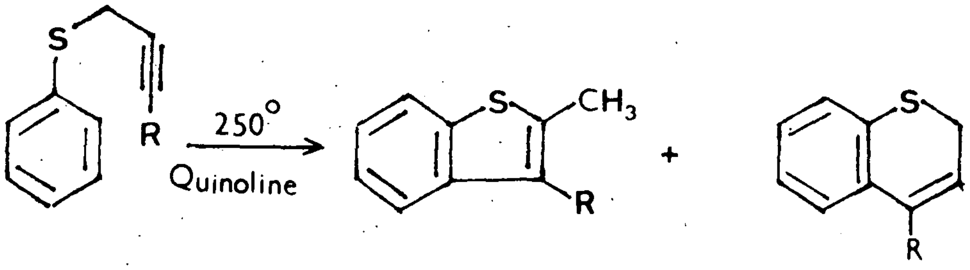
The Claisen rearrangements of 2-allylthio derivatives of imidazoles and indoles demonstrate the efficient rearrangements of prop-2-enyl thioethers[30]. Some examples are shown in scheme (15)



(44) (45) (46) (47)

Scheme (15)

Reports on the thermal behaviour of the prop-2-ynyl phenyl thioethers are limited to (48) and (49). Scheme (16)[31].



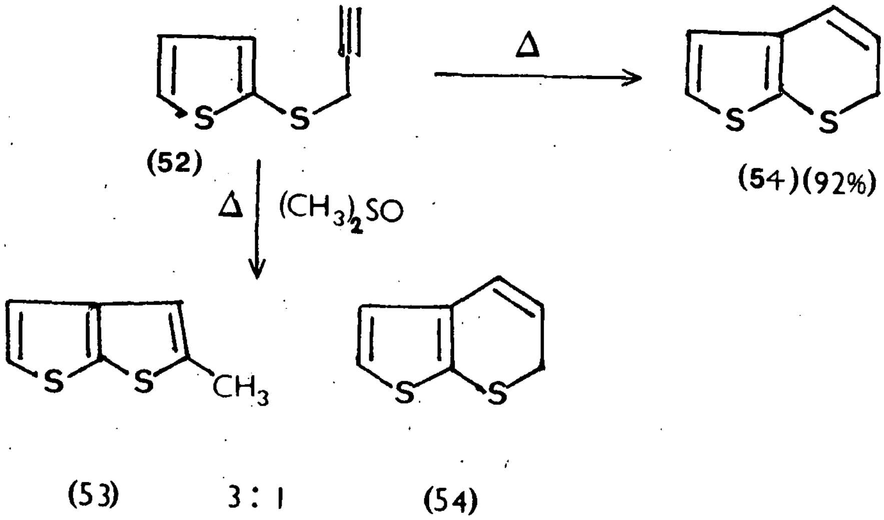
R=H (48)
R=CH$_3$(49)

(50)

(51)

Scheme (16)

The rearrangements of prop-2-ynyl thioethers of heterocylic nuclei are more common and proceed more readily. The study of 2- and 3- thienyl sulphides once again revealed a dependance of the product distribution on the reaction conditions[31]. Scheme (17).

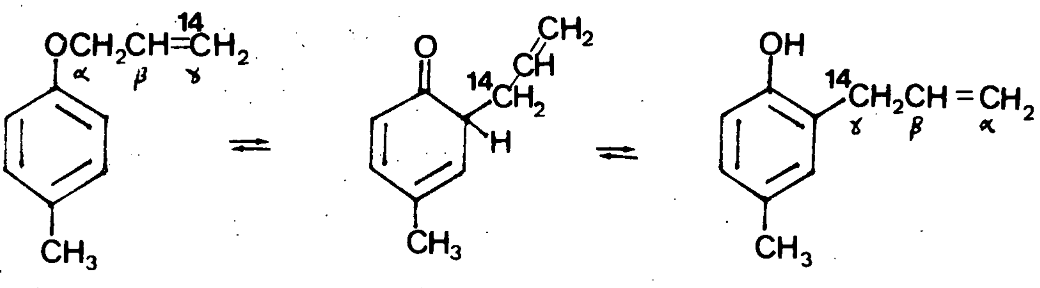


Scheme (17)

The fact that the Claisen rearrangement is less facile for thioethers than for ether compounds can be attributed to either the cyclic transition state having higher relative energy or the overall $\Delta$ G associated with the transformation being less favourable, or a combination of both these effects[32]. The suggestion that the oxy-Claisen rearrangements could be thermodynamically more favourable is based on the energy change associated with the C - X being transformed to C = X; the transformation for X = O compared with X = S is more exothermic to the extent of 23k cal $mol^{-1}$[32].

## 1.5. Mechanism and Stereochemistry of the Claisen Rearrangement

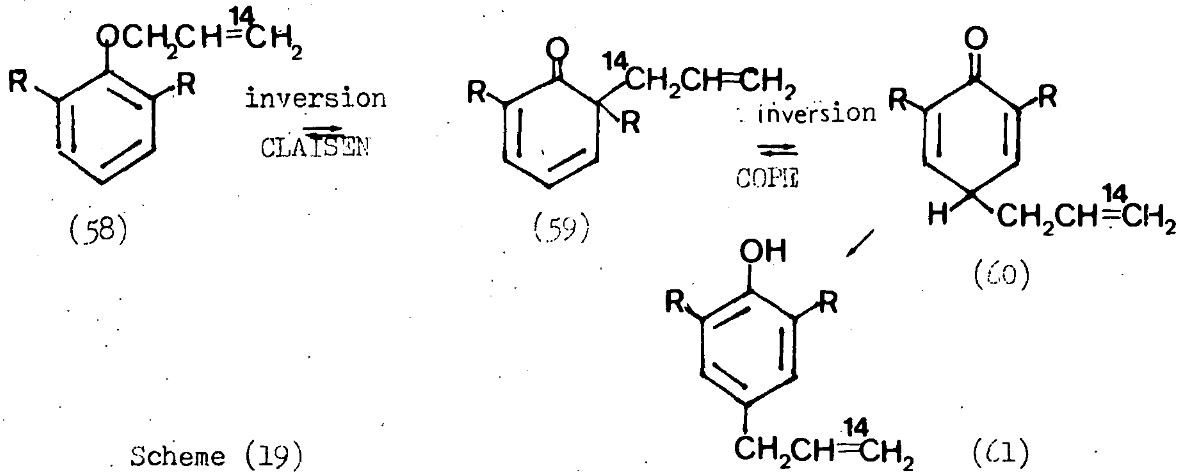
The Claisen rearrangement was for many years conspicuous by virtue of the absence of evidence relating to reactive intermediates, as the rearrangement is mainly insensitive to ionic and free radical probes. The intramolecular nature, exact stereospecificity and failure to respond to catalysts other than heat and light led to a proposal of a neutral cyclic transition state in which a concerted bond reorganisation was depicted by a cyclic movement of electrons[33]. Schmid et al demonstrated the inversion of the simplest possible rearranging group, the prop-2-enyl group[34], in a series of experiments by labelling the $\gamma$-carbon with $^{14}C$ and blocking the para position on the aromatic ring. In explaining the formation of (57) Schmid[34b] (Scheme 18) proposed the intermediacy of an ortho-dienone (56).



(55) (56) (57)

Scheme (18)

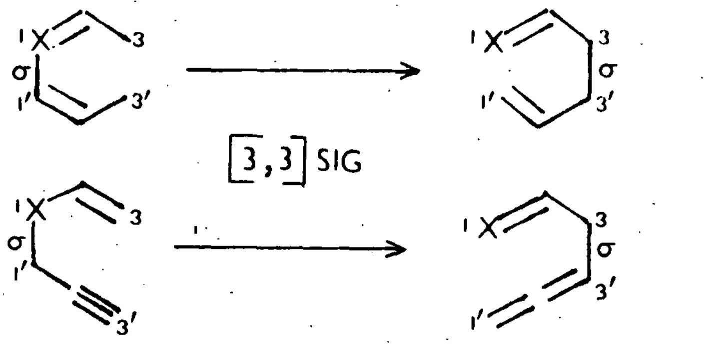
Repeating the experiment using a system in which both ortho-positions are blocked gave a product resulting from a para-Claisen rearrangement and the rearranging group was shown to have retained its original stereochemistry.[35] The para-Claisen rearrangement was thought to proceed in a similar fashion to the ortho-Claisen rearrangement but with two migrations of the prop-2-enyl group. However, the second migration, identified as a Cope rearrangement also fell into what at the time was called a 'no-mechanism' mechanism. (Scheme (19).



Scheme (19)

It was not until 40 years after the observation of the Claisen rearrangement that its mechanism was defined. This followed a publication of a series of rules by Woodward and Hoffmann[36-37] which could predict the ease and the steric course of all such concerted reactions known thereafter as sigmatropic shifts.

Woodward and Hoffmann defined the migration of a σ-bond flanked by one or more π bonds to a new position in the molecule, as an [i, j] sigmatropic rearrangement, where i and j refer to the number of the atoms to which each end of the migrating σ-bond becomes attached. In both the Claisen and Cope rearrangements (Scheme (20) ), the σ-bond migrates from position $1,1'$ to position $3,3'$ and is termed a [3,3] sigmatropic shift.



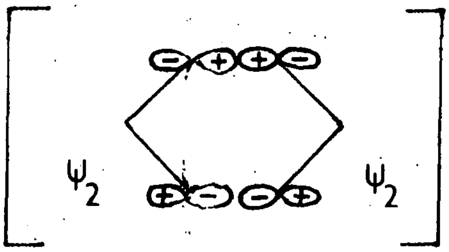
x = C - COPE
x = O - CLAISEN

(Scheme 20)

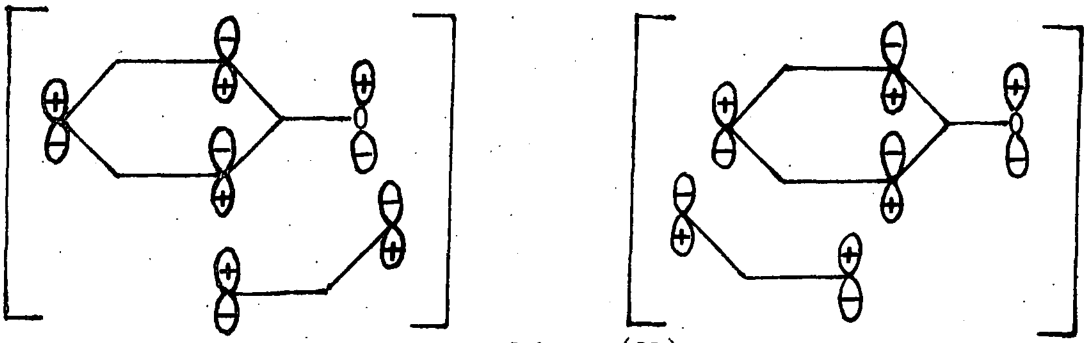
For the reaction to be concerted, the rearrangement requires a cyclic transition state in which an orbital lobe(s) of the migrating group overlap(s) in a bonding mode with both ends of the $\pi$-system to which the group migrates. If in the rearrangement the migrating group is associated at all times with the same face of the $\pi$-framework the migration is termed suprafacial. However, if the migrating group crosses the nodal plane of the $\pi$-system, the shift is defined as antarafacial. Both types of migration can result in retention or inversion of the migrating group, which allows four possible modes of sigmatropic shift.

A simple way of analysing these sigmatropic shifts is provided by Dewar's Perturbational Molecular Orbital (PMO) method which approximates the transition state energies by regarding the transition state as being constructed from two alternant radicals. It is the non-bonding molecular orbitals (which always have the phase-alternating form + o − o + o −) that form the basis of the PMO technique, as the dominant attractive interaction between the two alternant radicals is that between the singly occupied Non Bonding Molecular Orbitals (NBMO). The transition state stability of the Claisen and Cope rearrangements can be assessed by breaking down the transition states into a pair of component odd alternant radicals and then combining them, taking careful note of matching and non-matching wave functions. The Claisen rearrangement transition state can be represented by a phenoxy radical and an allyl radical[38] (by associating one electron of the O-$CH_2$ bond with the allyl group) which have single electrons occupying NBMO's. Whereas, the Cope rearrangement transition state can be represented by combining two odd alternant allyl radicals (Scheme 21).

a) Cope T.S.

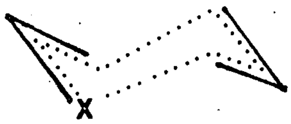


b) Ortho-Claisen T.S. Para-Claisen T.S.

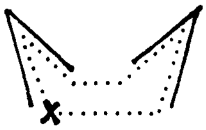


Scheme (21)

Inspection of the orbitals shows why the migration of the allyl group is to the ortho-position and why a further migration to the para-position may take place, for there will again be overlap of like orbitals. Inspection also predicts a duplicate reaction involving an -ynyl group as its corresponding N.M.B.O. has the same symmetry as the singly occupied allyl N.B.M.O.. Because the Claisen and Cope rearrangements for steric reasons must proceed via suprafacial-suprafacial (3,3) sigmatropic processes, the resultant 6-membered cyclic transition states have a number of possible geometries related to a) the chair arrangement (62) or b) the 6-centred boat arrangement (63). Scheme (22).



(62)

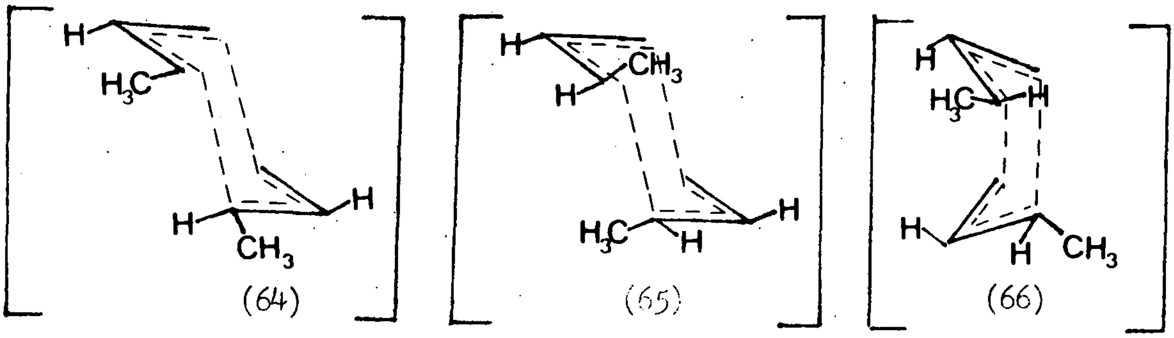


(63)

X =O or C

Scheme (22)

A series of experiments considering the stereochemical relationship between the reactant and product, using E- and Z- phenyl 1-methylbut-2-enylether[39] and erythro and threo-2-(1-methyl prop-2-enyl)-2,6-dimethylcyclohexa-3,5-dienone[40] demonstrated the preference to proceed via a chair geometry (64) (which minimises the pseudo-1,3-diaxial interactions) as opposed to (65) and the energetically least favourable boat - form (66). Scheme (23).



(64) (65) (66)

Scheme (23)

While the chair transition state geometry is preferred, there are many examples in the chemical literature for certain sterically constained molecules in which the boat arrangement represents the only available pathway[41-44].

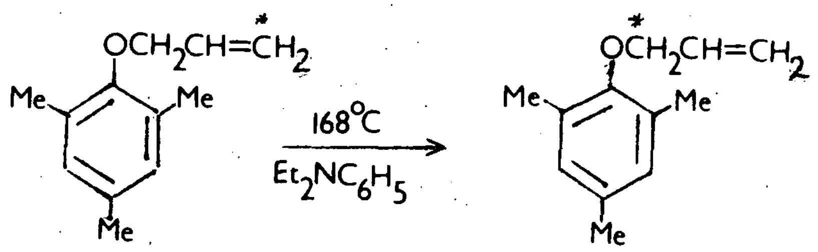
# Chapter 2 Reactions following an Initial Claisen Rearrangement Reaction

## 2.1. Introduction

This chapter reviews some of the reactions of the respective Claisen rearranged intermediates, derived from prop-2-enyl and prop-2-ynyl systems, when enolisation to the 2- and 4- phenol derivatives is not possible.

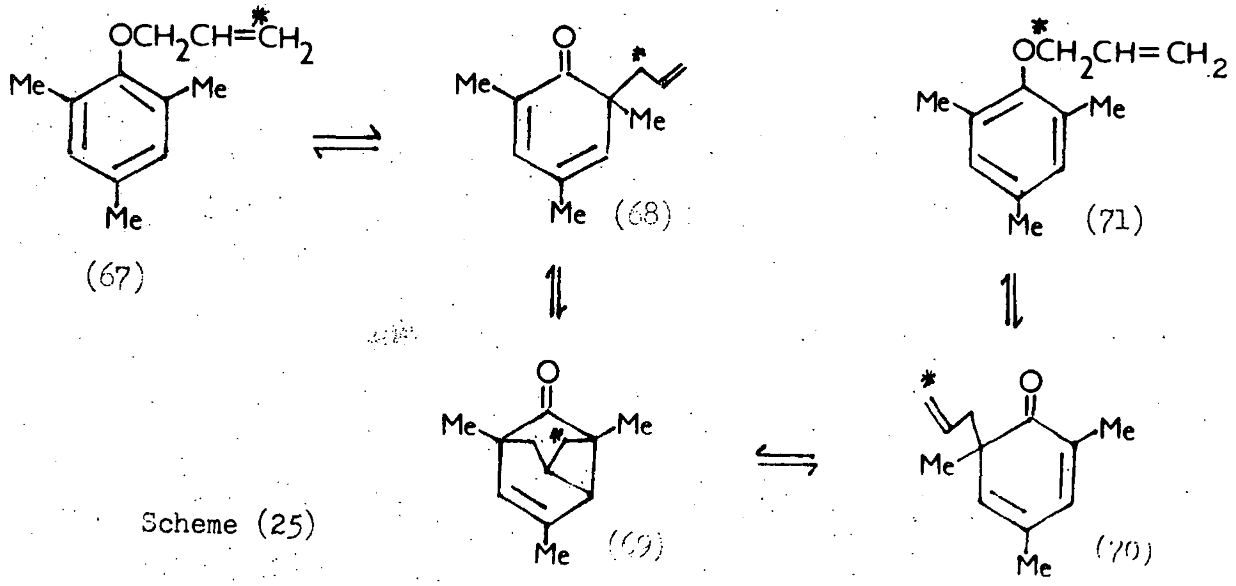
## 2.2. Internal Diels-Alder Reactions

The (2+2) cycloaddition reaction of an ortho-Claisen intermediate has been recorded in many prop-2-enyl and prop-2-ynyl systems[45-46]. It was first postulated by Schmid et al in trying to account for the observed distribution of radioactivity, when $^{14}$C-labelled 2,4,6-trimethylphenyl prop-2-enyl ether was heated at 168°C for 24 hrs. in diethylaniline[47]. (Scheme 24).



(67) Scheme (24) (71)

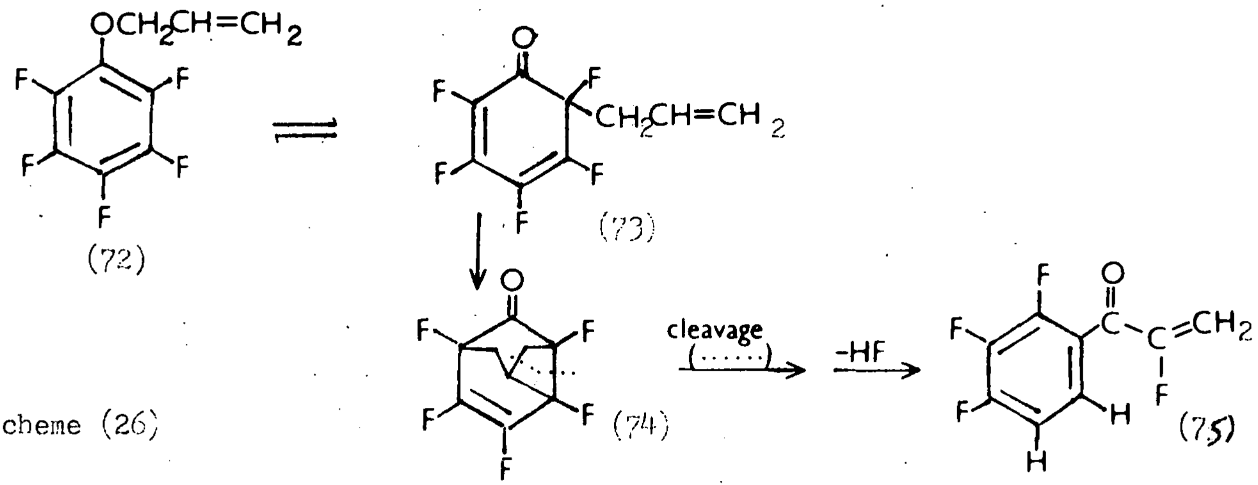
Schmid accounted for the observed radioactive distribution by invoking the intermediacy of an intramolecular Diels-Alder adduct (69) which undergoes preferential cleavage of the strained 4-membered ring, to give the ortho-dienone (70), in which the $^{14}$C-labelled atom is no longer attached to the aromatic ring (Scheme 25).



(67) (68) (71) (69) (70)

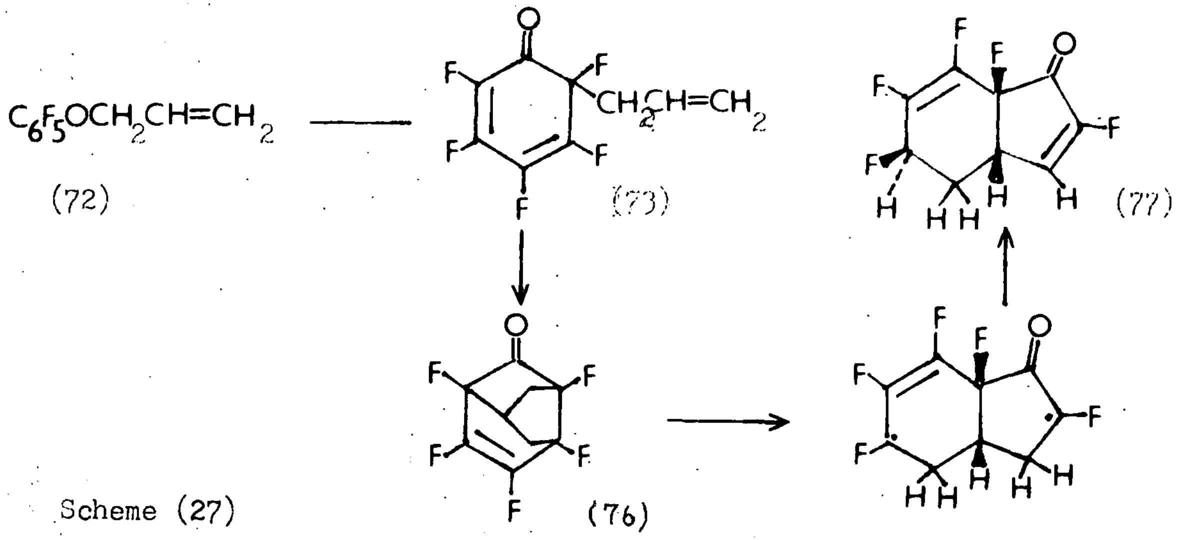
Scheme (25)

An analogous intramolecular Diels-Alder addition reaction intermediate was also invoked to account for the products formed in the thermolyses of pentafluorophenyl prop-2-enyl ether (72)[48-50], in particular the formation of the(1-fluorovinyl)-2,3,4-trifluorophenyl ketone (75). (Scheme 26).



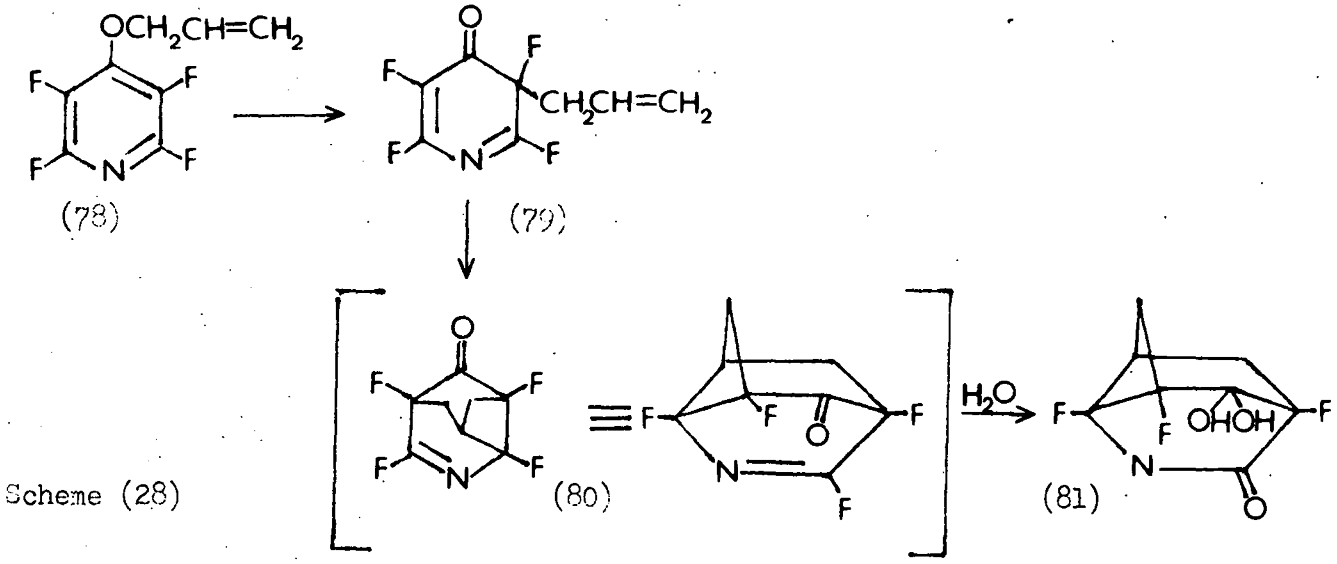
Scheme (26)

Moreover, the internal Diels-Alder adduct (74) was isolated when the ether (72) was heated under milder conditions (See sec 3.2 ). Interestingly, the study with pentafluorophenyl prop-2-enyl ether gave a product (77) whose formation was rationalized on the basis of the alternative possible internal Diels-Alder adduct (76).[48] (Scheme 27).



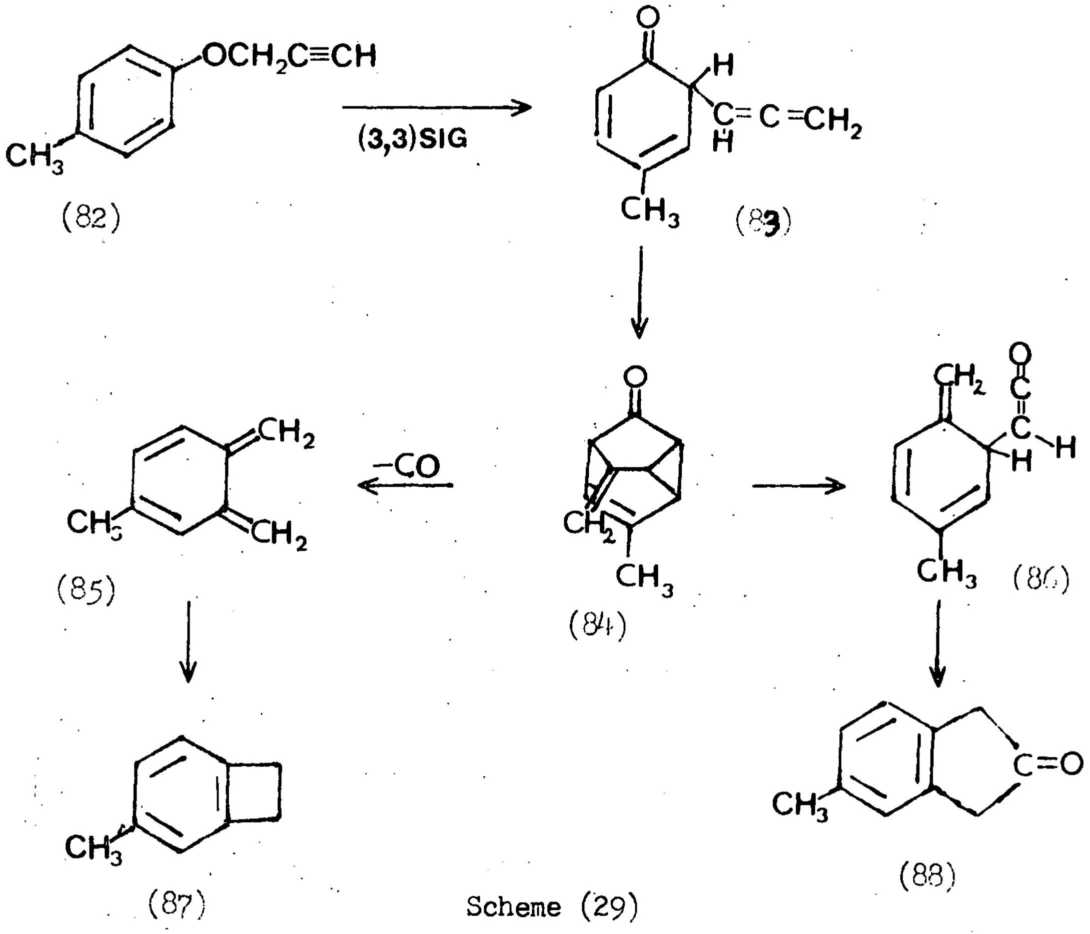
Scheme (27)

Internal Diels-Alder adducts and their derivatives have also been observed in the thermolyses of tetrafluoropyridyl prop-2-enyl ethers[51]. Heating 2,3,5,6-tetrafluoro-4-pyridyl prop-2-enyl ether in the vapour phase at 138°C for 10d gave 15% of 3-aza-2,4,5,7-tetrafluoro-tricyclo $(3,3,1,0^{2,7})$ non-3-en-6-one(80) and 9% of its hydrated hydrolysis product (81) (Scheme 28), which arises because of the susceptibility of the N=CF bond in the intramolecular Diels-Alder adduct to reaction with water.



Scheme (28)

The intervention of an intramolecular Diels-Alder addition in a prop-2-ynyl system was proposed in the flash vacuum pyrolysis at 480°C of 4-methyl prop-2-ynyl ether (82) which gave a mixture of the indan-2-one (88) and 1,2-dihydrobenzocyclobutene (87). (Scheme 29)[52,53].



Scheme (29)

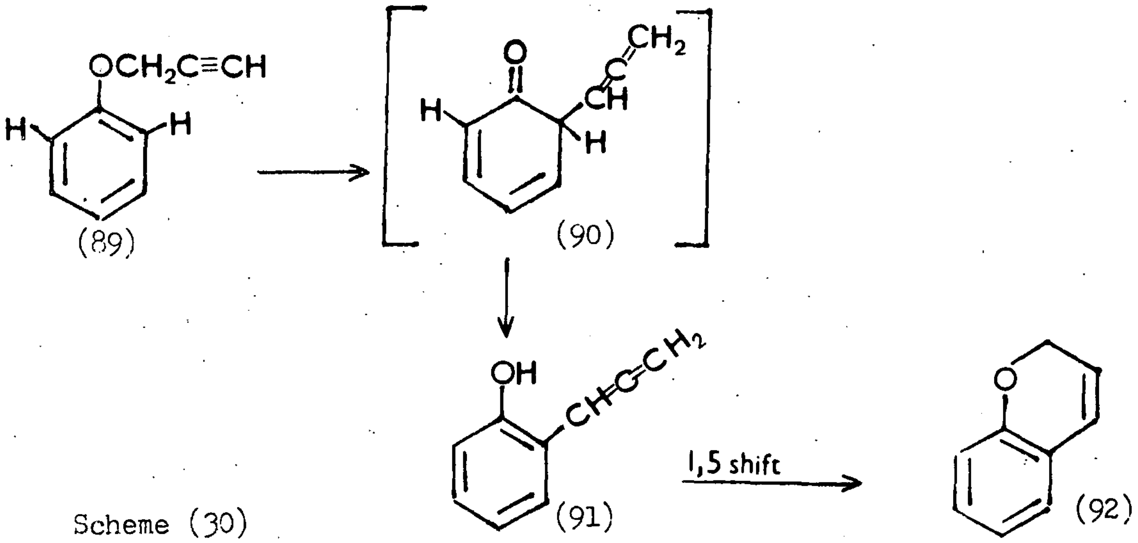
Schmid et al demonstrated that 2,6-dimethylphenyl prop-2-ynyl ether and its derivatives[19] rearranged thermally to give 1,5-dimethyl-6-methylenetricyclo $(3,2,1,0^{2,7})$ oct-3-en-8-one and related compounds. This requires an internal cycloaddition of the respective ortho allenyldienones. (Scheme 8). On further examination of these prop-2-ynyl systems it became clear that an internal Diels-Alder addition reaction of the Claisen intermediate was dependant upon the ortho substituent to the O-prop-2-ynyl group. If the ortho-substituent was hydrogen then the ether was shown not to undergo a cycloaddition but a preferential cyclisation to the 2H-chromene derivative.

These observations clearly demonstrate the viability of an internal Diels-Alder addition reaction of the Claisen rearranged intermediates derived from phenyl prop-2-enyl and prop-2-ynyl ether systems. The intramolecular Diels-Alder addition reactions have been invoked only as transitionary intermediates in some naphthalene compounds as these involve unfavourable loss of aromaticity during the reaction. To date there have been no reports of intramolecular Diels-Alder addition reactions involving aryl prop-2-enyl or prop-2-ynyl thioethers. In all the thermolyses reported the thioethers have shown a preference to undergo alternative cyclisation reactions.

## 2.3. Alternative Cyclisation Reactions

The cyclisations of Claisen rearrangement intermediates other than via a Diels Alder reaction have been known to take place with numerous prop-2-enyl and prop-2-ynyl systems. While H. Schmid was first to propose that the thermal cyclisation to the chromene derivative involved a preliminary (3,3) sigmatropic rearrangement, many other workers established and confirmed his proposals in later years. An investigation of phenyl prop-2-ynyl derivatives had shown that blocking of the ortho-position prevents cyclisation to the 2H-chromene. Although

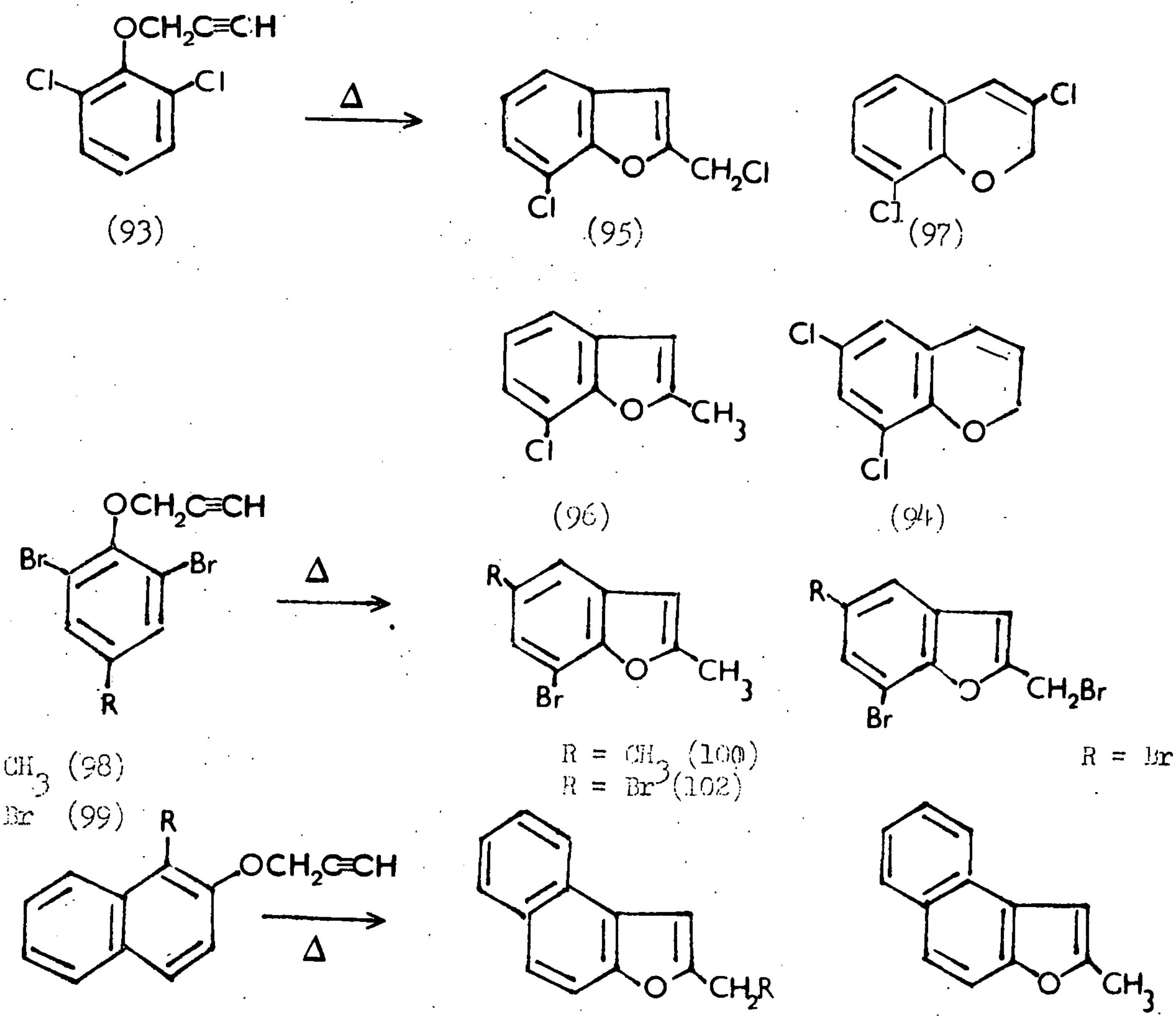
Schmid predicted that a hydrogen atom in the ortho postion would lead to enolisation of the dienone (90) followed by a 1,5-sigmatropic shift to give



Scheme (30)

(92),the formation of a 2H-Chromene on heating the phenyl and naphthyl prop-2-ynyl ethers was also postulated by Iwai and Ide. However, they presumed that the chromene resulted from a direct cyclisation[20].

The thermal behaviour of 2,6-dihalophenyl prop-2-ynyl ethers has been investigated. Both the chloro and bromo-derivatives thermolysed to give cyclisation products. (Scheme 31). Heating 2,6-dichlorophenyl prop-2-ynyl ether (93) in vacuo at 230°-260°C in n-decane gave 4-6% 6,8 dichloro-2H-chromen (94) and 33% 7-chloro-2-chloromethylbenzofuran (95) as the main products accompanied by (96) and (97) in much smaller quantities[54]. Thermolysis of the dibromo analogue (98) at 235°C gave only 21% 7-bromo-2,5-dimethyl benzo(b)furan (100), whereas the 2,4,6-tribromophenyl prop-2-ynyl ether (99) gave both the benzofuran derivatives (101) and (102) containing one bromine atom less per molecule[54]. (Scheme 31). The corresponding naphthyl prop-2-ynyl ethers (103) and (104) as expected rearranged more efficiently and at a lower temperature (180°) to give the naphthofurans (105), (107) and (106)[54].



(93) (95) (97)

(96) (94)

R = $CH_3$ (98)
R = Br (99)

R = $CH_3$ (100)
R = Br (102)

R = Br (101)

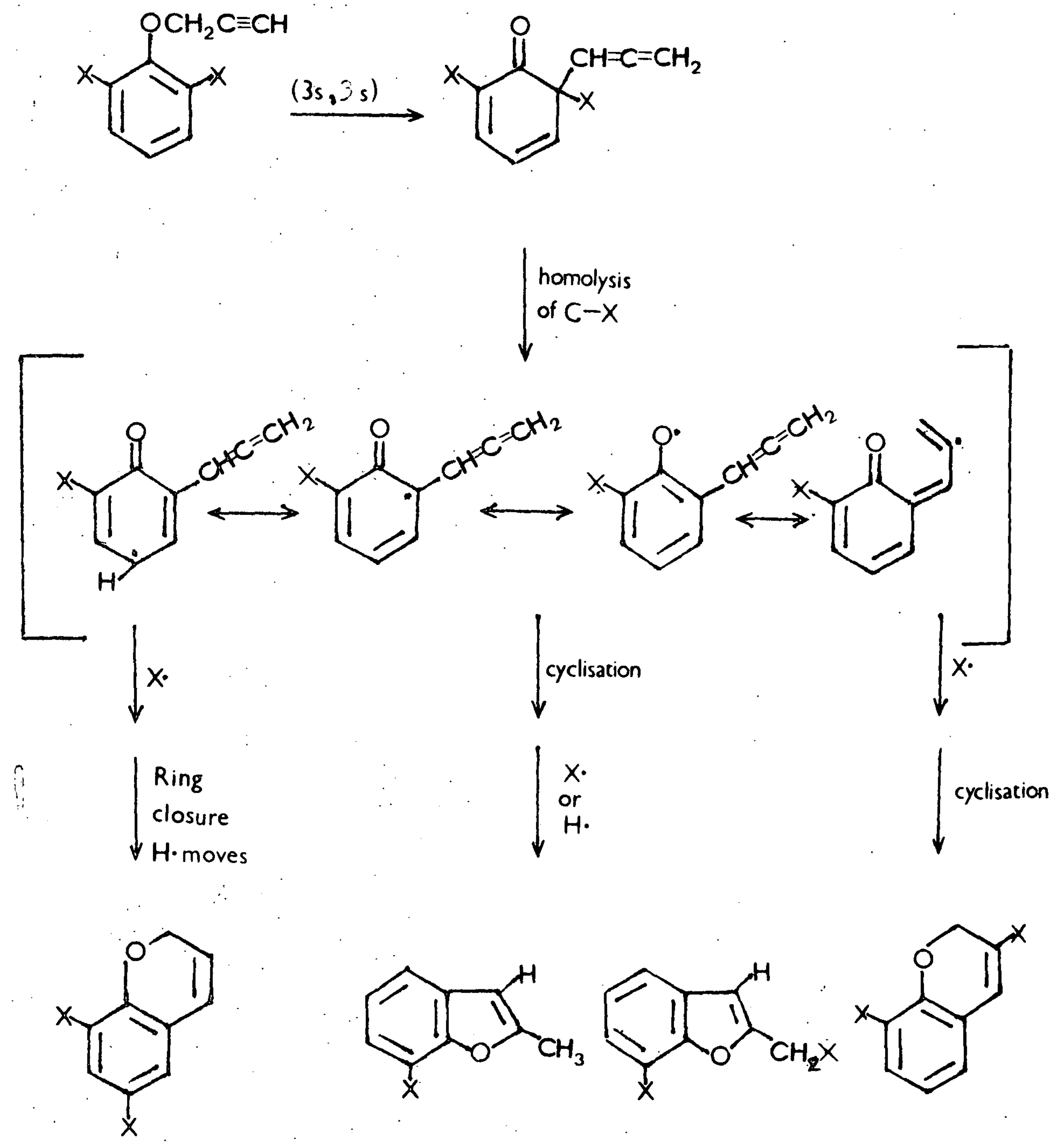
R = Cl (103)
R = Br (104)

R = Cl (105)
R = Br (107)

(106)

Scheme (31)

Schmid proposed an initial (3,3) sigmatropic rearrangement to the 6-allenyl-6-halogeno cyclohexa-2,4-dienones followed by a series of radical pathways to account for the observed products as illustrated for 2,6-dichlorophenyl prop-2-ynyl ether in Scheme (32).

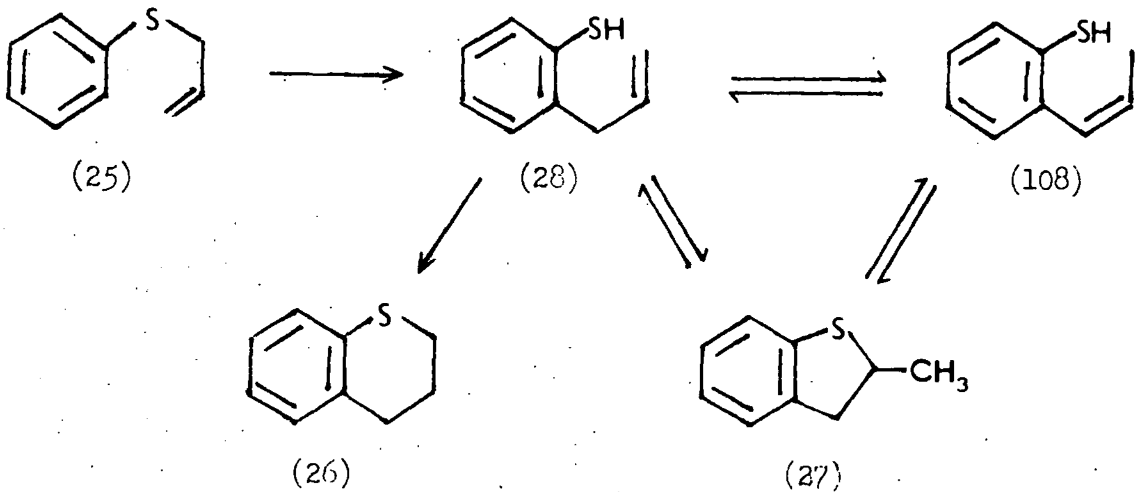


X = Cl X = Br

Scheme (32)

The thermolyses of prop-2-enyl and prop-2-ynyl thioethers have been shown to give only cyclisation products (not internal Diels-Alder adducts)(Sec1.4 ),[28,31] and it is in the study of these compounds alone that the nature of the solvent has been shown to have a very important role. While a Claisen intermediate has not been isolated, the similarities of the product with those formed in the oxygen series has led to simple analogy. Indeed, it is thought that the special facility for cyclisation in the sulphur series prevents the isolation of the initial thio-Claisen intermediate.

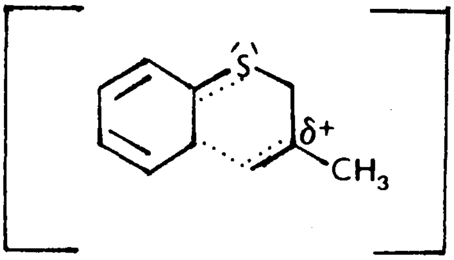
Kwart and Evans proposed an interelation between the thiacoumaran (27) and thiachroman(26)[25]. (Scheme 33). However, this is far from undisputed[56,57,55].



Scheme (33)

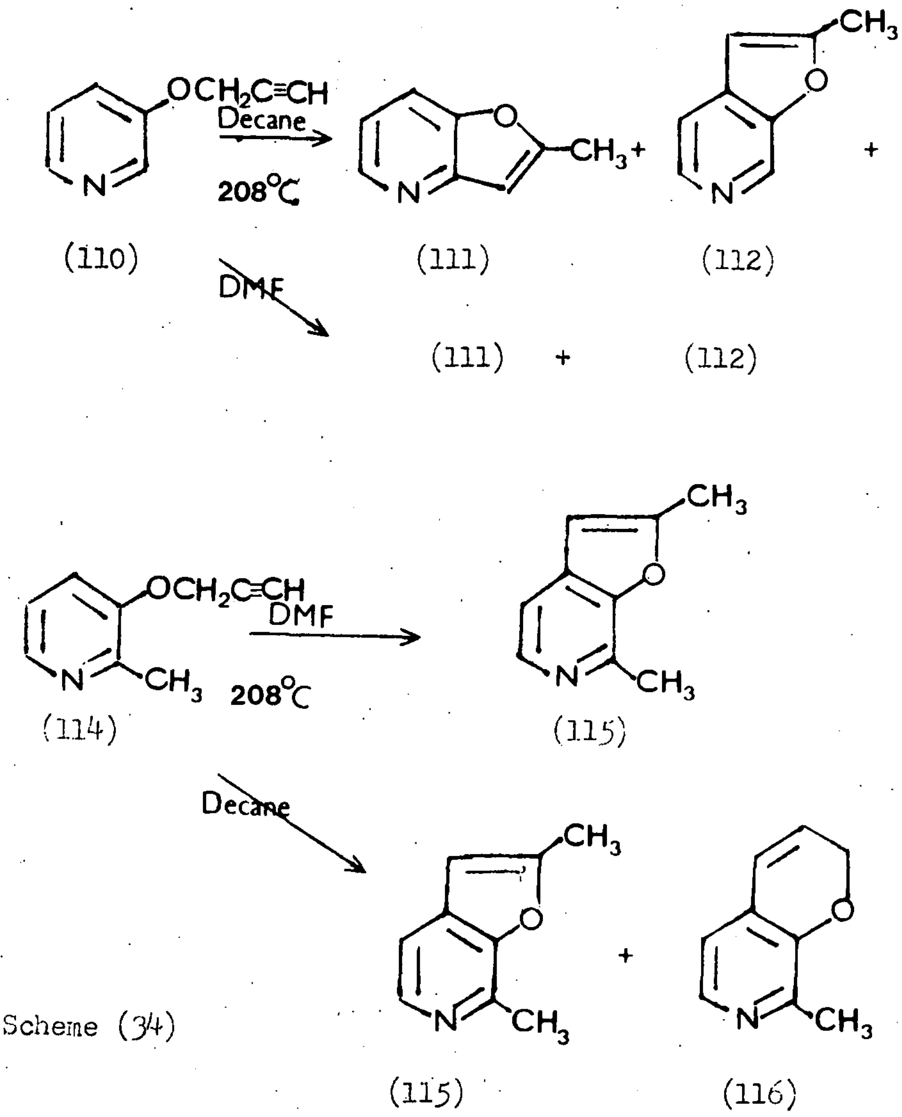
The formation of the cyclised products was rationalised in terms of competitive ionic and radical additions of the thiol function to the double bond in the 2-prop-2-enyl group[56]. Ordinarily the thio-Claisen rearrangement does not occur without the aid of a high boiling amine solvent, which may be taken as an indication of the greater need for charge transfer in a thio-Claisen activated complex.

The cyclisation of a prop-2-enyl derivative was shown to occur in the absence of a solvent by substituting a methyl group for H at C-2. The 2-methyl group was thought to lower the energy of activation of the cyclic transition state by a) helping to maintain a 6-membered arrangement by imposing restraints on the free rotations of the bonds and b) stabilizing the developing +ve charge on the developing 3 position in the transition state (109)[57].



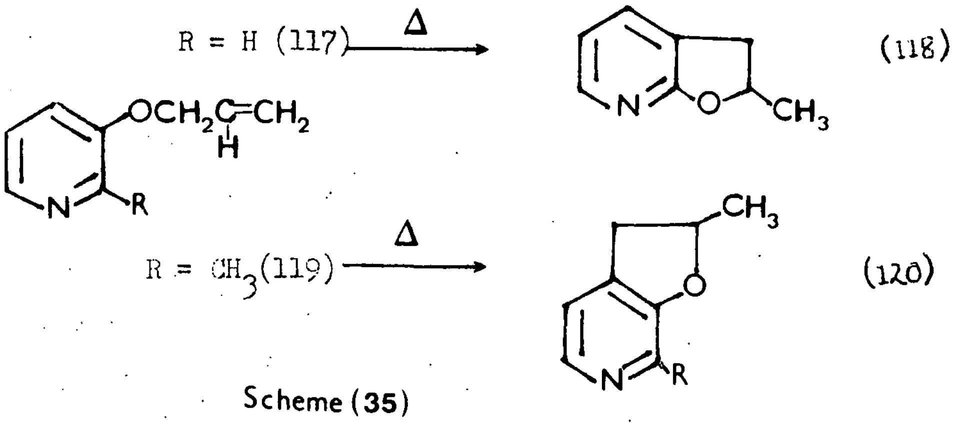
(109)

The cyclisation of Claisen intermediates was also observed in various pyridyl prop-2-enyl[58] and prop-2-ynyl ethers[58]. Schmid investigated the thermolysis of prop-2-ynyl (3-pyridyl) ether (110) at 208°C in DMF which gave the furanopyridines (111) and (112). Changing the solvent to n-decane gave an additional product, the pyranopyridine (113) (Scheme 34). The same reactions took place using (2-methyl-3-pyridyl) prop-2-ynyl ether (114). In DMF, only (115), and in decane (116) as well as (115) were formed (Scheme 34).



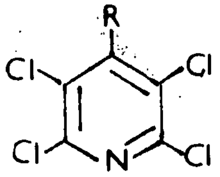
Scheme (34)

To extend the study an investigation into the thermolysis of the prop-2-enyl (3-pyridyl) ethers (117) and (119) was carried out. As expected they gave the different furano pyridines (118) and (120). The prop-2-ynyl (3-pyridyl) ether thermolyses also illustrated that blocking of C-2 results in a (3,3) sigmatropic rearrangement to the alternative adjacent carbon at position 4.



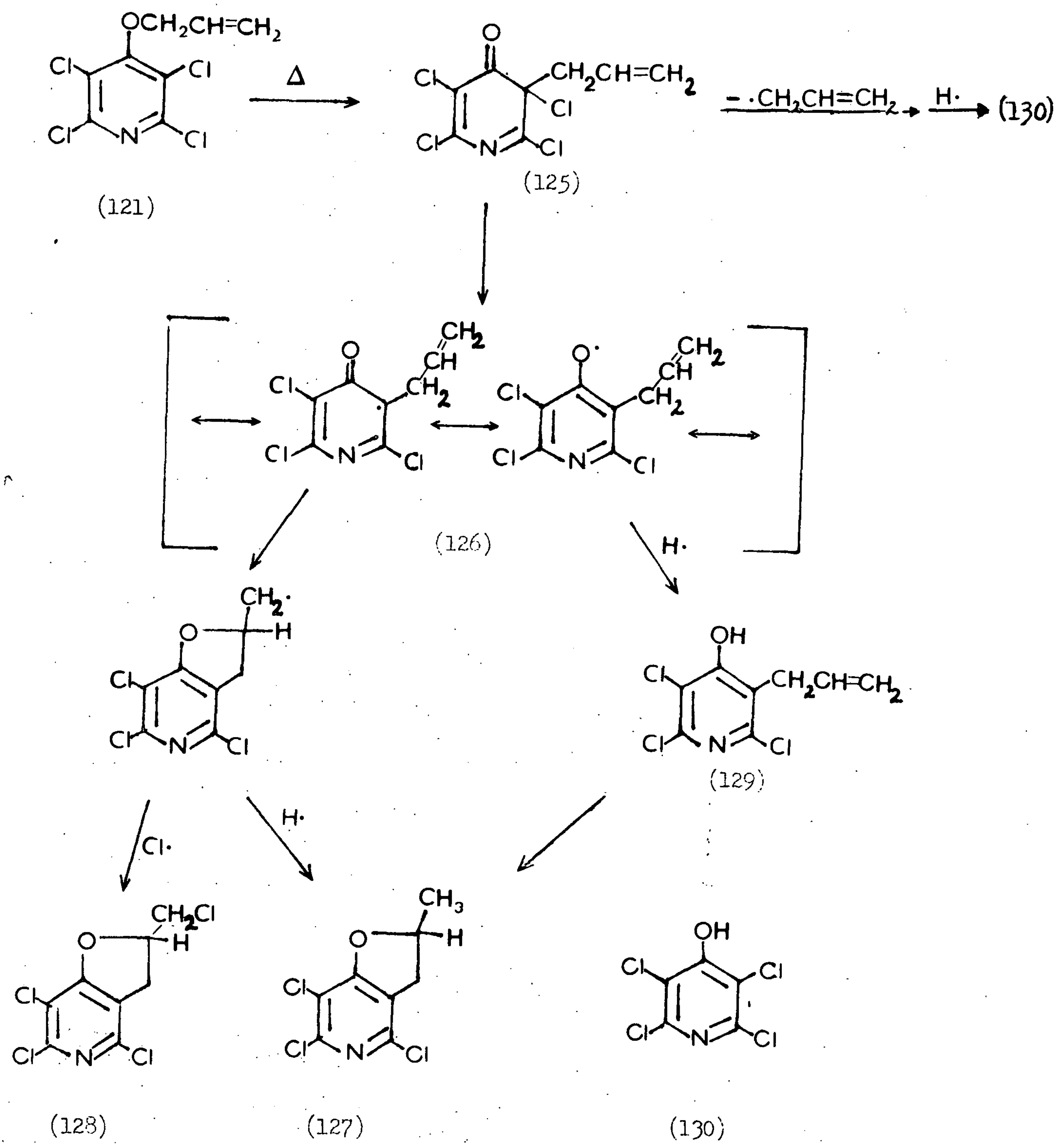
Scheme (35)

A thorough study into the thermal behaviour of some polychloropyridines was



(121) R - $OCH_2CH=CH_2$
(122) R = $OCH_2C\equiv CH$
(123) R = $SCH_2CH=CH_2$
(124) R = $SCH_2C\equiv CH$

reported by Iddon and co-workers[59]. The report confirmed the ability of the prop-2-enyl ether grouping to rearrange with displacement of the ortho-chlorine, which, from the product study, was shown to be either be lost or to migrate to another position. Heating the prop-2-enyl ether(121) at 190°C for 90min in sulpholan gave 10.5% 4,6,7-trichloro-2,3,-dihydro-2-methylfuro (3,2-c)pyridine (127) 6%, 4,6,7-trichloro-2-chloromethyl-2,3-dihydrofuro (3,2-c)pyridine (128) 26% 3-allyl-2,5,6-trichloro-4-hydroxypyridine (129) and 6% tetrachloro-4-hydroxypyridine (130). This was the first report of the formation of a chloromethyl derivative during Claisen rearrangements of allyl heteroaryl ethers. Iddon rationalised the formation of the products (Scheme 36) in terms of an initial Claisen rearrangement to the intermediate (125) followed by homolytic cleavage at the $Sp^3$ carbon to lose either a chlorine radical or an allyl radical. The cyclised products were thought to arise from the intermediate radical (126) followed by either hydrogen abstraction or chlorine atom combination. (Scheme 36).



Scheme (36)

The attempts to rearrange the corresponding prop-2-enyl (123) and prop-2-ynyl thioethers (124) thermally gave only intractable products. However, work by Brooke and Wallis on the thermal behaviour of polyfluoroaromatic prop-2-enyl and prop-2-ynyl systems proved much more successful and is reported in chapter 3.

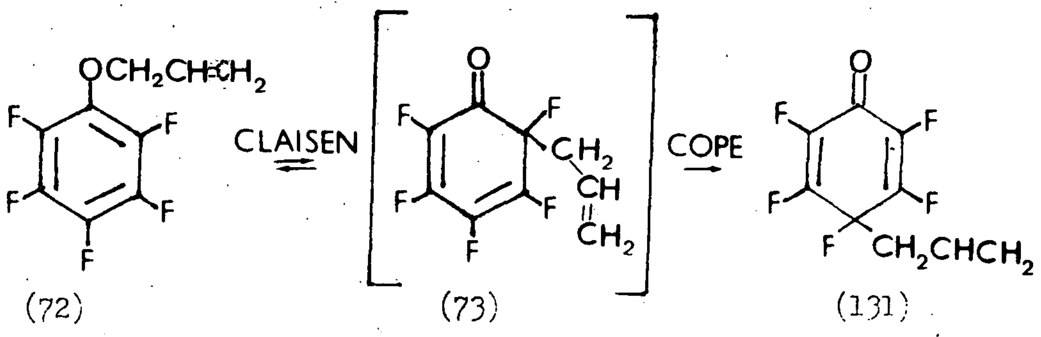
# Chapter 3: The Claisen Rearrangement and Reactions of Polyfluoroaromatic Prop-2-enyl and Prop-2-ynyl Systems.

## 3.1. Introduction.

This chapter surveys recent work carried out with polyfluoroaryl prop-2-enyl and prop-2-ynyl ethers and prop-2-enyl thioethers in which the ortho or para-positions do not bear hydrogen atoms.

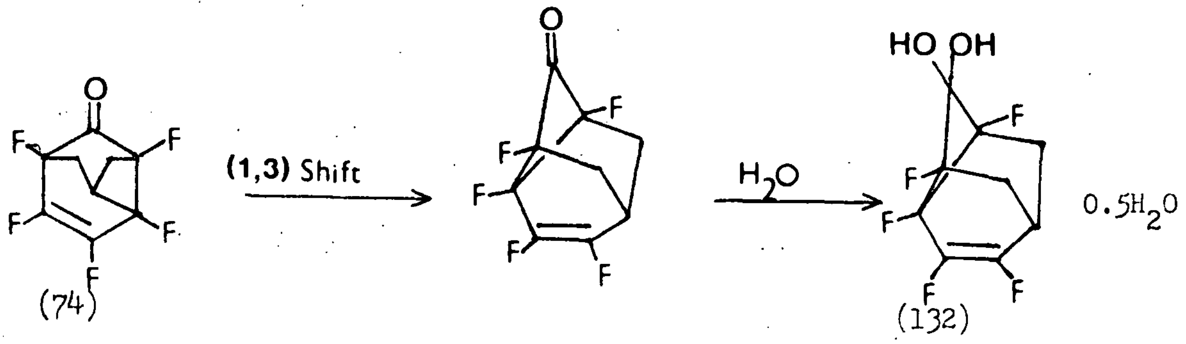
## 3.2. The Claisen Rearrangement and Reactions of Pentafluorophenyl Prop-2-enyl Ether (72).

An early investigation of pentafluoro-phenyl prop-2-enyl ether (72) showed that pyrolysis at 365°C[48] in the vapour phase gave as the major product, 32%, 4-allyl-2,3,4,5,6-pentafluoro-2-,5-cyclohexadienone (131) (Scheme 37). When the reaction termperature was raised to 480°,2,5β,6,7,7aβ pentafluoro -3a β,4,5,7a-tetrahydroinden-1-one (77) (33%) and 2,3,4-trifluorophenyl 1-fluorovinyl ketone (75) (40%) are formed as shown previously in Schemes (26) and (27) respectively.



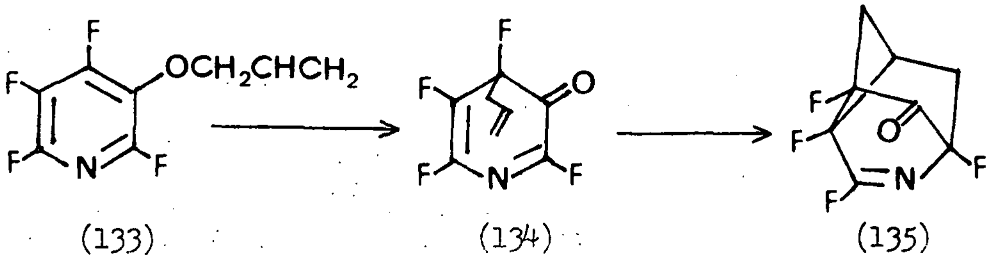
Scheme (37)

The prolonged heating of the ether (72) in the vapour at 137-141° gave another product; the hydrated compound (132) which was shown later to arise from a stepwise (1,3) rearrangement of the internal Diels-Alder adduct (74) (Scheme 38).[48b]



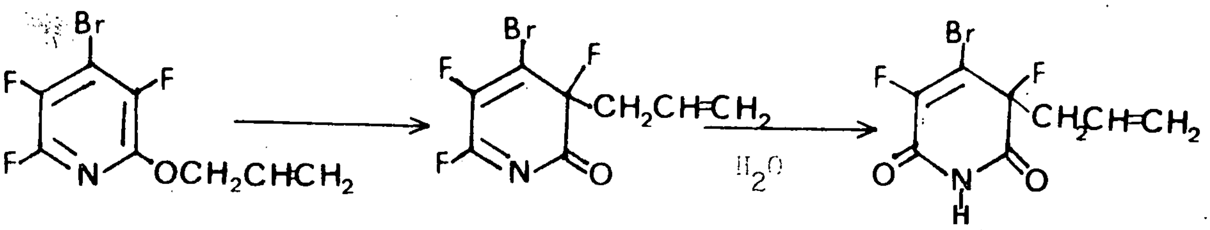
Scheme (38)

A similar series of pyrolyses on pentafluorophenyl 2-methyl-prop-2-enyl ether at 310°C and 410°C reflected the observations made with pentafluorophenyl prop-2-ynyl ether (72) and supported the formation and decomposition of Diels-Alder adducts following an initial Claisen rearrangement . Brooke[51] also investigated the thermal behaviour of polyfluoro-2-,-3-, and -4-pyridyl prop-2-enyl ethers which produced a variety of products, all derived from an initial (3,3) sigmatropic shift, This study showed the formation of intramolecular Diels-Alder adducts and derived products from the reactions of 2,3,5,6-tetrafluoro-4-pyridyl prop-2-enyl ether (78) ( Scheme 28) and of 2,4,5,6-tetrafluoro-3-pyridyl prop-2-enyl ether (133), Scheme (39). However,



Scheme (39)

with 4-bromo-2,3,5-trifluoro-6-pyridyl prop-2-enyl ether (136), the only product which was isolated was the cyclic imide (137) Scheme (40).

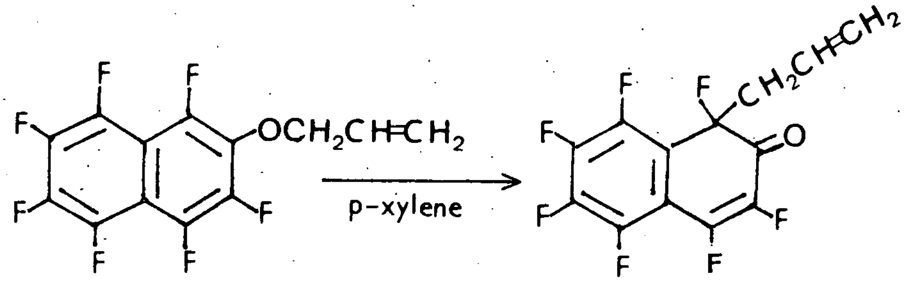


(136)

(137)

Scheme (40)

Interestingly, the polyfluoropyridyl systems showed no tendency to form the cyclisation products observed in the thermal rearrangements of the polychloropyridines (see Scheme (36) ) but showed a closer resemblance to the behaviour of the pentafluorophenyl ether (72). The formation of an ortho Claisen rearrangement intermediate was inferred from all the reactions with the polyfluoro compounds studied. However only one example of the isolation of such an intermediate has been discovered: the thermally induced reaction of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-enyl ether (138), gave the stable dienone (139)[60]. Scheme (41).



(138)

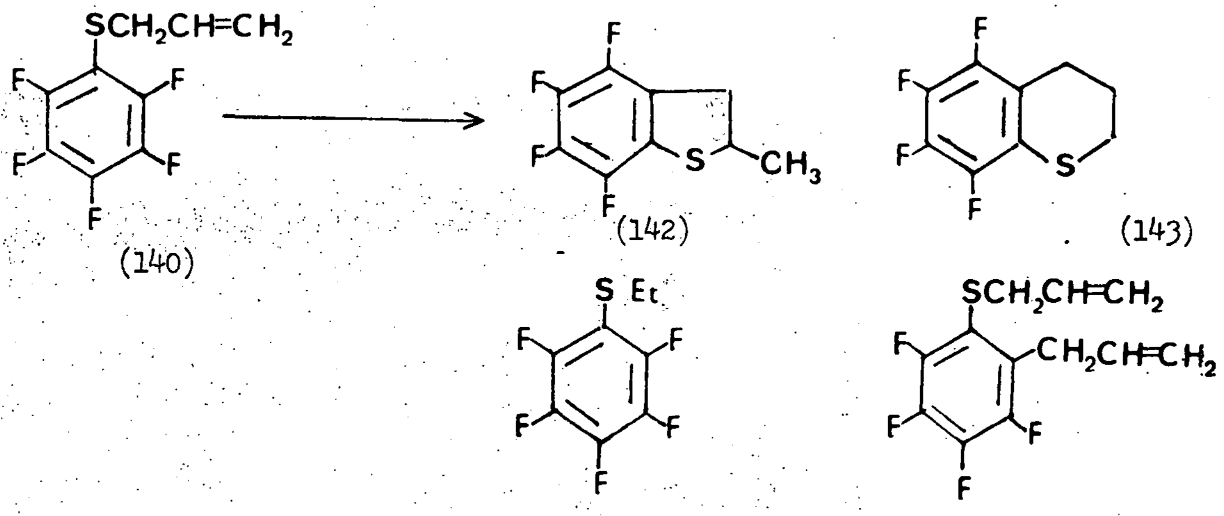
(139)

Scheme (41)

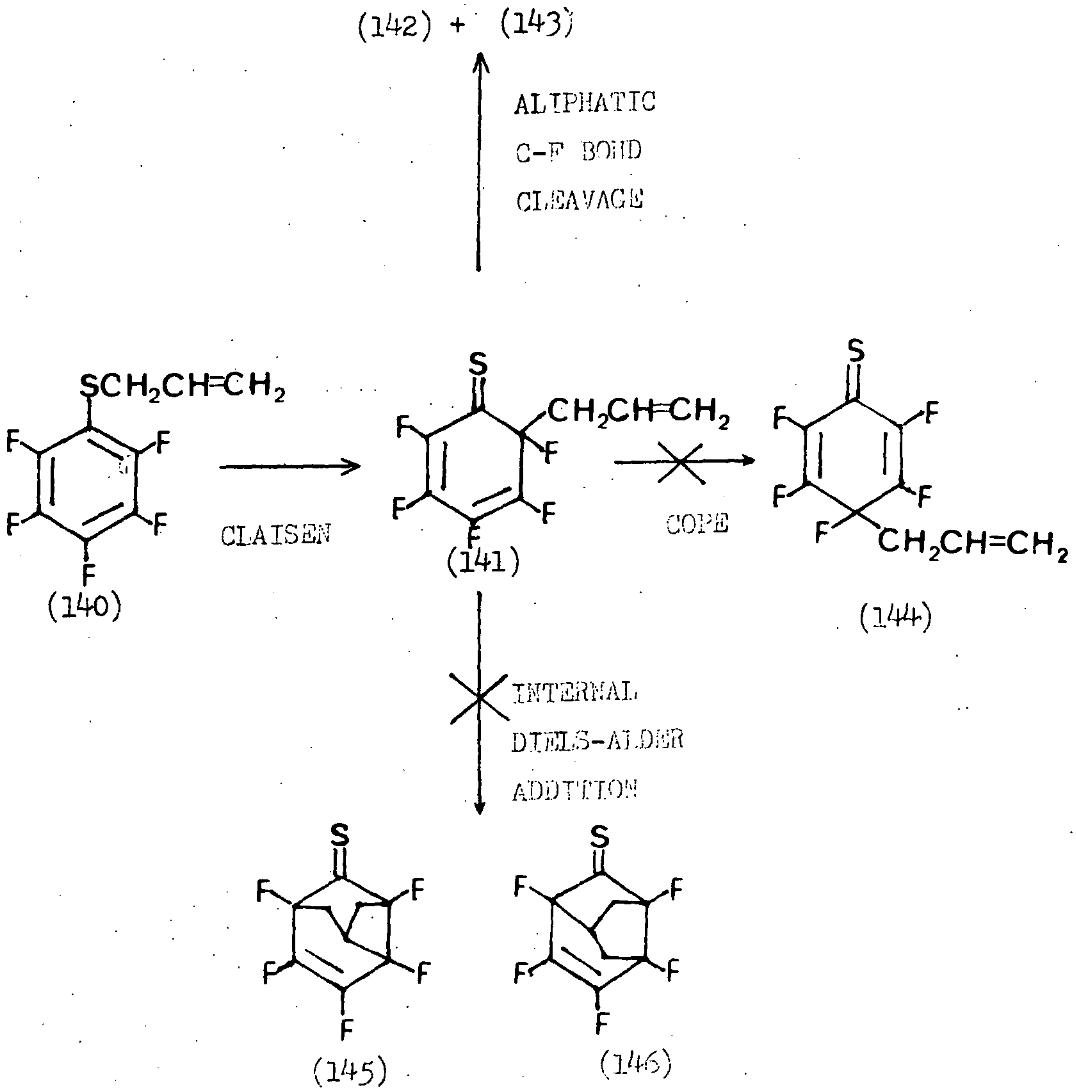
The first dienone ever to be isolated in an ortho Claisen rearrangement reaction had been reported previously by Green[61]; 1,1-di(prop-2-enyl)naphthalen-2-one was obtained from 1-prop-2-enyl-2-napthyl prop-2-enyl ether.

## 3.3. The Claisen Rearrangement and Reactions of Pentafluorophenyl Prop-2-enyl Thioether (140)

The investigation into the thermally induced reactions of pentafluorophenyl prop-2-enyl thioether[63,62] illustrated the outstanding influence of the heteroatom on the reactivity of the molecule. Thus while pentafluorophenyl prop-2-enyl ether (72), 2,3,4,6-tetrafluoro-4-pyridyl prop-2-enyl ether (78) and 2,4,5,6-tetrafluoro-3-pyridyl prop-2-enyl ether (133) gave a variety of products all derived from the corresponding 2,4-dienone intermediate, pentafluorophenyl prop-2-enyl thioether (140) was recovered unchanged under corresponding conditions[63,62]. However, as has been noted earlier (sec 1.4) N,N-diethylaniline was found to promote the initial rearrangement reaction. Thus, when the prop-2-enyl thioether (140) was heated under reflux in boiling N,N-diethylaniline for 23h a complex product was obtained which contained at least fourteen compounds. Four compounds were identified in this mixture: 4,5,6,7-tetrafluoro-2,3-dihydro-2-methyl-1-benzothiophen (142) (5%), 5,6,7,8-tetrafluorothiachroman (143) (2%), ethylpentafluorophenyl sulphide (6%) and prop-2-enyl 3,4,5,6-tetrafluoro-2-(prop-2-enyl) phenyl sulphide. The thermolysis of pentafluorophenyl prop-2-enyl thioether (140) did not yield derivatives of the internal Diels-Alder adducts (145) or (146) which had been the only products observed in the corresponding ether (72). (Scheme 42.).



Scheme (42)

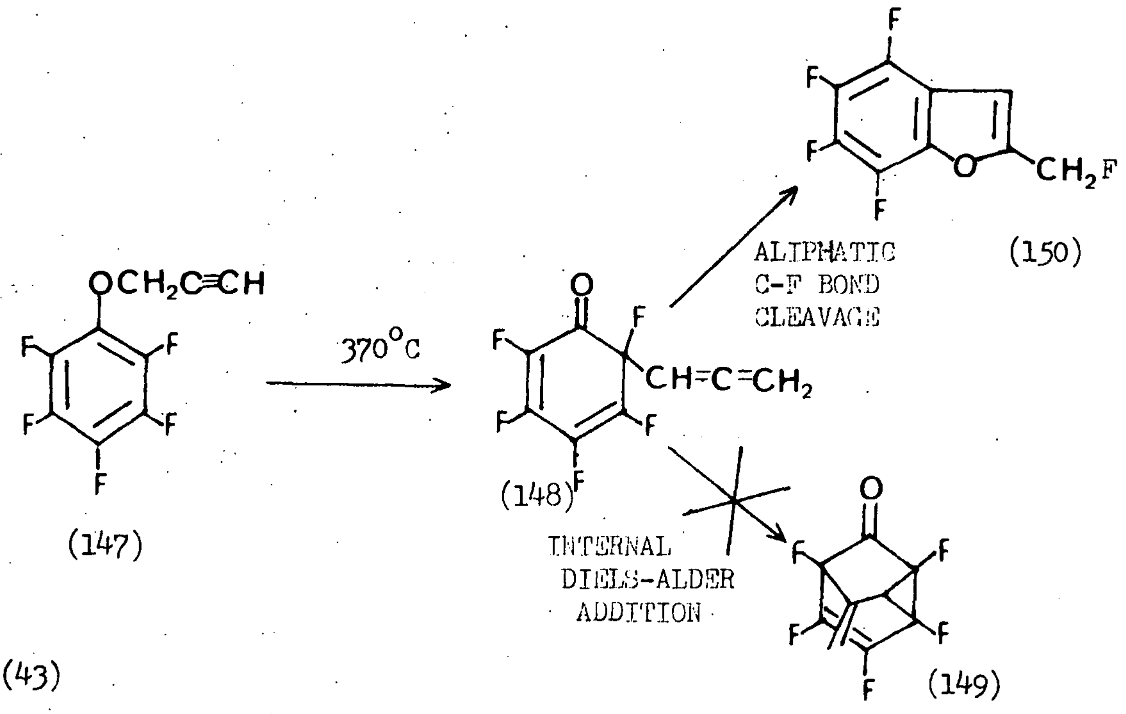

(142) + (143)
ALIPHATIC
C-F BOND
CLEAVAGE
SCH₂CH=CH₂
(140)
CLAISEN
CH₂CH=CH₂
(141)
COPE
CH₂CH=CH₂
(144)
INTERNAL
DIELS-ALDER
ADDITION
(145)
(146)
S
F

Scheme (42)

A homolytic cleavage of the $sp^3$C-F bond in the presumed ortho thio-Claisen rearrangement intermediate was originally proposed to account for the formation of all the identified products, though later it was realised that a heterolytic cleavage was also possible[63]

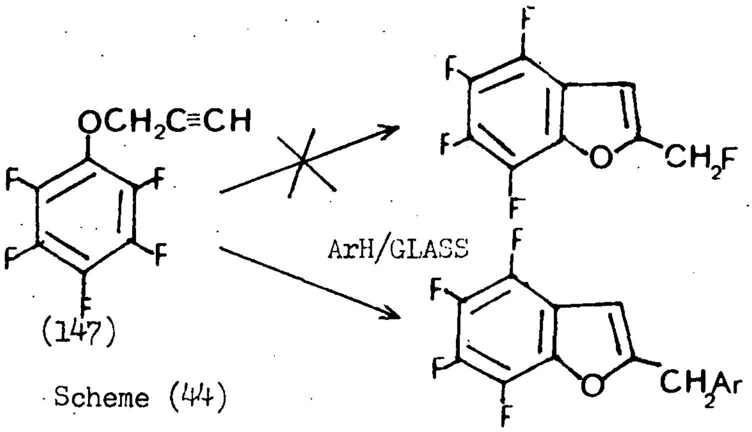
## 3.4. The Claisen Rearrangement and Reactions of Polyfluoroaromatic Prop-2-ynyl Ethers.

The formation of the tricylic derivative (19) from the thermolysis of 2,6-dimethylphenyl prop-2-ynyl ether (16) had been rationalised on the basis of an intramolecular Diels-Alder reaction of the Claisen rearrangement intermediate (17) (Scheme 8,p 5 ) and it was expected that an analogous product would be formed when the pentafluorophenyl containing starting material was used. However, the static phase thermolyses of pentafluorophenyl prop-2-ynyl ether were unsuccessful under the conditions used: a) 148°C for 17.5h and b) 138-140°C for 95h both gave unchanged starting material and a complex black residue respectively. However, flow pyrolysis at 370°C through a silica tube packed with quartz wool gave 8%,2-fluoromethyl-4,5,6,7-tetrafluorobenzo (b) furan (150) but no tricyclic ketone (149) (Scheme 43).



Scheme (43)

In an attempt to induce the isomerisation of the pentafluorophenyl prop-2-ynyl ether (147) to the benzofuran derivative (150) at lower temperatures, the ether (147) was heated in the presence of benzene in a sealed glass tube at 140°C for 116h. The reaction yielded 28%, 2-benzyl-4,5,6,7-tetrafluorobenzo (b) furan (151) and no 2-fluoromethyl-4,5,6,7-tetrafluorobenzo (b) furan (150). Repeating the thermolysis using p-xylene, again in glass apparatus, for 118h also gave the substitution product, 2-(2,5-dimethylbenzyl)-4,5,6,7-tetrafluorobenzo (b) furan (152) (21%) (Scheme 44).



(150)

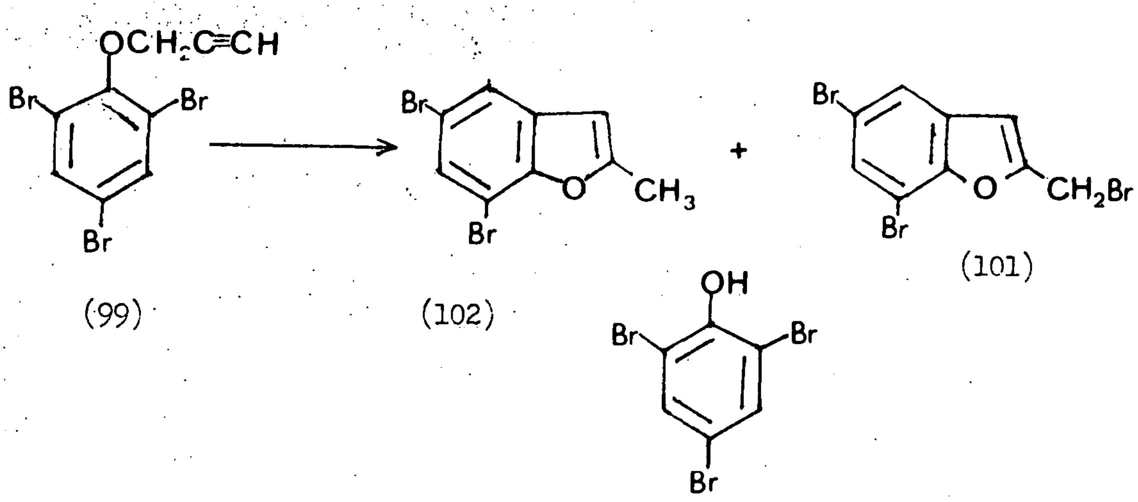
Ar = $C_6H_5$ (151)

Ar = $(CH_3)_2C_6H_3$ (152)

(147)

Scheme (44)

The first mechanism proposed to account for these products was based, by analogy upon the homolytic process previously put forward to explain the behaviour of 2,4,6-tribromophenyl prop-2-ynyl ether (99) in decane at 230°C[54], which had given 2-methyl-5,7-dibromobenzo(b) furan (102)(18%), 2-bromomethyl-5,7-dibromo benzo (b) furan (101) (1-2%) and 2,4,6-tribromophenol (153) (7%) (Scheme 45)



(99)

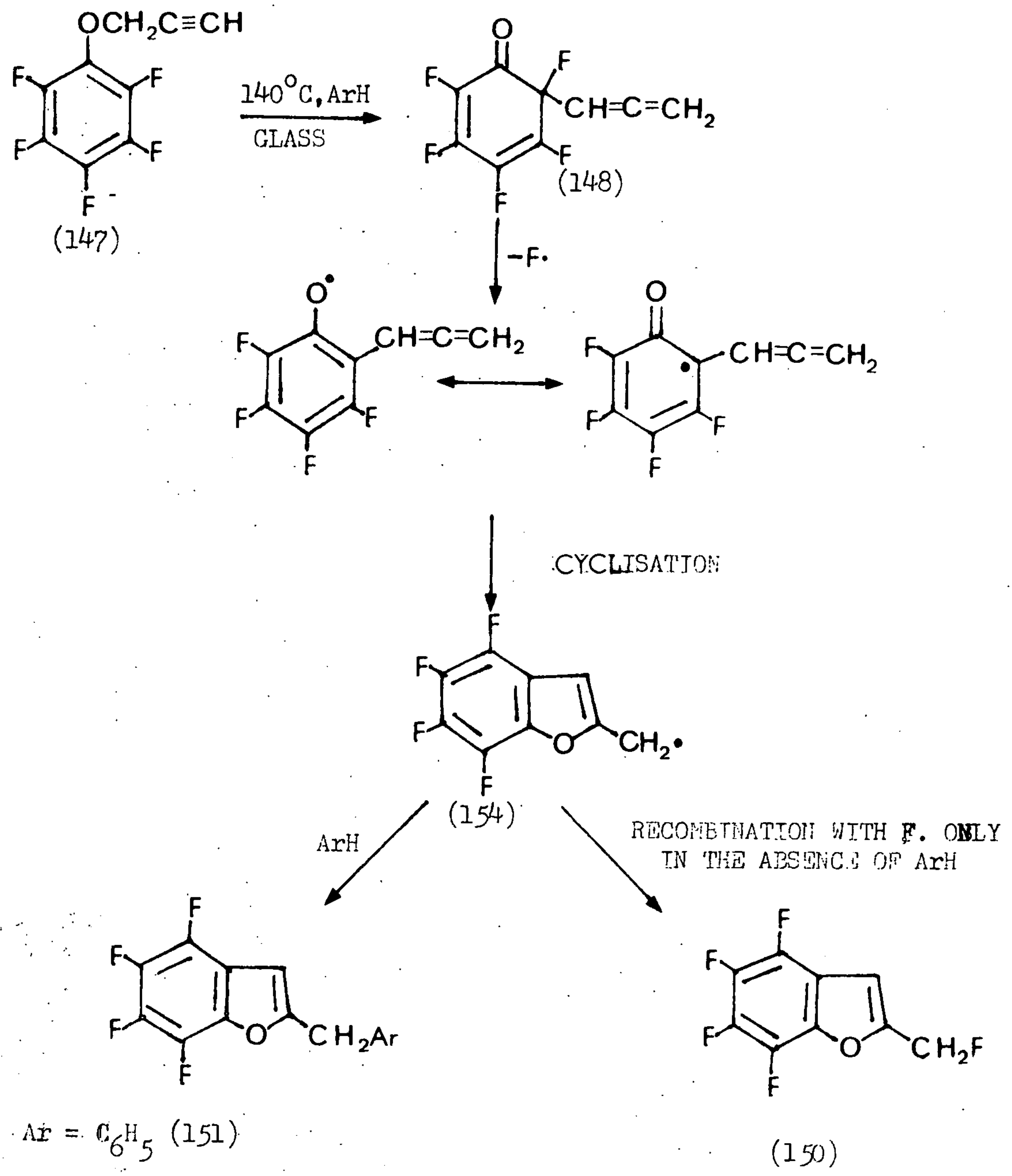
(102)

(101)

(153)

Scheme (45)

With the fluorine containing compounds, it was suggested that a homolytic cleavage of the $sp^3$C-F bond of the intermediate ortho-propa-1,2-dienone (148) is followed by cyclisation to give the heterocyclic radical (154), which it was maintained, would only recombine with a fluorine atom in the absence of a hydrocarbon solvent. In the presence of an aromatic solvent, the radical (154) brought about homolytic substitution of hydrogen. (Scheme 46).

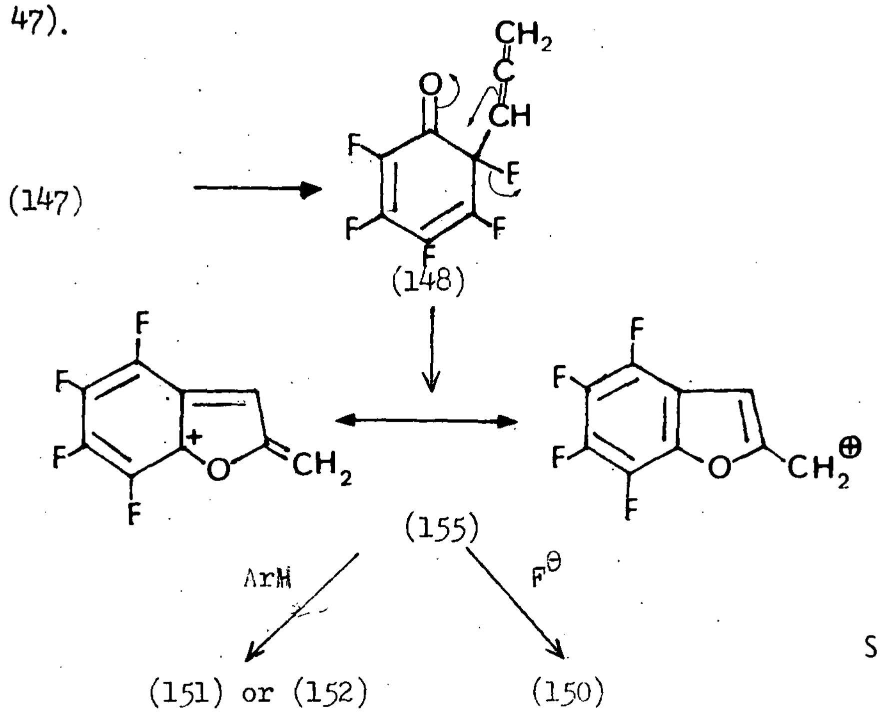


Ar = $C_6H_5$ (151)

Ar = $(CH_3)_2C_6H_3$ (152)

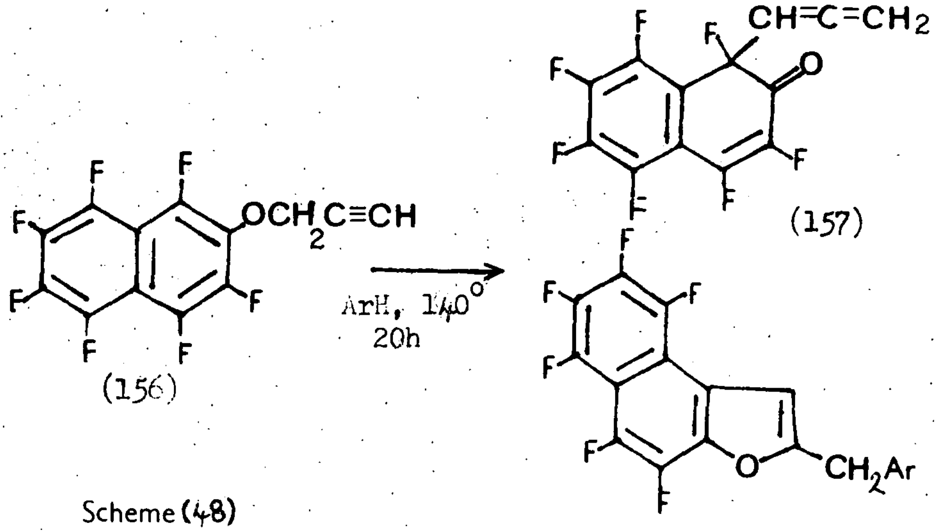
Scheme (46)

An alternative heterolytic process was later proposed by a referee to account for the formation of the products in the reactions already described. In this mechanism the aliphatic C-F bond of the Claisen intermediate (148) is cleaved heterolytically with concurrent cyclisation. The resulting carbo-cation (155), must maintain a close association with the departing fluoride ion in the vapour phase to recombine with it to give the 2- fluoromethyl compound (150), while in an aromatic solvent electrophilic substitution of hydrogen takes place, (Scheme 47).



Scheme (47)

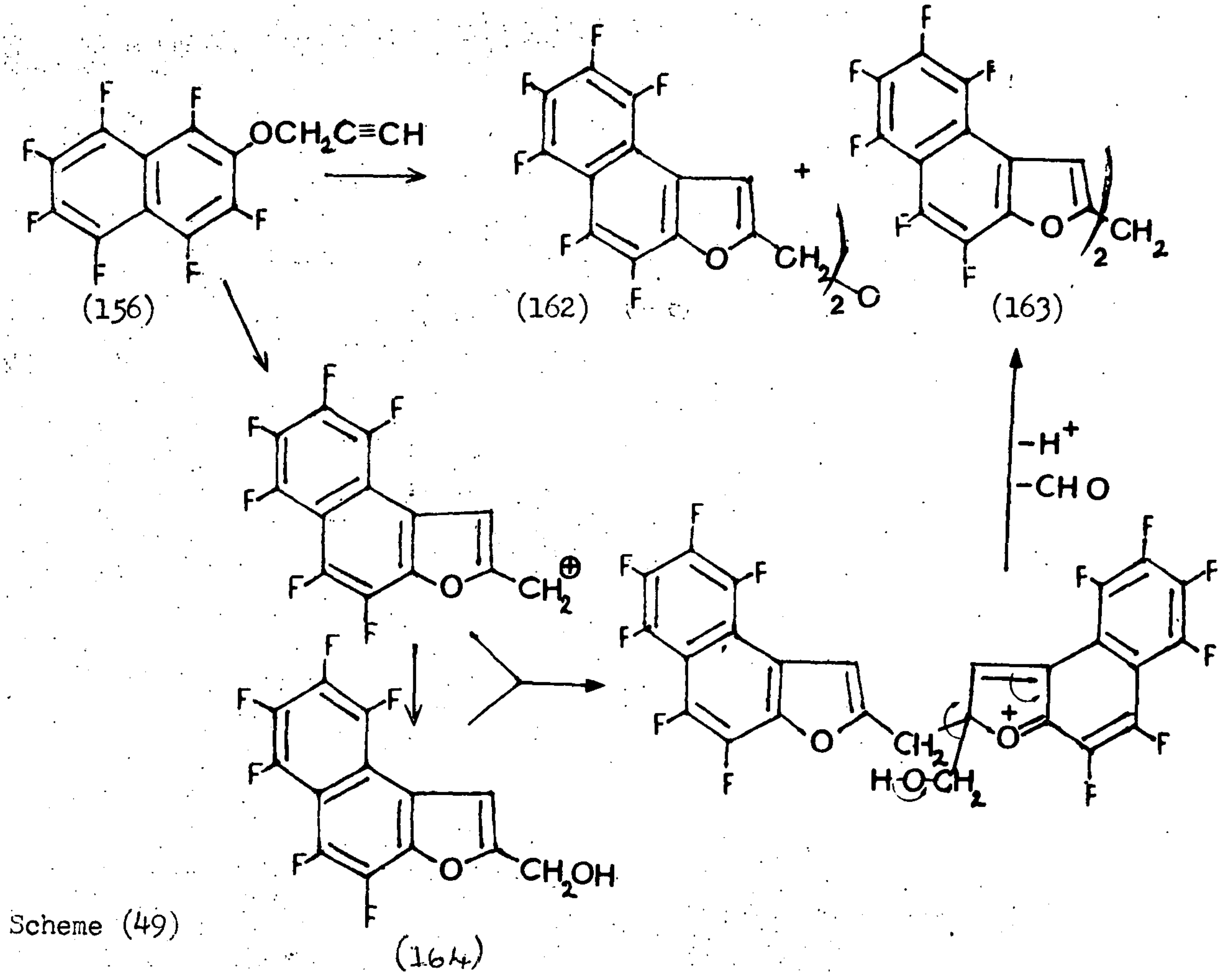
The cyclisation reactions of the prop-2-ynyl ether (147) were also investigated using 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156), as it was expected to react more efficiently. Suprisingly, the vapour phase thermolysis was never attempted even though the 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156) reacted in a manner analogous to the pentafluorophenyl compound (147) when thermolysed in benzene and p-xylene at 140°C in glass apparatus. When the heptafluoro-2-napthyl prop-2-ynyl ether (156) was reacted with boiling isopropylbenzene, in addition to the formation of 2-$\underline{CH_2}$Ar products, the Claisen intermediate 13,4,5,6,7,8-heptafluoro-1-(propa-1,2-dienyl)-naphthalen-2-one (157) was isolated in 10% yield. This observation warranted a re-examination of the reactions of the ether (156) with benzene and p-xylene at 140°C in glass apparatus. The naphthalenone (157), in addition to the substitution products described earlier, was detected in 26% yield in the reaction with benzene; surprisingly, however, (157) was not detected in the reaction with p-xylene. (Scheme 48).



Ar = $C_6H_5$ (158)
Ar = $(CH_3)_2\ C_6H_3$ (159)
Ar = $(C_6H_4)CHMe_2$ (160)

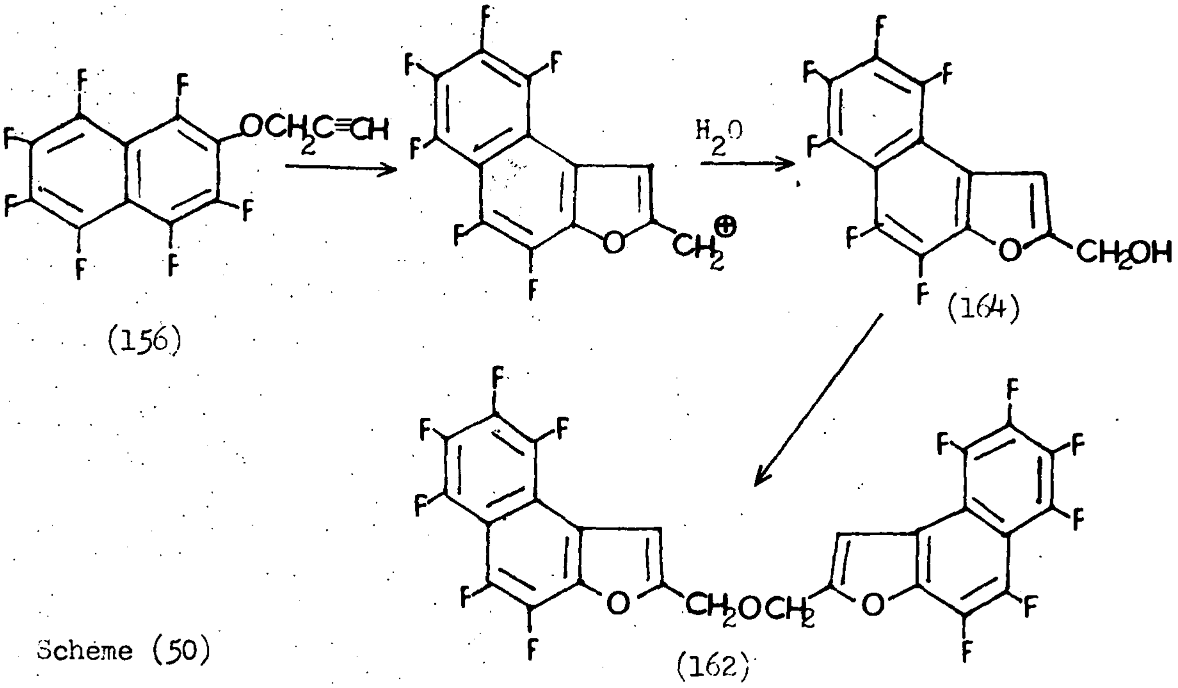
Scheme (48)

The thermolyses of (156) in aromatic solvents has failed to produce any observable isomerisation product (161). Consequently, the experiment was repeated in a non-hydrogen-containing solvent $CF_2ClCFCl_2$ in a glass Carius tube. Under strictly anhydrous conditions no 2-fluoromethyl compound (161) was obtained; the major products were the dimethyl ether derivative (162) (29%) and the bis-methane derivative (163) (Scheme 49).



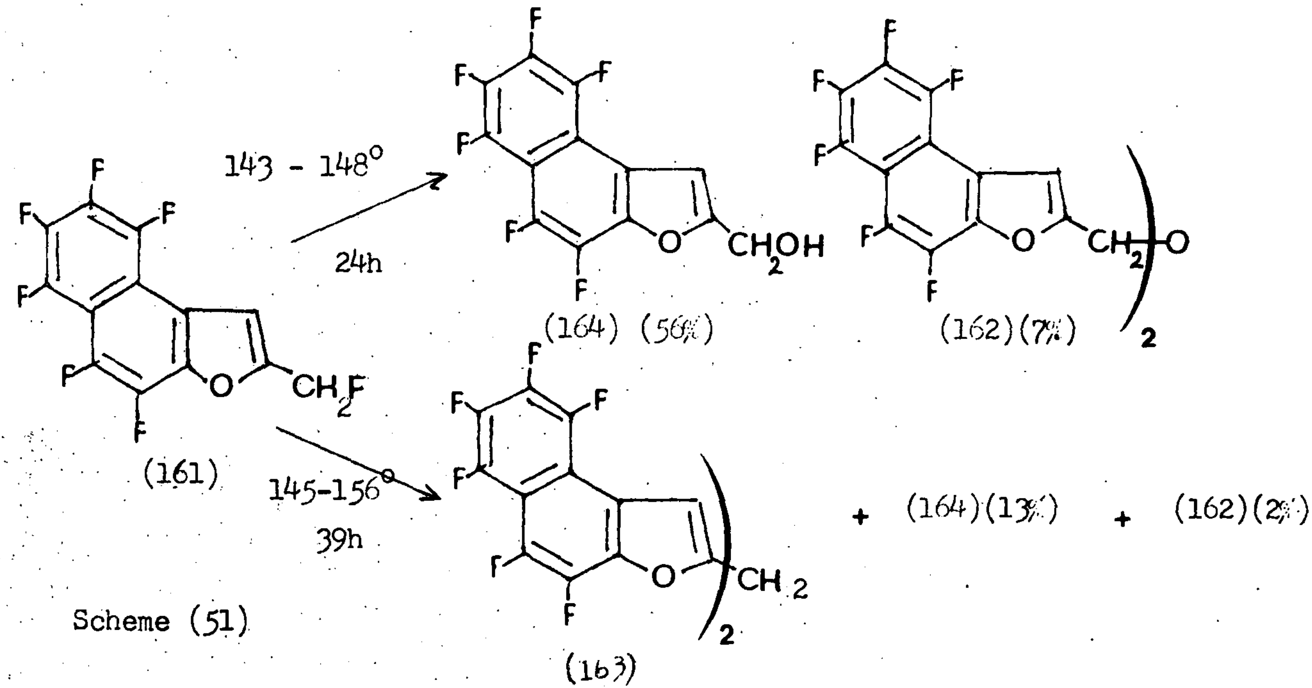
Scheme (49)

It was concluded that water was generated during the experiment due to the reaction of HF with the glass walls of the reaction vessel and this provided the oxygen in compound (162) (Scheme 50).



Scheme (50)

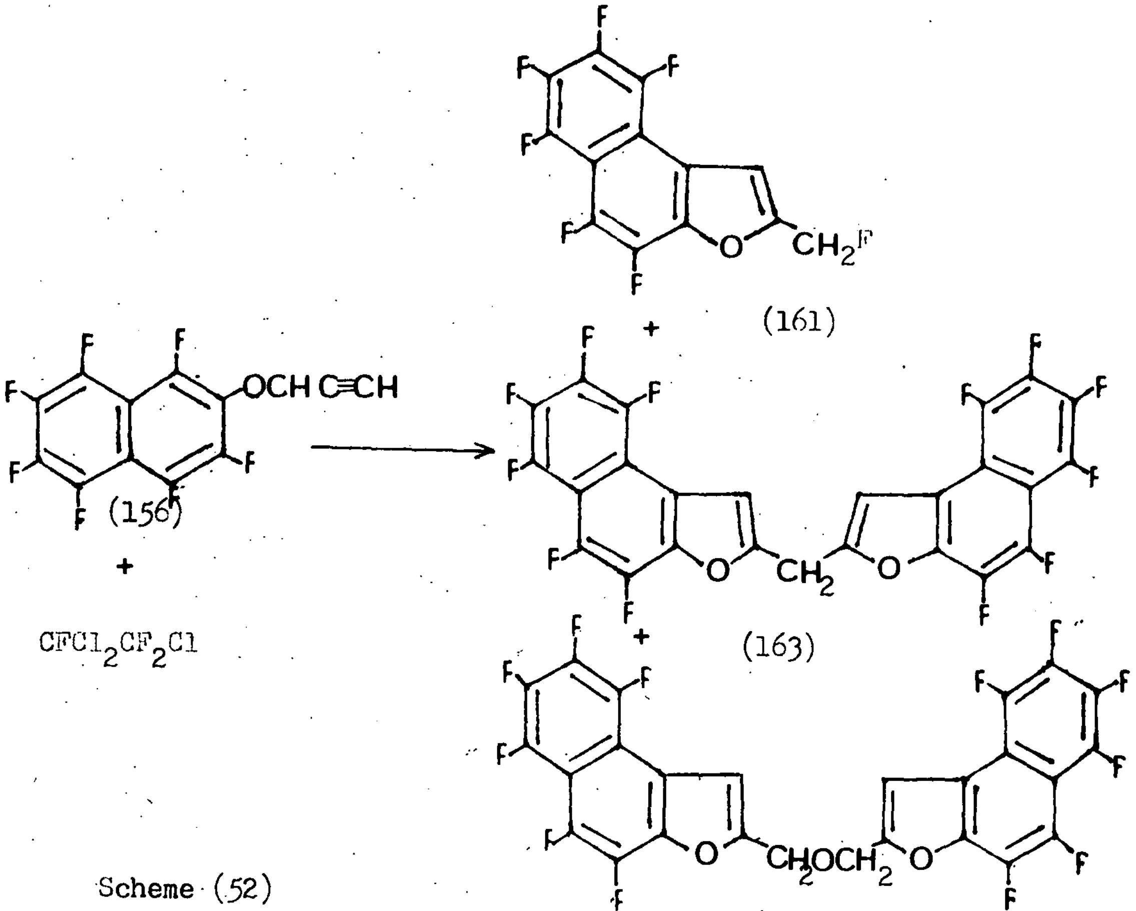
Experimental support for this proposal involving water was provided by performing hydrolysis reactions of the 2-fluoromethyl derivative (161) under various experimental conditions. (Scheme 51).



Scheme (51)

As will be seen later, the loss of fluoride ion at the surface of the glass can provide both HF and a carbocation capable of undergoing further reactions to give either the dimethyl ether (162) (via the furan-2-yl methyl alcohol) or the bis-methane derivative (163) by electrophilic substitution of formaldehyde with the furan-2-yl methyl alcohol.

In order to avoid any intervention of water, the naphthyl ether (156) was thermolysed in 1,1,2-trichloro-1,2,2,-trifluoroethane in a sealed nickel tube at 150°C for 18h. The products were 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) (42%), di-(4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan-2-yl methyl) ether (162) (6%) and bis-(4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan-2-yl) methane (163)(3%)[64]. (Scheme 52).



(156) (161) (163) (162)

Scheme (52)

Despite taking every precaution to exclude moisture from the system the bis ether (162) and bis methane derivative (163) were prominent in the reaction product.

The thermolysis of pentafluorophenyl prop-2-ynyl ether (147) was later repeated in $CF_2ClCFCl_2$ in a nickel tube at 150°C for 120h and gave the isomerisation product (150)(19%) and di-(4,5,6,7-tetrafluorobenzo (b) furan-2-yl methyl) ether (162)(20%); this compound resulted from not having strictly anhydrous conditions.

# Chapter 4: Synthesis and Reactions of Pentafluorophenyl Prop-2-ynyl Thioether

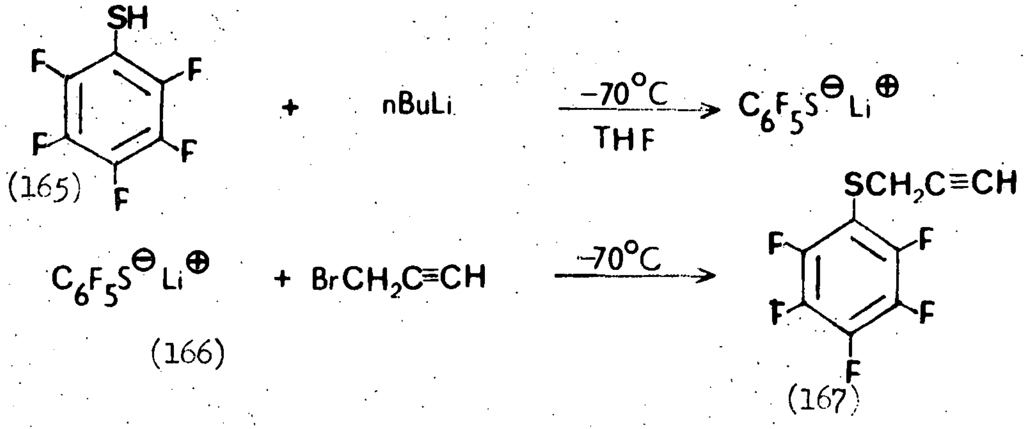
## 4.1. Introduction

The diversity in the Claisen rearrangement of ether and thioether derivatives involving pentafluorophenyl systems was highlighted in Chapter 3. Thus the prop-2-enyl ether (72) gave the internal Diels-Alder adduct (74) via the corresponding ortho-dienone (73)[48], whereas the pentafluorophenyl prop-2-enyl thioether (140) (in diethylaniline) gave the cyclisation product (142) via cleavage of the Sp$^3$ carbon-fluorine bond of the orthodiene thione (141). These observations indicated that the heteroatom was playing a significant role in determining the course of the reaction. Similarly, changing the prop-2-enyl ether to a prop-2-ynyl ether grouping once again rendered the corresponding Claisen intermediate (148), (Scheme 46), susceptable to a thermolytic cleavage of the aliphatic C-F bond, in preference to an internal Diels-Alder addition.

The work described in this chapter is the investigation of the combined effect of both a prop-2-ynyl linkage and a sulphur atom in the rearranging group by studying the thermal behaviour of pentafluorophenyl prop-2-ynyl thioether (167).

## 4.2. Synthesis of Pentafluorophenyl Prop-2-ynyl Thioether (167)

The prop-2-ynyl thioether (167) was prepared in 71% yield by reacting pentafluorothiophenol (165) with n-butyllithium in tetrahydrofuran at-70°C, followed by reaction of the lithium sulphide derivative with prop-2-ynyl bromide at the same temperature (Scheme 53).

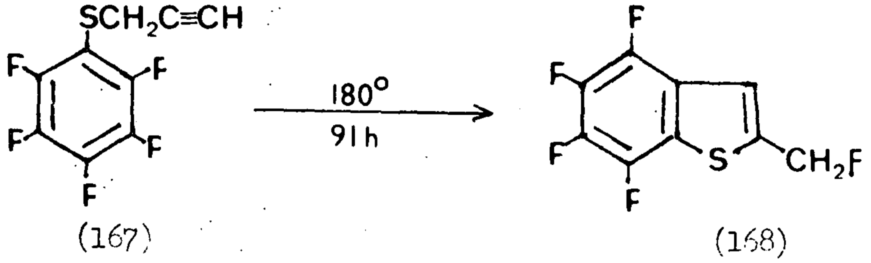


Scheme (53)

The low temperature was chosen so as to minimize the possiblity of polymerisation of the intermediate $C_6F_5S^\ominus$ species which may occur by successive nucleophilic substitutions of fluorine to give perfluoro (polyphenylene sulphide)[65] $(-C_6F_4S)_n$.

## 4.3. Thermolysis of Pentafluorophenyl Prop-2-ynyl Thioether (167) in 1,1,2-Trichloro-1,2,2-Trifluoroethane

The prop-2-ynyl thioether (167) was sealed in a nickel Carius tube with 1,1,2-trichloro-1,2,2-trifluoroethane and heated at 180°C for 91h to yield a dark brown tar. The crude product was initially analysed by $^{19}F$ n.m.r., which revealed a high field triplet characteristic of a fluoromethyl compound (There was no evidence to suggest the presence of a Diels-Alder adduct). Attempts were then made to optimize the degree of isomerisation by adjusting the temperature and reaction time. However, this resulted in either a smaller degree of conversion of the starting material (167) or a more complex product mixture, characteristic of the prop-2-enyl thioether[63]. Distillation and flash chromatography of the crude product gave unchanged starting material (6%) and the isomerisation product, 2-fluoromethyl -4,5,6,7-tetrafluorobenzo (b) thiophen (168) (13%) (Scheme 54).



Scheme (54)

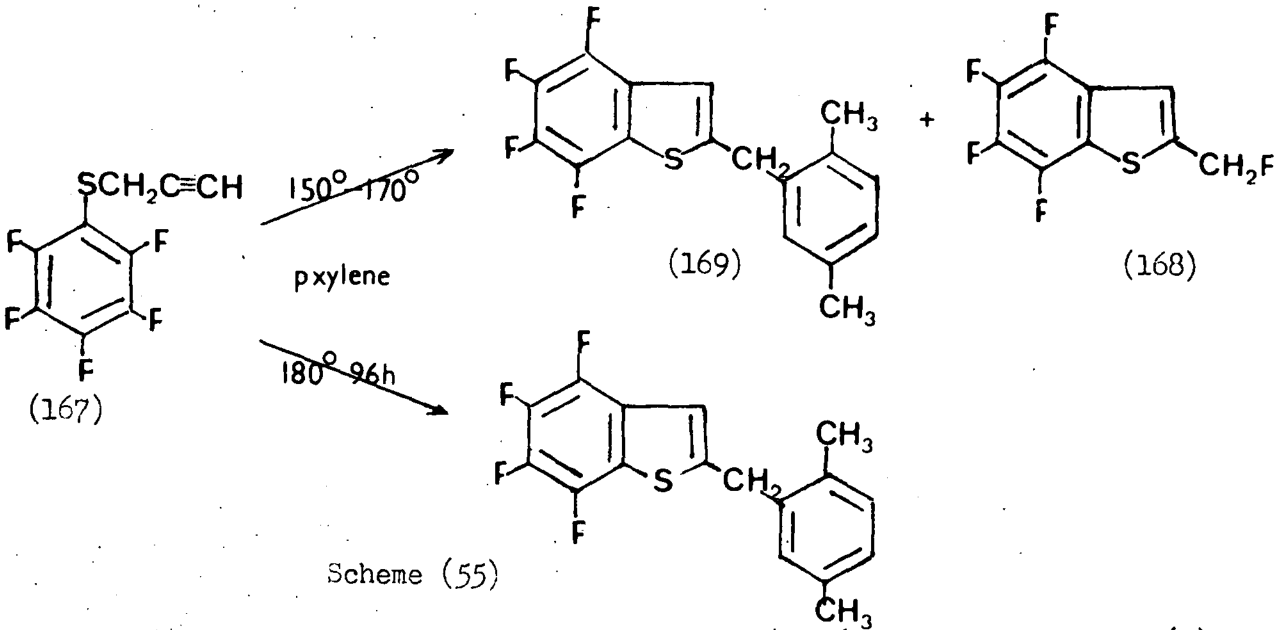
## 4.4. Reaction of Pentafluorophenyl Prop-2-ynyl Thioether (167) with p-Xylene and with Benzene.

The thermolysis of pentafluorophenyl prop-2-ynyl thioether (167) was investigated in two solvents - benzene and p-xylene, the intention being to assess whether the behaviour was analogous to the oxygen-containing compounds. However, unlike previous experiments using the prop-2-ynyl ether (147) in which glass apparatus was used, in this work nickel Carius tubes were used, primarily in an effort to prevent the intervention of any water in the reaction and also to be able to conduct the experiments at temperatures even higher than the boiling point of p-xylene.

Pentafluorophenyl prop-2-ynyl thioether (167) and benzene were sealed in a nickel Carius tube and heated at 180° for 96h. A black tar was formed which, on exhaustive distillation, gave a distillate containing a least six compounds (TLC) and no attempt was made to isolate 2-benzyl-4,5,6,7-tetrafluorobenzo (b) thiophen (170) from the mixtures although its presence could be inferred from TLC data (using material prepared by another method (See page 43 )).

The thermolysis of the thioether (167) in p-xylene proved more successful. Heating these components in a sealed nickel Carius tube at 180°C for 96 h produced a black oil, which on distillation in vacuo yielded 2-(2,5-dimethylbenzyl) -4,5,6,7-tetrafluorobenzo (b) thiophen (169) (7%).

A number of experiments were undertaken in order to optimize the yield of the 2-(2,5-dimethylbenzyl) derivative (169) using various experimental conditions. Under milder reaction conditions (150-170°C) the isomerisation compound, 2-fluoromethyl-4,5,6,7-tetrafluorobenzo (b) thiophen (168) was observed by $^{19}$F n.m.r. spectroscopy in the crude reaction products. In general the proportion of the fluoromethyl derivative (168) decreased on increasing the severity of the conditions. Indeed under the optimum conditions adopted to maximise the yield of 2-(2,5 dimethylbenzyl) derivative (169) the fluoromethyl compound (168) was not observed in the reaction product. (Scheme 55.)



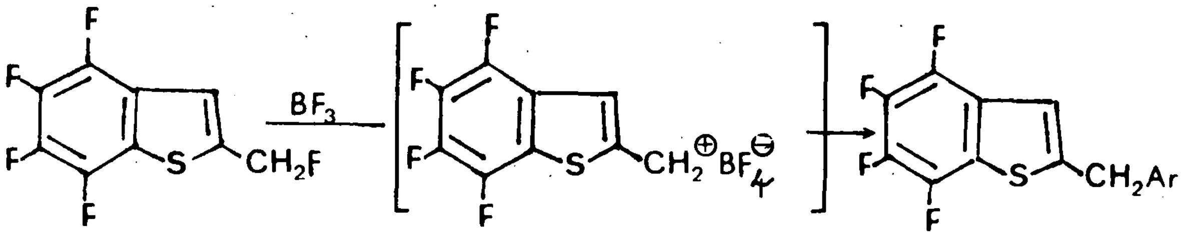
Scheme (55)

## 4.5. The FriedelCrafts Reaction of 2-Fluoromethyl-4,5,6,7-Tetrafluorobenzo (b) Thiophenol (168) with p-Xylene and with Benzene in the presence of Boron Trifluoride.

The fluoromethyl compound (168)was dissolved in ether and mixed with the aromatic solvent. The Lewis acid, boron trifluoride etherate, was then added and the homogeneous solution was stirred at 25°C for 150 mins. Successive reactions with p-xylene and benzene gave only one reaction product.

The reaction with p-xylene gave 2-(2,5-dimethylbenzyl-4,5,6,7-tetrafluorobenzo (b) thiophen (169)(94%) which confirmed that the carbocation had substituted into the aromatic species essentially quantitatively. The 2-benzyl derivative (170) had not been isolated in the reaction with benzene, owing to the complexity of the reaction product. However, reacting the fluoromethyl compound (168) with benzene in the presence of $BF_3$ gave 2-benzyl-4,5,6,7-tetrafluoro benzo (b) thiophen (170) in 93% yield.

Both of the Friedel-Crafts reactions involving the 2-fluoromethyl-4,5,6,7-tetrafluorobenzo (b) thiophen (168) demonstrated that once the carbocation (168a) was generated it would quantitatively substitute into the aromatic ring of the aromatic species present.



(168) (168a) Ar = $C_6H_5$ (170)

Scheme (56) Ar = $(CH_3)_2C_6H_3$ (169)

## 4.6. Summary

The reactions of the pentafluorophenyl prop-2-ynyl thioether (167) in both the 1,1,2-trichlorotrifluoroethane and aromatic solvent is less efficient than those observed with the pentafluorophenyl prop-2-ynyl ether (147). However, the isomersation product 2-fluoromethyl-4,5,6,7-tetrafluorobenzo(b) thiophen (168) was observed in an aromatic solvent by adopting milder reaction conditions in the thermolysis of the prop-2-ynyl thioether (167) in p-xylene.

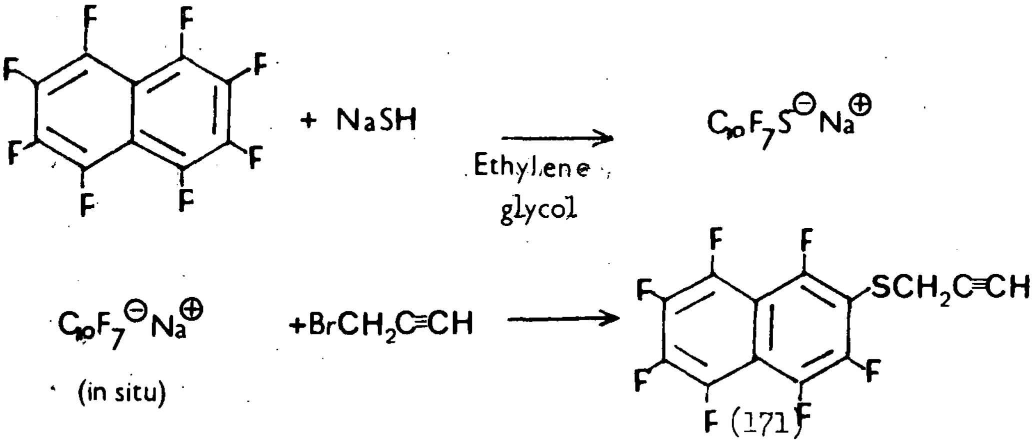
The Friedel Crafts reaction (sec 4.5) also demonstrated the viability of a heterolytic fission of the aliphatic C-F bond and subsequent electrophilic substitution into the aromatic species to give the substitution products (169) and (170), once the fluoromethyl compound is formed. Both observations were considered significant to the interpretation of the reaction pathway in the thermolysis of the thioether (167) in an aromatic solvent.

These observations and the apparent significance of the reaction environment adopted were investigated in greater detail using 1,3,4,5,6,7,8-heptafluoronaphthyl prop-2-ynyl thioether (171), which was expected to react more efficiently.

# Chapter 5: Synthesis and Reactions of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Thioether (171).

## 5.1. Synthesis

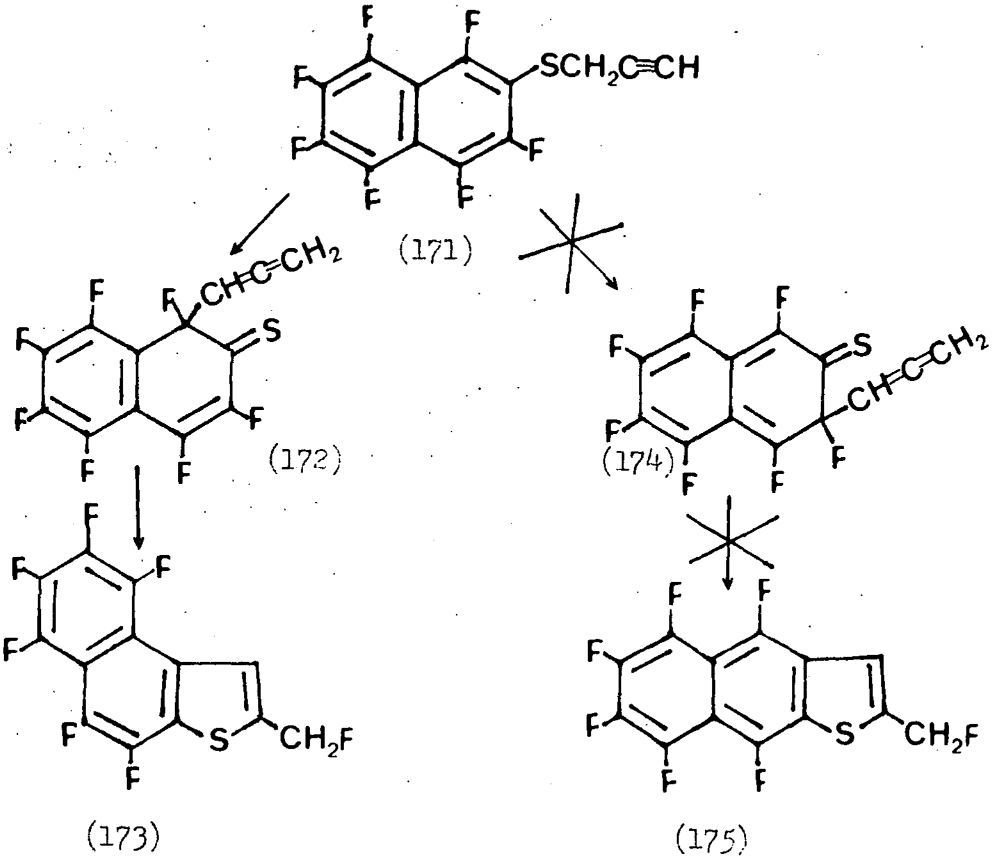
1,3,4,5,6,7,8-Heptafluoro-2-naphthyl prop-2-ynyl thioether (171) was synthesised by reacting octafluoronaphthalene with sodium hydrosulphide in N, N-dimethylformamide and ethylene glycol, followed by reaction with prop-2-ynyl bromide in situ. (G.M. Brooke personal communication) (Scheme 56a).



Scheme (56a)

## 5.2. Thermolysis of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Thioether (171) in 1,1,2-Trichloro-1,2,2-Trifluoroethane.

The prop-2-ynyl thioether (171) was thermolysed in anhydrous 1,1,2-trichloro -1,2,2-trifluoroethane at 160°C for 24h in a sealed nickel Carius tube. The 2-fluoromethyl derivative (173) was isolated from the reaction product in 41% yield: the $^{19}F$ n.m.r. spectrum of the cyclisation product identified its structure as the presence of one large peri $J_{F-F}$ coupling constant, (66 Hz), was consistent only with the structure (173) and showed that the initial 3,3-sigmatropic shift was to the C-1 atom and not the C-3 atom. Migration to C-3 would have given structure (175) which would have had two large peri $J_{F-F}$ coupling constants.



Scheme (56b)

The significant factor in maximizing the yield of the fluoromethyl derivative (173) appeared to be the precautions taken to exclude moisture from the system Noticeably, when no effort was made to prevent water from the atomosphere being contained in the reaction vessel the yield of the fluoromethyl compound (173) was consistantly reduced to between 24 and 30%. An attempt was made to identify the Claisen rearranged intermediate (172) from (171) in reactions carried out under milder conditions. However, thermolysis of the thioether (171) in $CF_2ClCFCl_2$ in a nickel tube at 125°C for 21h yielded only unreacted thioether (171) and the expected fluoromethyl compound (173). No trace of the thione (172) was ever observed in any of the experiments in this study.

## 5.3. The Vapour Phase Isomerisation of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Thioether (171).

### a ) Static Phase Thermolysis

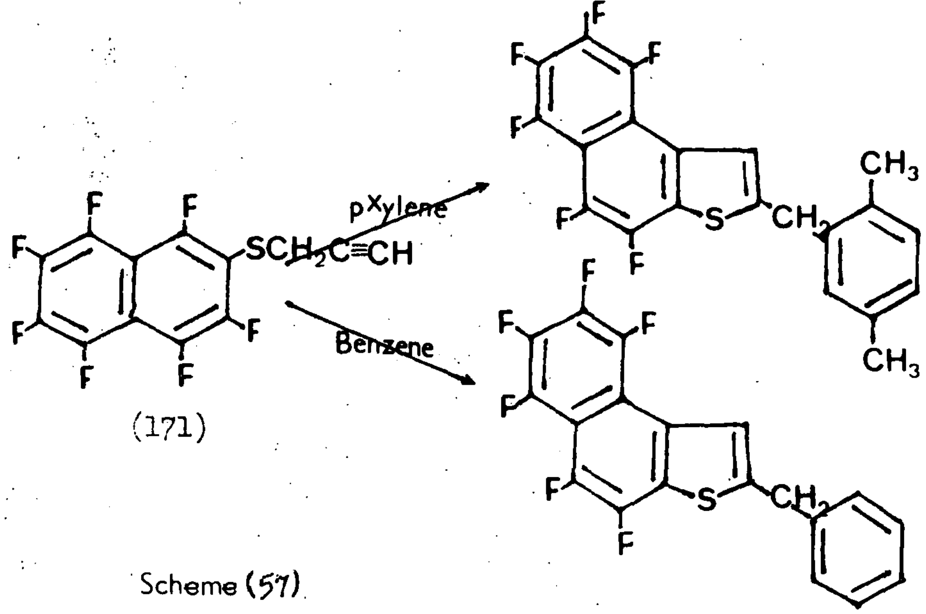
As an initial investigation into the isomerisation in the vapour phase, the thioether (171) was sealed in a 1 litre glass bulb in vacuo and heated under various conditions. The reaction products, observed by $^{19}$F n.m.r. spectroscopy, showed only unreacted starting material or, under more severe conditions (p.82), black tars containing no fluoromethyl derivative (173) or the Claisen rearranged intermediate (172). Because of the unpromising nature of this approach the static phase thermolyses were abandoned and a flow pyrolysis system was examined.

### b ) Vapour Phase Pyrolysis

The thioether (171) was distilled through a quartz tube packed with silica fibre maintained at temperatures ranging from 330 to 390°C / 0.005 mmHg. On each occasion the pyrolysis gave one major compound, identified as the isomerisation product 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (173). Under optimum conditions (360°C) the 2-fluoromethyl derivative (173) was formed in 81% yield.

## 5.4: Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Thioether (171) with P-Xylene and Benzene.

The thioether (171) was sealed with the aromatic solvent in a nickel Carius tube and heated at 160°C. The reaction in the benzene solvent produced a dark brown oil containing at least six compounds (TLC). The presence of the 2-fluoromethyl derivative (173) was inferred by the characteristic high field triplet ($CH_2F$) in the $^{19}$F n.m.r. spectrum of the crude reaction product. However, in optimising the yield of the benzyl derivative (176) (16%), by extending the reaction time to 25hs, no 2-fluoromethyl-4,5,6,7,8,9-hexafluoro naphtho (2,1-b) thiophen (173) could be detected in the crude reaction product. The thermolysis of the thioether (171) in p-xylene in a sealed nickel Carius tube at 160°C for 24h proved to be more efficient, yielding a single major compound which was identified as the substitution product, 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (177) (51%) (Scheme 57).



(171) (177) (176)

Scheme (57)

### 5.5. A Semi-Kinetic Study of the Reaction between 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Thioether (171) and p-Xylene at 160°C in a Nickel Tube.

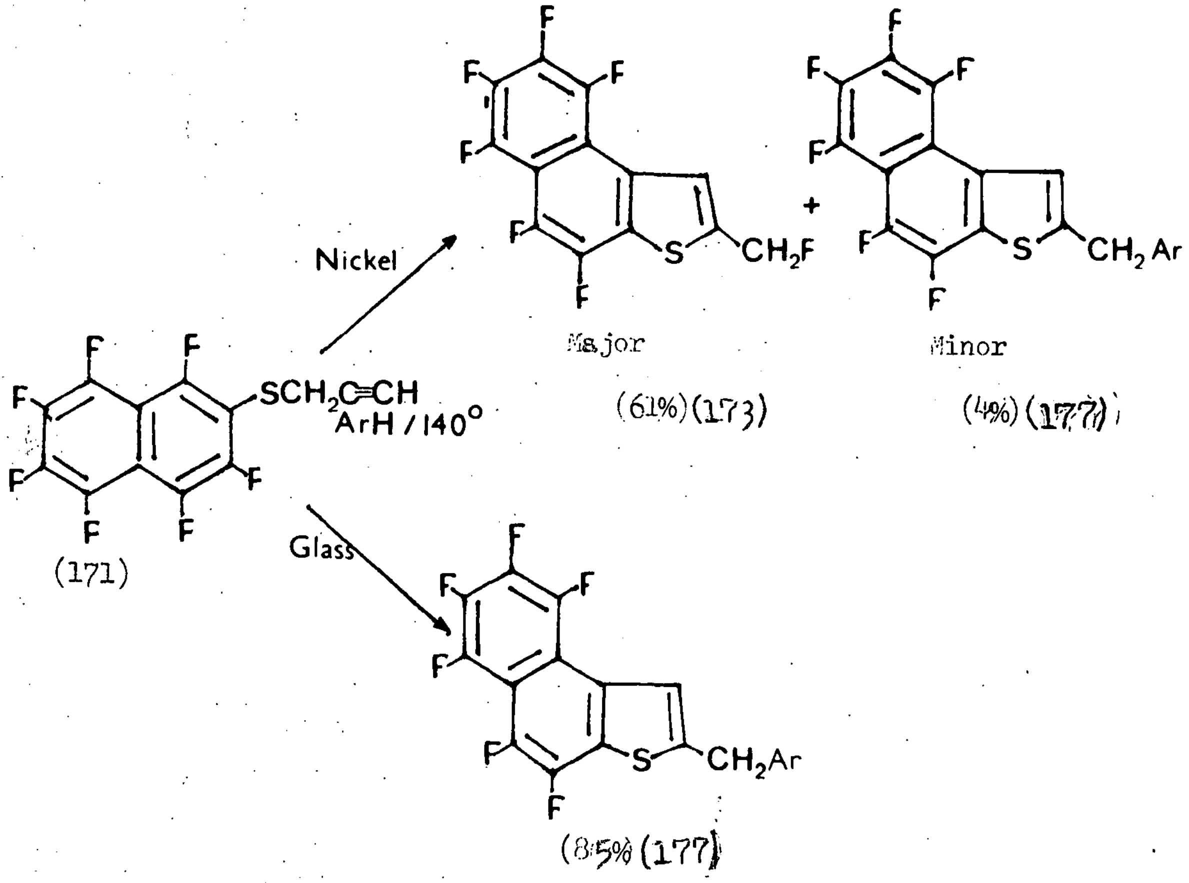
If the fluoromethyl compound (173) was an intermediate in the reaction between the thioether (171) and aromatic solvent then the ratio (2-fluoromethyl compound)/(substitution product) as a function of time would decrease. A product study was conducted on incomplete reactions, in an effort to record this ratio and identify any significant trend. The reactants, 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (171) and p-xylene, were sealed in a nickel Carius tube and heated at 160° in separate experiments over 6, 12, 18 and 24h. The reaction products were analysed using $^{19}F$ n.m.r. spectroscopy and the results are tabulated below. (Table 1.)

| TIME (hs) | (173) | (177) |
|---|---|---|
| 6 | 75 (64%)* | 25 (21%)* |
| 12 | 61 | 39 |
| 18 | 47 | 53 |
| 24 | 0 | 100 (50%)* |

*are actual yields.

The results clearly demonstrate a decrease in the fluoromethyl compound (173) as a function of time, with a concurrent build up of the substitution product (177).

In the original work, using 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156), on refluxing in glass apparatus at 140°C with p-xylene for 20h,[64] only only one identifiable product, namely the substitution compound 2-(2,5-dimethylbenzyl)derivative(159), was obtained. The absence of any 2-fluoromethyl compound (161) seems very unusual in view of the observations made using a sealed nickel tube with the corresponding thioether (171). The thioether (171) was therefore thermolysed using identical experimental conditions (140°C, 24h) in nickel and glass environments. The reaction product from the nickel tube contained 61% 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (173) and 4% 2-(2,5 dimethyl benzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (177), whereas in glass there was only unreacted starting material (171) (15%) and the 2-(2,5-dimethylbenzyl) compound (177) (85%) but <u>no</u> 2-fluoromethyl compound (173), Scheme (58). Two conclusions can be drawn from these experiments: (i) the ability of the thioether (171) to be isomerised to the 2-fluoromethyl compound (173) at relatively low temperatures even in an aromatic solvent, provided nickel apparatus is used, and (ii) the profound effect which the nature of the reaction vessel-nickel or glass-has on the course of the reaction.

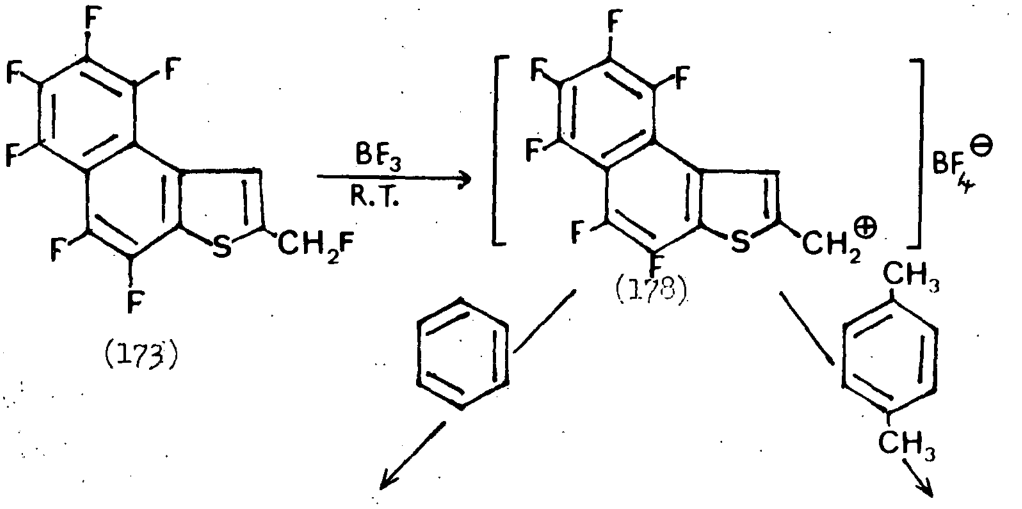


Scheme (58)

The results suggest that the glass has a destabilizing effect on the C-F bond either in the Claisen rearrangement intermediate (172) or in the fluoromethyl compound (173), which promotes substitution into the aromatic ring of the solvent. From these observations it is possible to speculate that the failure to observe the isomerisation reaction of the oxygen compound 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156) to the 2-fluoromethyl compound (161) in an aromatic solvent was because the experiment had been performed in glass apparatus.

## 5.6. The Friedel-Crafts Reaction of 2-Fluoromethyl-4,5,6,7,8,9-Hexafluoro Naphtho (2,1-b) Thiophen (173) with p-Xylene and with Benzene in the presence of boron trifluoride.

The fluoromethyl compound (173) was dissolved in the aromatic solvent (p-xylene, benzene) mixed with boron-trifluoride etherate and stirred at room temperature for 15 mins. The reactions with benzene and p-xylene proceeded quantitatively to give the corresponding substitution derivatives (176) and (177) (Scheme 59).



(176) Scheme (59) (177)

To complete the mechanistic study of the thermal prop-2-ynyl rearrangement, a series of experiments using 1,3,4,5,6,7,8-heptafluoro naphthyl prop-2-ynyl ether (156) were conducted and are reported in the following chapter.

# Chapter 6: Reactions and Thermolyses of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Ether (156)

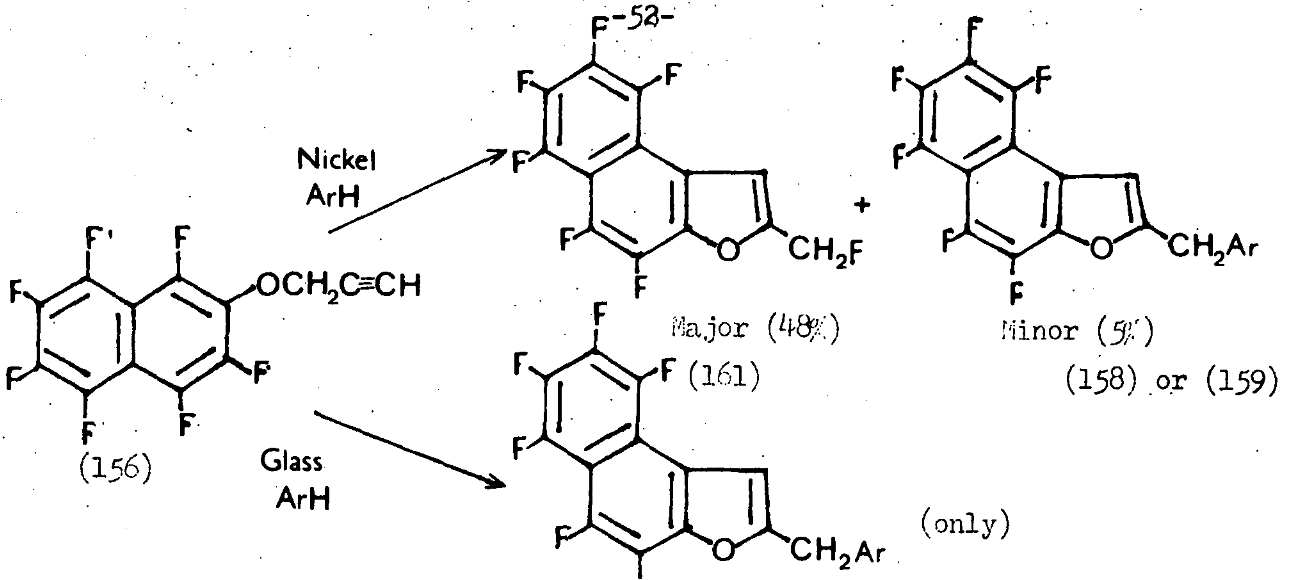
## 6.1. Introduction

Previous work on the thermolyses of the naphthyl prop-2-ynyl ether (156) using various aromatic solvents[66], in glass apparatus, had been shown to give the aromatic substitution derivatives as the only reaction product. However, in Chapter (5) the thioether (171) was shown in corresponding reactions to give the aromatic substitution product in glass, and the isomeric 2-fluoromethyl-4,5,6,7,8,9-hexafluoro naphtho (2,1-b) thiophen (173) when the experiment was conducted in a nickel Carius tube.

In this Chapter, the course of the reactions of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-enyl ether (156) in aromatic solvents in nickel apparatus is examined.

## 6.2. Comparison of The Reaction of the Ether (156) with p-Xylene, in Nickel and in Glass Apparatus at 140°C.

The reaction of the ether (156) in refluxing p-xylene (140°C)in glass apparatus gave the substitution derivative (159) (62%) and no isomerisation product (161). However, when the same reaction was conducted under identical conditions in a sealed nickel tube the reaction yielded 48% 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) and only 5% of the 2-(2,5-dimethylbenzyl) derivative (159) (Scheme 60). These observations are in total agreement with previous observations made using glass apparatus and also show that the oxygen compound behaves in a manner similar to the sulphur compound (171) giving products which depend on whether the reactions are performed in glass or in nickel apparatus.



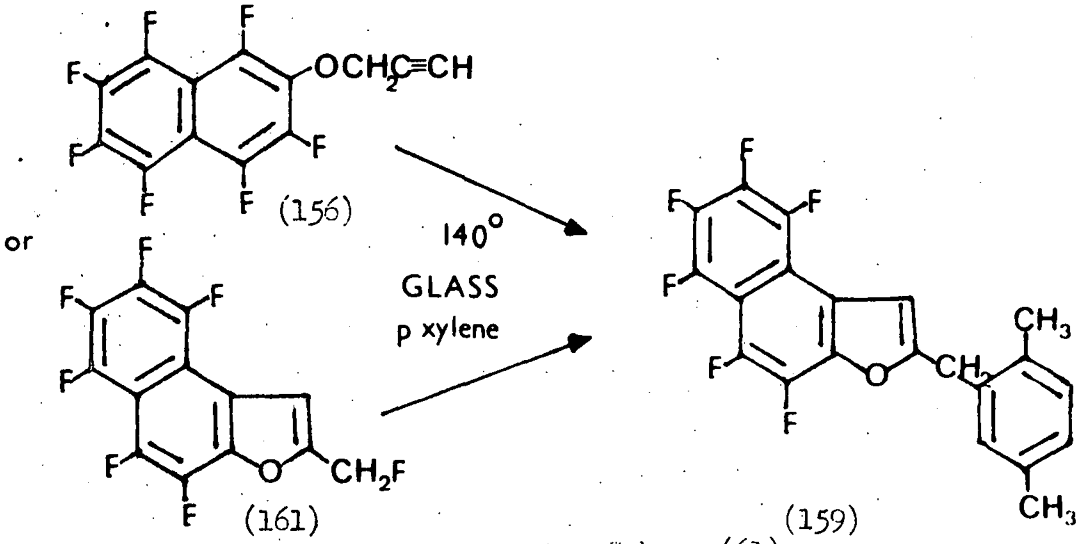
Scheme (60)

## 6.3. A Comparison between the Reactions of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (156) and of 2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) with p-Xylene in Glass Apparatus.

The thermolysis of the ether (156) in p-xylene under reflux at 140°C for 20h in glass apparatus has been shown in the current work (sec 6.2) to give 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (159) in 62% yield; no 2-fluoromethyl compound (161) was present in the crude reaction product.

In Chapter 5, section 5.6., it was suggested that the glass of the reaction vessel has a profound influence on the course of the thermolysis reaction of the thioether (171) in aromatic solvents, and in the previous section (6.2.) it is clear that the oxygen-containing compound (156) is influenced in a similar manner. It was of interest to discover whether or not the 2-fluoromethyl compound (161) was stable when heated with aromatic solvents in glass apparatus. This experiment had been tried previously[64] and had been shown to give 75% of the 2-(2,5-dimethylbenzyl) substitution product (159) but some unchanged 2-fluoromethyl compound (161) (17%) remained in the product.

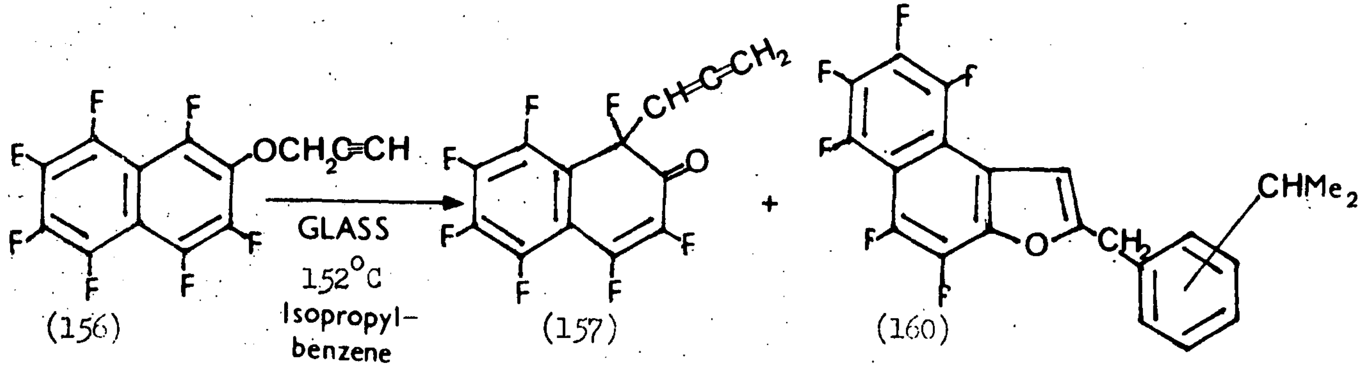
The fluoromethyl derivative (161) and p-xylene were heated under reflux, in glass, under identical experimental conditions to those used in the thermolysis of the parent ether (156). The single reaction product was identified as the substitution compound, 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (159) (78% after one recrystallisation from ethanol) (Scheme 61); moreover, the crude reaction product was shown by $^{19}$F and $^{1}$H n.m.r. spectroscopy to be completely free from unreacted 2-fluoromethyl compound (161) unlike the experiment performed previously.[64] This result clearly demonstrates the catalytic effect which glass has in promoting the substitution in the aromatic ring.



Scheme (61)

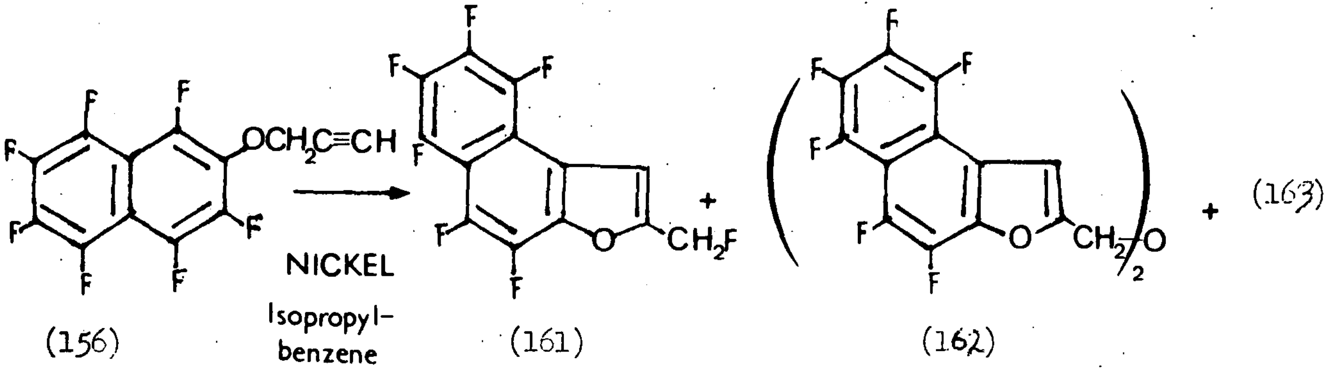
## 6.4. The Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (156) with Isopropylbenzene in a Nickel Tube at 140°C.

This reaction was originally attempted in an effort to differentiate between the two plausible mechanisms (radical and ionic) proposed for the reaction between the prop-2-ynyl ether (156) and an aromatic solvent[66]. The ether (156) was heated in isopropylbenzene under reflux, in glass apparatus, for 24hs to yield 10% 1,3,4,5,6,7,8-heptafluoro-1-(propa-1,2-dienyl)naphthalen-2-one (157) and a 42% mixture containing at least two isopropylbenzene substitution derivatives (160) (Scheme 62).



Scheme (62)

The reaction failed to yield any 2-fluoromethyl compound (161) which is entirely consistent with what would be expected now for a reaction performed in an aromatic solvent in glass apparatus. However, when the ether (156) was heated in the presence of isopropyl benzene in a sealed nickel tube at 142°C for 24h, three major identifiable products were observed : 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) (18%), di-(4,5,6,7,8,9-hexafluorobenzo(2,1-b) furan-2-ylmethyl) ether (162) (6%) and isomeric 2-(isopropylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furans (160) (5%). Under more rigorously controlled anhydrous conditions the same reaction gave 65% of the isomerisation product (161), 7% of the bis-ether (162) and ca. 2% of the bis methane (163) (Scheme 63).



(156) (161) (162)

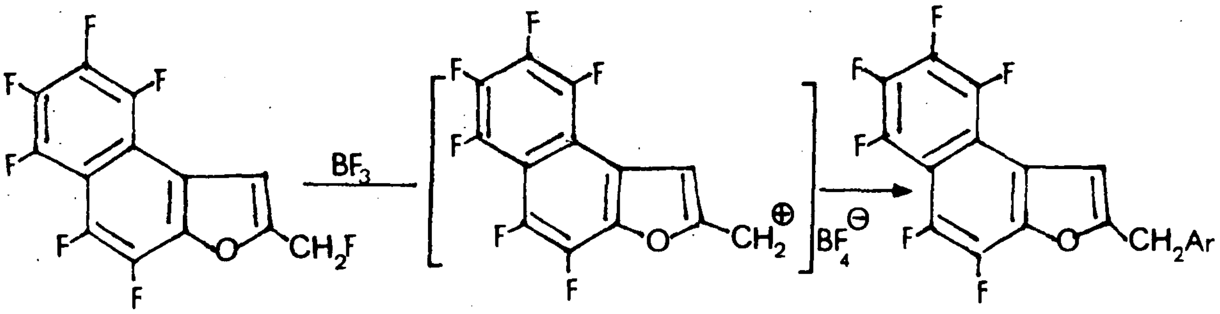
Scheme (63)

## 6.5. The Vapour Phase Pyrolysis of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (156)

One attempt was made to effect the isomerisation reaction of the ether (156) in the absence of a solvent cage by distilling it through a quartz tube packed with silica fibre maintained at 360°C / 0.005 mmHg. The experiment yielded a crude green product the sublimation of which gave 43% of the isomerisation product 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan.

## 6.6. The Friedel-Crafts Reaction of 2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) with p-Xylene and with Benzene in the presence of Boron Trifluoride

The fluoromethyl compound (161) was dissolved in a mixture of diethyl ether and the aromatic solvent (p-xylene; and benzene). The Lewis acid, boron trifluoride etherate was then added at room temperature. After stirring for 150min each individual mixture yielded a single product: the respective substitution products (158) and (159) both in essentially quantitative yields. (Scheme 64).



(161) (179)

Ar = $C_6H_5$ (158)

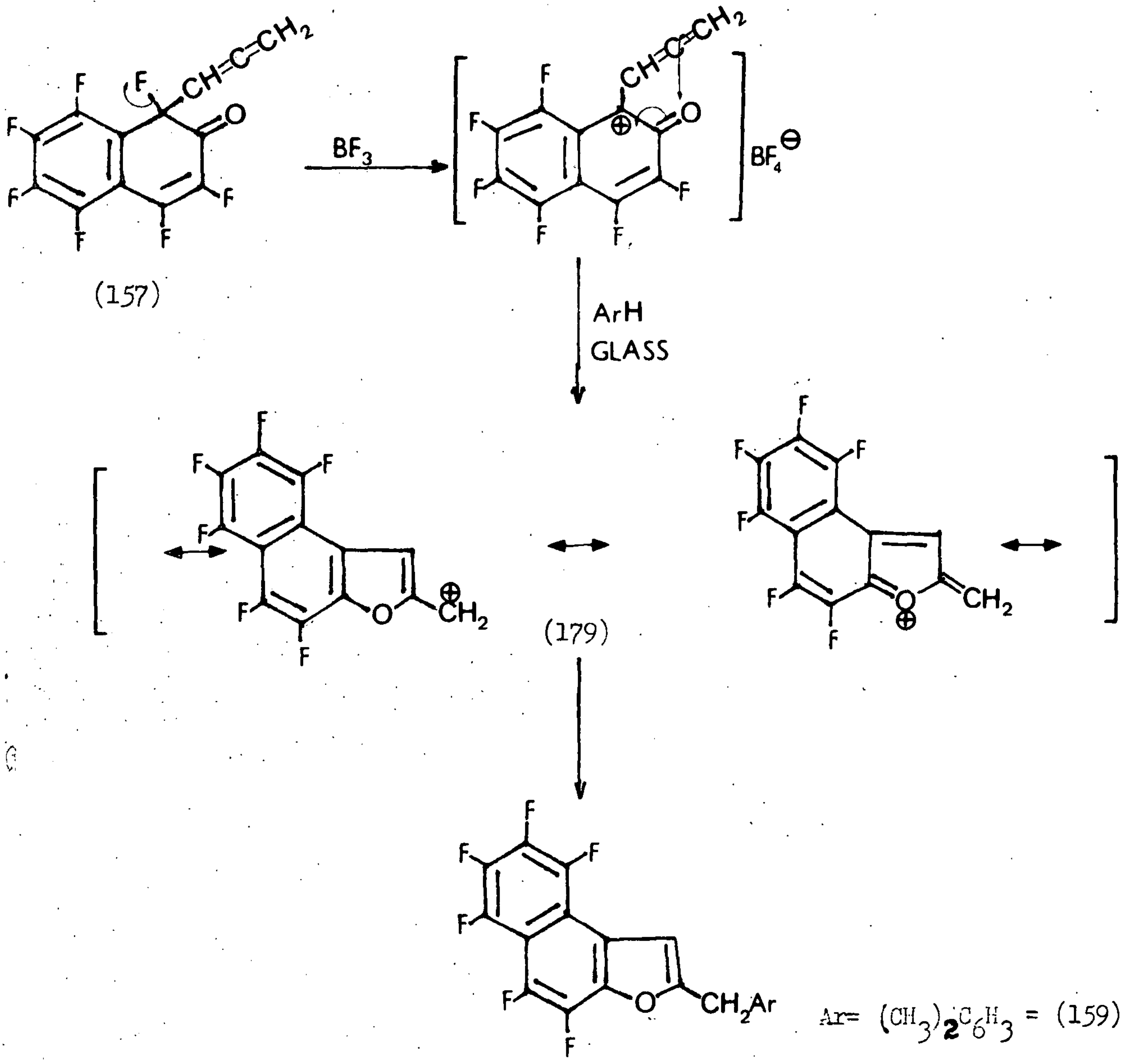
Ar = $(CH_3)_2C_6H_5$ (159)

Scheme (64)

## 6.7. Reaction of 1,3,4,5,6,7,8-Heptafluoro-1-(propa-1,2-dienyl)-naphthalen-2-one (157) with p-Xyleneand Borontrifluoride

The previous section demonstrated the Friedel-Crafts reaction of the 2-fluoromethyl compound (161) with aromatic solvents, in the presence of a Lewis-acid, under very mild conditions. Using the naphthalen-2-one (157), which is the intermediate in all the reactions with 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156) the possibility of removing the fluorine at C-1 in (157) with boron trifluoride, and thereby promoting the cyclisation reaction, was investigated in p-xylene.

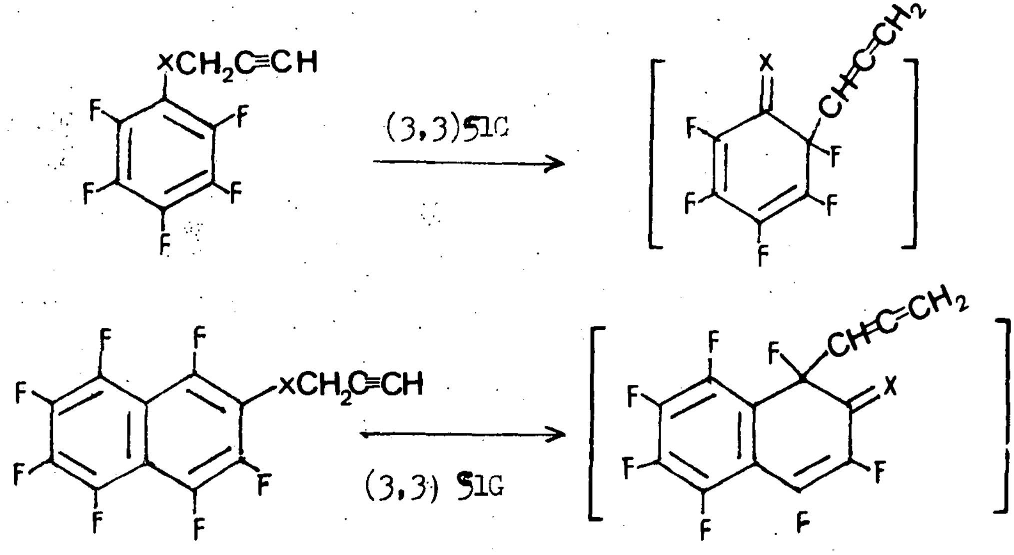
The reaction of the naphthalen-2-one (157) with p-xylene in the presence of boron trifluoride etherate was attempted at room temperature and at 100°C (5h) but both sets of conditions failed to induce any reaction. (Owing to the small quantities of 1,3,4,5,6,7,8-heptafluoro-1- (propa-1,2-dienyl)-naphthalen-2-one (157) available, the reaction products were analysed using $^1$H n.m.r. spectroscopy, without isolation.) However, when the reactants were heated at 120°C for 180 min, unreacted starting material and ca 12% of 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoro napththo (2,1-b) furan (159) were shown to be present in the mixture. (Scheme 65). The experiment succeeded in demonstrating that the cyclisation can occur via an ionic mechanism.



Scheme (65)

## Chapter 7: Concluding Remarks Concerning the Claisen Rearrangement of Polyfluoroaromatic Prop-2-ynyl Ethers and Thioethers

(i) The Claisen rearrangement of an aromatic prop-2-ynyl ether is a well established reaction . Indeed it is the formation of a reactive ortho-propa-1,2-dienyl derivative (Scheme 66) that gives the parent compound such an interesting and varied thermal chemistry. The actual isolation of the Claisen intermediate does require an additional stablising factor, which can be realised by using a polynuclear aromatic compound. 1,3,4,5,6,7,8-Heptafluoro-1-(propa-1,2-dienyl) naphthalen-2-one (157) was isolated from the thermolyses of 1,3,4,5,6,7,8-heptafluoronaphthyl prop-2-ynyl ether (156) in the presence of both isopropylbenzene (9%) and benzene (26%)$^{66}$. In experiments with the analogous thioether (171) it was expected that 1,3,4,5,6,7,8-heptafluoro-1-(propa-1,2-dienyl) naphthalen-2-thione (172) would be observed, However thermolyses in both the liquid and vapour phases failed to reveal any of this compound. This can only be due to the effect of the heteroatom, which clearly facilitates the subsequent cyclisation reaction. Although no Claisen intermediate was isolated, rationalisation of the observed products in the thermolyses of prop-2-ynyl thioether compounds (167) & (171) pre-supposes an initial and efficient ortho-Claisen rearrangement, to give the thiones (167a) & (172) respectively.



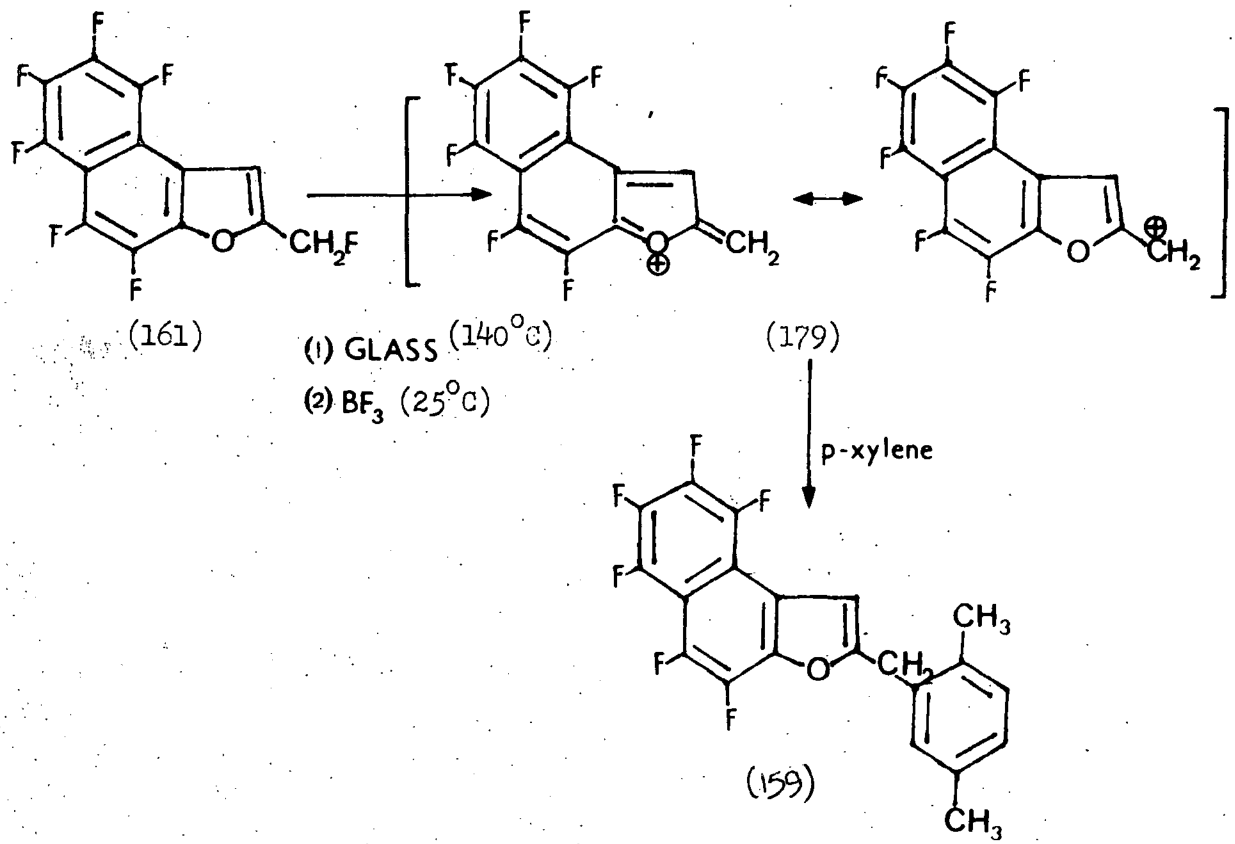
X = O (147),(148)
X = S (167),(167a)

X = O (156),(157)
X = S (171),(172)

Scheme (66)

(ii) Two possible reaction mechanisms have been proposed to account for the thermolysis reactions of pentafluorophenyl prop-2-ynyl ether (147) (and by analogy, of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156)): (a) A homolytic process (Ch3,p35) and (b) a heterolytic process (Ch6,p56) In this section all the data given in Chapters 4,5 and 6 are considered together in conjunction with one crucial experiment (which has not yet been reported in this thesis) in an attempt to define a general mechanism for the cylisation reactions of propa-1,2-dieneones and propa-1,2-dienethiones.

The experiments described in Chapters 5 & 6 demonstrated the profound effect which the reaction vessel (glass or nickel) had in determining the products formed from the thermolyses of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156) and thioether (171). The conversion of 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) in p-xylene in glass apparatus to 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (159) clearly implies the surface of the glass is behaving as a Lewis-acid catalyst, promoting the formation of a carbocation of considerable inherent stablility. Scheme (67). The same reaction has been shown to take place at room temperature in the presence of $BF_3$-etherate, a much more effective Lewis-acid.



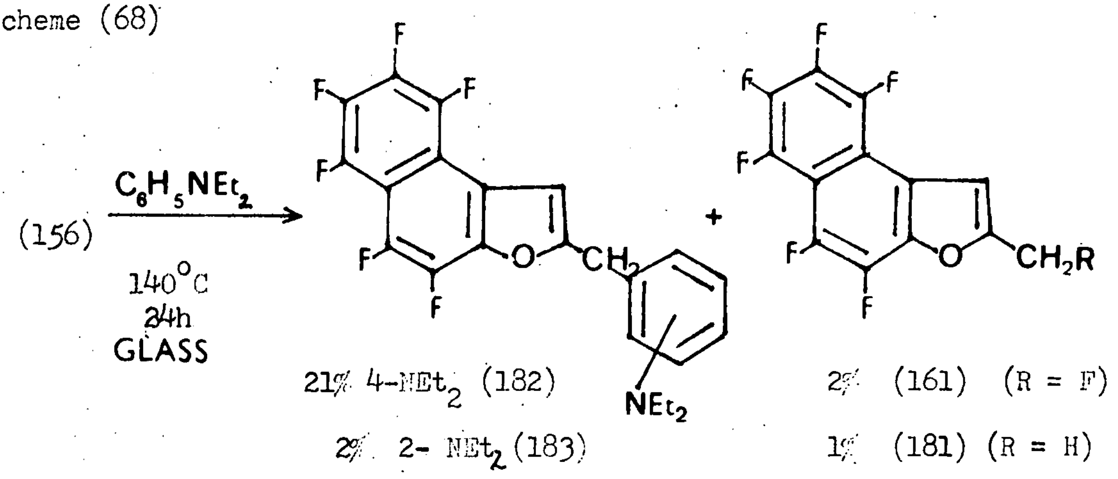
Scheme (67)

When the ether (156) is reacted with p-xylene in nickel apparatus, the major product is the 2-fluoromethyl compound (161). From this it can be concluded that in the intervening period between conversion of the 1,3,4,5,6,7,8-heptafluoro-1-(propa-1,2-dienyl)-naphthalen-2-one (157) to (161) (the process which, from the mechanistic point of view is the most interesting factor in all the studies undertaken with propynyl ethers (and thioethers)) there is insufficient cationic character of the type represented by (179) (Scheme 67) present for electrophilic substitution to take place in p-xylene. Consequently, the reaction in nickel terminates with the formation of the 2-fluoromethyl compound (161).

In Chapter 6, sec. 6.7 it was noted that the naphthalenone (157) with $BF_3$-etherate and p-xylene is not converted into the substitution product (159) until at least 120°C, clearly the Lewis acid is exercising some catalytic effect. The glass surface alone <u>could</u> also act as a Lewis acid in this process, albeit at a higher working temperature, so in <u>glass</u> apparatus it is not possible to say categorically that the 2-fluoro-methyl compound (161) is a definite intermediate in the conversion of the ether (156) in p-xylene to the substituted xylene derivative (159).

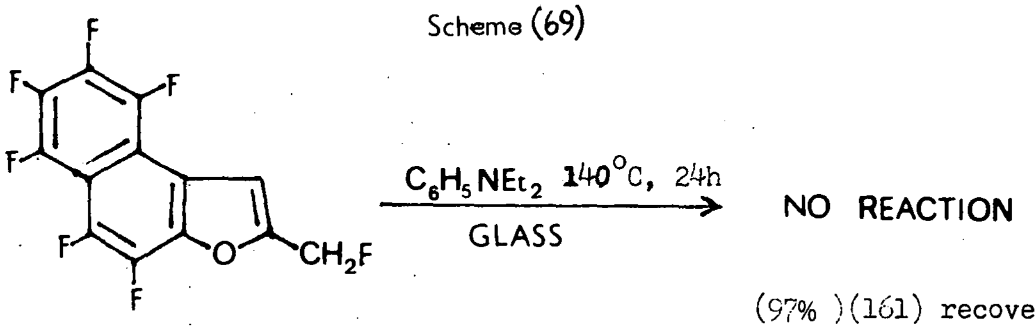
(iii) There is one experiment in the literature and one recent observation which really does shed light on the process involved in the conversion of the intermediate naphthalenone (157) into a naphtho (2,1-b) furanyl derivative. In 1982 the results of the thermolysis of the ether (156) in N,N-diethylaniline in glass were published[63]. The experiment has been repeated in a glass Carius tube, under carefully controlled conditions (140°C, 24h) (Scheme 68) and the original findings have been confirmed.

Scheme (68)



The presence of the 2-fluoromethyl compound (161) (2%) is particularly important since it has been shown that this material is recovered unchanged (97%) when heated with N,N-diethylaniline in a glass Carius tube at 140°C for 24h; no semblance of any substitution products was detected[67] . (scheme 69). (It is this observation that is the crucial factor referred to in Sec. 7.2).

Scheme (69)



(97% )(161) recovered)

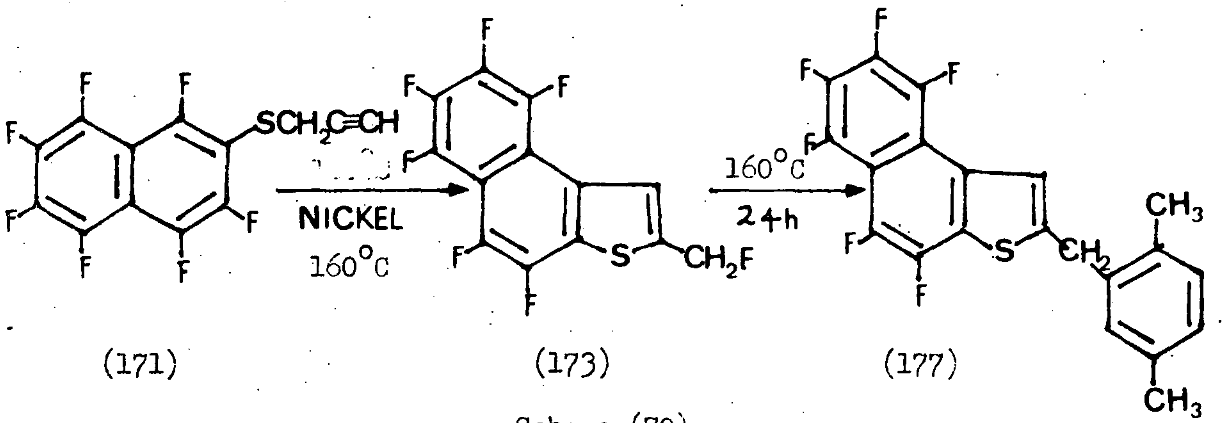
The Lewis-acid catalysing effect of the glass walls must have been effectively neutralised by the solvent acting as a base. (Similarly, 2-fluoromethyl-4,5,6,7-tetrafluorobenzo(b) furan is recovered (98%) from a reaction attempted in N,N-diethylaniline at 150°C - 154°C for 114hs in glass apparatus[67] .) There remains, however, the rationalisation for the formation of the substituted diethylaniline derivatives (182) and (183) starting from the ether (156).

(IV) There is a problem regarding the mechanism of substitution of aromatic hydrogen in N,N-diethylaniline; neither homolytic nor Friedel-Crafts substitution reactions have ever been reported. However, in the absence of a Lewis acid which would otherwise have converted a highly activating Et$_2$ N-group into a highly deactivating quaternary ammonium substitutent, an electrophilic substitution reaction provides a satisfactory rationalisation for the formation of the substituted N,N-diethylaniline derivatives. During the transformation of the naphthalenone (157) to the 2-fluoromethyl compound (161) (2% is formed in the reaction), <u>sufficient</u> cationic character must develop on the 2-CH$_2$ substitutent of the furan ring during cyclisation for it to be captured to a major extent by the nucleophilic N,N-diethylaniline . With Xylene as solvent in nickel apparatus, the fluoride ion is the more effective nucleophile which accounts for the high pro-

proportion (48%) of 2-fluoromethyl compound (161) compared to the substituted p-xylene derivative (159) (5%) in the product. Using the freon solvent ($CF_2ClCFCl_2$), the 2-fluoromethyl compound (161) can be obtained in yields as high as 81%.

It is clear from these considerations that a heterolytic rather than homolytic process is being invoked to account for the chemistry of the propa-1,2-dienones derived from pentafluorophenyl and 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ethers (147) and (156) respectively. This process also provides a very satisfactory explanation for the vapour phase isomerisations of (156) and (171) where a pre-condition for the overall 1,4-fluorine shift is that the fluorine should not depart very far from the organic moiety: the presence of charged species and their electrostatic attraction provides the necessary intimacy.

7.5. The semi-kinetic study of the thermolysis of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl thioether (171) with p-xylene in nickel apparatus at 160°C does show that the 2-fluoromethyl derivative (173) is a definite intermediate prior to the formation of the substituted p-xylene derivative (177) (Scheme 70). When the same reaction was carried out in glass apparatus at 140°C, <u>only</u> the substituted p-xylene derivative (177)(85%) was formed. The glass was clearly acting as a Lewis-acid catalyst, as in the reactions with the ethers (i.e. oxygen analogues), but it is not possible to say categorically whether the 2-fluoromethyl compound (161) is an intermediate. The higher temperature (160°C) presumably is sufficient to cause the heterolysis of the $CH_2$-F bond in (173) in nickel apparatus in the absence of a Lewis-acid catalyst, though it has to be admitted that the homolytic cleavage of



Scheme (70)

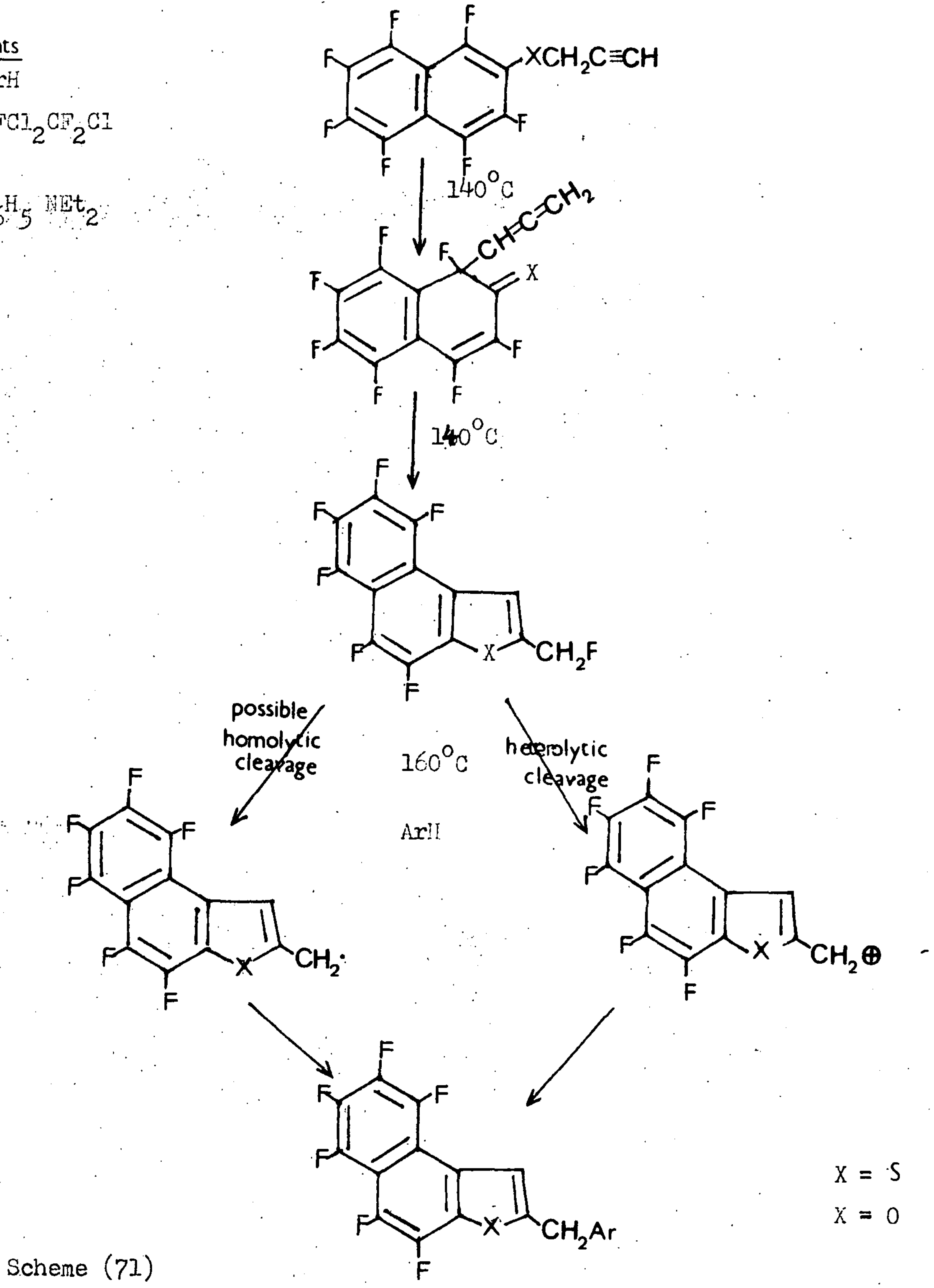
the $CH_2$-F bond in (173) could lead to the p-xylene substitution product (177).

The facile isomerisation of the thioether (171) in the vapour phase at 360°C to give the 2-fluoromethyl compound (173) (81%) is best explained in terms of a heterolytic fission of the aliphatic C-F bond in the intermediate propa-1,2-dienethione (172) for the same reason as has been given for the isomerisation of the ether compound (156). Schemes(71) and (72) provide the mechanistic overview of all the major reactions involving the naphthalene derivatives.

## (I) IN NICKEL

Solvents

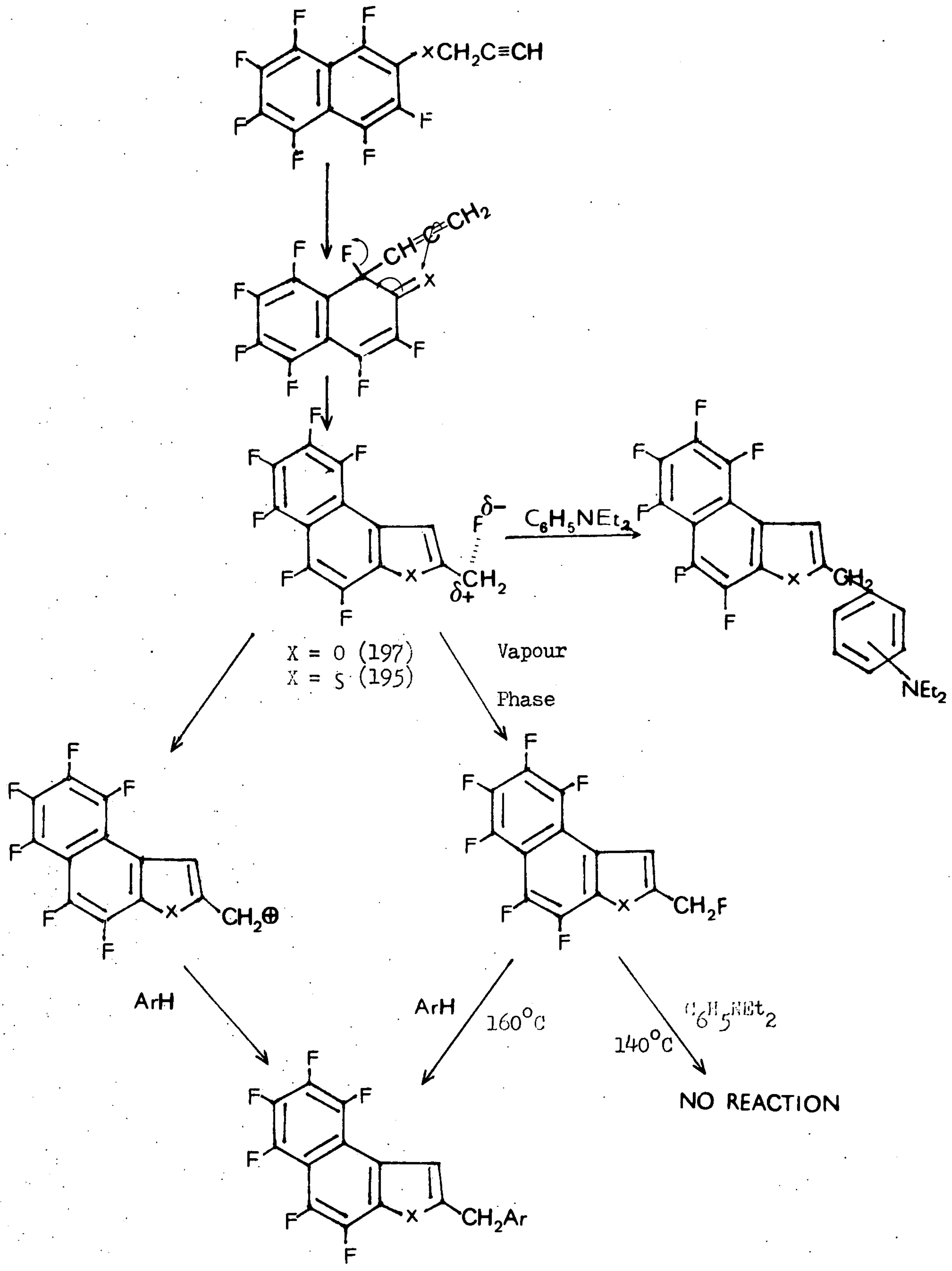
1) ArH
2) $CFCl_2CF_2Cl$
or
3) $C_6H_5NEt_2$



X = S
X = O

Scheme (71)

## (2) IN GLASS



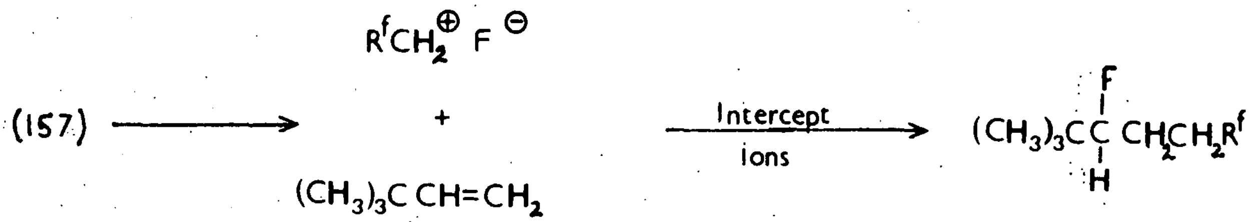
Scheme (72)

# Chapter 8: The Reaction of 2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) with 3,3-Dimethylbut-1-ene in the presence of a Lewis-Acid

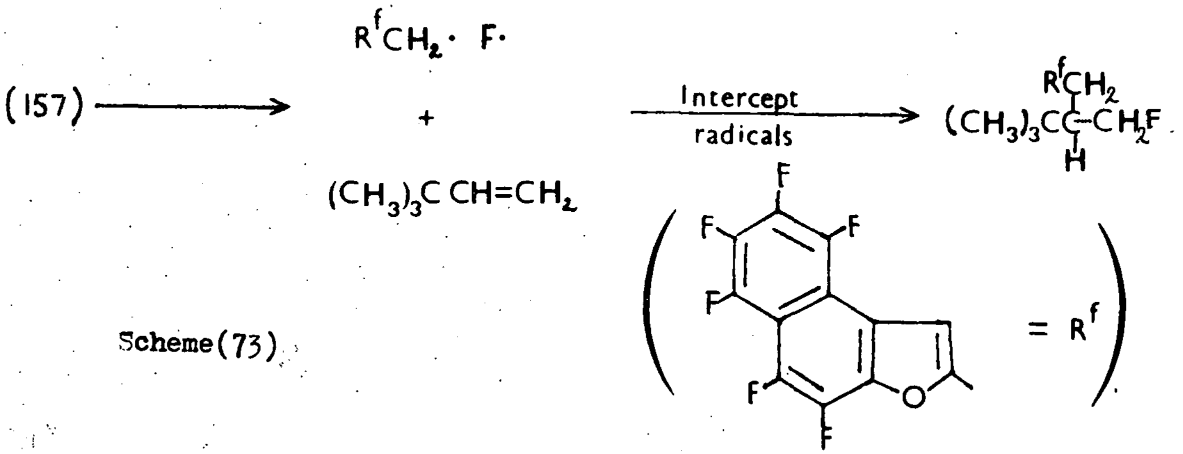
## 8.1. Introduction

The thermolysis of 1,3,4,5,6,7,8-heptafluoro-naphthyl prop-2-ynyl ether (156) in 3,3-dimethylbut-1-ene was originally undertaken in an attempt to determine whether radical or ionic species were involved during the course of cyclisation reactions of the initially formed 1,3,4,5,6,7,8-heptafluoro-1-(propa-1,2-dienyl)naphthalene-2-one (157). It was hoped that the orientation of the addition across the double bond would reveal the nature of the attacking species.

1. Heterolytic Cleavage

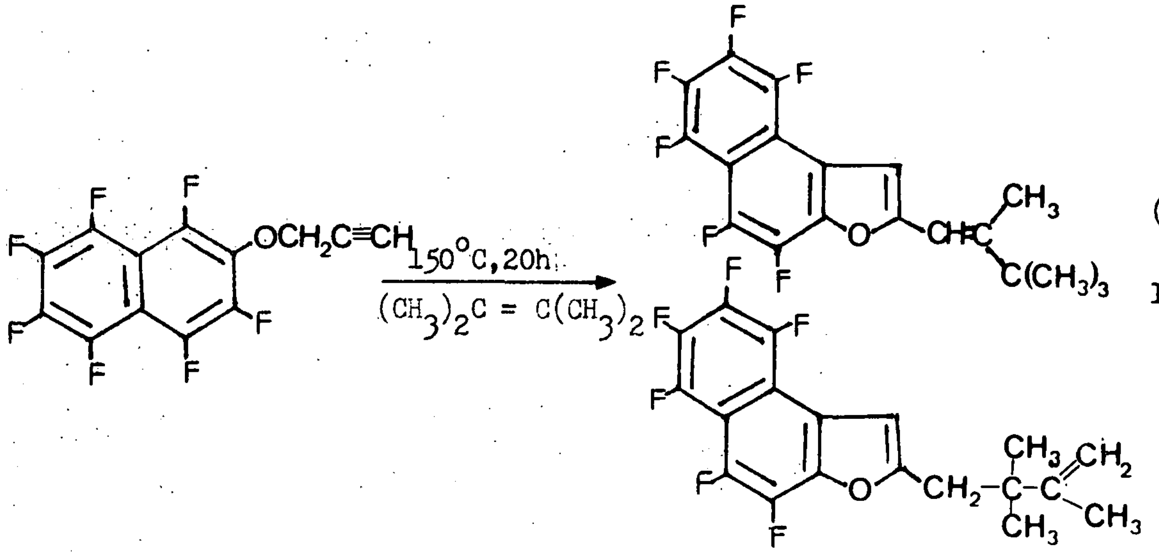


2. Homolytic Cleavage



Scheme(73)

Preliminary experiments carried out with the ether (156) in the presence of excess 2,3-dimethylbut-2-ene in a sealed nickel Carius tube at 150°C over 20hs failed to yield a simple adduct. Two substitution products (54%) were isolated 2-(2,3,3,-trimethylbut-1-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (187) and an isomer 2-(2,2,3-trimethylbut-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (186) (Scheme 74).



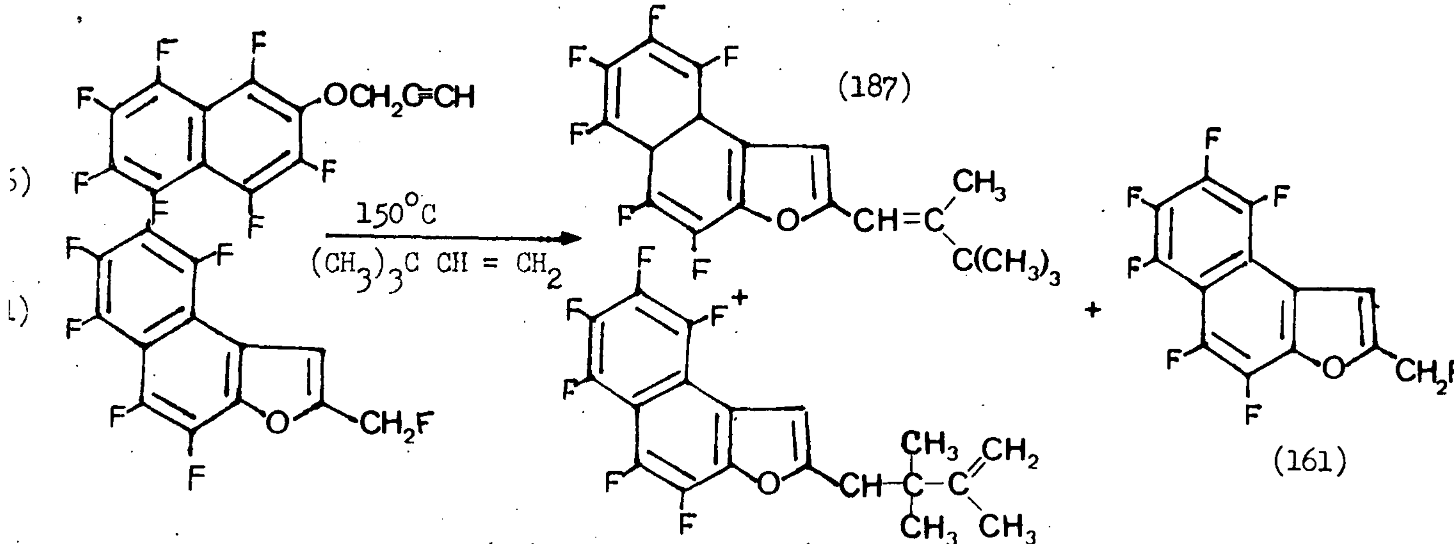
(187)
1 part

(186)
99 parts

Scheme (74)

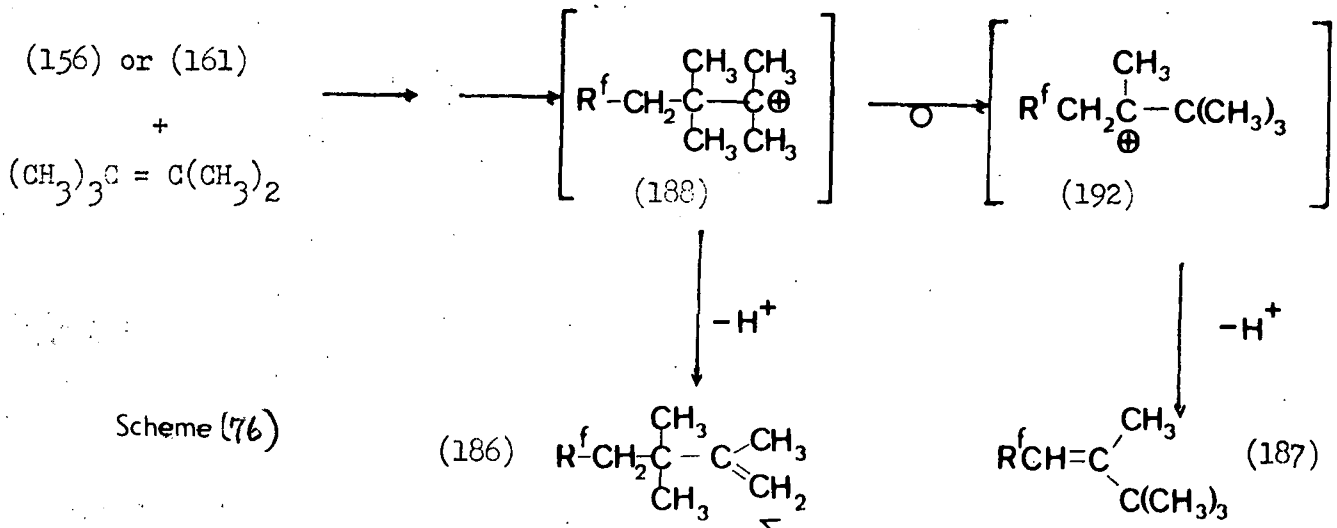
Substitution products (186) and (187) (58% overall) , in the ratio of 92 parts to 8 parts respectively, were obtained when the 2-fluoromethyl compound (161) was heated with excess 2,3-dimethylbut-2-ene at 150°for 72h.

The thermolysis of 1,3,4,5,6,7,8-heptafluoronaphthyl prop-2-ynyl ether (156) in 3,3-dimethylbut-1-ene at 150°C for 20h gave a complex mixture of alkene substitution products (43%), in which suprisingly the two compounds which had been prepared in the reaction with 2,3 -dimethylbut-1-ene ((186) and (187)) were present in the ratio 93 parts to 7 parts respectively with 41 parts unaccounted for; a small proportion of 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) (3.5%) was also isolated from the reaction product. When the 2-fluoromethyl derivative (161) was heated with 3,3-dimethylbut-1-ene at 150°C for 68h in a nickel tube, a complex mixture of products was again obtained. The alkene substitution components (20%) contained (186) and (187) in the ratio 80 parts to 20 parts respectively with 65 parts unaccounted for. Significantly the reaction products contained 55% of unreacted 2-fluoromethyl compound (161) (Scheme 75).



Scheme (75) (186)

In rationalising the formation of the 2-(2,3,3-trimethylbut-1-enyl) derivative (187) in the reactions of either the ether (156) or the 2-fluoromethyl compound (161) with 2,3,-dimethylbut-2-ene it is necessary to invoke a (1,2) methyl shift. This rearrangement excludes a reaction mechanism involving a radical species, as 1,2-shifts of alkyl radicals (and hydrogen atoms) are unknown. However as (1,2) migrations are a feature of carbocation chemistry, the reaction mechanism proposed involves the carbocation (188) as the source of both substitution products of the rearranged and unaltered $C_6$-alkene skeleton. (Scheme 76).

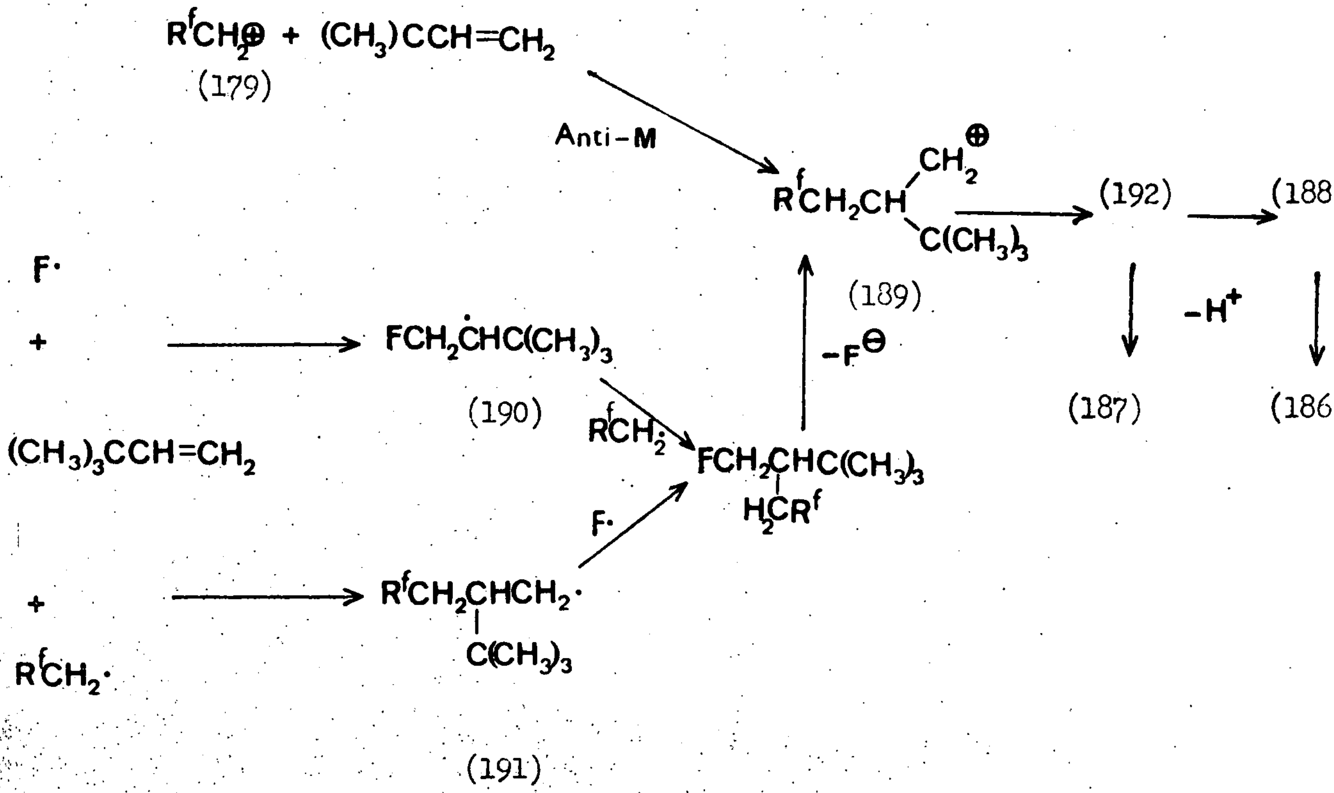


Scheme (76)

It was observed that the cation (188) could have arisen either by an initial attack by the carbocation R$^f$ CH$_2^+$, or alternatively by an initial attack by either R$^f$CH$_2$· or F· to give an adduct which then lost fluoride ion.$^{64}$.

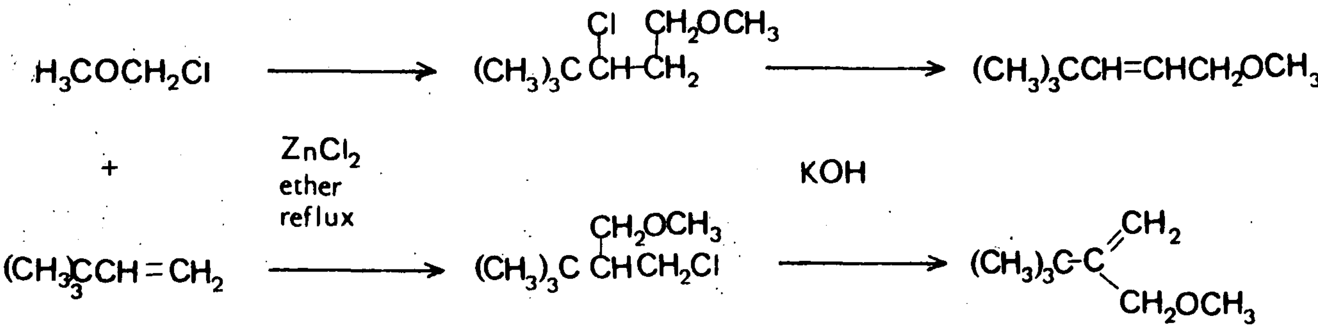
The suprising formation of the same alkene substitution products in the thermolysis reactions of the ether (156) or the 2-fluoromethyl coumpound (161) in 3,3-dimethylbut-1-ene led the author[64] to offer two suggestions to rationalise these data: (a) one involving an initial Anti-Markovnikov addition to the terminal double bond by the attacking species; and (b) one involving the acid catalysed isomerisation of the 3,3-dimethylbut-1-ene to 2,3-dimethylbut-2-ene and subsequently undergoing reaction via (188).

The essence of the Anti-Markovnikov reaction requires the intermediacy of the cation (189). (Scheme 77). The proposed



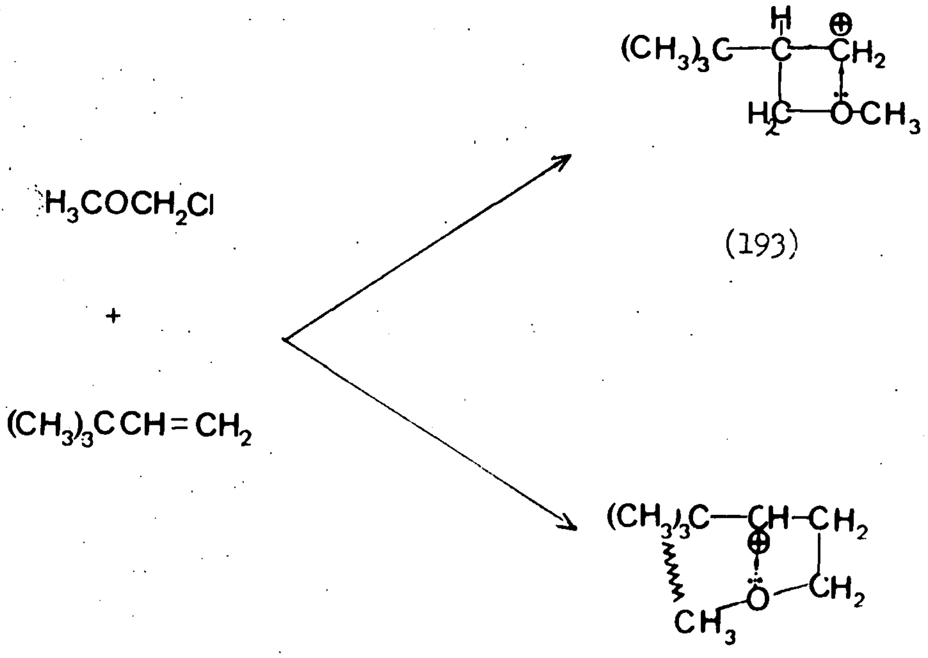
Scheme (77)

Anti-Markovnikov reaction was based on a publication by the Russian workers A.Z. Shikhmamedbekova and F.M. Akhmedara$^{68}$, who claimed to have identified both Markovnikov and anti-Markovnikov addition products from the reaction of chloromethyl methyl ether with 3,3-dimethylbut-1-ene, when refluxed in diethyl ether, in the presence of $ZnCl_2$ (Scheme 7a).



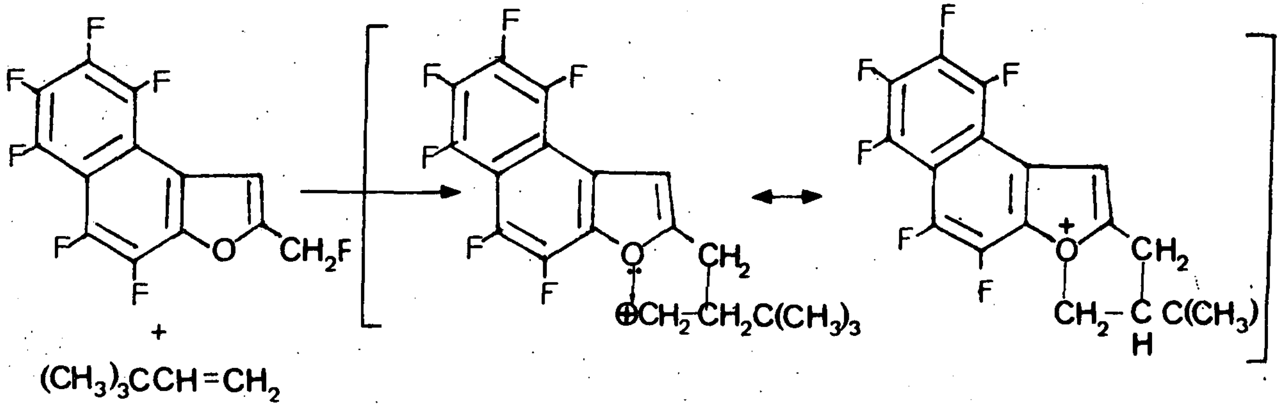
Scheme (7a)

These results could be explained in terms of a partially bridged (and therefore stabilized) cationic species (193), being formed during the reaction, since molecular models reveal some unfavourable steric effects if such an interaction is invoked in the ion leading to the Markovnikov adduct.



(193)

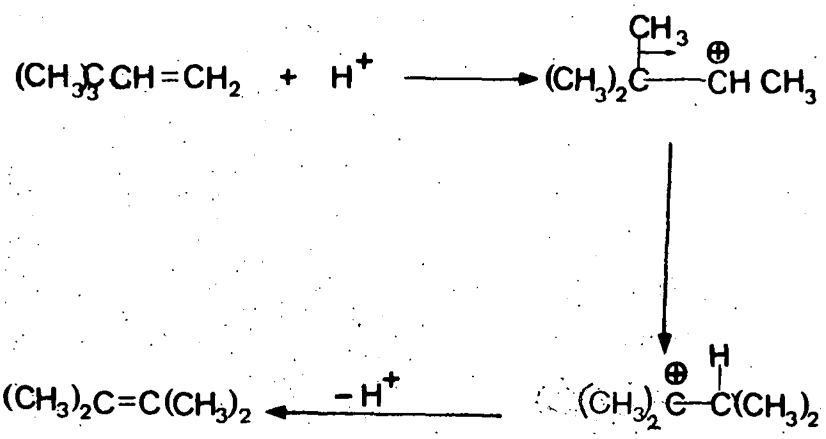
It had been suggested that this argument could be extended to the particular system under investigation, which would produce a primary carbocation (189) of a more favourable geometry (Scheme 78).



(189)

Scheme (78)

The second suggestion to account for the presence of the substituted alkenes (186) and (187) in reactions of the ether (156) and the 2-fluoromethyl compound (161) with 3,3-dimethylbut-1-ene required the isomerisation of this alkene to 2,3-dimethylbut-2-ene. This reaction, which in principle could be brought about by just one $H^+$ ion, is well known (Scheme 79).



Scheme (79)

The work described in the following sections examines these two suggestions, presupposing the formation of the carbocation(179), by reacting the 2-fluoromethyl compound (161) with 3,3-dimethylbut-1-ene in the presence of a Lewis-acid. The study also pays particular attention to the possible isomerisation of 3,3-dimethylbut-1-ene to 2,3-dimethylbut-2-ene under the various experimental conditions adopted in the reactions already described; this possibility is reported first.

## 8.2 Isomerisation of 3,3-Dimethylbut-1-ene

In order to assess whether the isomerisation of the 3,3-dimethylbut-1-ene to 2,3-dimethylbut-2-ene occurred under the reaction conditions used for the thermolysis of the 2-fluoromethyl compound (161) in 3,3-dimethylbut-1-ene, it is necessary to estimate the maximum amount of HF which would be produced in a typical reaction. The use of 2g of 1,3,4,5,6,7,8-heptafluoronaphthyl prop-2-ynyl ether (156) (in 3,3-dimethylbut-1-ene, 12ml) would produce ca. 0.13g HF. When liquid HF (0.3g) and 3,3-dimethylbut-1-ene (10mls) were heated at 150°C for 20hs, the integrated $^1$H n.m.r. of the hydrocarbon product revealed a 24% isomerisation to 2,3-dimethylbut-2-ene, corresponding to 1.57g. A simple calculation shows that the thermolysis of the prop-2-ynyl ether (156) (2g) in 3,3-dimethylbut-1-ene at 150°C for 20h would produce ca 0.68g of 2,3-dimethylbut-2-ene. 1,3,4,5,6,7,8-Heptafluoronaphthyl prop-2-ynyl ether (156) (2g) requires only 0.55g of2,3-dimethylbut-2-ene for complete reaction, while the amount required to yield the substitution products (186) and (187) in Table (2) requires only 0.17g. The experimental (data) evidence shows that pre-isomerisation of 3,3-dimethylbut-1-ene to 2,3-dimethylbut-2-ene followed by direct reaction with the 2-fluoromethyl derivative (161) can comfortably account for the formation of 2-(2,3,3-trimethylbut-2-enyl)4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (187) and 2-(2,2,3-trimethylbut-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (186) without having to invoke an initial anti-Markovnikov reaction with the terminal alkene. It is expected that the rate of electrophilic addition to the but-2-ene derivative (giving a tertiary carbocation) would be very much faster than the rate of addition to the but-1-ene derivative (which would produce a secondary carbocation).

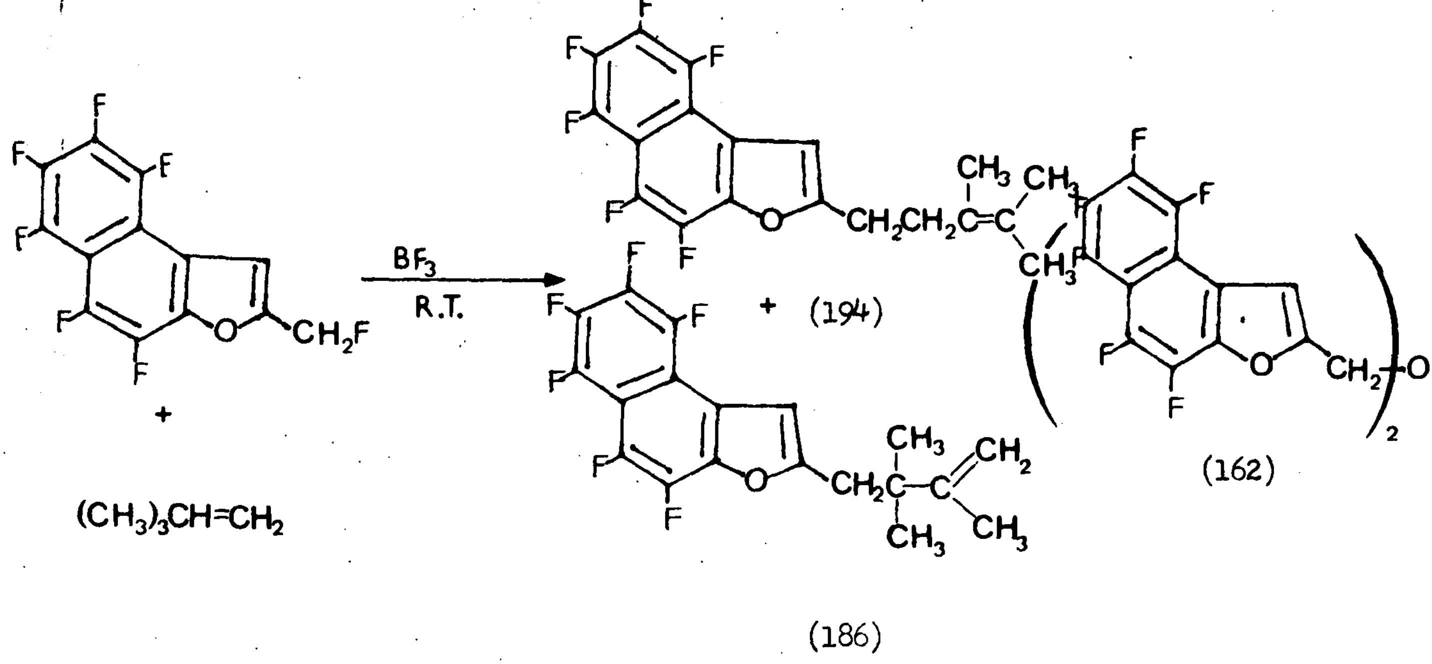
## 8.3. Reaction of 2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) with 3,3-Dimethylbut-1-ene in the presence of Borontrifluoride

Having observed the isomerisation of 3,3-dimethylbut-1-ene to 2,3-dimethylbut-2-ene at 150°C, it was necessary to find a system which would render possible the reaction of the $R^fCH_2^{\oplus}$ species with the terminal alkene under conditions which would minimise the degree of isomerisation of the 3,3-dimethylbut-1-ene. In this way the true orientation of the initial electrophilic attack could be determined. In order to cleave the $CH_2$-F bond of the 2-fluoromethyl compound (161) heterolytically at room temperature, a Lewis-acid, boron trifluoride-etherate, was used. The system was tested first by adding the aromatic species, benzene or p-xylene, to a $R^fCH_2F/BF_3/(C_2H_5)_2O$ mixture at room temperature (sec 6.6). The $R^fCH_2\oplus$ cation (179) substituted into the aromatic ring quantitatively to give (158) and (159) respectively.

2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) and 3,3 dimethylbut-1-ene were stirred in the presence of $BF_3{:}(C_2H_5)_2O$ at room temperature for 180mins and at -50°C for 30 mins. Both reactions gave, as the major product 2-(3,4-dimethylpent-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (194) accompanied by a small proportion of 2-(2,2,3-trimethylbut-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (186). (Table 2). The subsitution products were accompanied by the coupling derivative di-(4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan-2-yl methyl) ether (162) (c.a. 40%) (Scheme 80).

| $R^fCH_2F/BF_3(C_2H_5)_2O$<br>$(CH_3)_3CCH{=}CH_2$ | YIELD | (194) | (186) | UNKNOWN |
|---|---|---|---|---|
| 25°C | 26% | 94 | 6 | 27 |
| -50°C | 37% | 92 | 8 | 47 |

TABLE (2)



Scheme (80)

These experiments were the first ones to give a substitution product derived from an initial Markovnikov addition to 3,3-dimethylbut-1-ene. Nevertheless, compound (186) was again present in the reaction product so it was necessary to investigate whether the 3,3-dimethylbut-1-ene had isomerised to 2,3-dimethylbut-2-ene in the present Lewis-acid system.

## 8.4: Sami-Quantitative Estimation of the Degree of Isomerisation of 3,3-Dimethylbut-1-ene to 2,3-Dimethylbut-2-ene in the presence of Borontrifluoride.

A series of control experiments with $BF_3{:}(C_2H_5)_2O$ and 3,3-dimethylbut-1-ene at room temperature in the absence of the 2-fluoromethyl compound $R^{f'}CH_2F$( 161) revealed that no isomerisation took place. However the addition of HF (0.008g - 0.62g) to the reaction mixture in a second series of control experiments brought about a small but significant degree of isomerisation to 2,3-dimethylbut-2-ene corresponding to a 0.2 - 2% conversion. In a typical experiment described in Sec 8.3. a simple calculation shows that 0.5g of $R^fCH_2F$ (161) if completely converted would generate 0.032gm of HF which would produce 0.0068g of 2,3-dimethylbut-2-ene. The presence of this amount of internal alkene is more than sufficient to give the 6 parts of (186) present in the 26% yield of $R^{f'}C_7H_3$ compounds reported in the previous section.

The experiment between $R^fCH_2F$ (161), 3,3-dimethylbut-1-ene ($7 \times 10^{-4}$ mole) and $BF_3$-etherate was repeated, the mixture treated with water and the volatile components in the organic phase (ether and hydrocarbon) were distilled in vacuo to separate them from involatile materials. GLC analysis of this mixture showed that it contained ($2.09 \times 10^{-4}$ mole) of 2,3-dimethylbut-1-ene which again is far more than is necessary to account for the amount of the substitution product (186) formed. This experiment implies that the alkene isomerisation takes place during and continues after the consumption of all of the 2-fluoromethyl compound (161).

## 8.5 Reaction of 2-Chloromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161a) with 3,3-Dimethylbut-1-ene in the presence of Zinc Chloride.

Shikmamedbekova[68] had reported the formation of anti-Markovnikov adducts in the reaction of $CH_3OCH_2Cl$ with $(CH_3)_3CH{=}CH_2$. Consequently in an attempt to produce an alkene adduct, 2-chloromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161a) was prepared from the 2-fluoromethyl compound (161) by a halogen exchange reaction using aluminium trichloride dissolved in acetonitrile. The 2-chloromethyl compound (161a) was dissolved in diethyl ether and refluxed under nitrogen with 3,3-dimethylbut-1-ene in the presence of anhydrous zinc chloride for 22 hs. The reaction failed to yield an alkene adduct but produced the substituted alkene compounds already identified in previous work (sec 8.3). The $^1H$ n.m.r analysis of the separated alkenes is shown in the Table (3).

| $R^fCH_2Cl/(CH_3)_3CH = CH_2$<br>$ZnCl_2$ - Reflux | YIELD | (186) | (194) | (196) | UNKNOWN |
|---|---|---|---|---|---|
| 22hs | 55% | 68parts | 17parts | 15parts | 30parts |

TABLE (3)

It is noteworthy that the 2-(2,3,3,-trimethylbut-1-enyl) - 4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (196) had a different geometrial configuration to the material prepared previously (187) (sec 8.2). This was clearly shown by the $^1H$ n.m.r. signal of its protons at position 3 in the furan ring and position 1 in the side chain, which were centred at $\delta$ 7.042 and 6.368 respectively whereas before the corresponding signals were centred at $\delta$ 7.118 and 6.382 in (187); the remaining $^1H$ shifts were unaltered.

As the major product was (186) it was necessary to once again consider the isomerisation of the 3,3-dimethylbut-1-ene to 2,3-dimethylbut-2-ene under the same reaction conditions. Refluxing excess $ZnCl_2$ and diethylether with 3,3-dimethylbut-1-ene for 21h did not promote any isomerisation of the alkene. However, under the same experimental conditions in the presence of $R^fCH_2Cl$ (161a) ($3.5x10^{-4}$mole) an examination of the ether-hydrocarbon component at the end of the experiment (using GLC) revealed the presence of $2.9x10^{-4}$mole of 2,3-dimethylbut-2-ene.

The course of the reaction of the 2-chloromethyl compound (161a) with 3,3-dimethylbut-1-ene in the presence of the Lewis acid $ZnCl_2$ is very similar to that of the 2-fluoromethyl compound (161) with the same alkene at 150°C, in that the main reaction products arise primarily from reaction with 2,3-dimethylbut-2-ene, formed by pre-isomerisation of the 3,3-dimethylbut-1-ene. Clearly the ionisation (or, it must be admitted the homolytic fission) of the $CH_2$-F bond in (161) in the absence of a Lewis-acid and the ionisation of the $CH_2$-Cl bond in (161a) in the presence of $ZnCl_2$ must be slow compared with the rate of isomerisation of the terminal alkene to the internal alkene under the prevailing reaction conditions.

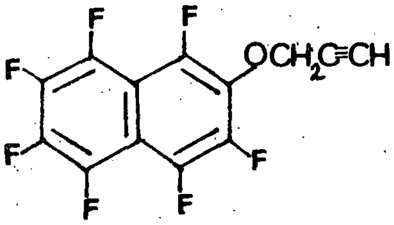
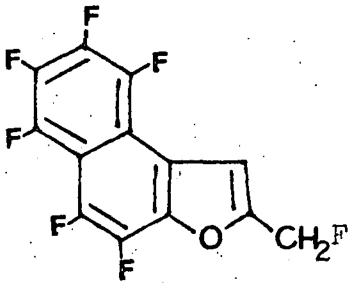
## 8.6; Concluding Remarks

(i) The thermolysis of 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156) and of 2-fluoromethyl-4,5,6,7,8,9-hexafluoro (2,1-b) furan (161) in 3,3-dimethylbut-1-ene at 150° in a nickel tube has been shown to give 2-(2,2,3-trimethylbut-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho (1,2-b) furan (186) and 2-(2,3,3-trimethylbut-1-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (187) not as a result of reaction <u>with</u> the terminal alkene, but rather by reaction with 2,3-dimethylbut-2-ene which is formed <u>from</u> it by acid catalysis.

(ii) The 2-fluoromethyl compound (161) has been shown to react with 3,3-dimethylbut-1-ene at room temperature under the influence of the Lewis-acid $BF_3$-etherate to give 2-(3,4-dimethylpent-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (194) by an initial Markovnikov cationic attack.

The isolation of (194) has enabled its presence to be sought in the products obtained from the reactionsof both (156) and (161) with 3,3-dimethylbut-1-ene at

150° in a nickel tube. It is indeed present, and Table (4) gives the new analysis of the products obtained in the earlier work.[64] Clearly some reaction has occurred with unisomerised 3,3-dimethylbut-1-ene.

| Experiment | Worker | Yield | (186) | (187) | (194) | Unknown |
|---|---|---|---|---|---|---|
| <br>+<br>$(CH_3)_3CCH = CH_2$ | AGM | 43% | 77 | 6 | 17 | 16 |
| <br>+<br>$(CH_3)_3CCH = CH_2$ | AGM | 20%<br>(68h) | 65 | 16 | 19 | 34 |
| | AGM | 33% | 86 | 7 | 7 | 30 |
| | GMB | 21% | 57 | 24 | 19 | 34 |

(iii) The reaction of the 2-fluoromethyl compound (161) with 3,3-dimethylbut-1-ene in nickel at 150°C showed that the fisson of the $CH_2$-F bond is slow at this temperature. However, in the reaction of the ether (156) with 3,3-dimethylbut-1-ene at 150°C, only 3.5% of the 2-fluoromethyl compound (161) is isolated in the product; the major components are the substituted alkenes (186) and (194). Consequently, the alkene which has reacted - 2,3-dimethylbut-2-ene via pre-isomerisation of 3,3-dimethylbut-1-ene-must have largely intercepted the transformation of the naphthalen-2-one (157) to the 2-fluoromethyl compound (161) before the $CH_2$-F had formed. (in exactly the same way as N,N-diethylaniline did in Section 7.3) This can be taken as further evidence for the development of cationic character on the 2-$CH_2$ substituent of the furan ring during the cyclisation reaction.

# EXPERIMENTAL

## Synthesis of Pentafluorophenyl Prop-2-ynyl Thioether (167)

Pentafluorothiophenol (50.0g) and dry tetrahydrofuran (400 ml) were cooled to -70°C under nitrogen and n-butyllithium solution (156 ml, 1.6 M) was added over a period of 2h, maintaining a temperature ≑ - 70°C. The last traces of n-butyllithium were introduced to the reaction mixture by washing with further dry tetrahydrofuran (50 ml). Prop-2-ynyl bromide (37 gm, 80% w/w in toluene) was then added over 50 min at -70°C. The mixture was allowed to warm to room temperature over 3h, diluted with water (800ml), acidified with hydrochloric acid (50ml, 11M) and extracted with diethyl ether (2 x 300ml). Unreacted pentafluorothiophenol present in the reaction mixture was removed by shaking with sodium carbonate solution (100ml, 1M). The organic extracts were dried ($MgSO_4$), the solvents evaporated and the product distilled in vacuo to give Pentafluorophenyl prop-2-ynyl thioether (167) (42.21g; 71%) bp. 93°C at 18mmHg (Found : C, 45.1; H, 1.0%. $C_9H_3F_5S$ requires C, 45.4; H, 1.3%) $\delta_F$ ($CDCl_3$), (2:1:2), 133.8, 153.8 and 163.2 ppm upfield from external $CFCl_3$. $\delta_H$ ($CDCl_3$) 2.25 (t, $-C{\equiv}C\underline{H}$) and 3.73 (d, $-C\underline{H}_2-$).

## Isomerisation of Pentafluorophenyl Prop-2-ynyl Thioether (167) In 1,1,2,-Trichloro-1,2,2,-trifluoroethane.

The thioether (167) (3.35g) and dry 1,1,2-trichloro-1,2,2-trifluoroethane (30ml), were sealed in a nickel Carius tube and heated at 180°C for 91h. The resulting brown oil was washed from the tube using diethyl ether, and the solvents removed by distillation through a 60cm Vigreaux column. The residue was distilled in vacuo and onefraction (0.643g) bp. 80°C at 0.01mmHg, was collected. Analytical TLC of the distillate (on silica using light petroleum (bp 30-40°C) as elutant) showed two components, one of which was unreacted thioether (167) and

$^{19}$F n.m.r. indicated the presence of 2-fluoromethyl-4,5,6,7-tetrafluorobenzo (b) thiophen (168) (0.43g; 13%) in the mixture. The distillate was separated by chromatography on silica (6" x 2.5") using light petroleum (bp. 30-40°C) as elutant. The slower component, a solid, was sublimed at 40°C, 0.05mmHg and recrystallised from light petroleum (bp. 40-60°C) to give pure 2-fluoromethyl - 4,5, 6,7-tetrafluorobenzo (b) thiophen (168) M.P. 49.5 - 50°C. (Found : C, 45.66; H, 0.90%.$C_9H_3F_5S$ requires C, 45.4; H, 1.3%). $\delta_f$ ($CDCl_3$) 141.4 (t), 144.5 (t), 159.1 (t), 160.0 (t) and 201.9 ppm (t, $CH_2\underline{F}$) in the ratio 1:1:1:1:1 respectively; J gem - F,H 47Hz ; $\delta_H$ ($CDCl_3$), 7.38 (3-$\underline{H}$) and 5.56 (d,$C\underline{H}_2$).

### Reaction of Pentafluorophenyl Prop-2-ynyl Thioether (167) with p-Xylene.

The thioether (167) (2.0g) and dry p-xylene (10ml) were sealed in a nickel Carius tube and heated at 180°C for 96h. The contents of the tube were removed using diethyl ether, the solvent was evaporated and excess p-xylene removed by distillation in vacuo at 40°C/0.005mmHg using a 60 cm Vigreaux column. The residue, a black oil, which was shown to contain 4 components by TLC on silica (light petroleum (bpt - 40-60°C) as elutant) was exhaustively distilled at 0.005 mmHg using an oil bath maintained at 190°C. The distillate (0.54 gm) was analysed by $^{19}$F n.m.r. and it was estimated that 2- (2,5 - dimethylbenzyl) - 4,5,6,7-tetrafluorobenzo (b) thiophen (169) was present to the extent of 35% by weight, representing an overall yield of (0.189gm,7%).

From a number of identical experiments a combination of distillation, flash chromatography, sublimation and crystallisation from light petroleum (bp. (40 - 60°C)) gave pure 2-(2,5- dimethylbenzyl - 4,5,6,7- tetrafluorobenzo (b) thiophen (169), mp.83.5 - 84°C. (Found: C,63.3;H, 4.0%. $C_{17}H_{12}F_4S$ requires C, 63.0; H, 3.7%); $\delta_F$ ($CDCl_3$) 142.4 (t), 146.0 (t), 161.4 (t) and 162.2 (t) upfield from internal $CFCl_3$, in the ratio 1:1:1:1: $\delta_H$ ($CDCl_3$) 2.25 ($C\underline{H}_3$), 4.127 (-$C\underline{H}_2$), and 7.02 (overlapping 3$\underline{H}$ and - $C_6\underline{H}_3$).

## Reaction of Pentafluorophenyl Prop-2-ynyl Thioether (167) with Benzene.

The thioether (167) (2.0g) and dry benzene (10ml) were sealed in a nickel Carius tube and heated at 180°C for 96h. The reaction product was washed from the tube with acetone and the solvents were evaporated from the mixture. The crude residue was distilled at 0.005 mmHg with an external temperature of 200°C. The distillate (0.9g) was shown by analytical T.L.C. analyses to be an extremely complex mixture (at least six components) and no attempt was made to isolate the benzyl derivative (170).

## Reaction of 2-Fluoromethyl - 4,5,6,7 - Tetrafluorobenzo (b) Thiophen (168) with p-Xylene in Boron trifluoride Etherate.

The fluoromethyl compound (168)(0.07g), dissolved in anhydrous ether (1ml), was mixed with dry p-xylene (1ml), boron trifluoride etherate (0.5ml) was added and the solution stirred at 25°C for 150min. The mixture was diluted with water, and the reaction products extracted with diethyl ether. The extracts were dried ($MgSO_4$), the ether was evaporated and the excess p-xylene removed by distillation at 25°C and 0.005 mmHg. The reaction product, shown to be a single component by analytical T.L.C. (on silica using $CHCl_3$ /$CCl_4$ 50 ; 50 solution as solvent), was sublimed at 70°C / 0.005 mmHg to give 2- (2,5-dimethylbenzyl) - 4,5,6,7 - tetrafluorobenzo (b) thiophen (169) (0.090g) (94%) mp. 83.5-84°C., which was identified by direct comparison of its I.R, $^{19}F$ and $^{1}H$ n.m.r. spectra with those of authentic material.

## Reaction of 2-Fluoromethyl - 4,5,6,7-Tetrafluorobenzo (b) Thiophen (168) With Benzene in Boron Trifluoride - Etherate.

The 2-fluoromethyl-compound (168) (0.056g), dissolved in anhydrous diethyl ether (1ml), was mixed with dry benzene (1ml). Boron trifluoride etherate (0.5ml) was added and the mixture stirred at room temperature for 150 min. The mixture was diluted with water and extracted with ether. The extracts were dried ($MgSO_4$), the solvents were evaporated and the reaction product, a single component by analytical T.L.C. (on silica using light petroleum bp. 40-60°C as the solvent) was sublimed at 70°C / 0.005 mmHg to give <u>2-benzyl - 4,5,6,7-tetrafluorobenzo (b) thiophen (170)</u> (0.065g, 93%) mp. 91.5 - 92°C (Found: C, 60.78; H, 2.48% $C_{15}H_8F_4S$ requires C, 60.8; H, 2.7%), $\delta_f$ ($CDCl_3$) 142.77 (t), 146.4 (t), 161.7 (t) and 162.4p.p.m. (t) in the ratio 1:1:1:1. $\delta_H$ ($CDCl_3$) 4.19 (S, $C\underline{H}_2$), 7.09 (3 - $\underline{H}$) and 7.30 (S, - $C_6\underline{H}_5$).

## 1,3,4,5,6,7,8 - Heptafluoro - 2 - naphthyl Prop-2-ynyl Thioether (171)

This material was prepared by the reaction of octafluoronaphthalene with sodium hydrosulphide in NN-dimethyl formamide / ethylene glycol followed by the reaction with prop-2-ynyl bromide <u>in situ</u> (G.M. Brooke personal communication).

## Isomerisation of 1,3,4,5,6,7,8-Heptafluoro - 2-naphthyl Prop-2-ynyl Thioether (171) in 1,1,2 - Trichloro - 1,2,2,-trifluoroethane

The thioether (171) (0.880g) and dry 1,1,2 -trichloro - 1,2,2 - trifluoroethane (20ml) were sealed, under nitrogen, in a nickel Carius tube and heated at 160°C for 24h. The orange reaction product was washed from the tube using freshly distilled acetone. The solvents were evaporated and the crude product was fractionally sublimed at 50-60°C and 0.005 mmHg and the sublimate (0.3646g, 41%) was recrystallised from light petroleum (b.p. 80-100°C) to give pure <u>2- fluoromethyl - 4,5,6,7,8,9 hexafluoronaphtho (2,1-b) thiophen (173)</u> m.p. 78-79°C. (Found: C, 48.4; H, 0.6%; $C_{13}H_3F_7S$ requires C, 48.2; H, 0.9%, M, 324): $\delta_F$ ($CDCl_3$) 139.7 (d), 142.5 (t), 145.4 ( d of t, peri - F $J_{7,8}$ 66Hz), 149.7 (d of d, peri-F), 156.7 (m) and 198.1 p.p.m. (t) in the ratio of 1:1:1:1:2:1 $\delta_H$ ($CDCl_3$) 5.75 (d, $C\underline{H}_2F$; J gem - F,H 49Hz) and 8.2 (m) with intensities in the ratio 2:1 respectively.

### Attempted Static Phase Isomerisation of 1,3,4,5,6,7,8 - Heptafluoro -2-naphthyl Prop-2-ynyl Thioether (171).

The thioether (ca.0.2g) was sealed in a glass bulb (1 litre) in vacuo and heated at various temperatures and time periods (140°C for 23h and 5h, 126°C for 21h) in an attempt to induce isomerisation to the 2-fluoromethyl derivative (173). The reaction products (brown/black oils) were analysed by $^{19}F$ n.m.r. which indicated the presence of unreacted starting material, but no thione (172) or 2 - fluoromethyl compound (173) was observed.

### The Vapour Phase Pyrolysis of 1,3,4,5,6,7,8 - Heptafluoro - 2 - naphthyl Prop-2-ynyl Thioether (171).

The thioether (171) (0.215g) was distilled through a silica tube (60cm x 1.5cm diam.) packed with silica fibre, (20cm x 1.5cm diam.) and heated to 360°C into a trap cooled with liquid air, connected to a high vacuum system (0.005 mmHg). The product was collected and sublimed at 50-60°C and 0.005 mmHg to yield 2-fluoromethyl - 4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (173) (0.1740g) (81%), which was identified by direct comparison of its I.R, $^{19}F$ and $^{1}H$ n.m.r. spectra with those of authentic material, previously prepared.

### Reaction of 1,3,4,5,6,7,8 - Heptafluoro - 2 - naphthyl Prop-2-ynyl Thioether (171) with p-xylene at 160°C in a Nickel Tube.

The thioether (171) (0.8554g) and dry p-xylene (10ml) were sealed in a nickel Carius tube and heated at 160°C for 24h. The red reaction product was washed from the tube using acetone, the solvent was then evaporated and the excess p-xylene removed by freeze drying at 0.005 mmHg. The crude product was sublimed at 100°C / 0.005 mmHg and the sublimate chromatographed on silica (20cm x 6cm diam.) (using a 70:30 v/v mixture of carbon tetrachloride and chloroform respectively as the elutant.) The major component (0.557g; 51%) was crystallised from light petroleum (bp. 80-100°C) to give 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (177) mp 110-111°C. (Found: C, 61.2; H,3.3%. $C_{21}H_{12}F_6S$ requires

C,61.5; H,3.0%) $\delta_F$ ($CDCl_3$) 139.6(d), 142.0 (t), 145.9(d of m, peri-F $J_{7,8}$ 64Hz), 152.3(d of d, peri-F) and 157.7 ppm (bd) in the ratio 1:1:1:1:2 $\delta_H$ ($CDCl_3$) 2.31($C\underline{H}_3$ 2.28($C\underline{H}_3$), 4.25(S,$C\underline{H}_2$), 7.03(m, $C_6\underline{H}_3$) and 7.70 ($\underline{H}$ at ring position 3).

### Reaction of 1,3,4,5,6,7,8 - Heptafluoro -2-naphthyl Prop-2-ynyl Thioether (171) With Benzene at 160°C in a Nickel Tube.

The thioether (171) (0.4516g) and dry benzene (10ml) were sealed in nickel Carius tube and heated at 160°C for 25h. The crude product (a dark brown oil) was washed from the tube with acetone and an analytical T.L.C. of this solution showed there were at least 4 compounds present in the product mixture. Fractional sublimation of the crude product at 60, 80, 100°C / 0.005 mmHg, followed by flash chromatography of the sublimate (using 70:30 solution of carbon tetrachloride and chloroform as elutant) gave 2-benzyl- 4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (176) (0.083g) (16%). Crystallisation from light petroleum (bp. 60-80°C) gave the pure compound (176) m.p. 95-96°C, identified by comparing its I.R. and $^{19}F$ n.m.r. spectra with those of authentic material (see page 84).

### Reaction of 2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) Thiophen (173) With p-xylene in Boron Trifluoride etherate.

The fluoromethyl compound (173) (0.117g) was dissolved in dry p-xylene (2ml) and boron trifluoride etherate (1ml) was added to the mixture. The solution was stirred for 15 min. at 25°C, generating a dark blue colour which disappeared on dilution with water. The reaction product was extracted with ether, the extracts dried ($MgSO_4$) and the solvent was evaporated; the excess p-xylene was distilled at 25°C /0.005 mmHg. The single reaction product (shown by analytical TLC on silica using a 70:30 mixture of carbon tetrachloride and chloroform as the solvent) was sublimed at 80°C / 0.005 mmHg to give the 2-(2,5 dimethylbenzyl) derivative (177) (0.1294g; 87%) which was identified by comparing its I.R. spectrum with that of an authentic sample.

## Reaction of 2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) Thiophen (173) With Benzene in Boron Trifluoride Etherate.

The 2-fluoromethyl derivative (173) (0.116g) was dissolved in dry benzene (1ml) and boron trifluoride etherate (1ml) was added to the mixture. The solution was stirred at room temperature for 15min, generating a deep purple colour which disappeared on dilution with water. The product was extracted with ether, the extracts dried ($Mg\ SO_4$) and the solvents evaporated. The single reaction product (Shown by analytical T.L.C. on silica, using 70:30 mixture of carbon tetrachloride and chloroform as solvent) was sublimed at 70°C and the sublimate (0.122g; 89%) was recrystallised from light petroleum (bp. 60-80°C) to give the pure 2-benzyl-4,5,6,7,8,9-hexafluoronaphtho-(2,1-b) thiophen (176) m.p. 95-96°C (Found: C,59.4; H, 2.0%. $C_{19}H_8F_6S$ requires C,59.7; H,2.1% $\delta_F$ ($CDCl_3$) 140.9(d), 143.6(t), 146.8(d of m, peri- F, $J_{7,8}$ 64Hz), 152.7 (d of d, peri-F) and 158.4 p.p.m. (bd) in the ratio of 1:1:1:1:2; $\delta_H$ ($CDCl_3$) 4.3(s, $C\underline{H}_2$), 7.3(s, $C_6\underline{H}_5$) and 7.8 p.p.m. (m,3-$\underline{H}$).

## A Semi-Kinetics Study of the Reaction Between 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Thioether (171) and p-Xylene at 160°C In a Nickel Tube.

The thioether (171) and dry p-xylene (20ml) were sealed in a nickel Carius tube and heated at 160°C for xh. (x = 6,12,18, and 24). The products were washed from the tube with acetone, which was then removed by evaporation. The excess p-xylene was removed by distillation in vacuo at 25°C and 0.005 mmHg, via a cold finger to ensure no loss of the relatively volatile fluoromethyl compound (173). The integrated $^1H$ and $^{19}F$ n.m.r. spectra were recorded (see table) and the crude products were fractionally sublimed at 60 and (90-100)°C. (in an attempt to record absolute yields). The reaction products were identified as: 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (173) and 2-(2,5 dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (177) by comparison of I.R. and

$^{19}$F n.m.r. spectra with those of authentic samples.

| TIME | (173) | (177) |
|---|---|---|
| 6 | 75 (64%*) | 25 (21%*) |
| 12 | 61 | 39 |
| 18 | 47 | 53 |
| 24 | 0 | 100 (50%) |

* Are actual yields.

## Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Thioether (171) With p-Xylene at 140°C in a Nickel Tube.

The thioether (0.265g) and dry p-xylene (20ml) were sealed in a nickel Carius tube and heated at 140°C for 24h. The crude yellow product was washed from the tube with acetone, which was then removed by evaporation. The excess p-xylene was removed at 25°C and 0.005 mmHg via a cold finger to prevent possible loss of the relatively volatile fluoromethyl compound (173). The crude product was sublimed at 60°C to give 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) thiophen (173) (0.1628, 61%) which was identified by comparing its I.R. spectrum with that of an authentic sample. The presence of 2-(2, 5- dimethyl benzyl) - 4,5,6,7,8,9 -hexafluoronaphtho (2,1-b) thiophen (177) in the residue which did not sublime was inferred from $^{1}$Hn.m.r. data, and its yield was estimated, by using 2-fluoromethyl -4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furan (173) as an internal standard, as 4%.

## Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Thioether (171) With p-Xylene at 140°C in Glass Apparatus.

The thioether (171) (0.5734g) and dry p-xylene (30ml) were heated under reflux at 140°C for 24h. The excess p-xylene was evaporated at 25°C / 0. 005 mmHg via a cold finger to ensure no possible loss of the relatively volatile fluoromethyl compound (173). The crude reaction product was examined by $^{19}F$ n.m.r. spectroscopy which showed that the 2-fluoromethyl compound (173) was <u>not</u> present. The crude product was fractionally sublimed at 80°C causing rapid sublimation of unchanged starting material (0.089g, 15%) (identified by $^{19}F$ n.m.r.), followed more slowly by the 2-(2,5 - dimethylbenzyl) derivative (177) (0.6236g, 85%) (identified by comparison of its I.R. spectrum with that of the authentic material).

### Attempted Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Thioether (171) with Benzene in Glass Apparatus.

The thioether (171) (0.2087g) and dry benzene (15ml) were heated under reflux at 78°C. 5ml solutions were withdrawn from the reaction mixture at 24 and 48h, and analysed by $^{19}F$ n.m.r. spectroscopy. The $^{19}F$ n.m.r. spectra showed <u>only</u> unchanged starting material, and consequently the reaction was terminated, as the conditions were considered too mild to induce a reaction.

### The Vapour Phase Pyrolysis Of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Ether (15

The ether (156) (0.175g) was distilled by gentle warming through a silica tube (60cm x 1.5 cm diam., the central section (20cm) being packed with silica fibre) and heated to 360°C into a trap cooled by liquid air, connected to a high vacuum system (0.005 mmHg). The yellow/green product was shown by $^{19}F$ n.m.r. and analytical T.L.C. data to contain the 2-fluoromethyl compound (161) as the major component as well as several unidentified compounds. Preparative thick layer chromatography of the crude product on silica (50:50 v/v mixture carbon tetrachloride and chloroform) followed by sublimation of the enriched product at 50°C / 0.005 mmHg gave the pure 2-fluoromethyl compound (161) (0.076g, 43%) which was confirmed by analysis of its $^{19}F$ n.m.r. and I.R. spectrum.

### Reaction of 1,3,4,5,6,7,8 Heptafluoro-2-naphthyl Prop-2-ynyl Ether (156) With p-Xylene at 140°C in a Nickel Tube.

The ether (156) (0.284g) and dry p-xylene (20ml) were sealed in a nickel Carius tube and heated at 140°C for 20h. The contents of the tube were removed by washing with acetone, and the solvents were distilled at 12 mmHg (to remove the acetone), and then at 0.005mmHg / 25°C to remove the p-xylene via a cold finger to ensure no loss of the relatively volatile fluoromethyl compound (161). The crude product was sublimed at 80°C / 0.005 mmHg and the sublimate (0.157g) was analysed by $^1H$ n.m.r., 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) and 2-(2, 5-dimethylbenzyl)-4,5,6,8,9-hexafluoronaphtho (2, 1-b) furan (159) were present to the extent of 90 parts and 10 parts respectively. (representing yields of 48% and 5% respectively.).

### Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Ether (156) With p-Xylene at 140°C In Glass Apparatus.

The ether (156) (0.257g) and dry p-xylene (20ml, distilled from $P_2O_5$) were heated together under reflux at 140°C in a glass reaction vessel for 20h. The excess p-xylene was removed by distillation at 25°C / 0.005 mmHg. via a cold finger to ensure no loss of the relatively volatile 2-fluoromethyl compound (161), and the crude product was sublimed at 80°C / 0.005 mmHg. Examination of the sublimate by $^{19}F$ and $^1H$ n.m.r. failed to reveal the presence of any fluoromethyl compound (161); only one product was present, identified by I.R. spectroscopy as 2-(2, 5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furan (159) (0.2046g 62%

### Reaction of 2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furan (161) With p-Xylene at 140°C In Glass.

The fluoromethyl derivative (161) (0.2814g) and dry p-xylene (20ml) were heated under reflux in a glass reaction vessel for 20h at 140°C. The excess p-xylene was removed by distillation at 25°C / 0.005 mmHg via a cold finger to ensure no possible loss of the relatively volatile starting material. Examination of the crude reaction product by $^{19}$F and $^{1}$H n.m.r. spectroscopy confirmed the absence of any unreacted starting material. The reaction product was crystallised from ethanol to give 2-(2, 5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furan (159) (0.2802g, 78%) which was identified by I.R. spectroscopy.

## Reaction of 1,3,4,5,6,7,8-Heptafluoro-1-(propa-1,2-dienyl) - Naphthalen - 2 - one (157) With p-Xylene In Boron Trifluoride Etherate.

The propa-1,2 diene (157) (0.029g) was dissolved in dry p-xylene (1ml) and boron trifluoride etherate (0.5ml) was added to the mixture. Preliminary experiments at 25°C (140min) and 100°C (300min) gave only unreacted staring material, so the solution was heated under reflux at 120°C with an external bath temperature of 140°C for 180 min. The reaction mixture was diluted with water, extracted with ether and the extracts dried ($MgSO_4$). The ether was evaporated and the excess p-xylene distilled at 25°C / 0.005 mmHg via a cold finger to prevent possible loss of the relatively volatile 2-fluoromethyl compound (161). The reaction product was analysed using $^{1}$H n.m.r. and it was found that 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161) was <u>not</u> present and that the ratio of 2-(2, 5-dimethylbenzyl) - 4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (159) to the unreacted propa-1,2-diene was 15;85 respectively.

## Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Ether (156) And Isopropylbenzene At 142°C In A Nickel Tube.

The ether (156) (0.5547g) and isopropylbenzene (10ml) were sealed in a nickel Carius tube and heated at 142°C for 24h. The reaction product was washed from the tube using acetone and the solvent was distilled using a rotary evaporator. The excess isopropylbenzene was removed by distillation at 40°C / 0.005 mmHg via a cold finger to prevent possible loss of the relatively volatile fluoromethyl compound (161). Analytical TLC (on silica using a 50:50 v/v solution of carbon tetrachloride and chloroform as the solvent) of the crude product indicated the presence of three major compounds, which were fractionally sublimed and identified by $^{19}F$ n.m.r. analysis as : 2-fluoromethyl-4,5,6,7,8,9 hexafluoronaph (2,1-b) furan (161) (0.102g; 18%), di-(4,5,6,7,8,9-hexafluoronaphtho (2, 1-b)-furan-2-yl methyl) ether (162) (0.062g; 6%) and isomeric 2-(isopropylbenzyl) 4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furans (160) (0.035g; 5%).

## Isomerisation Of 3,3-Dimethylbut-1-ene With HF.

3,3-Dimethylbut-1-ene (10ml, 6.505g) was placed in a nickel Carius tube (vol. 80ml) at 0°C, which was then weighed. Liquid hydrogen fluoride from a cylinder was then dropped into the tube which was rapidly reweighed sealed and heated at 150°C for 20h. The contents of the tube were diluted with water and the organic layer was separated and dried (Mg $SO_4$). The $^1H$ n.m.r. spectrum of the hydrocarbon was recorded and the degree of isomerisation calculated from the integrated spectrum. It was found that 0.3g HF induced 24% isomerisation, i.e. 1.57g $(CH_3)_2C{=}C(CH_3)_2$ was produced in the experiment. In a typical reaction of 13,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (156) (2g) and 3,3-dimethylbut-2-ene (12ml) the maximum amount of HF which could be produced is ca 0.13g. Assuming that the amount of 2,3-dimethylbut-2-ene formed in the isomerisation reaction is directly proportional to the amount of HF present (and ignoring the difference in volume of the terminal alkene used in the control experiment and in a typical experiment with (156)) the maximum amount of $(CH_3)_2C{=}C(CH_3)_2$ which would be produced by 0.13gHF inducing isomerisation of 3,3-dimethylbut-1-ene is 0.68g, and only 0.55g would be required for a complete reaction with 2g of ether (156). (To produce a mixture of (186) and (187) in the amount given in Table (1) would require only 0.17g $(CH_3)_2C{=}C(CH_3)_2$.)

### Reaction of 2-Fluoromethyl-4,5,6,7-tetrafluorobenzo (b) Furan (150) with p-Xylene in Boron Trifluoride - Etherate.

The furan derivative (150) (0.053g) was dissolved in dry p-xylene (1ml) and boron trifluoride etherate (0. 5ml) was added to the mixture. The homogeneous solution was stirred for 150min. at room temperature, diluted with water, and then extracted with ether. The extracts were dried ($MgSO_4$), the ether removed by rotary evaporation and the excess p-xylene removed by distillation in vacuo at 40°C and 0.005 mmHg. Analytical TLC of the residue (on silica using light petroleum (bp30-40°C) as the elutant), showed there was only one component present, which was identified as 2-(2,5-dimethylbenzyl)-4,5,6,7-tetrafluorobenzo (b) furan (152) (0.072g) (98%) by direct comparison of its I.R. spectrum with that of an authentic sample.

### Reaction of 2-Fluoromethyl-4,5,6,7,8,9-Hexafluoronaphtho (2,1-b) Furan (161) With p-Xylene in Boron Trifluoride - Etherate.

The furan derivative (156) (0.071g) was dissolved in diethyl ether (1ml) and added to dry p-xylene (1ml). Boron trifluoride-etherate (0.5ml) was added to the mixture and the homogeneous solution stirred at room temperature for 150min. The mixture was diluted with water, extracted with ether and the extracts dried ($Mg\ SO_4$). The solvent ether was evaporated and the excess p-xylene was removed by evaporation in vacuo at room temperature at 0.005 mmHg. Analytical TLC of the residue (on silica using light petroleum b.p. 30-40°C as the solvent) showed that only one component was present which was identified as, 2-(2,5-dimethylbenzyl) -4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furan (159) (0.089g) (98%) by direct comparison of its I.R. and N.m.r. spectra with those of an authentic sample.

### Reaction of 2-Fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) Furan (156) With 3,3- Dimethylbut-1-ene in Boron Trifluoride Etherate.

### (a) Isolation of Major Component 2-(3,4-dimethylpent-3-enyl)-4,5,6,7,8,9-Hexafluoronaphtho (2, 1-b) furan (194)

The 2-fluoromethyl compound (161) (0.498g) dissolved in diethyl ether (5ml) was mixed with 3,3-dimethylbut-1-ene (5ml). Boron trifluoride etherate (2.5ml.) was added to the mixture which was stirred at 25$^{\circ}$C for 180 min. The solution was diluted with water, extracted with ether and the extracts dried (Mg SO$_4$). Analytical TLC (on silica using light petroleum b.p. 30-40$^{\circ}$C as the solvent) of the ether extracts showed there to be a fast moving fraction, containing at least three components and a single slower moving component. The fast moving components were separated from the major slower moving compound by subliming the crude product at 70-80$^{\circ}$C / 0.005 mmHg. Flash chromatography of the sublimate (0.132g.;22%) (on silica using light petroleum b.p. 30-40$^{\circ}$C as elutant) and recrystallisation from light petroleum b.p. 40-60$^{\circ}$C gave pure 2-(3,4 -dimethylpent-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furan (194) m.p. 87.5-88.5$^{\circ}$C. Found: C,61.5; H,4.0%; $M^+$,372. $C_{19}H_{14}F_6O$ requires C,61.3; H,3.8%; M,372); $\delta_F$(CDCl$_3$) 145.3-146.8 (broad m), 151.9 (d of d, peri- F $J_{7,8}$ 62Hz), 157.8-159.4 p.p.m. (broad m), with intensities in the ratio 2:1:3 respectively; $\delta_H$(CDCl$_3$) 1.643 (m, 2 x $C\underline{H}_3$), 1.697(m,1 x $C\underline{H}_3$), 2.52(t, $C\underline{H}_2$), 2.92(t, $C\underline{H}_2$) and 6.96 (overlapping d of d, $\underline{H}$ at ring position 3.).

The slower moving component was shown by $^1$H n.m.r. and i.r. spectroscopy to be di-(4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furan-2-ylmethyl) ether (162).

(b) Determination of the Product Ratios

(i) At 25°. The experiment described in (a) was repeated at 25° with the fluoromethyl compound (161) (0.512g) diethylether (5ml), 3-3dimethylbut-1-ene (5ml) and boron trifluoride etherate (2.5ml). The mixture of fast moving components (by TLC) was first separated from the slower moving component by flash chromatography on silica using light petroleum (bp40-50°), then sublimed at 70-80° / 0.005mmHg. and the sublimate (0.160g, 26%) analysed by $^1$H nmr spectroscopy. The ratio of identifiable components (186) : (194): unidentified material was 6;94 ; 27.

A simple calculation shows that the amount of compound (186) in the sublimate (0,16x6/127g) requires 0.0017g $(CH_3)_2C=C(CH_3)_2$ for its formation; for an experiment on 1/5 scale (i.e. using 0.1g (156)) 0.00034g$(CH_3)_2C=C(CH_3)_2$ would be required (see C later).

(ii) At -50°. The 2-fluoromethyl compound (161) (0.222g) dissolved in diethylether (3ml) was added over 5 min. to a mixture of 3,3-dimethylbut-1-ene (3ml) and boron trifluoride etherate (1.5ml) pre-cooled to -70°. The mixture was stirred for 30min at -30° and then allowed to warm to room temperature over 1h. The work up procedure described in (a) was repeated and the crude reaction product was sublimed at 70-80° / 0.005 mmHg. The sublimate (0.098g, 37%) was analysed by $^1$H n.m.r. The ratio of identifiable compounds (186):(194): Unidentified material was 8:92:47. The non-sublimable residue was compound (162.)

(c) Demonstration of the formation of 2,3-dimethylbut-2-ene during the reaction (experiment done on 2/5 scale of experiment (b)).

A solution of the 2-fluoromethyl compound (161) (0.217g; 7x10-4 mole) in diethylether (2ml) and 3,3-dimethylbut-1-ene (2ml) was stirred with boron trifluoride etherate (1ml) at 25°C for 180min. The volatile components were distilled at room temperature / 0.005 mmHg and collected using a vacuum line technique. The analysis of this distillate by G.L.C. (column O, 10% SE 30 at 53°), showed qualitatively that 2,3-dimethyl but-2-ene was present in the mixture.

Quantitative estimation of this alkene was made using a standard injection procedure (by comparing the result with those obtained from standard solutions made from known volumes of 2,3-dimethylbut-2-ene added to diethylether (2vol) 3,3-dimethlbut-1-ene (2vol) and $BF_3$-etherate (1vol) and which had been worked up from water as before)

The analysis showed that 2,3-dimethylbut-2-ene (2.1x10$^{-4}$ mole) was present in the reaction mixture <u>after</u> the reaction of the 2-fluoromethyl compound (161) (7x10$^{-4}$ mole) with 3,3-dimethylbut-1-ene had taken place. Assuming that the same proportion of compound (186) is formed in this experiment as is found in experiment (b) the amount of $(CH_3)_2C{=}C(CH_3)_2$ required for its production is 0.00068g (0.0017 x 2/5g, 8x10$^{-6}$mole). This clearly demonstrates that far more internal alkene than is necessary is produced.

The isomerisation of the terminal alkene to the internal alkene had presumably occured due to the release of HF during the reaction. This hypothesis was tested by adding known amounts of HF (instead of compound (161)) to a mixture of diethylether (2vol), 3,3-dimethylbut-1-ene (2vol) and $BF_3$-etherate (1vol), stirring the mixtures at 25° for 150min. and finally adding water and using the injection procedure as was used with the standard solutions of 2,3-dimethylbut-2-ene prepared for the calibration.

(i) Five standard solutions, containing 3,3-dimethylbut-1-ene (1ml), boron trifluoride-etherate (0.5ml), diethyl ether (1ml, used to homogenize the mixture) and x of 2,3-dimethylbut-2-ene (where x = a) 2µl b) 4µl c) 8µl d) 16µl and e) 32µl) were prepared at room temperature diluted with water and the organic layer dried over $MgSO_4$ and analysed using G.L.C. on Column O (10% SE 30) at 46°C.

(ii) A further five solutions containing 3,3-dimethylbut-1-ene (1ml), boron trifluoride etherate (0.5ml) and diethyl ether (1ml) (i.e. the same amounts as in the controlled experiments in (i)) and x drops of hydrogen fluoride (where x = a) 0: b) 1: d) 4: and e)8 ) were prepared, stirred at room temperature for 150min. and then diluted with water. The surface layer was pipetted off, dried over $MgSO_4$ and analysed by GLC.

(The HF was introduced dropwise into the reaction vessels using a constant flow rate in an attempt to keep each drop a constant weight. The weight of one drop of HF in this experiment was estimated to be 0.0077g, determined by dropping 10 drops of the HF into an ice-cooled preweighed flask).

Results

Standard Solutions of $Me_2\ C = C\ Me_2$ (X µl) In $CH_3C(CH_3)_2CH = CH_2$(1ml) $Et_2\ O$ (1ml) And $BF_3\ (C_2\ H_5)_2\ O$(0.5ml)

| $Me_2\ C = C\ Me_2$ (X µl) | (Corresponding) Area for a 5µl injection cm² |
|---|---|
| 2 | 0.0525 |
| 4 | 0.1 |
| 8 | 0.1925 |
| 16 | 0.375 - 0.40 |
| 32 | 0.75 - 0.80 |

| Drops of HF | Wt. of HF (g) | Area of $Me_2C{=}CMe_2$ for a 5µl injection (CM²) | Equivalent Volume of $Me_2C{=}CMe_2$ | Equivalent Wgt. of $Me_2C{=}CMe_2$ | % Isomerisation |
|---|---|---|---|---|---|
| 1 | 0.0077 | 0.0525 | 2 | 0.0014 | 0.2% |
| 2 | 0.0154 | 0.1275 | 5 | 0.0035 | 0.54% |
| 4 | 0.0308 | 0.225 | 9 | 0.0064 | 1% |
| 8 | 0.0616 | 0.43 | 17 | 0.0121 | 1.9% |

It is estimated that 0.0065g of HF (which would be released by the complete reaction of 0.1g of the 2-fluoromethyl compound (161))would produce $1.20 \times 10^{-3}$g $(CH_3)_2C{=}C(CH_3)_2$, which is more than three times the amount required ($3.4 \times 10^{-4}$g) to produce the small proportion of compound (186) formed in experiment (b)(i).

## The Preparation of 2-Chloromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan.

The 2-fluoromethyl compound (161) (0.1755g) dissolved in 1,1,2-trichloro-1,2,2-trifluoroethane (5ml) was mixed with aluminium trichloride in acetonitrile (1ml, 0.87M). The solution was heated under reflux for 3h, diluted with water, and extracted with ether. The extracts were dried ($MgSO_4$) and the ether evaporated. The single reaction product (indicated by analytical TLC on silica using a 50:50 mixture of carbon tetrachloride and chloroform as solvent) was sublimed at 60°C / 0.005 mmHg and the sublimate (0.1289g: 70%) was crystallised from light petroleum (b.p. 40-60°C) to give <u>2-chloromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161a)</u> m.p. 73.5-74°C. (Found: C, 48.4; H, 1.3%. $C_{13}H_3ClF_6O$ requires C, 48.1; H, 0.9%) $\delta_F$ ($CDCl_3$) 144.5-146.5 (broad m), 148.8 (d of d, peri- F $J_{7,8}$ 67Hz), 154.9-158.1 (broad m) in the ratio 2:1:3 respectively; $\delta_H$ ($CDCl_3$) 4.82 (S, $C\underline{H}_2$) and 7.37 (t, <u>H</u> at ring position 3.)

## Reaction of 2-Chloromethyl-4,5,6,7,8,9-hexafluoronaphtho (2, 1-b) furan (161a) With 3,3-Dimethylbut-1-ene in the presence of Zinc Chloride

The chloromethyl compound (161a) (0.1133g; $3.5 \times 10^{-4}$ mole) in diethyl ether (1ml) was added to anhydrous $ZnCl_2$ (0.091g) stirred and kept under a nitrogen atmosphere throughout the experiment. 3,3-Dimethylbut-1-ene (1ml) was added and the mixture was heated under reflux (42°C under $N_2$) for 22h. The reaction mixture was diluted with water, the ether layer separated and the volatile components were distilled at room temperature / 0.005 mmHg using a vacuum line technique. G.L.C analysis of the distillate (Column O, 10% SE 30 at 52°C) showed the presence of 2,3-dimethylbut-2-ene which was estimated to be present to the extent of $2.9 \times 10^{-4}$ mol using the analytical method described previously. The residue from the distillation was sublimed at 70-80°C/·005mm Hg and the sublimate (0.1031g) was chromatographed (on silica using freshly distilled light petroleum b.p. 40-60°C as elutant) to isolate a mixture of faster moving components of similar $R_f$ values. $^1H$ n.m.r. spectroscopic analysis of this material showed that it contained compounds (196),(186),(194),and unidentified material in the ratio 15:68:17:30 respectively (0.672g; 55%). It seems that in this product, compound (196) has a different geometrical configuration about the double bond compared to the material isolated previously, in that the hydrogen at C-3 in the furan ring has $\delta$H7.04 compared to $\delta$H7.12 before; the shifts of other protons are essentially unchanged.

## Attempted Isomerisation of 3,3-Dimethylbut-1-ene in the presence of Zinc Chloride And Diethyl Ether.

Excess zinc chloride (0.8736g), diethyl ether (1ml) and 3,3-dimethylbut-1-ene (1ml) were mixed together and heated under reflux at 42°C for 21h. The solution was analysed using G.L.C. on Column, 0.10% SE 30 at 52°C. The G.L.C. data showed no trace of 2,3-dimethylbut-2-ene. (By passing standard solutions through the column it was possible to demonstrate the presence of 2$\mu$l of 2,3-dimethylbut-2-ene in 2 ml of diethyl ether).

## Appendix I : Analytical Instrumentation

I.R. : Perkin-Elmer 597 infra-red spectometer (4000 - 200 $cm^{-1}$)

N.m.r : The majority of $^1H$ and $^{19}F$ n.m.r. spectra reported in this thesis were recorded using either a Varian EM 360 spectrometer ($^1H$ at 60MHz; $^{19}F$ at 56.46 MHz) or a Bruker WX 90E spectrometer ($^1H$ at 90MHz, $^{19}F$ at 84.68 MHz).

However, in the experiments involving the reaction of 2-fluoronaphtho (2,1-b) furan (161) and 2-chloromethyl-4,5,6,7,8,9-hexafluoronaphtho (2,1-b) furan (161a) with 3,3-dimethylbut-1-ene in boron trifluoride etherate, the Bruker WH 360 spectrometer ($^1H$ at 360 MHz) was utilized.

Chemical shifts $\delta_F$ are upfield from internal $CFCl_3$ (except where stated); $\delta_h$ are downfield from internal TMS.

G.L.C. :PYE 104 Chromatograph, Column O, packed with 10% silicone elastomer (SE-10) on chromosorb P.

Elemental Analysis: Perkin-Elmer 240-C,H,N elemental analyser.

## Appendix (11) : Infra-red Spectra

SPECTRUM I : Pentafluorophenyl prop-2-ynyl thiother(I67)
(liquid film)

SPECTRUM 2 : 2-fluoromethyl-4,5,6,7-tetrafluorobenzo(b)thiophen(168)
(nujol mull)

SPECTRUM 3 : 2-benzyl-4,5,6,7-tetrafluorobenzo(b)thiophen(170)
(nujol mull)

SPECTRUM 4 : 2-(2,5-dimethyl)-4,5,6,7-tetrafluorobenzo(b)thiophen(169)
(nujol mull)

SPECTRUM 5 : 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho(2, 1-b)thiophen(173)
(nujol mull)

SPECTRUM 6 : 2-benzyl-4,5,6,7,8,9-hexafluoronaphtho(2,1-b)thiophen(176)
(nujol mull)

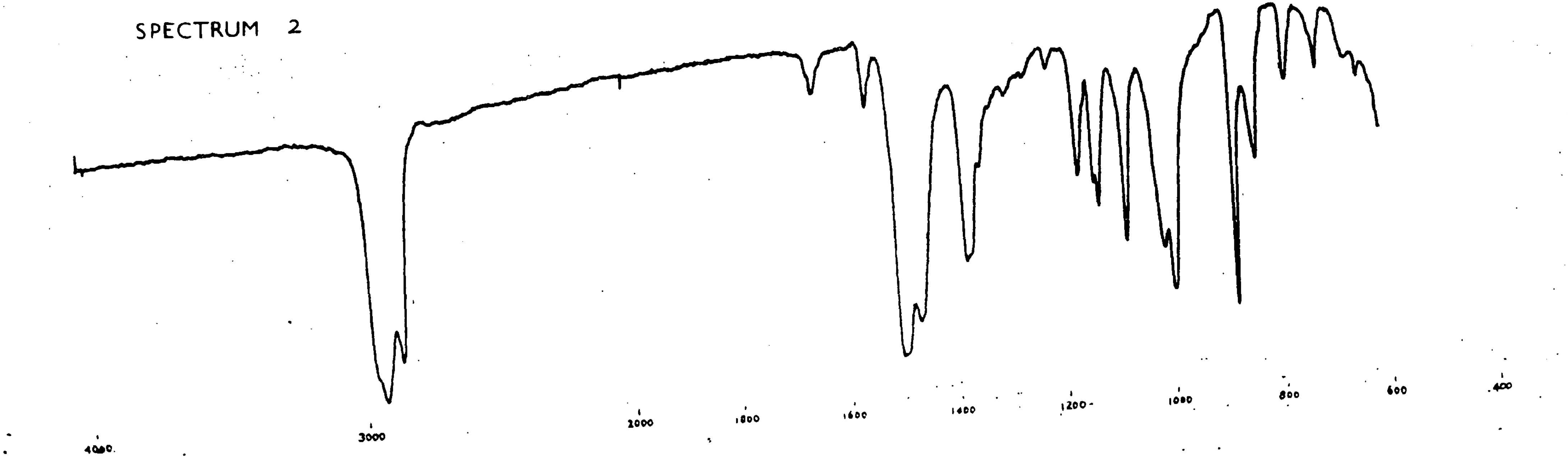
SPECTRUM 7 : 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho(2,1-b)
(nujol mull) thiophen(177)

SPECTRUM 8 : 2-chloromethyl-4,5,6,7,8,9-hexafluoronaphtho(2,1-b)furan(161)
(nujol mull)

SPECTRUM 9 : 2-(3,4-dimethylpent-3-enyl)-4,5,6,7,8,9-hexafluoro-
(nujol mull) naphtho(2,1-b)furan(194)

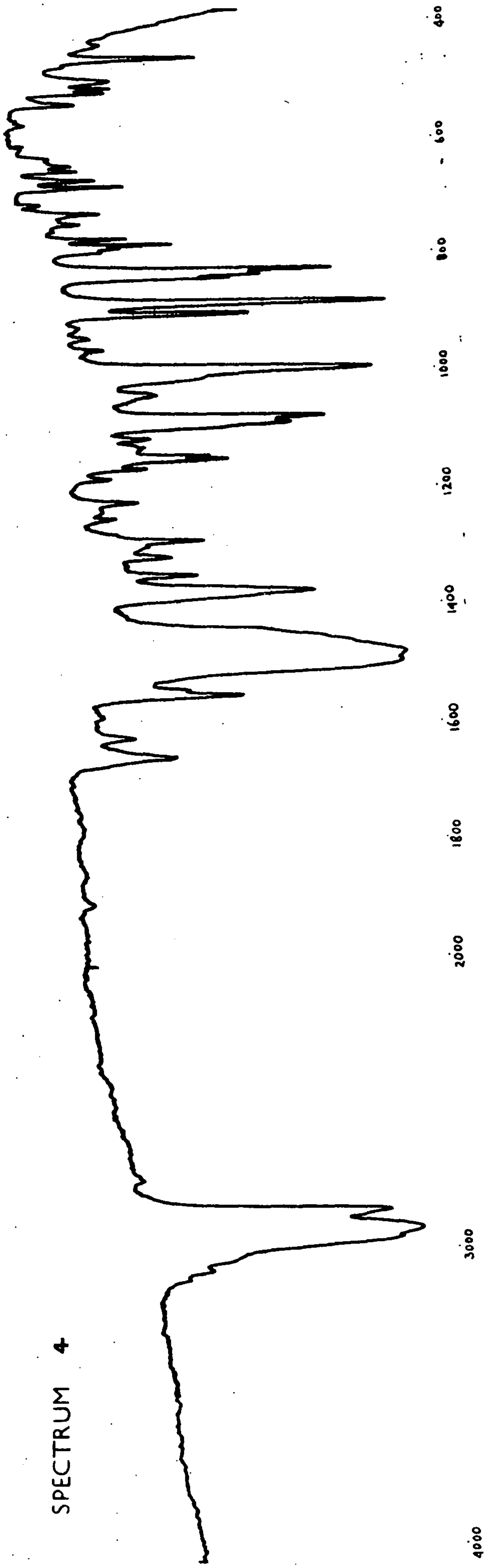
SPECTRUM 1

SPECTRUM 2

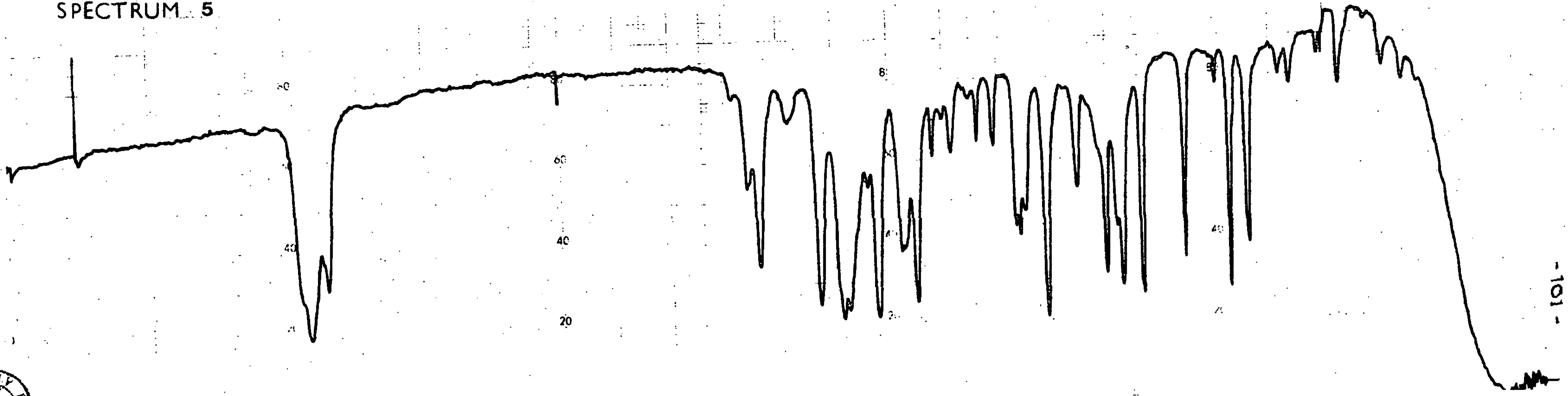


SPECTRUM 3

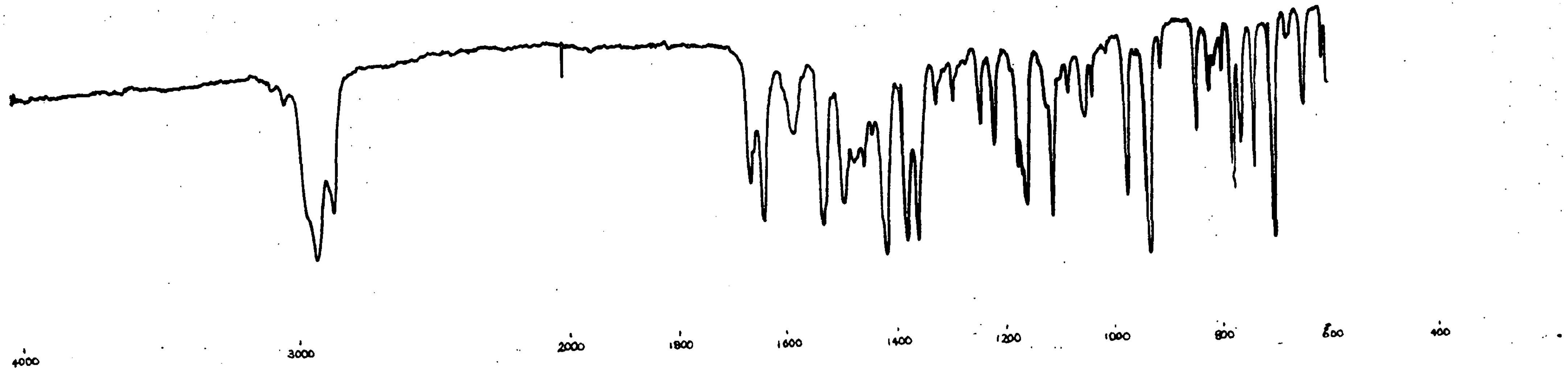
SPECTRUM 4



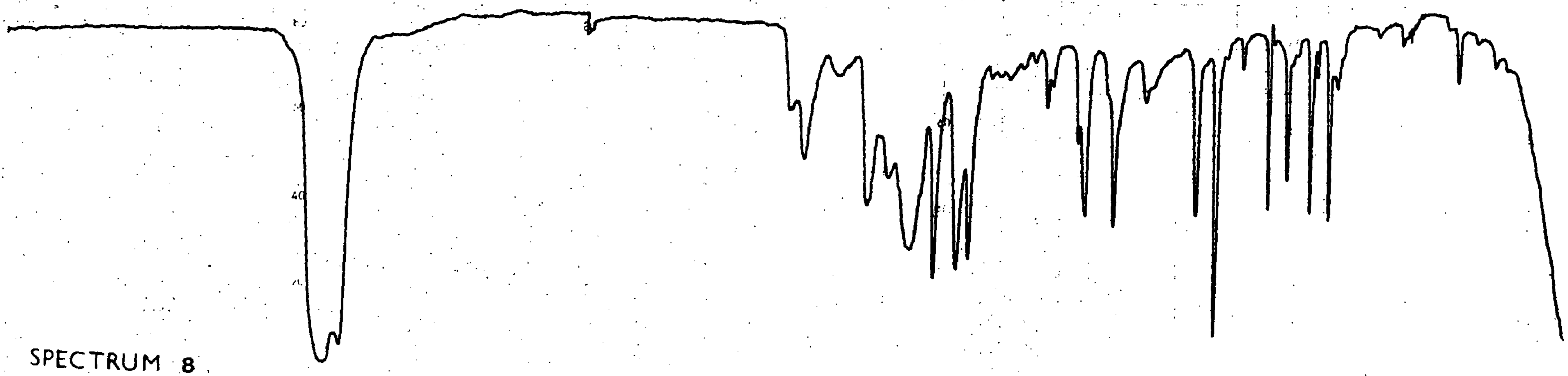
SPECTRUM 5



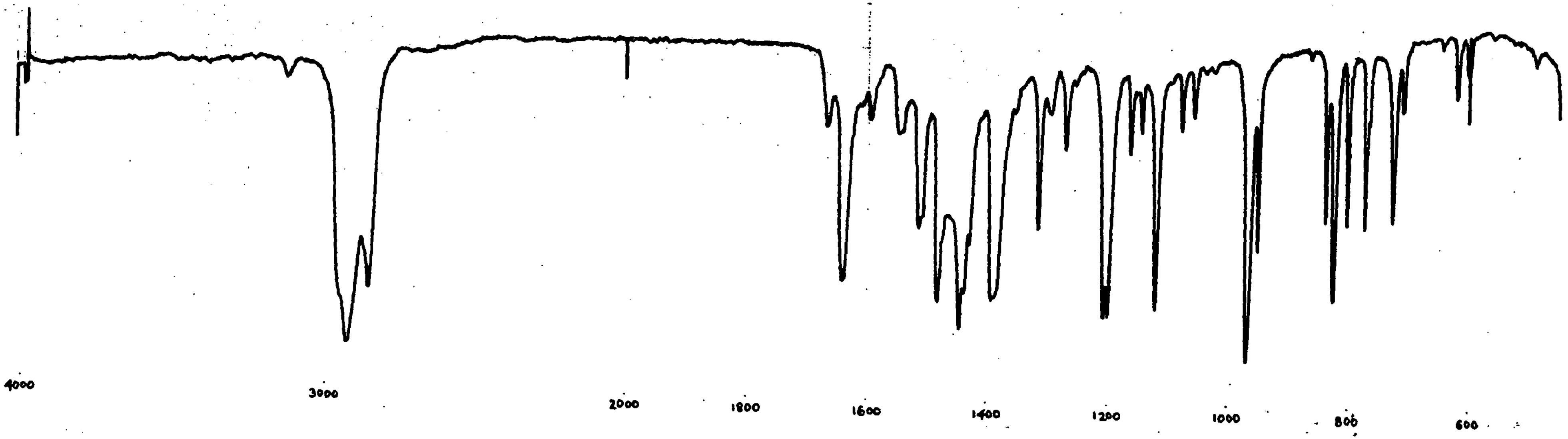
SPECTRUM 6

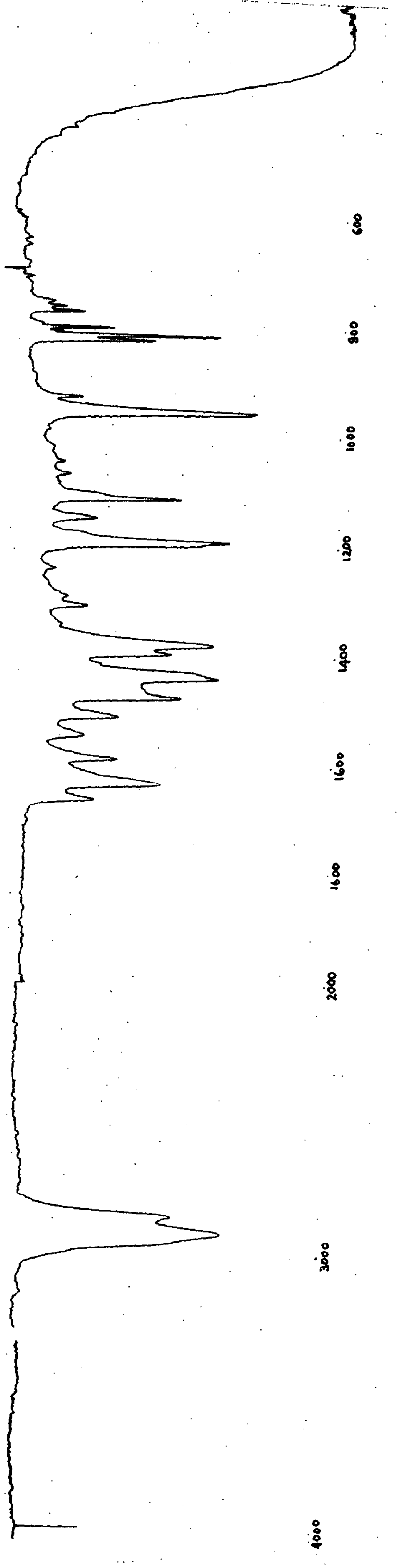


SPECTRUM 7



SPECTRUM 8





SPECTRUM 9

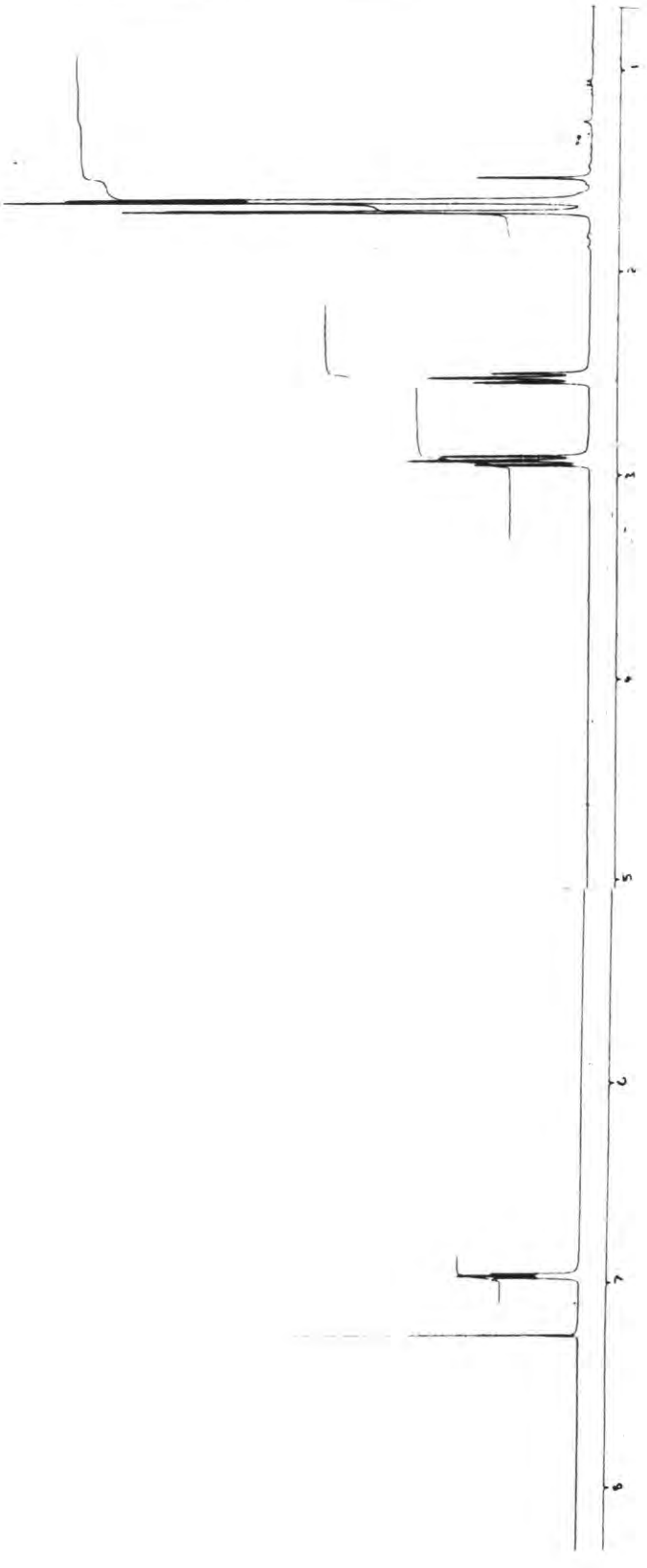
## Appendix(111) : Proton N.m.r. Analyses

SPECTRUM 10 : 2-(3,4-dimethylpent-3-enyl)-4,5,6,7,8,9-hexafluoronaphtho(2,1-b)furan(194)

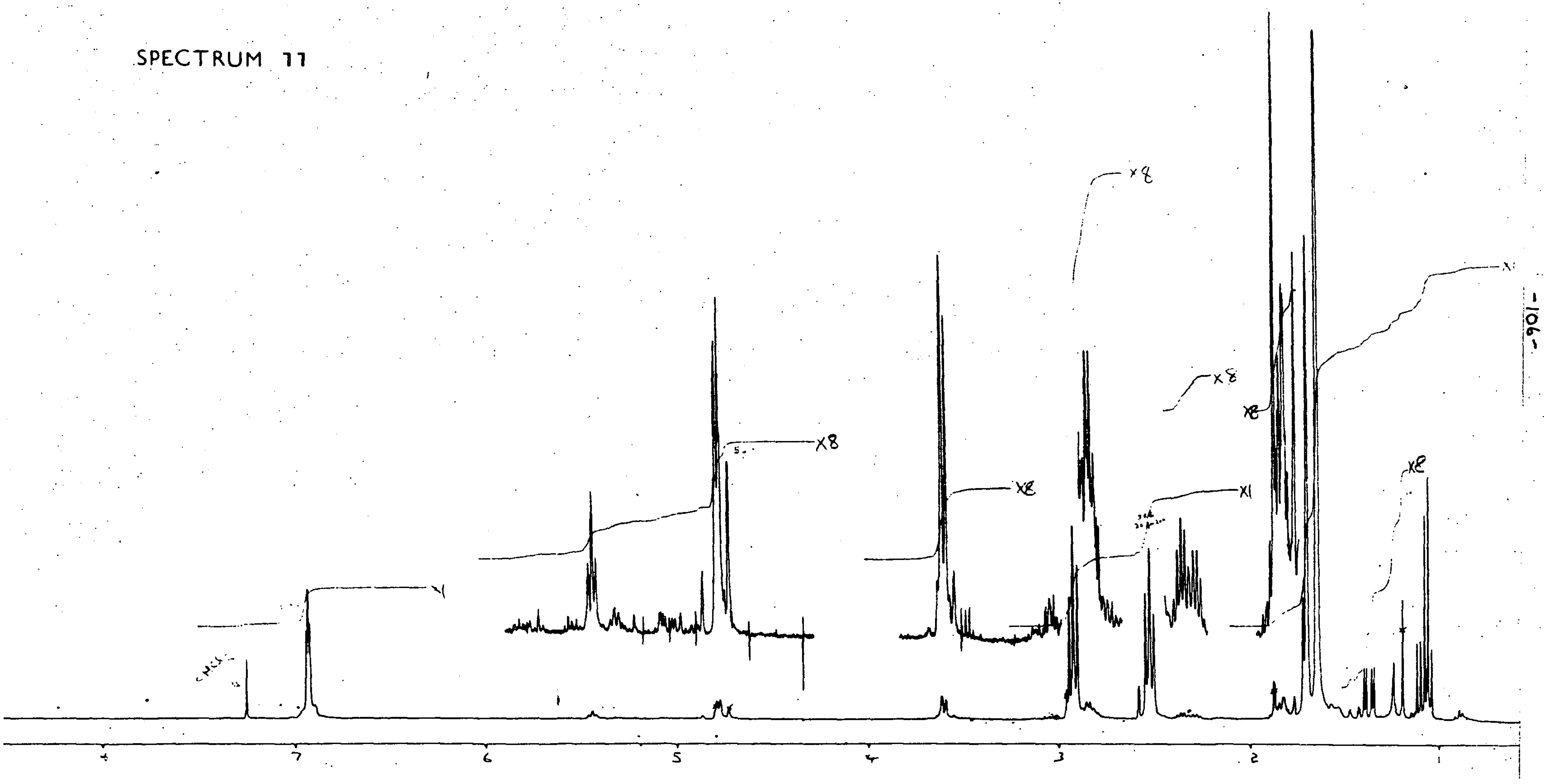
SPECTRUM 11 : Reaction of 2-fluoromethyl-4,5,6,7,8,9-hexafluoronaphtho-(2,1-b)furan(161) with 3,3-dimethylbut-1-ene in the presence of $BF_3.(C_2H_5)_2O$ at 25 C.

SPECTRUM 12 : Reaction of 2-chloromethyl-4,5,6,7,8,9-hexafluoronaphtho-(2,1-b)furan(161a) with 3,3-dimethylbut-1-ene in the presence of $ZnCl_2$.

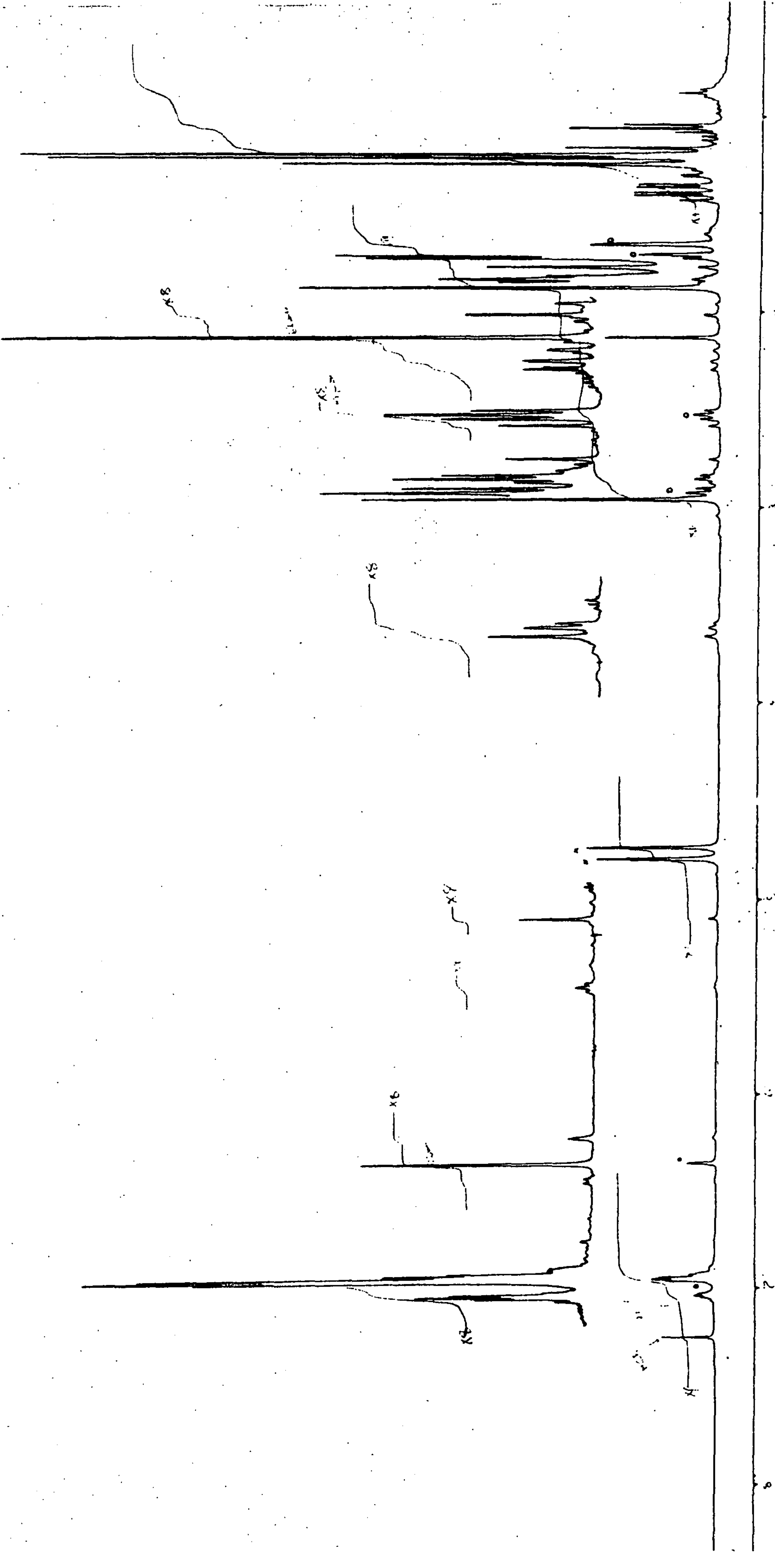
SPECTRUM 10



SPECTRUM 11



SPECTRUM 12



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