A study of the chemistry of some polyfluoroaromatic prop-2-ynyl ethers and prop-2-enyl thioethers

Derek Ian Wallis

A STUDY OF THE CHEMISTRY OF SOME POLYFLUOROAROMATIC PROP-2-YNYL ETHERS AND PROP-2-ENYL THIOETHERS

by

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TO MY PARENTS

Abstract

This work involves vapour phase and solution-phase studies of several polyfluoroaromatic prop-2-ynyl ethers and prop-2-enyl thioethers. When the prop-2-enyl thioether has a hydrogen ortho to the sulphur then a conventional thio-Claisen rearrangement occurs. However, if there are fluorine substitutents ortho to the sulphur then rearrangement to an ortho-dienethione is followed by homolysis of the carbon to fluorine bond of the carbon to which the prop-2-enyl group has migrated. Claisen rearrangement followed by homolytic cleavage of the carbon to fluorine bond of the carbon to which the prop-2-ynyl group migrates occurs for the prop-2-ynyl ethers, which have fluorine substitutents ortho to the oxygen.

The thesis is divided into six main parts. Chapter one deals with the literature on the Claisen and thio-Claisen rearrangements including the mechanistic development of the Claisen rearrangement.

Chapters two and three are concerned with the thermal reactions of pentafluorophenyl, 2,3,4,5-tetrafluorophenyl, and 2,3,5,6-tetrafluorophenyl prop-2-enyl thioethers. Chapter four describes attempted syntheses of the compounds arising out of the reaction of pentafluorophenyl prop-2-enyl thioether in N,N-diethylaniline.

Chapters five and six discuss the thermal chemistry of pentafluorophenyl and 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ethers.

The thesis ends with a general conclusion tying together the work on the prop-2-enyl thioethers with that on the prop-2-ynyl ethers.

Acknowledgements

I wish to thank Dr. G.M. Brooke for his considerable assistance and encouragement throughout the supervision of this work. I am grateful to Dr. R.S. Matthews for his help with n.m.r. spectra and to Dr. M. Jones for his help with mass spectra.

I would also like to thank the technical staff for their support, particularly Mr. R. Hart and Mr. T. Holmes. I am indebted to Dr. S. Bartlett for the presentation of the typescript and to my friends for their interest and encouragement.

Declaration

The work in this thesis was carried out in the Chemistry Laboratories of the University of Durham between October 1977 and August 1980. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

Notes to the Reader

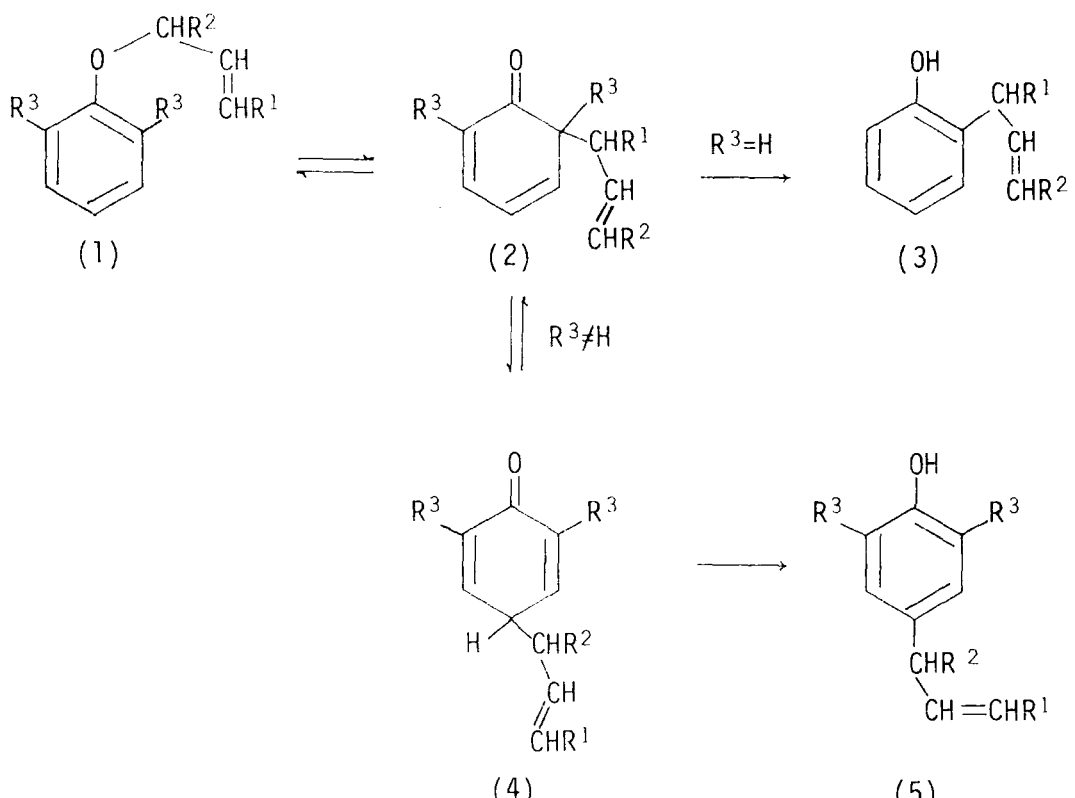
Throughout this thesis a number of abbreviations have been used regularly, these are: infra-red spectroscopy (i.r.); gas-liquid chromatography (g.l.c.); nuclear magnetic resonance spectroscopy (n.m.r.) and thin layer chromatography (t.l.c.).

Contents

Chapter 1 The Aromatic Claisen and Thio-Claisen Rearrangements

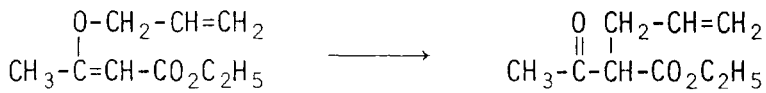
1.1 Introduction

The aromatic Claisen rearrangement involves the thermal transformation of a prop-2-enyl phenyl ether (1) into a 2-(prop-2-enyl)-cyclohexa-3,5-dienone (2), and there are many reviews on this subject[1]. When R^3 = H, the dienone (2), usually known as the ortho-dienone, rapidly tautomerises to the 2-(prop-2-enyl)-phenol (3). This overall process is known as the ortho-Claisen rearrangement. If $R^3 \neq H$, the dienone (2) undergoes a Cope rearrangement to give a 4-(prop-2-enyl)-cyclohexa-2,5-dienone (4), usually termed the para-dienone. The para-dienone (4) rapidly tautomerises to the para-substituted phenol (5) and this overall transformation is termed the para-Claisen rearrangement.



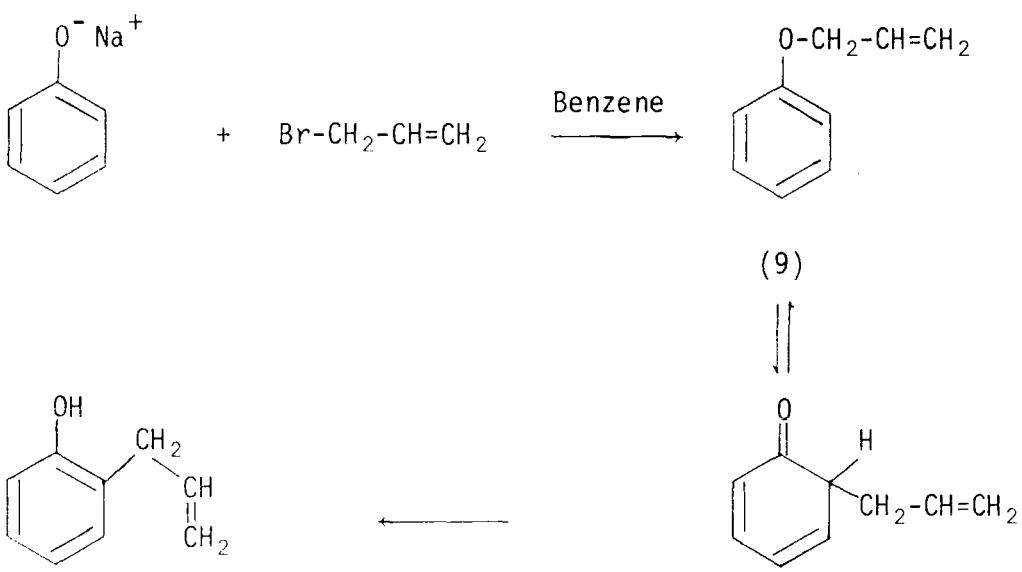
1.2 The Development of the Claisen Rearrangement of Aryl Prop-2-enyl Ethers

Claisen first reported the rearrangement of a prop-2-enyl vinyl ether (6) into ethyl prop-2-enylacetoacetate (7) during distillation at atmospheric pressure in the presence of ammonium chloride[2].



(6) (7)

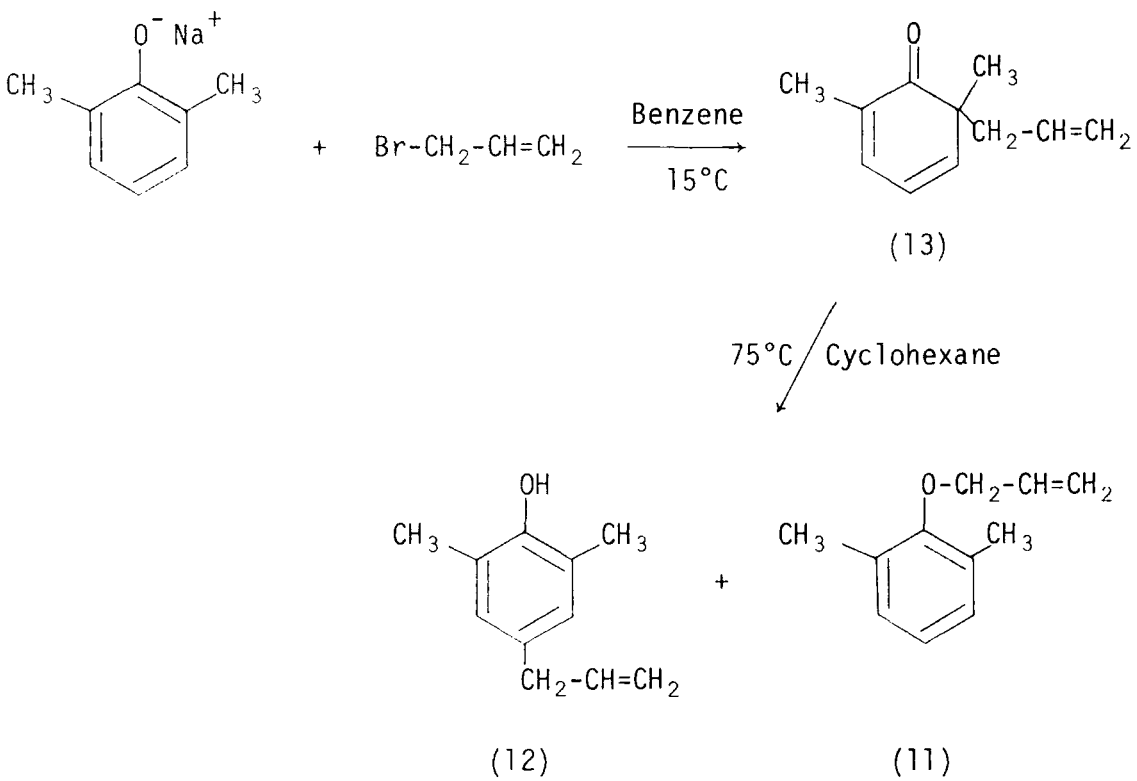
Soon after he noted that the reaction of sodium phenoxide and prop-2-enyl bromide in warm benzene gave 2-(prop-2-enyl)-phenol (8) and not the expected phenylprop-2-enyl ether (9)[3]. This reaction was thought to involve an intermediate ortho-dienone (10) by a process similar to the aliphatic ether (6) rearrangement[4].



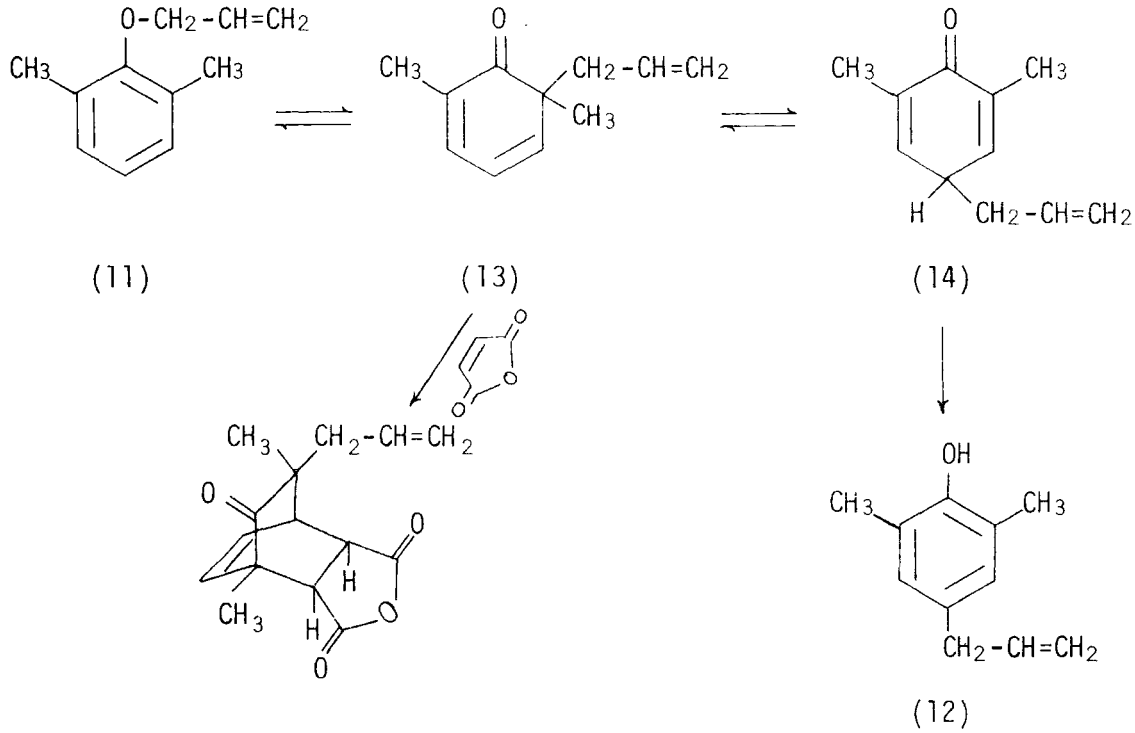
(8) (9) (10)

Furthermore the para-Claisen rearrangement of 2,6-dimethylphenyl prop-2-enyl ether (11) to 4-(prop-2-enyl)-2,6-dimethylphenol (12)

was shown to involve an ortho-dienone. Reaction of sodium 2,6-dimethylphenoxide and prop-2-enyl bromide in benzene at 15°C gave the ortho-dienone (13)[5]. This rearranged at 75°C in cyclohexane to give the prop-2-enyl phenyl ether (11) and the para-substituted phenol (12).

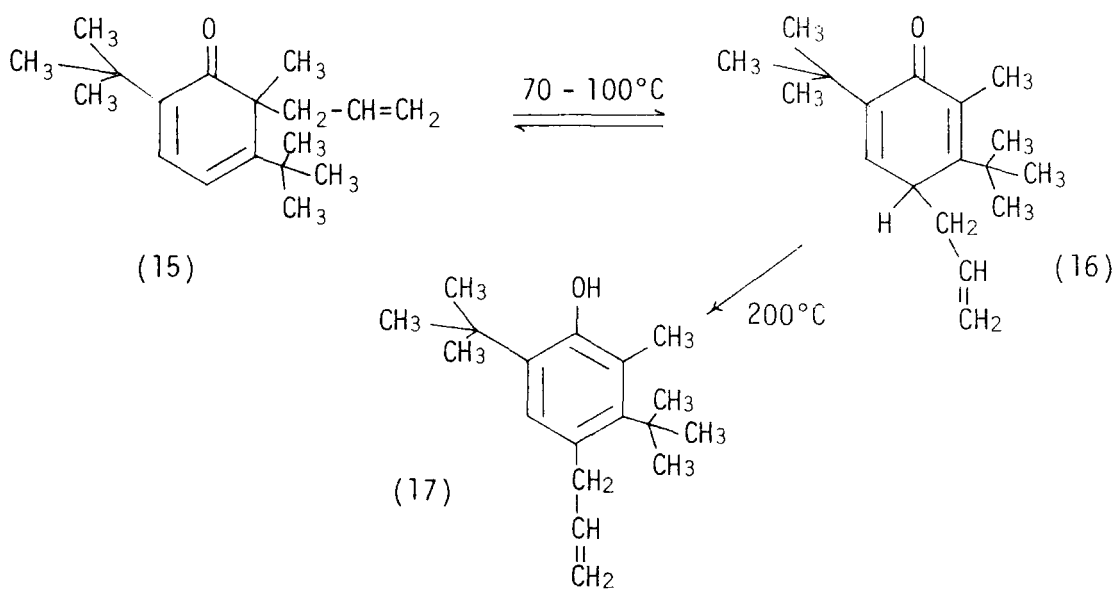


This showed that the ortho-dienone must be an intermediate in the aromatic Claisen rearrangement, and that the reaction must occur reversibly. The ortho-dienone (13) had previously been trapped out of the reaction mixture from the thermolysis of the ether (11), using maleic anhydride as the dienophile[6]. With the ortho positions blocked by methyl groups, the ortho-dienone (13) could not tautomerise and so an equilibrium was set up between the ether (11) and the two dienones (13) and (14). An excess of maleic anhydride ensured that reasonable quantities of the adduct were produced, since the removed dienone was replaced by re-establishment of the equilibrium.



(11) (13) (14) (12)

The stable 2-methyl-2-(prop-2-enyl)-3,6-di(1,1-dimethylethyl)-cyclohexa-3,5-dienone (15) rearranged to the para-dienone (16) between 70 - 100°C [7]. The latter tautomerised to the para-substituted phenol (17) on heating above 200°C. The stability of the para-dienone (16) is due to the large steric strain which develops in the aromatised product as a result of having an adjacent prop-2-enyl and 1,1-dimethylethyl group in the same plane. This reaction showed that para-dienones are intermediates in the para-Claisen rearrangement.

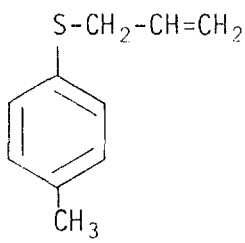


(15) (16) (17)

1.3 The Thio-Claisen Rearrangement of Aryl Prop-2-enyl Thioethers

Although most work on the Claisen rearrangement has been concentrated on aryl prop-2-enyl ethers and vinyl prop-2-enyl ethers, there are many reports in the literature on the thermal behaviour of aryl prop-2-enyl thioethers[1].

4-Methylphenyl prop-2-enyl thioether (18) was reported to give 2-(prop-2-enyl)-4-methylthiophenol (19) on refluxing for four hours at 228 - 264°C[8]. However, this was later disproved and the reaction shown to give 4-methylphenyl prop-2-enyl thioether (20) and condensation products arising out of its decomposition[9].



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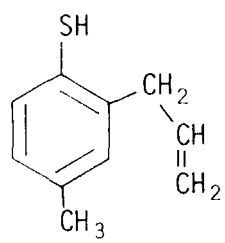

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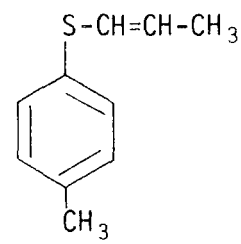
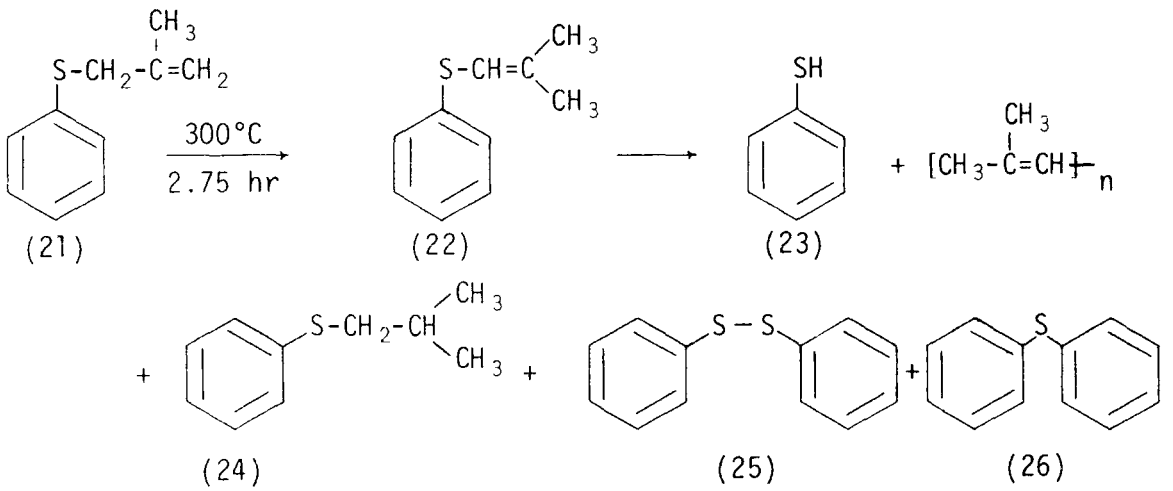


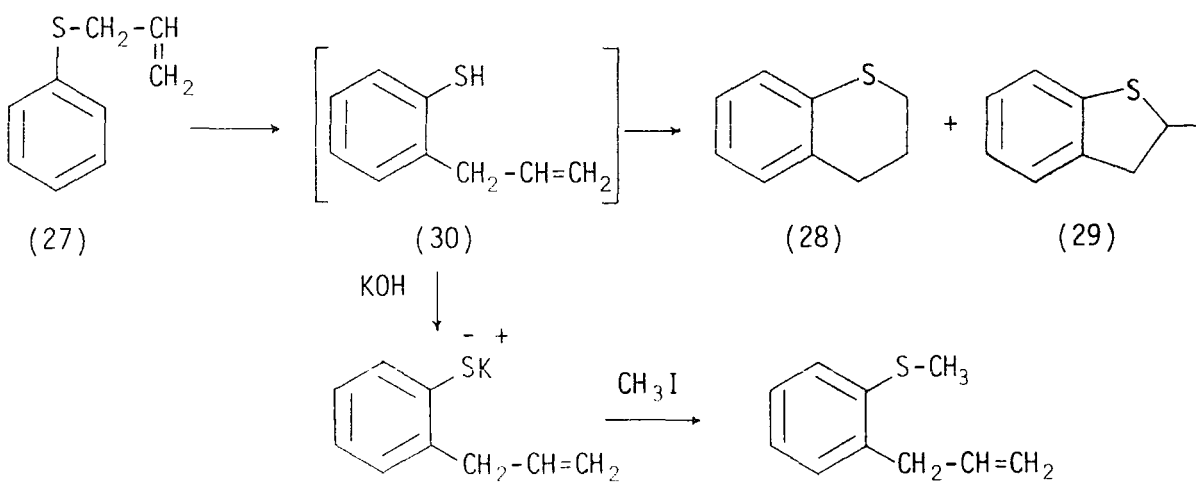
(20)

Similarly pyrolysis at 300°C of phenyl 2-methylprop-2-enyl thioether (21) led to isomerisation and decomposition[10]. The initial product, the thioether (22), was isolated in 1% yield, the rest undergoing cleavage to the thiophenol (23) and low boiling olefins. The thiophenol (23) attacked excess thioether (22) functioning as a reducing agent to give phenyl-2-methylpropyl thioether (24) and diphenyl dithioether (25), which gave diphenyl thioether (26) by loss of sulphur.

The thio-Claisen rearrangement of phenyl prop-2-enyl thioether (27) occurred in boiling diethylaniline or quinoline to give an equal mixture of thiachroman (28) and 2H,3H-2-methylbenzo (b) thiophene (29).



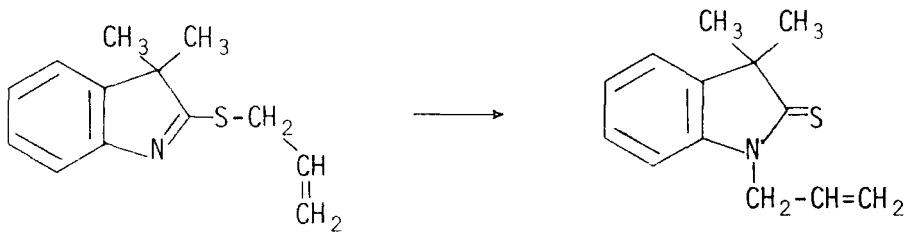
The first product was presumed to be 2-(prop-2-enyl)thiophenol (30) but this rapidly cyclised under the reaction conditions to the observed products. The intermediacy of (30) was shown in two other experiments. In the first experiment the thioether (27) was refluxed in quinoline for 1 hour (much less than the full reaction time) and potassium hydroxide was added. Addition of methyl iodide converted the trapped thiophenolate (30) to the corresponding methyl thioether (31) (Scheme 1)[11]. In the second experiment the thiophenol (30), prepared independently, produced the same products (28) and (29) in the same ratio as did the prop-2-enyl phenyl thioether (27).



SCHEME 1

The formation of the cyclised products has been rationalised as the result of competitive ionic and radical additions of the thiol function to the prop-2-enyl double bond[12].

The initial Claisen rearrangement products, the ortho-dienethiones, have not been isolated in the benzene series. However, the indole derivatives (32) gave stable thione products (33) in refluxing tetralin[13].



(32) (33)

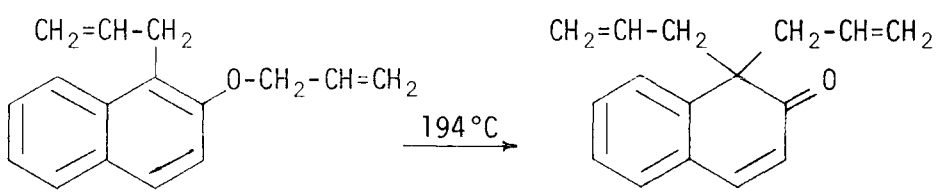
The thio-Claisen rearrangement is less facile than the oxygen counterpart. The reason may be kinetic in that the activation energy necessary to reach the strained cyclic transition state for the thioethers is so high that thermolysis or isomerisation reactions are kinetically easier. An alternative suggestion is that because the carbon to sulphur double bond is weaker than the carbon to oxygen double bond (the difference in bond energy of a C=S over C-S bond is ca. 62 kcal/mole whereas the difference in bond energy of a C=O over C-O bond is ca. 85 kcal/mole[14]), the thio-Claisen rearrangement is thermodynamically less favourable than the oxygen analogue[15].

1.4 A Comparison of Phenyl and Naphthyl Prop-2-enyl and Prop-2-ynyl Ethers in the Claisen Rearrangement

Kinetic studies on several prop-2-enyl aryl ethers have given the half-life, enthalpy of activation and entropy of activation for their thermal rearrangements[16,17]. Prop-2-enyl 4-methylphenyl ether at 170°C has a $\tau_{\frac{1}{2}}$ = 50 hours, a $\Delta H^{\ddagger}$ = 32 kcal/mole and a $\Delta S^{\ddagger}$ = -11.5 e.u.; prop-2-enyl naphth-1-yl ether has, at 172°C, a $\tau_{\frac{1}{2}}$ = 0.35 hours, a $\Delta H^{\ddagger}$ = 26.0 kcal/mole and a $\Delta S^{\ddagger}$ = -16 e.u.; prop-2-enyl naphth-2-yl ether has, at 172°C, a $\tau_{\frac{1}{2}}$ = 0.80 hours, a $\Delta H^{\ddagger}$ = 28.5 kcal/mole and a $\Delta S^{\ddagger}$ = -12 e.u.

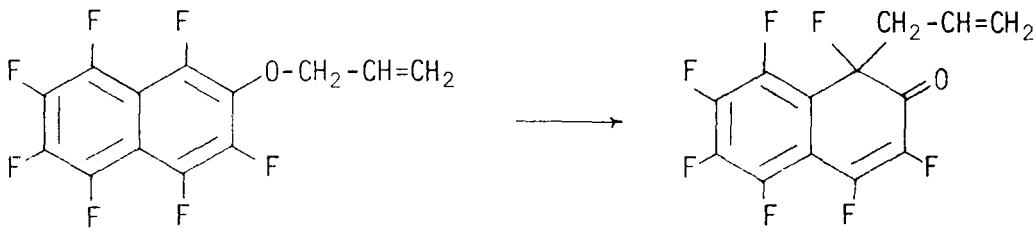
These results show that the primary rearrangement is easier for the naphthalene series than the benzene series, and the main cause is the lowering of the enthalpy of activation. A further difference is the ease of formation of Diels-Alder adducts. In order to undergo internal Diels-Alder addition the naphthalenones must lose aromaticity and this makes the cycloaddition less favourable for the naphthalene series than the benzene series. A consequence of this is that the initial Claisen rearrangement product can often be isolated in the naphthalene series in contrast to the benzene series.

The first example of rearrangement of an aryl prop-2-enyl ether to a stable dienone was reported for 1-(prop-2-enyl)-naphth-2-yl prop-2-enyl ether (34) which gave 1,1-di(prop-2-enyl)-naphthalen-2-one (35)[18].



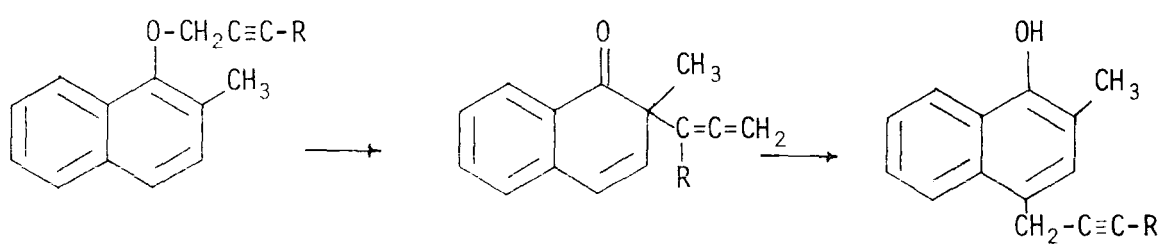
(34) (35)

Recently, 1,3,4,5,6,7,8-heptafluoronaphth-2-yl prop-2-enyl ether (36) has been shown to rearrange in boiling xylene over 2.5 hours to give 1,3,4,5,6,7,8-heptafluoro-1-(prop-2-enyl)-naphthalen-2-one (37)[19].



(36) (37)

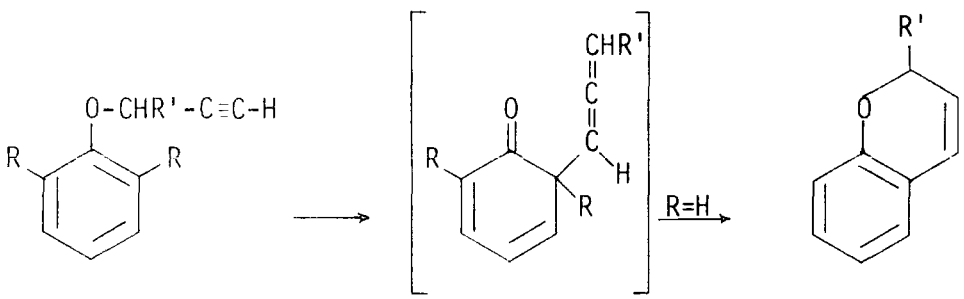
A similar difference in thermal behaviour is shown by phenyl and naphthyl prop-2-ynyl ethers. In no case was it possible to prove, directly, that a propa-1,2-dienyldienone was an intermediate in the Claisen rearrangement of phenyl prop-2-ynyl ethers. In contrast the 2-methylnaphth-1-yl prop-2-ynyl ethers (38) gave propa-1,2-dienyl dienones (39) at 160°C, which on further heating rearranged to the corresponding 4-(but-2-ynyl)-2-methylnaphth-1-ols (40)[20].



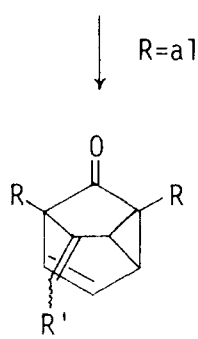
(38) (39) (40)

1.5 The Claisen Rearrangement of Aryl Prop-ynyl Ethers

A carbon carbon triple bond can take the place of a carbon carbon double bond in the Claisen rearrangement. Prop-2-ynyl phenyl ethers (41) rearrange to an ortho-dienone (42). If R = H, the ortho-dienone is rapidly converted into the 2H-chromene (43) via an ortho-propa-1,2-dienyl-substituted phenol. When R = alkyl, the dienone undergoes internal Diels-Alder addition to give the tricyclic ketone (44)[21].

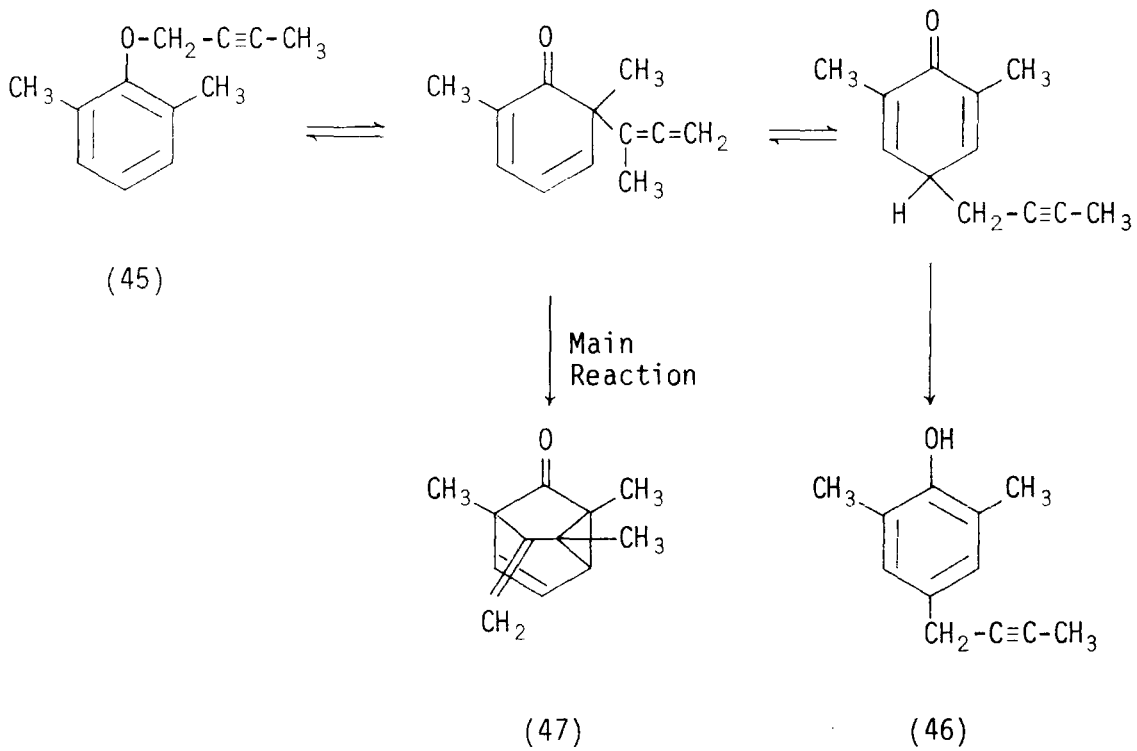


(41) (42) (43)



(44)

The para-Claisen rearrangement has been observed with but-2-ynyl - 2,6-dimethylphenyl ether (45)[21]. Some 4-(but-2-ynyl)-2,6-dimethyl phenol (46) was obtained but the main product was the Diels-Alder adduct (47) (Scheme 2).

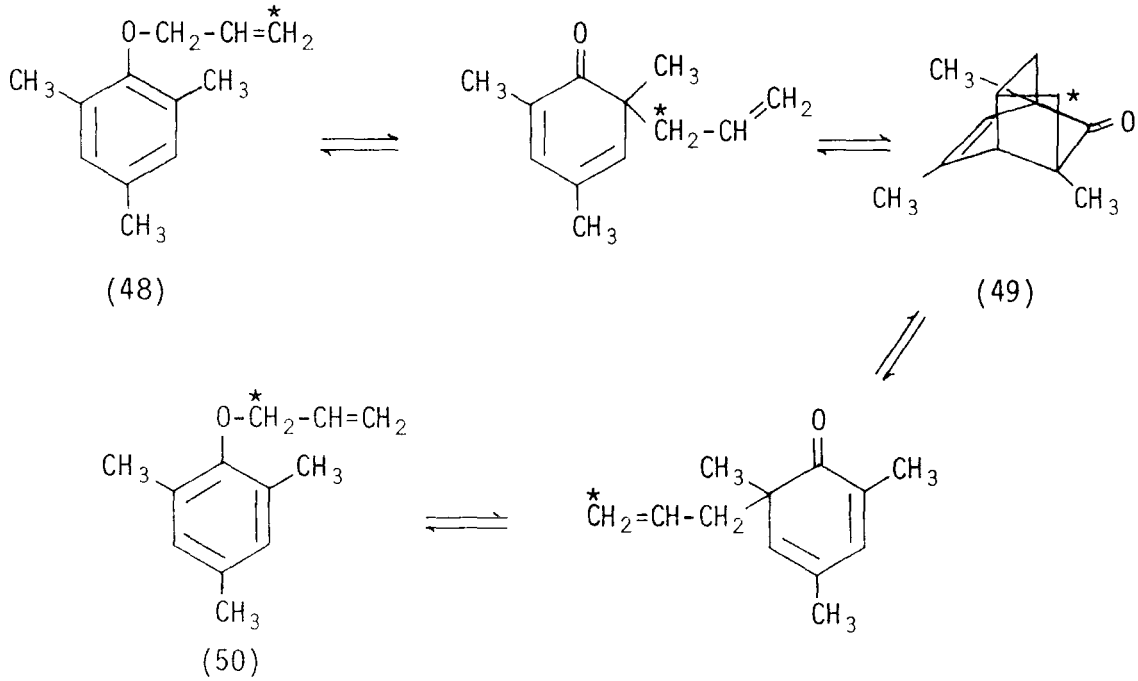


SCHEME 2

1.6 Internal Diels-Alder Adducts arising from the Claisen Rearrangement

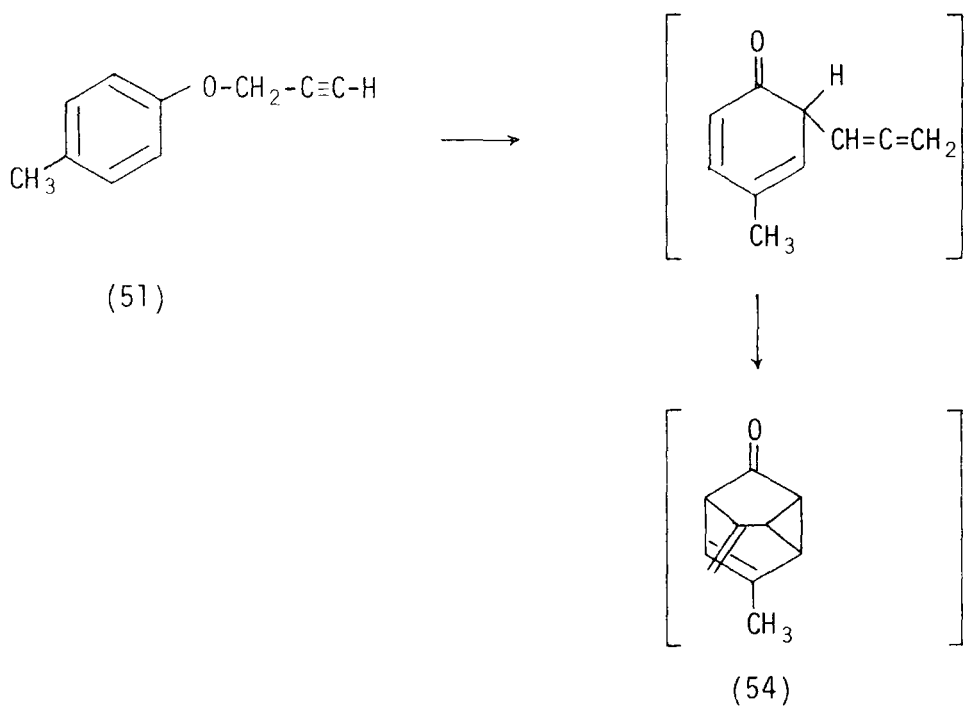
In studying the reversibility of the Claisen rearrangement Schmid et al. observed that on heating a ^{14}C-labelled 2,4,6-trimethylphenyl prop-2-enyl ether (48) the radioactivity became distributed between the 1 and 3 carbon atoms of the prop-2-enyl group[22]. This phenomenon is best accounted for by invoking the intermediacy of an intramolecular Diels-Alder adduct (49). Cleavage of the four-membered ring in (49) results in the formation of the rearranged isomer (50).

Flash vacuum pyrolysis of 4-methylphenyl prop-2-ynyl ether (51) at 480°C gave a mixture of indan-2-one (52) and 1,2-dihydrobenzocyclobutene (53)[23]. The formation of these products can be explained by invoking the Diels-Alder adduct (54) which rearranges



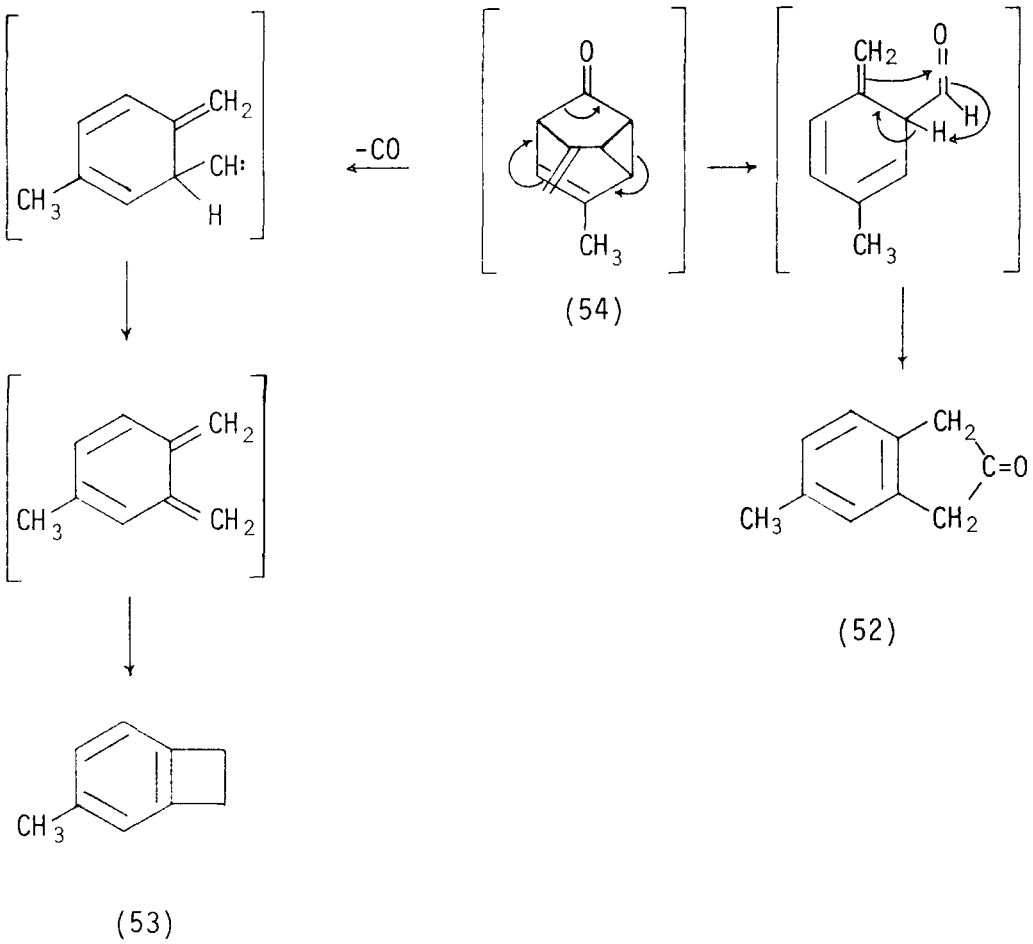
(48) (49) (50)

to the indan-2-one (52) or decarbonylates to give the 1,2-dihydrobenzocyclobutene (53) (Scheme 3).



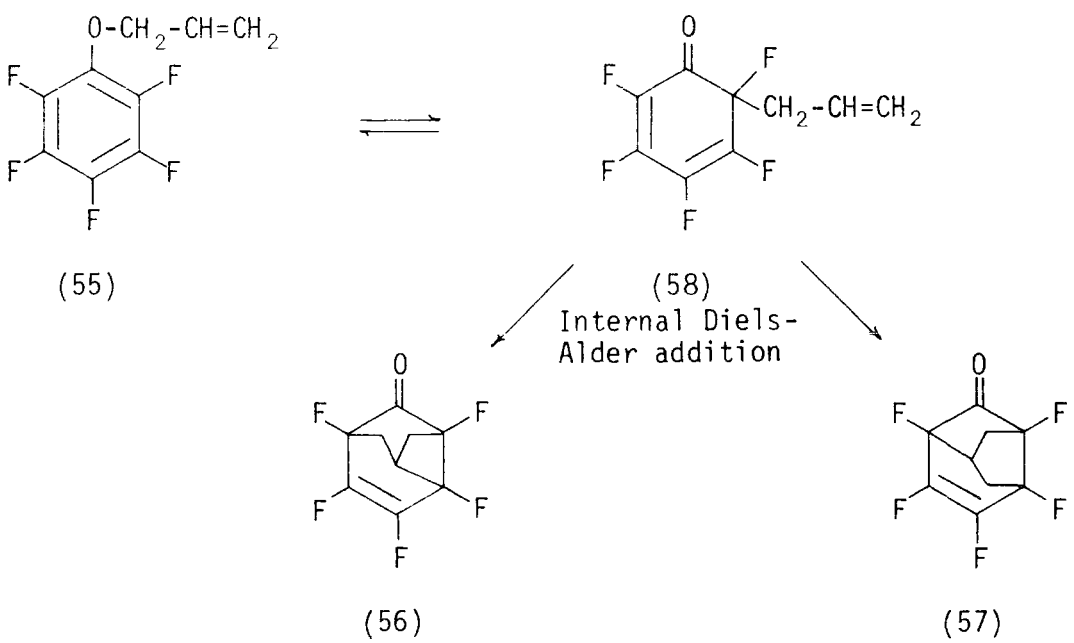
(51) (54)

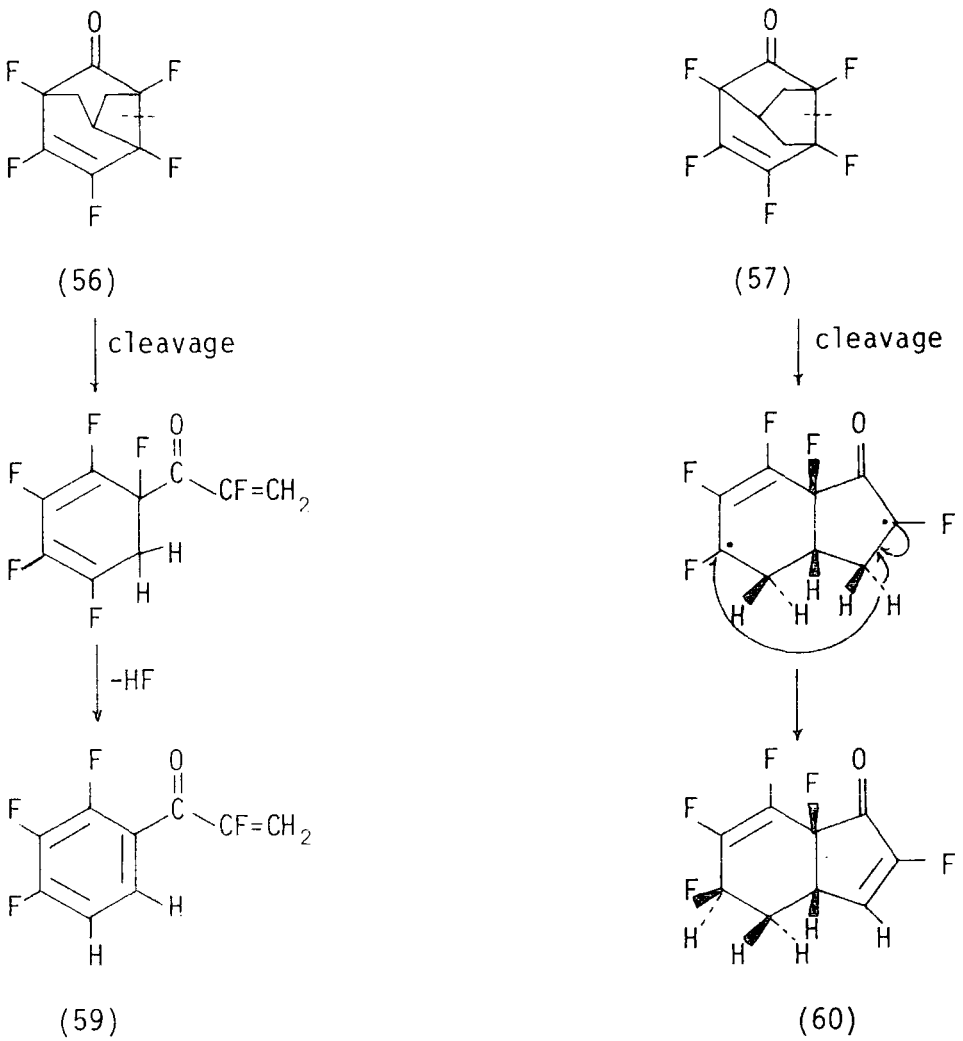
The vapour-phase pyrolysis of pentafluorophenyl prop-2-enyl ether (55) at 440 -480°C gives a variety of products. These are formed



SCHEME 3

by the reactions of both possible intermediate Diels-Alder adducts (56) and (57) arising from the initial Claisen rearrangement product, 2,3,4,5,6-pentafluoro-2-(prop-2-enyl)-cyclohexa-3,5-dienone (58) (Scheme 4)[24,25].

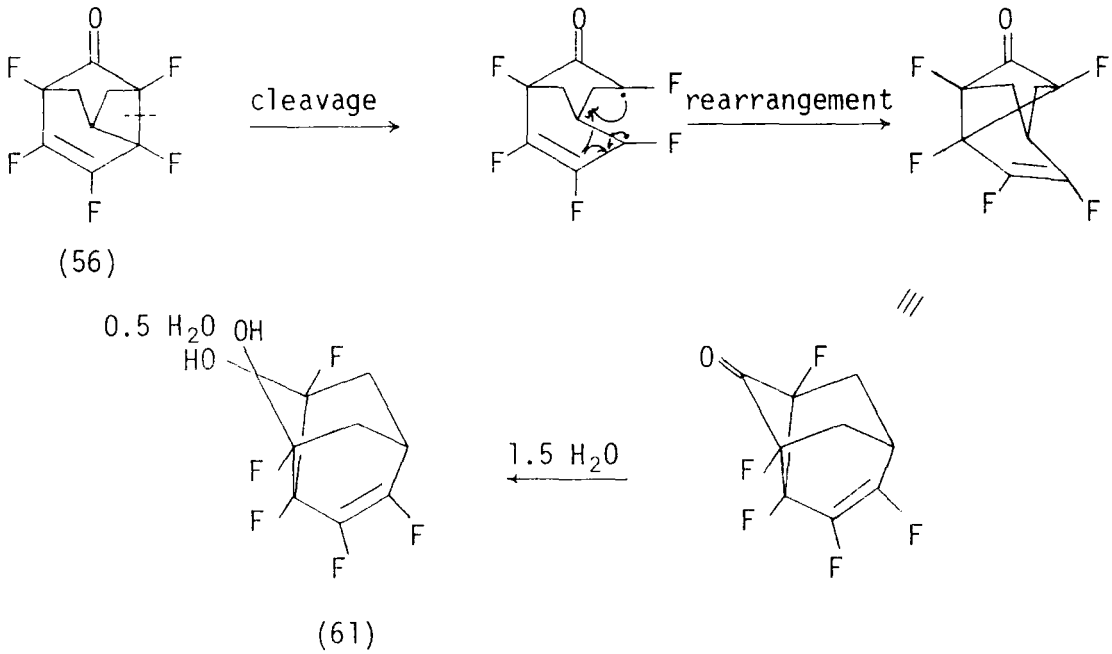




SCHEME 4

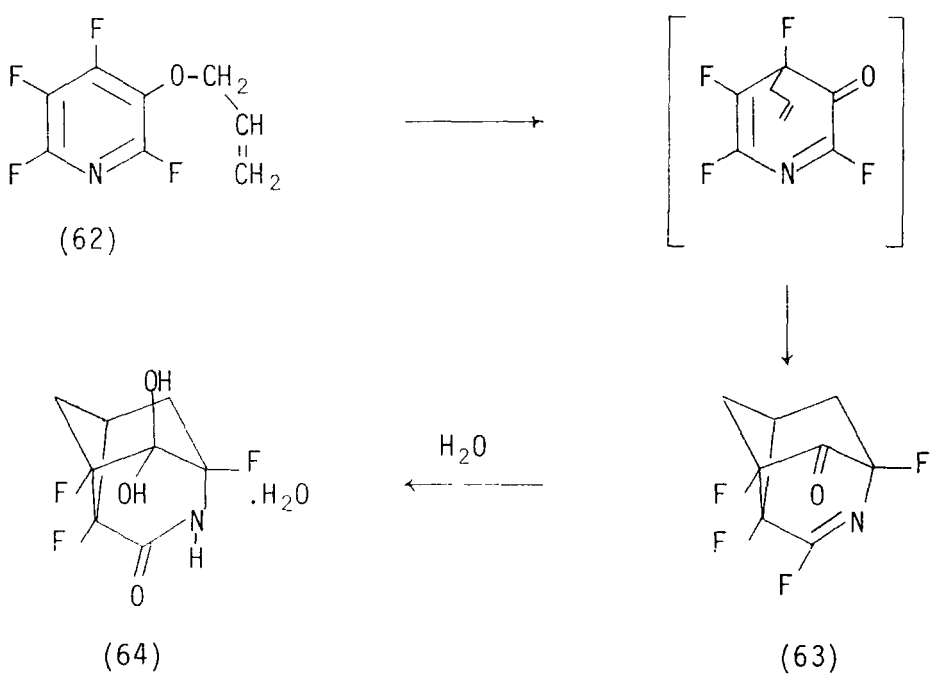
The products were a fluorovinyltrifluorophenylketone (59) and a fused bicyclic compound (60). Under milder conditions (137 - 141°C for 13 days) a hydrated gem diol (61) was isolated after work up. The formation of this product was explained in terms of a stepwise [1,3] sigmatropic rearrangement of the internal Diels-Alder adduct (56) and subsequent hydration (Scheme 5)[26].

Further work with tetrafluoropyridyl prop-2-enyl ethers has also given internal Diels-Alder adducts and hydrated derivatives of them[27]. Thermolysis of 2,4,5,6-tetrafluoro-3-pyridyl prop-2-enyl ether (62) at 185°C for 112.8 hours gave 14% of unchanged ether (62) and 81% of

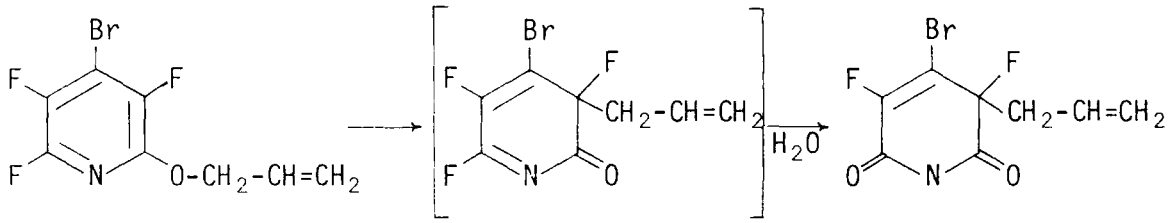


SCHEME 5

2,3,5,7-tetrafluoro-4-azatricyclo[3,3,1,$0^{2,7}$]non-3-en-6-one (63). Boiling the ketone (63) in aqueous acetone gave the hydrated hydrolysed product (64).



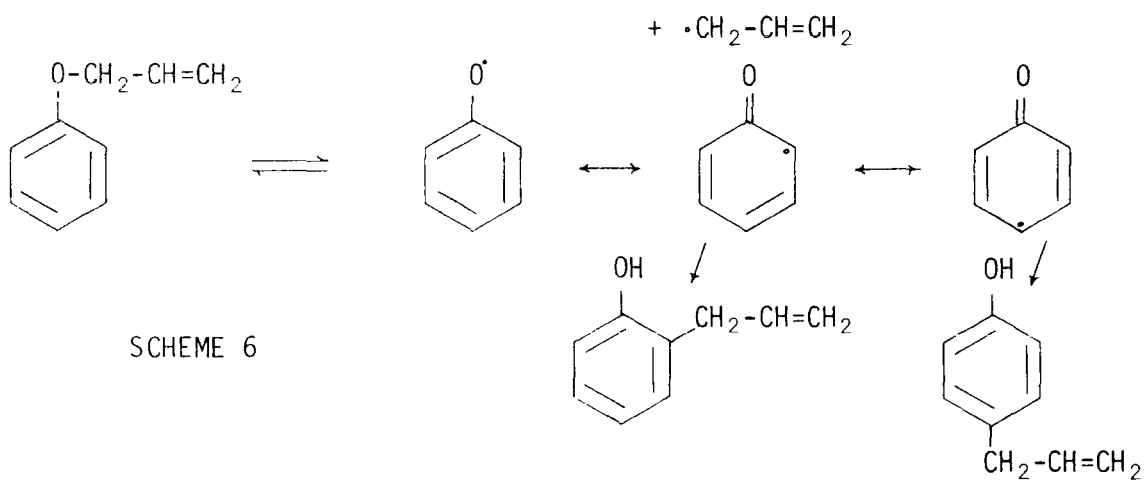
Interestingly, thermolysis of 4-bromo-2,3,5-trifluoro-6-pyridyl prop-2-enyl ether (65) at 160°C for 139 hours gave unchanged ether (65) (62%) and the imide (66) (7%), resulting from the hydrolysis of the intermediate dienone (67), but no Diels-Alder adduct[27].



(65) (67) (66)

1.7 The Mechanism of the Aromatic Claisen Rearrangement

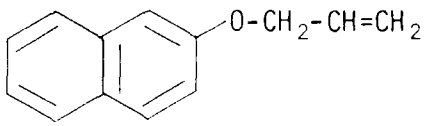
Once the reaction path of the aromatic Claisen rearrangement was known, much work was carried out investigating the mechanism. Claisen postulated that the rearrangement involved the participation of radicals. The ortho position is nearer than the para position to the prop-2-enyl group and by this simple steric argument, he explained the greater concentration of the ortho-substituted phenol (68) (Scheme 6).



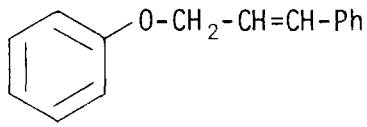
SCHEME 6

(68)

However, when naphth-2-yl prop-2-enyl ether (69) and phenyl (3-phenylprop-2-enyl) ether (70) were heated together only prop-2-enyl naphthols and phenylprop-2-enyl phenols were obtained[28].



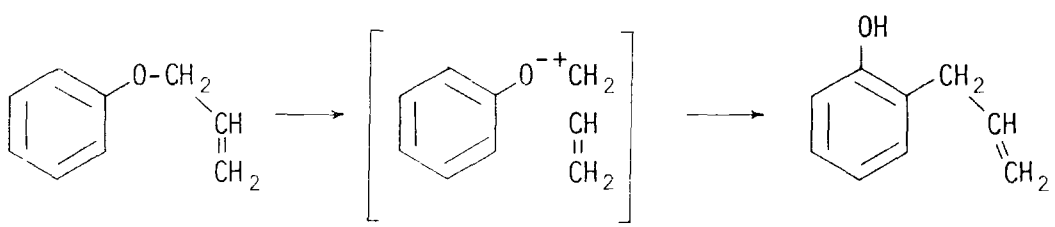
(69)



(70)

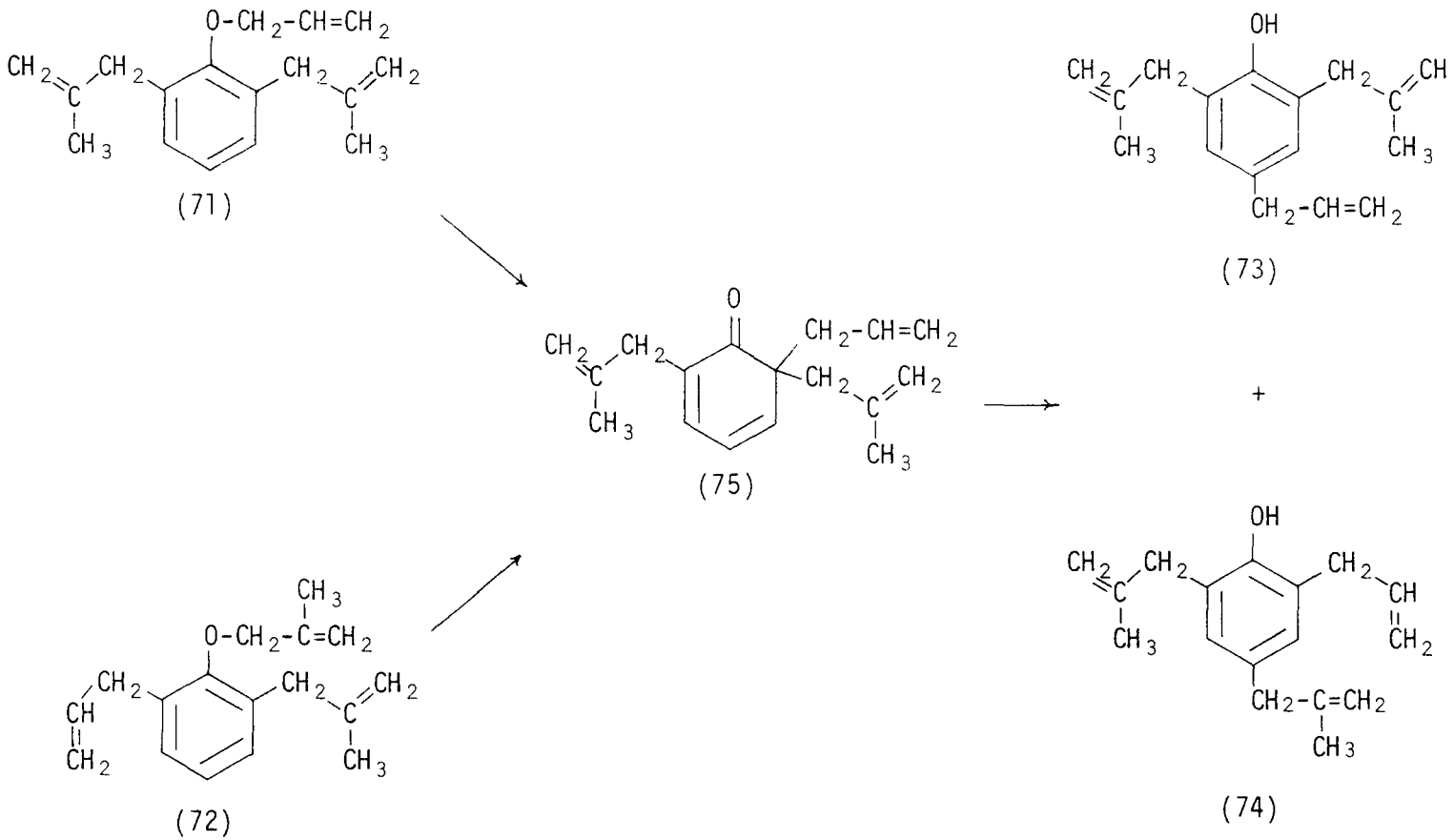
This experiment gave no crossover products and so it was concluded the rearrangement must be intramolecular - which ruled out a radical mechanism since it was unreasonable to expect a radical reaction to be exclusively intramolecular[29].

Another suggestion proposed that an ionisation occurred with the ions held together in a complex which collapsed to give the product (Scheme 7)[30].



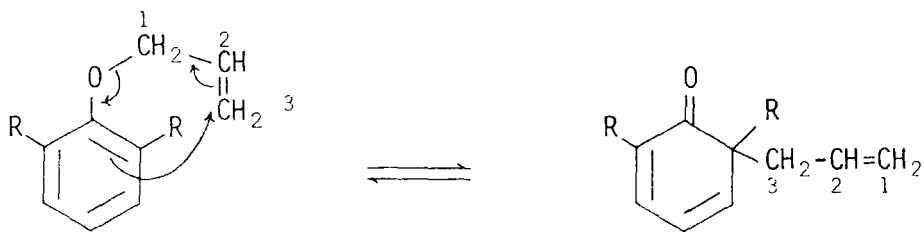
SCHEME 7

However, this theory failed to explain the result that isomeric ethers (71) and (72) rearranged to give an identical product distribution: 59% (73), 41% (74). The migration of the ortho substitutent could be explained if the ortho-dienone (75) was a common intermediate (Scheme 8)[31].


O-CH2-CH=CH2
CH2 CH2 CH2 CH2
C C
CH3 CH3
(71)
O
CH2-CH=CH2
CH2-C=CH2
CH3
(75)
OH
CH2-CH=CH2
(73)
+
CH3
O-CH2-C=CH2
CH2 CH2 CH2
CH CH2
CH2
(72)
OH
CH2-C=CH2
CH3
(74)

SCHEME 8

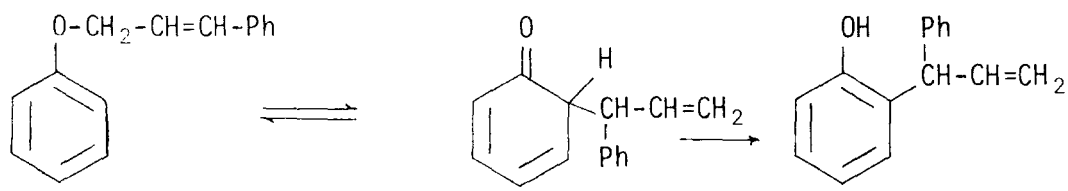
Hurd and Pollack offered a different mechanism. They suggested that the rearrangement occurred by concerted electron transfers with the migrating group moving around the ring in a cartwheel fashion[4]. Inversion of the prop-2-enyl group occurs during migration to the ortho position so that the 3 carbon of the prop-2-enyl group in the ether (76) becomes the 1 carbon of the prop-2-enyl in the ortho-dienone (77) (Scheme 9).



(76) (77)

SCHEME 9

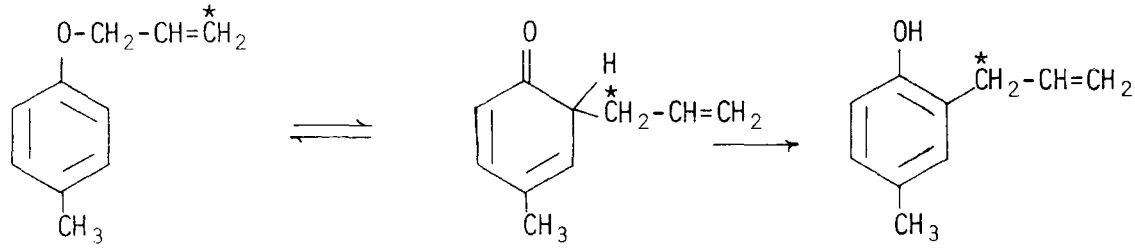
This mechanism was examined by labelling the prop-2-enyl group in either the 1 or 3 position and the product examined for inversion. Initially this was investigated using 3-phenylprop-2-enyl phenyl ether (70) in which it was noted that the phenyl group indeed had been transformed to the 1 position in the ortho-phenol (79)[28].



(70) (79)

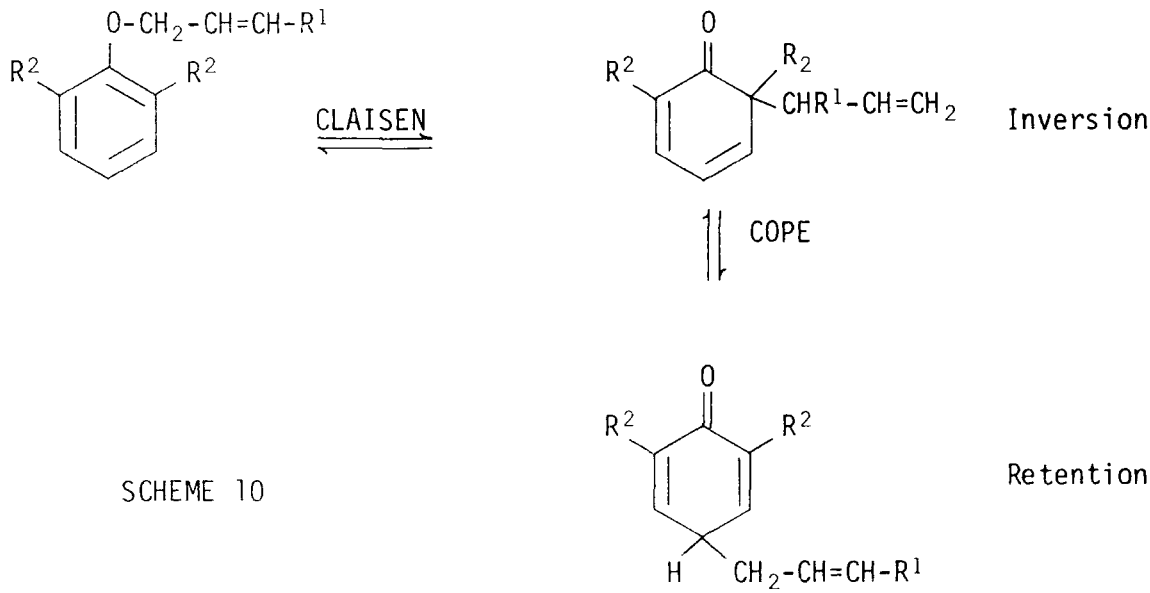
Using ^{14}C-labelled material (80) Schmid showed inversion of the prop-2-enyl group[32]. The methyl substitutent was present to prevent para-substituted phenol formation, which would have complicated the

study.



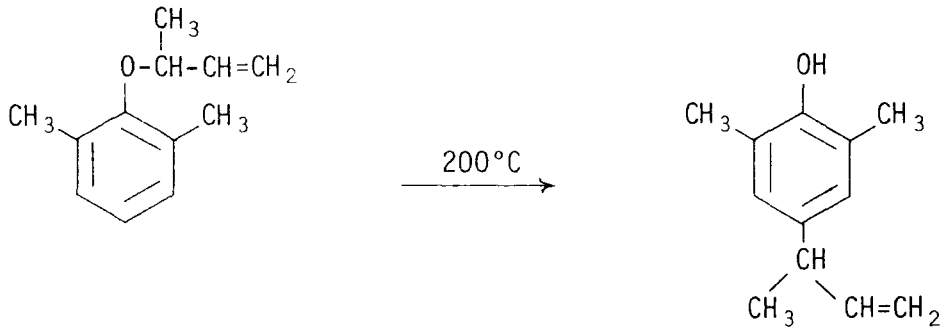
(80)

This gave the mechanism for the ortho-Claisen rearrangement. The para-Claisen rearrangement was expected to be similar but with two migrations of the prop-2-enyl groups leaving the stereochemistry retained (Scheme 10).

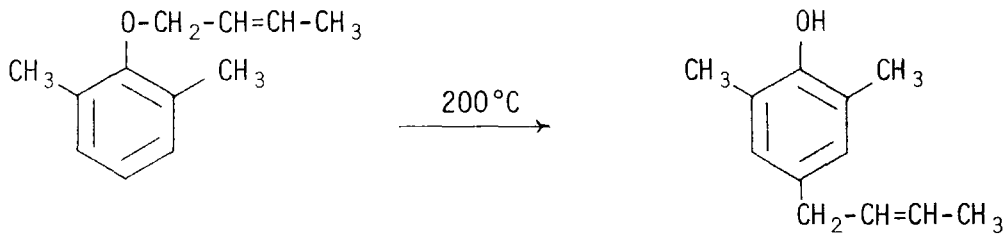


SCHEME 10

It was found that ethers (81) and (82) rearranged to give para-substituted phenols (83) and (84) respectively, in which the stereochemistry of the prop-2-enyl group was indeed retained[33]. This showed that the mechanism of the para-Claisen rearrangement was similar to the ortho-Claisen rearrangement.



(81) (83)



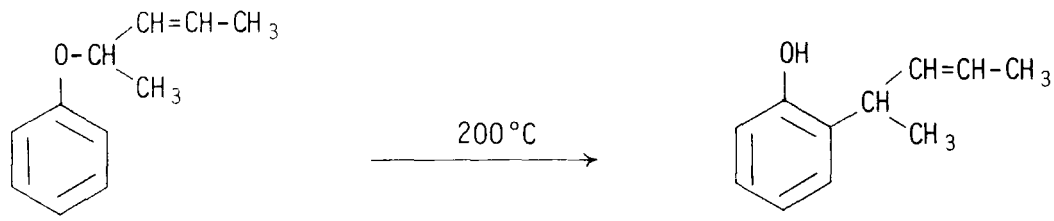
(82) (84)

1.8 The Stereochemistry and Nature of the Transition State of the Aromatic Claisen Rearrangement

Kinetic results have shown that both the ortho- and para-Claisen rearrangements are first order reactions, and the negative entropies of activation support the involvement of highly ordered transition states. Further details about the transition state are vague because the Claisen rearrangement is largely insensitive to probes for ionic and free radical character.

A more helpful approach is to consider the stereochemical relationship between reactant and product. Alexander and Kluiber found that optically active 1-methylbut-2-enyl phenyl ether (85) on heating at 200°C for 1 hour gave optically active ortho-1-methyl-but-2-enyl phenol (86)[34]. Since the activity was not destroyed then

the transition state must be stereospecific.



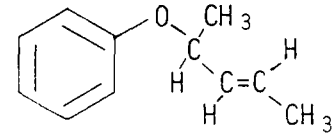
(85) (86)

α^{25}_{D} -0.10° α^{25}_{D} +0.48°

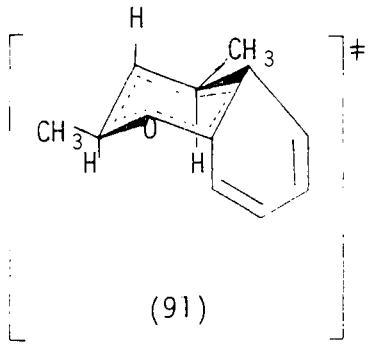
There are six atoms involved in the concerted electron transfer and so it was proposed that the transition state was based on a six membered ring. In addition it was postulated that two extreme forms existed approximating to the chair and boat forms of cyclohexane[35].

Detailed investigation showed that trans phenyl 1-methylbut-2-enyl ether (87) rearranged in mesitylene to give trans (88) and cis (89) 2-[1-methylbut-2-enyl]phenol in the ratio 82:18 (Scheme 11)[36]. The greater yield of the trans product (88) was explained by noting that trans alkenes are more stable than cis alkenes[37]. It was also found that cis phenyl 1-methylbut-2-enyl ether (90) rearranged to give the trans (88) and cis (89) phenols but in the ratio 98:2 (Scheme 12).

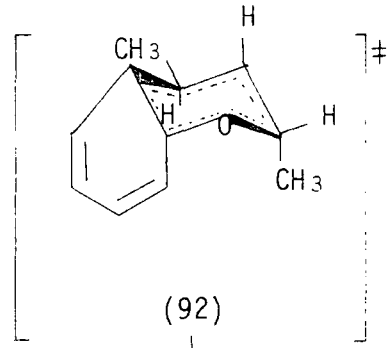
The product distribution can be explained by consideration of the stability of the possible transition states. Four possible transition states exist for both the trans and cis ethers (87) and (90), two chair forms and two boat forms. For the trans ether (87) consideration of steric interactions, especially axial-axial, predicts (91) to be more stable than (92), (93) to be more stable than (94) and the trans product will predominate (Scheme 11). The situation is different for the cis ether (90) because high steric interference in the transition state conformers (96) and (97) restricts the amount of cis alkene formed



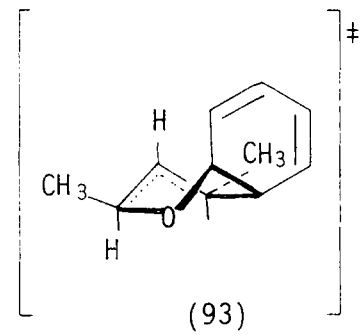
Trans (87)



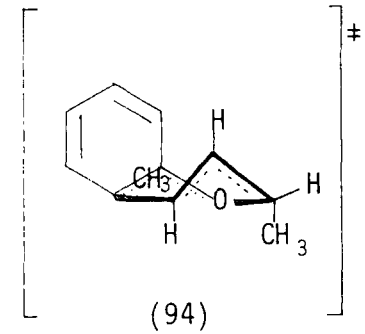
(91)



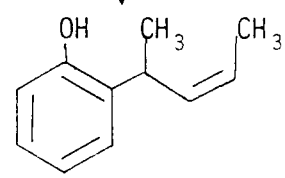
(92)



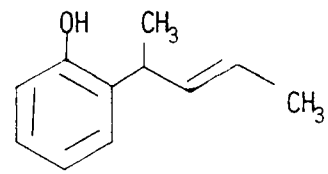
(93)



(94)

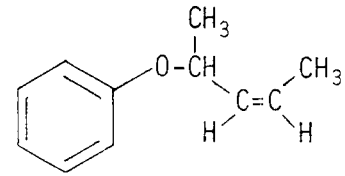


18% cis (89)

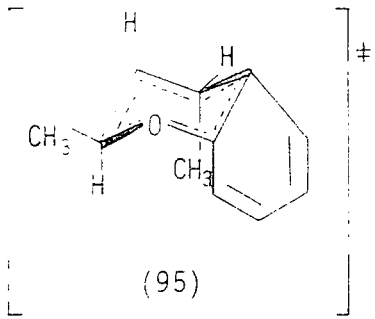


82% trans (88)

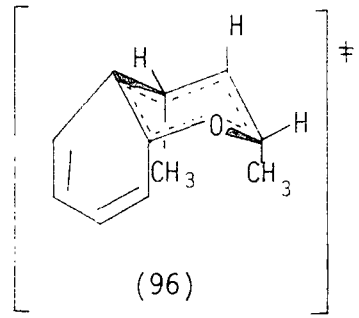
SCHEME 11



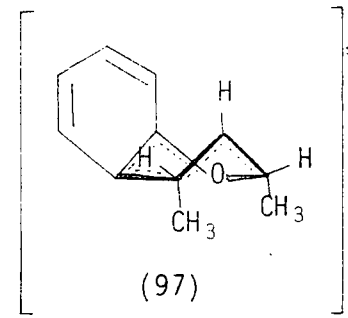
cis (90)



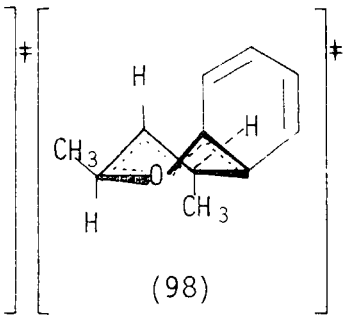
(95)



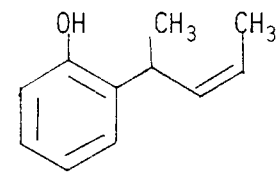
(96)



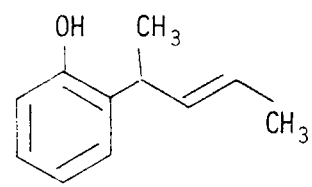
(97)



(98)



2% cis (89)



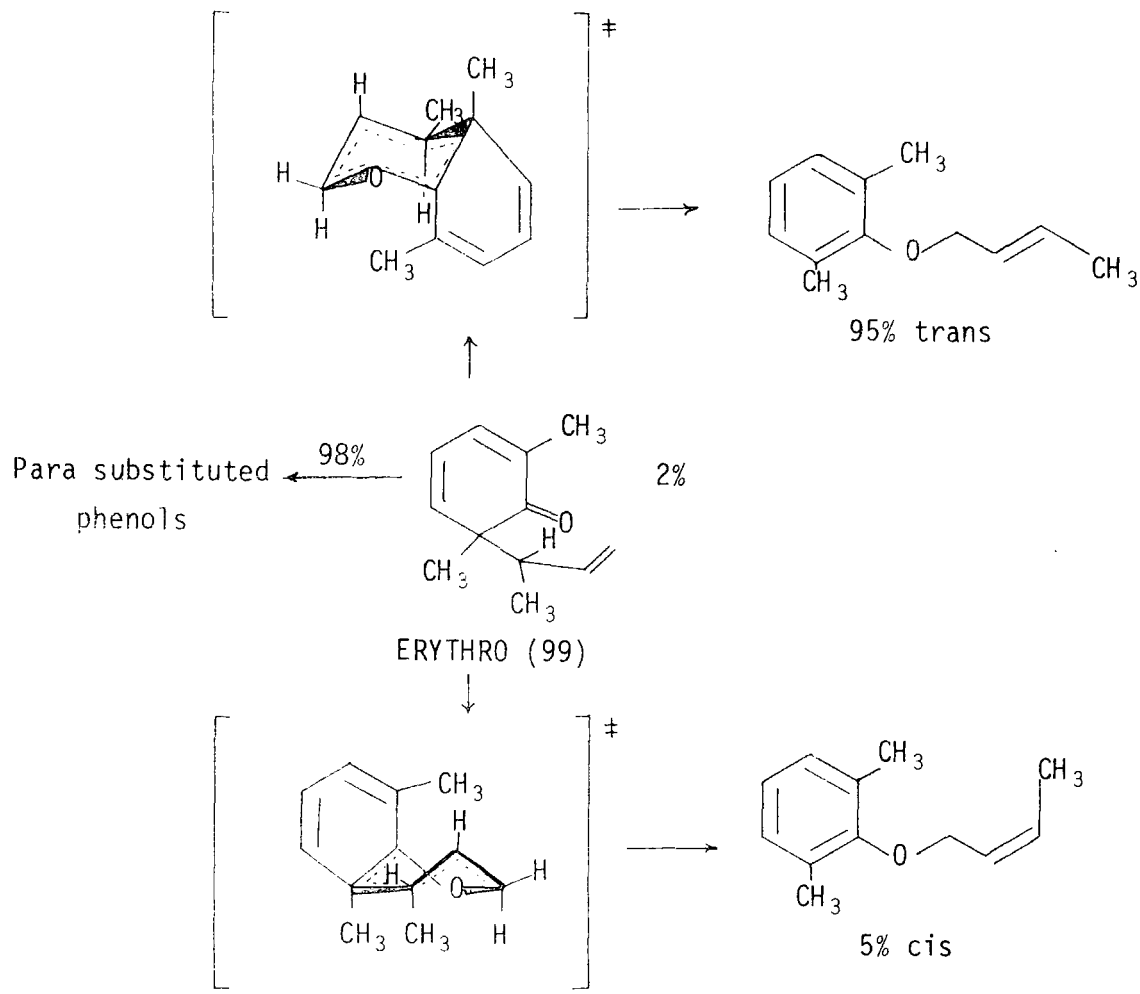
98% trans (88)

SCHEME 12

(Scheme 12).

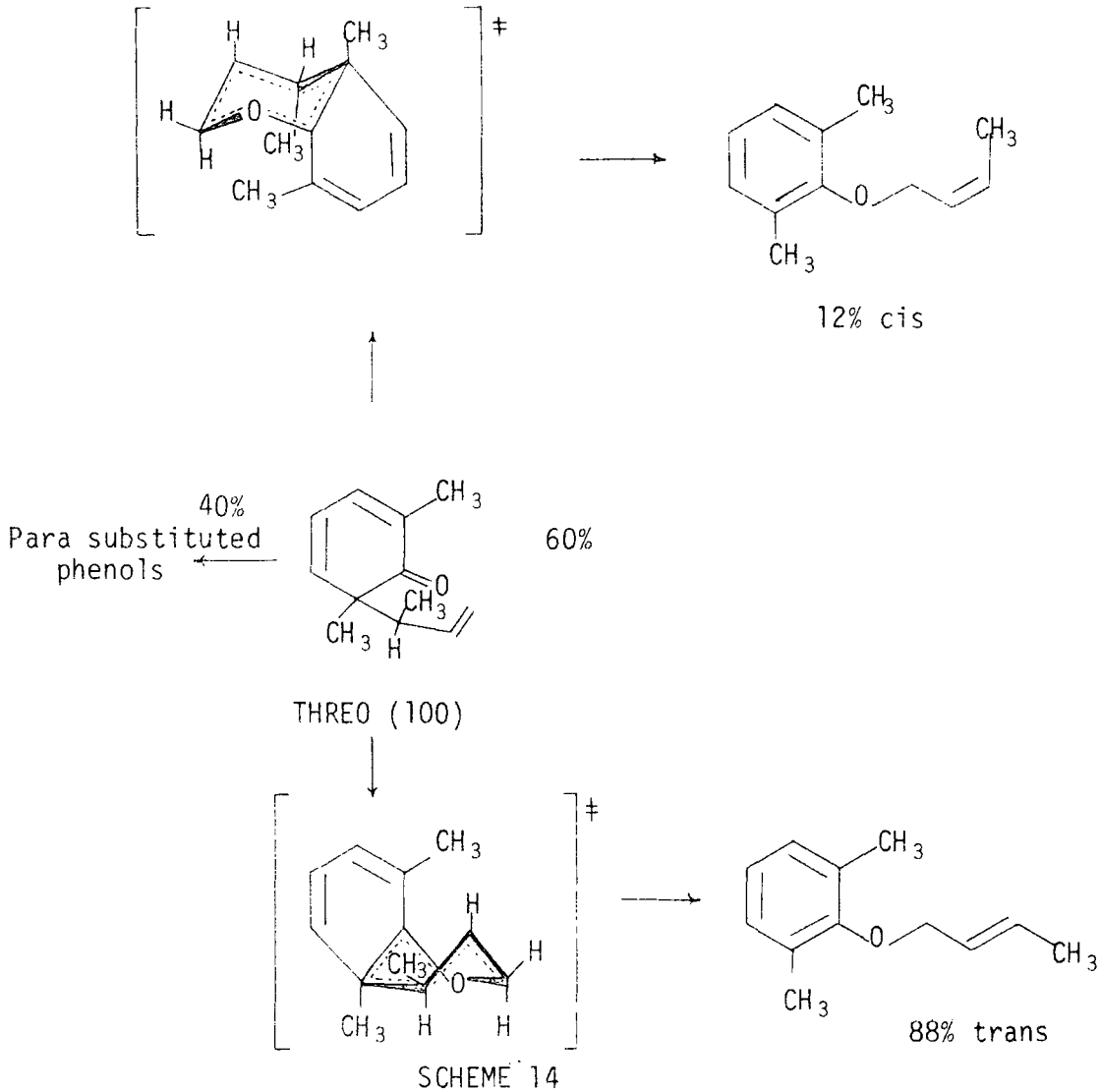
Each product molecule can be derived from either a boat or chair transition state and so no consideration can be made of the relative contributions of chair and boat conformers. Information on transition state conformers is obtained indirectly from the reaction of 2,6-disubstituted ortho-dienones, which may undergo a Cope rearrangement to give a para-dienone or a retro-Claisen rearrangement to give an ether.

Erythro-2-(1-methylprop-2-enyl)-2,6-dimethylcyclohexa-3,5-dienone (99) rearranges to a mixture of para phenols (98%) and a mixture of cis and trans but-2-enyl-2,6-dimethylphenyl ether (2%) (Scheme 13).



SCHEME 13

The products with a trans configuration, formed by a chair conformer, predominate (95%). Threo-2-(1-methylprop-2-enyl)-2,6-dimethylcyclohexa-3,5-dienone (100) also rearranges to give a mixture of cis and trans (but-2-enyl) 2,6-dimethylphenyl ether and here again the trans alkene predominates (88%). In this reaction it is the boat conformer that leads to the trans alkene (Scheme 14).



SCHEME 14

Secondary orbital symmetry effects predict preference for the chair conformation over the boat conformation in the transition state[38,39]. When, however, the chair conformation leads to the thermodynamically less stable product, or if pseudo diaxial 1,3 interaction in the chair conformation is high, then the boat conformation is preferred.

1.9 Symmetry Description of the Aromatic Claisen Rearrangement

In Woodward-Hoffmann terminology the Claisen rearrangement is an example of a sigmatropic shift of order [i,j] where i and j are both 3[40]. The order [i,j] refers to the extent of migration of a sigma bond along one or more π-electron systems during a concerted electron and bond reorganisation process, where the actual distance traversed is i-1 and j-1 atoms. It can be shown by use of the phase relationships of the highest occupied molecular orbital that for rearrangements of the order [i,j] in which i and j are both greater than unity, thermal changes are allowed if $(i + j) = 4n + 2$ while photochemically excited transformations are permitted when $(i + j) = 4n$.

The transition state for the Claisen rearrangement can be crudely constructed as a complex of interacting quasi-phenoxyl and quasi-prop-2-enyl radicals. The π-electron system of the quasi-prop-2-enyl radical can be described by three molecular orbitals ψ_1, ψ_2, ψ_3 using Hückel molecular orbital theory, where no more than two paired electrons can occupy a given orbital. The three orbitals are described in order of increasing energy as bonding, non-bonding and anti-bonding as in Fig. 1 where the positive and negative signs refer to the phase of the wave function. ψ_2, the non-bonding orbital, is the highest occupied molecular orbital with one electron.

The π electron system of the quasi-phenoxyl radical can be described in terms of seven molecular orbitals, of which ψ_4 is the highest occupied with one electron - Fig. 2[41].

The highest occupied orbitals ψ_4 (of the quasi-phenoxyl radical) and ψ_2 (of the quasi-prop-2-enyl radical) determine the course of the rearrangement. The stereochemical requirements for intramolecular

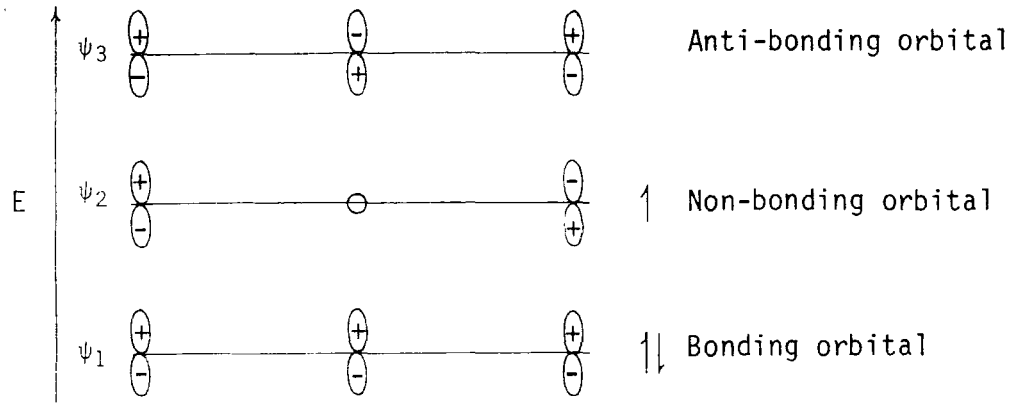

E
ψ3
ψ2
ψ1
Anti-bonding orbital
Non-bonding orbital
Bonding orbital

Fig. 1

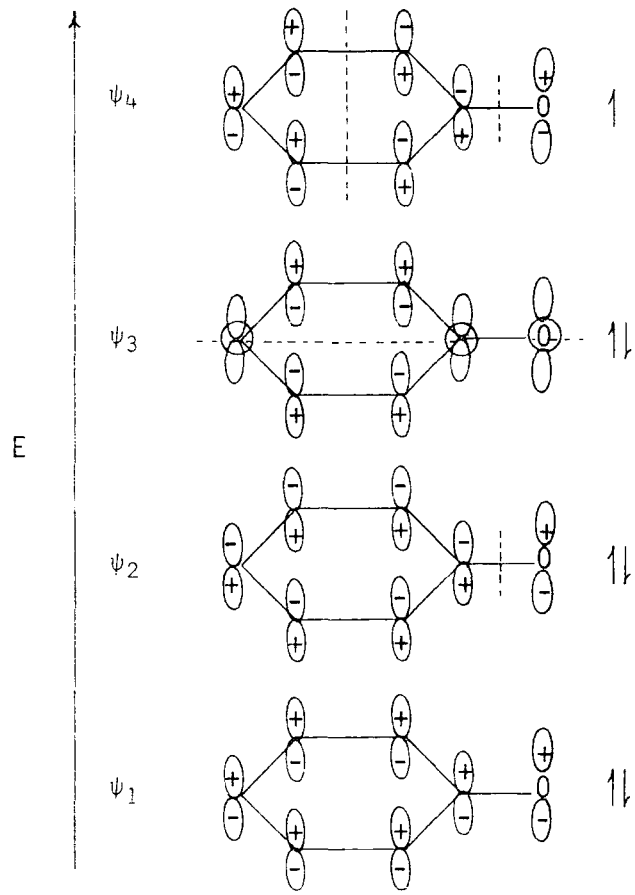
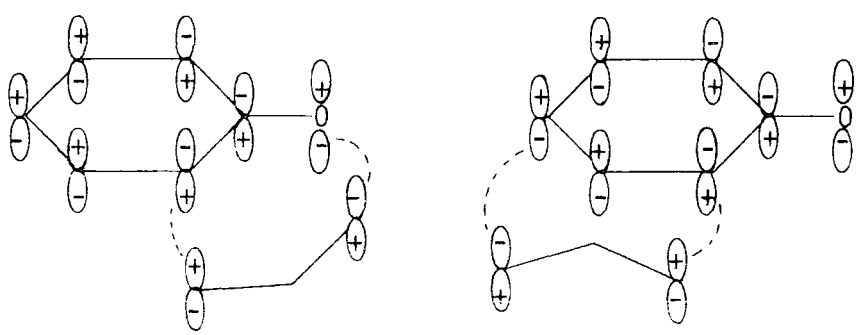

E
ψ4
ψ3
ψ2
ψ1

Fig. 2

prop-2-enyl migrations demand that bond breaking and bond formation occur on the same face of the prop-2-enyl group. For the quasi-prop-2-enyl radical there is a change of phase between atoms 1 and 3 in ψ_2. For the quasi-phenoxyl radical the phase of the wave function changes between the oxygen atom and the ortho position, and the phase changes again between the ortho and para positions.

Bonding can only occur between molecular orbitals of the same phase and assuming the rearrangement must occur suprafacially, then the transition state will be represented by ψ_2 of the quasi-prop-2-enyl radical and ψ_4 of the quasi-phenoxyl radical as in Fig. 3.

By the very symmetry of the wave functions, the migration of the prop-2-enyl group to the ortho position is thermally allowed as is the Cope rearrangement from the ortho to para positions. Equally, a 1,3 shift which is suprafacial is thermally forbidden with retention of stereochemistry in the migrating group.



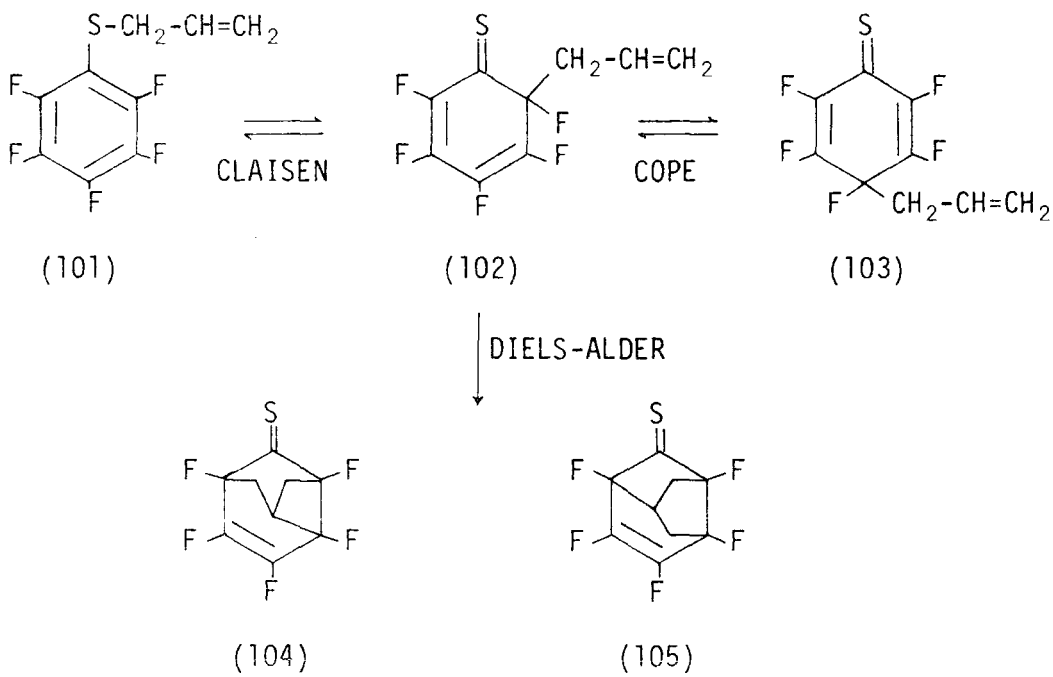
3,3 Claisen Shift 3,3 Cope Shift

Fig. 3

Chapter 2 Synthesis and Reactions of Pentafluorophenyl Prop-2-enyl-(101) and 2,3,4,5-Tetrafluorophenyl Prop-2-enyl-(107) Thioethers

2.1 Introduction

This work was intended to find out whether or not sulphur analogues behaved like the ether (55)[24-26]. If so, pyrolysis of pentafluorophenyl prop-2-enyl thioether (101) would promote thio-Claisen rearrangement to an ortho-dienethione (102), subsequent reaction of which would give a para-dienethione (103) and internal Diels-Alder adducts (104) and (105).



(101) (102) (103)

(104) (105)

The thioether (101) was synthesised (88% yield) by treatment of pentafluorothiophenol (106) with n-butyllithium and then prop-2-enyl bromide. The thioether (101) was subjected to both sets of conditions which brought about reaction with the corresponding ether (55). Vapour phase thermolysis at 250°C for 19 hours or flow pyrolysis

at 370°C through a silica tube packed with quartz wool gave no reaction. However, flow pyrolysis at 465°C induced limited decomposition to pentafluorothiophenol (106) and unidentified volatile materials, and flow pyrolysis at 510°C only gave (106) and volatile materials.

The thio-Claisen rearrangement is usually carried out in quinoline or N,N-diethylaniline[11]. In order to promote rearrangement, some preliminary experiments were carried out with the thioether (101) under standardised conditions in several solvents refluxing at length and the products obtained were distilled in vacuo ($\leq$ 120°C at 0.05 mm Hg) and were analysed by g.l.c.. n-Decane and N,N-dimethylaniline gave little or no reaction, whereas dimethylsulphoxide and quinoline gave mainly tar and N,N-diethylaniline gave ca. 60% of distillable material containing at least fourteen components.

2.2 Synthesis and Reaction in N,N-diethylaniline of 2,3,4,5-Tetrafluorophenyl Prop-2-enyl Thioether (107)

The reaction of the thioether (101) in N,N-diethylaniline could involve nucleophilic aromatic substitution of the para fluorine by the solvent in addition to rearrangement of the thioether (101), since secondary amines have been shown to substitute fluorine in hexafluorobenzene[42] .

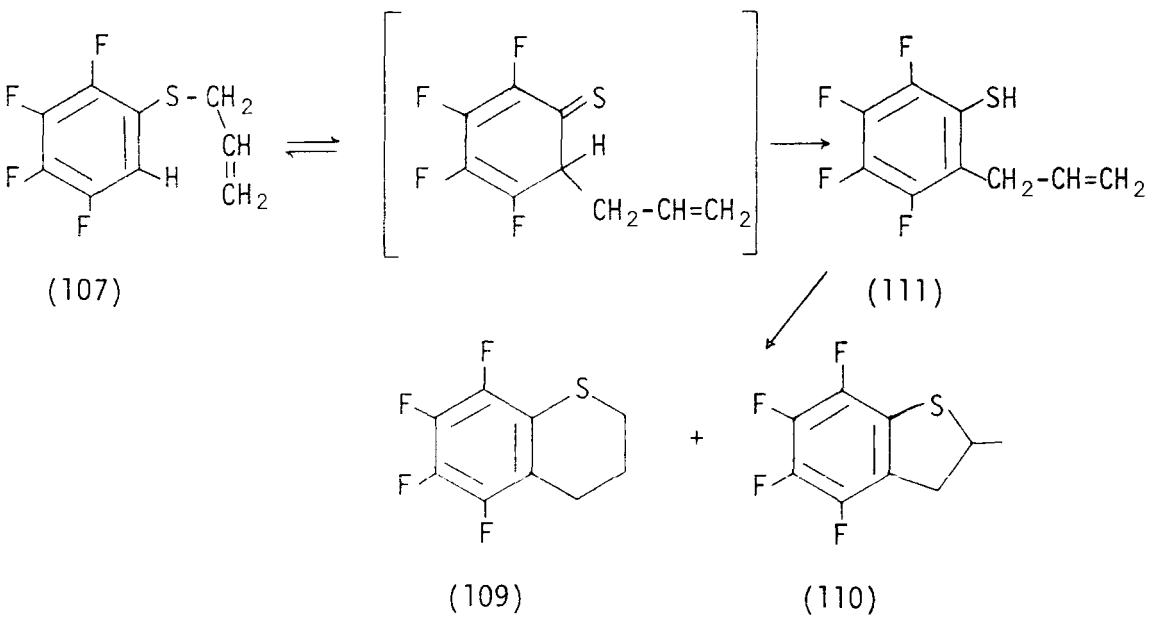
In order to study the conventional thio-Claisen rearrangement, 2,3,4,5-tetrafluorophenyl prop-2-enyl thioether (107) was synthesised (85% yield) from 2,3,4,5-tetrafluorothiophenol (108) by treatment with n-butyllithium followed by prop-2-enyl bromide. The thioether was then refluxed for 23 hours in N,N-diethylaniline and gave 40% of 5,6,7,8-tetrafluorothiachroman (109), and 30% of 2H,3H-2-methyl 4,5,6,7-tetrafluorobenzo (b) thiophene (110). The thiachroman (109)

was not obtained analytically pure but was identified by comparison with authentic material synthesised unambiguously (see chapter 4).

The ^{1}H n.m.r. spectrum of the thiachroman (109) showed a doublet at δ 2.14 for one CH_2 group and two overlapping signals at δ 2.74 and δ 2.96 for the other two CH_2 groups. The ^{19}F n.m.r. spectrum showed four signals of equal intensity at 143.6, 145.8, 162.5 and 165.5 ppm upfield from external $CFCl_3$.

The ^{1}H n.m.r. spectrum of the 2H,3H-2-methyl-benzo (b) thiophene (110) showed a doublet at δ 1.48 for the CH_3 group, a broad signal from δ 3.01 to δ 3.46 for the CH_2 group, and a signal at δ 4.12 for the CH group. The ^{19}F n.m.r. spectrum showed four signals of equal intensity at 140.0, 141.4, 157.4 and 161.5 ppm upfield from internal $CFCl_3$.

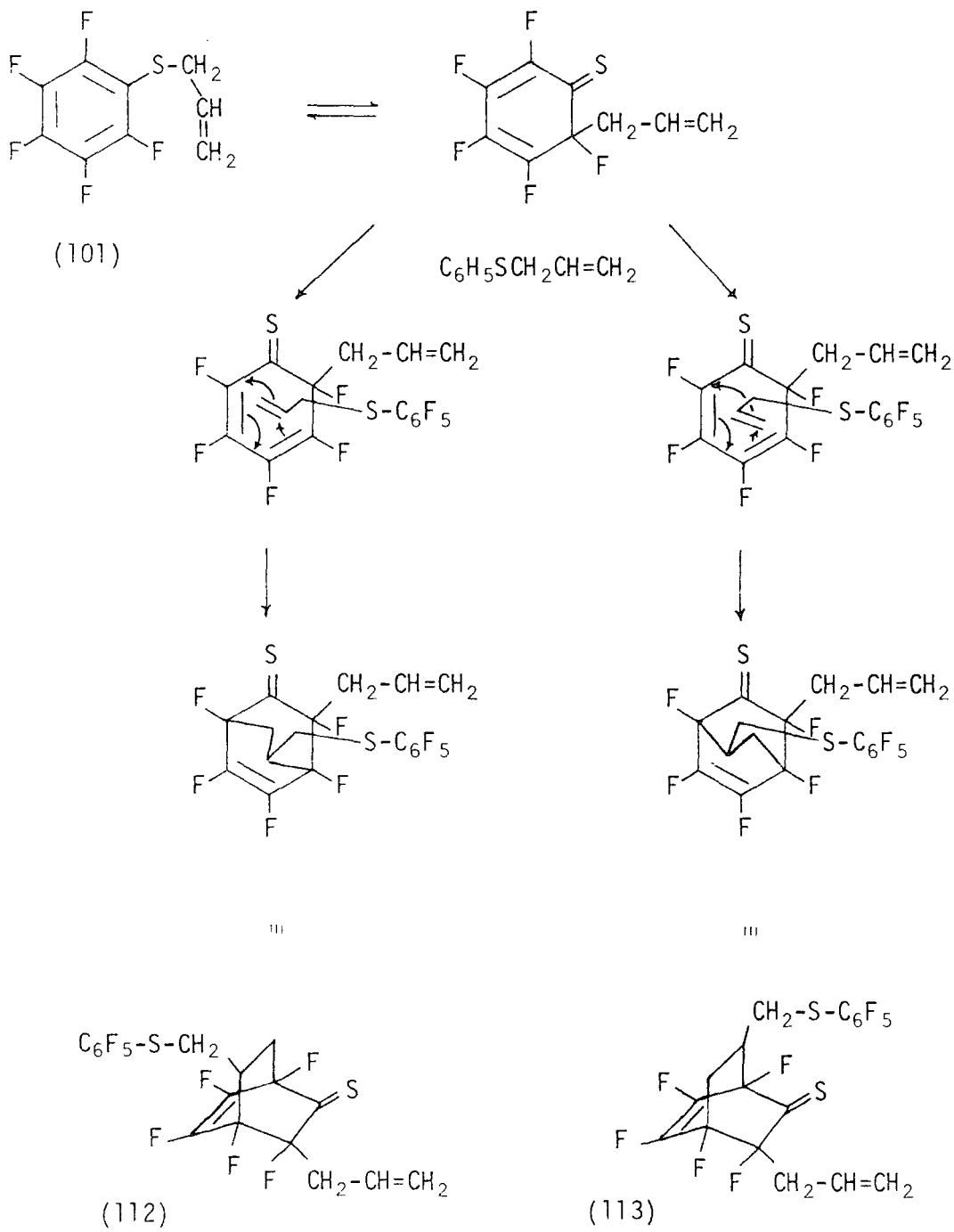
This reaction is a thio-Claisen rearrangement analogous to the reaction of phenyl prop-2-enyl thioether (27) in quinoline[11]. The reaction should proceed via initial formation of an ortho-dienethione which tautomerises to 2-(prop-2-enyl)-3,4,5,6-tetrafluorothiophenol (111) and this cyclises to the observed products (109) and (110).



(107) (111) (109) (110)

2.3 Reaction of Pentafluorophenyl Prop-2-enyl Thioether (101) in N,N-diethyl aniline

Evidence obtained with the ether (55) suggested that solution thermolysis of the thioether (101) would lead to dimers of the structures (112) and (113) arising from Claisen rearrangement followed by intermolecular Diels-Alder addition of the ortho-dienethione and the thioether (101) (Scheme 15)[43].



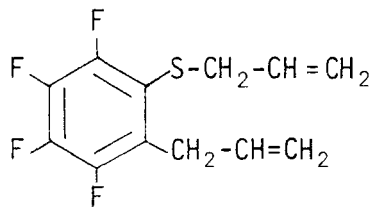
SCHEME 15

However, refluxing the thioether (101) for 23 hours in N,N-diethylaniline gave a complex mixture containing perfluoro(polyphenylene sulphide) (114) in ca. 6% yield and at least fourteen components by g.l.c.. The products were fractionally distilled in vacuo to give a mixture of starting material (101) with another component, identified in a later experiment as pentafluorophenyl ethyl thioether (115) (see chapter 3) in ca. 33% yield as the lowest boiling material, followed by fractions of increasing boiling-point and complexity. The higher boiling fractions were partially separated by both chromatography on silica and by g.l.c.. Three compounds were isolated from the distillate in sufficient purity to permit preliminary structural assignments to be made on the basis of spectroscopic data and these have been confirmed by independent syntheses of the pure materials. The most accessible component formed in ca. 8% yield, had M^+ 262 [starting material - 19 (fluorine) + 41 (prop-2-enyl)] and a large peak at m/e 41 (CH_2=CH-$\overset{+}{C}H_2$). The ^{19}F n.m.r. spectrum showed only four fluorines with shifts of 129.8, 142.3, 156.4 and 159.3 ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum showed a doublet at δ 3.73 (1 unit), a signal at δ 3.96 (1 unit), a signal at δ 5.26 (2 units) and a broad multiplet from δ 5.78 to δ 6.45 (1 unit). This compound has been confirmed as 2-(prop-2-enyl)-3,4,5,6-tetrafluorophenyl prop-2-enyl thioether (116) (see chapter 4).

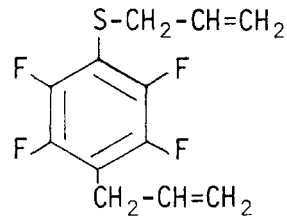
The other two compounds, isolated with more difficulty, were isomers with M^+ 222 and four fluorines in their ^{19}F n.m.r. spectra. These isomers have been confirmed as 5,6,7,8-tetrafluorothiachroman (109), obtained in ca. 2% yield, and 2H,3H-2-methyl-4,5,6,7-tetrafluorobenzo (b) thiophene (110), obtained in ca. 5% yield.

The most unusual feature of this reaction of the thioether (101) is the formation of 2-(prop-2-enyl)-3,4,5,6-tetrafluorophenyl prop-2-enyl

thioether (116). Also, the isomeric compound 4-(prop-2-enyl)-2,3,5,6-tetrafluorophenyl prop-2-enyl thioether (117), prepared independently,



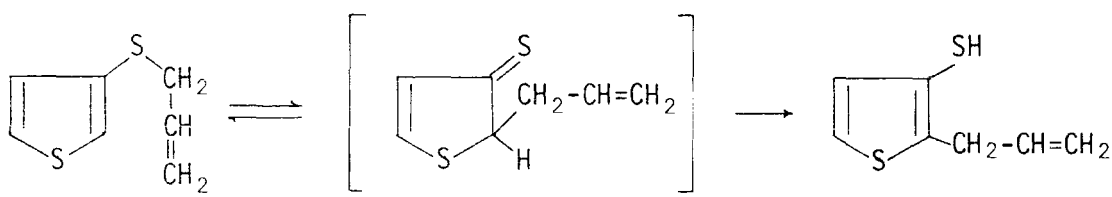
(116)



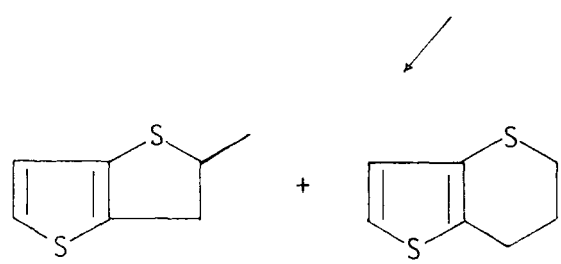
(117)

was shown not to be a product (by comparison of its g.l.c. retention time with the products in the reaction mixture).

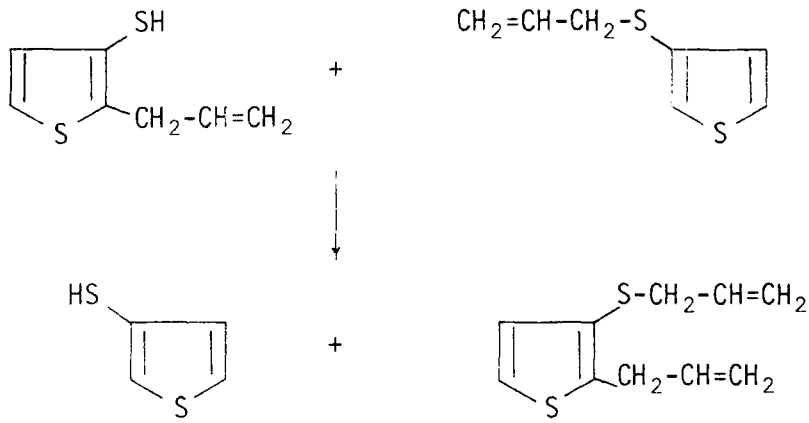
There is little precedent for this behaviour except for the reaction of prop-2-enyl 3-thienyl thioether (118) in N,N'-dimethyl-aniline[44]. The thioether (118) underwent thio-Claisen rearrangement to 2-(prop-2-enyl) 3-thienyl thiol (119) which cyclised to the thienyl thiophene (120) and the thienyl thiapyran (121). In addition the thiol (119) attacked more starting material (118) to give 3-thienyl thiol (122) and 2-(prop-2-enyl)-3-thienyl prop-2-enyl thioether (123).



(118) (124) (119)



(120) (121)



(122) (123)

Although this reaction gives products similar to those from pentafluorophenyl prop-2-enyl thioether (101) there is a major difference mechanistically. The intermediate thione (124) can tautomerise to the 3-thienyl thiol (119) whereas a similar process cannot occur with the thioether (101) which has the ortho and para positions blocked with fluorine as the substituent.

Work with 2,3,5,6-tetrafluorophenyl prop-2-enyl thioether (125) allowed a mechanism to be proposed for the reaction of (101) in N,N-diethylaniline and this will be discussed in chapter 3.

Chapter 2 Experimental

2.4 Synthesis of Pentafluorophenyl Prop-2-enyl Thioether (101)

Pentafluorothiophenol (106) (76.7g) and dry tetrahydrofuran (700 ml) were cooled to -75°C under nitrogen and n-butyllithium solution (320 ml, 1.28M) was added over 2 hours keeping the temperature below -73°C, the last traces being washed in with more dry tetrahydrofuran (100 ml). Prop-2-enyl bromide (52.9g) in dry tetrahydrofuran (100 ml) was added over 20 minutes at -70°C. The mixture was allowed to warm to room temperature over 4 hours, and was diluted with water (800 ml), acidified with hydrochloric acid (200 ml, 2M) and extracted with ether (3 x 300 ml). The extracts were dried ($MgSO_4$), the solvents were removed by distillation through a 60 cm column and the residue was distilled in vacuo to give pentafluorophenyl prop-2-enyl thioether (101) (81.4g), b.p. 76°C at 9.5 mm Hg. (Found: C, 45.23; H, 2.36%;M^+, 240. $C_9H_5F_5S$ requires C, 45.0; H, 2.08%; M, 240). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed signals at 131.7 (F ortho), 153.0 (F para), and 161.9 (F meta) ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a doublet at δ 3.53 (CH_2), a multiplet at 4.97 (vinylic CH_2) and a broad multiplet from 5.51 to 6.18 (vinylic CH).

2.5 Static thermolysis of Pentafluorophenyl Prop-2-enyl Thioether (101)

The thioether (101) was sealed in a 2 litre bulb evacuated to low pressure (0.01 mm Hg) and heated at 205°C for 16 hours and at 220°C for 72 hours. The products were condensed into a side-arm using liquid air, the vessel was opened and the mixture was washed out

using diethyl ether. The ether solution was dried ($MgSO_4$) and the solvent evaporated to give a residue which was analysed by g.l.c. (30% silicone elastomer at 150°C) showing only unchanged starting material (101). In another static thermolysis the thioether (101) (0.62g) was heated at 235°C for 15 hours, at 244°C for 8 hours, and at 254°C for 17 hours but no reaction occurred. Similarly in a further static thermolysis the thioether (101) (1.0g) was heated at 250°C for 19 hours but only gave unchanged starting material (101).

2.6 Flow pyrolysis of Pentafluorophenyl Prop-2-enyl Thioether (101)

The thioether (101) (0.35g) was distilled from a vessel through a silica tube (58 cm x 1.4 cm diam.) packed with quartz wool and heated in a cylindrical furnace at 370°C, into a trap cooled with liquid air, connected to a high vacuum system (0.001 mm Hg). The products thus obtained were analysed by g.l.c. (30% silicone elastomer at 165°C) which only showed unchanged starting material (101). Further pyrolysis of the thioether (101) (0.35g) at 465°C gave an orange oil containing starting material (101), pentafluorothiophenol (106), and two unidentified volatile components. Pyrolysis of the thioether (101) (0.3g) at 510°C gave a brown oil containing pentafluorothiophenol (106) and the same two unidentified volatile components.

2.7 Comparison of reaction of Pentafluorophenyl Prop-2-enyl Thioether (101) in various solvents

The thioether (101) was refluxed under nitrogen for 22 hours in various solvents using 10 ml of solvent per gramme of thioether (101).

The mixture was then treated with excess hydrochloric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue which was distilled in vacuo b.p. $\leqslant$ 120°C at 0.05 mm Hg. The distillate was analysed by g.l.c. (2-cyanoethylmethylsilicone at 190°C). The reaction in N,N'-dimethylaniline gave starting material (101) and an unidentified volatile component. The reaction in N,N'-diethylaniline gave ca. 60% distillate containing at least fourteen components. The reaction in quinoline gave ca. 10% distillate containing at least 6 components, and a tarry residue. The reaction in dimethylsulphoxide gave ca. 52% distillate containing starting material (101) and five other components, and a tarry residue. The reaction in n-decane only gave starting material (101).

2.8 Synthesis of 2,3,4,5-Tetrafluorophenyl Prop-2-enyl Thioether (107)

2,3,4,5-Tetrafluorothiophenol (108) (13.01g) and dry tetrahydrofuran (100 ml) were cooled to -76°C under nitrogen and n-butyllithium solution (51 ml, 1.43M) was added over 1 hour keeping the temperature below -60°C. The solution was stirred 1 hour at -76°C before adding prop-2-enyl bromide (11.09g) and allowing the mixture to warm to room temperature over 3 hours. The solution was diluted with water and extracted with ether. The extracts were dried ($MgSO_4$) and the solvent removed by distillation through a 60 cm column to give a residue which was distilled in vacuo to give 2,3,4,5-tetrafluorophenyl prop-2-enyl thioether (107) (13.51g) b.p. 76 - 78°C at 7 mm Hg. (Found: C, 48.93; H 2.90%; M^+, 222. $C_9H_6F_4S$ requires C, 48.65; H, 2.70%; M, 222). The ^{19}F n.m.r. spectrum (neat liq.) showed four signals of equal intensity at 135.1, 140.9, 156.7, and 158.3 ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum (neat liq.) showed a doublet at δ 3.65 (CH_2), a multiplet at 5.23 (vinylic CH_2),

a broad multiplet from 5.65 to 6.33 (vinylic CH), and a multiplet at 7.15 (aromatic CH).

2.9 Reaction of 2,3,4,5-Tetrafluorophenyl Prop-2-enyl Thioether (107) in N,N'-diethylaniline

The thioether (107) (5.05g) was refluxed in N,N'-diethylaniline (50 ml) under nitrogen for 23 hours. The mixture was acidified with hydrochloric acid (2M), extracted with ether, and the extracts dried ($MgSO_4$). The solvent was evaporated to give a residue which was distilled in vacuo to give a liquid (4.07g) b.p. $\leqslant$ 100°C at 0.05 mm Hg which contained three components by g.l.c. (2-cyanoethylmethylsilicone at 200°C). Chromatography of this liquid on silica (190 cm x 2.4 cm diam.) (light petroleum b.p. 30 - 40°C as eluent) gave a mixture of two components and then 5,6,7,8-tetrafluorothiachroman (109) (2.00g), identified by i.r.. The mixture of two components was separated by preparative g.l.c. (2-cyanoethylmethylsilicone at 200°C) to give two fractions: (i) 1.08g of a mixture of (110) and a more volatile material, which was not isolated, present in approximately equal amounts; and (ii) 2H,3H-2-methyl-4,5,6,7-tetrafluorobenzo(b)-thiophene (110) (0.91g) b.p. 40 - 45°C at 0.05 mm Hg. (Found: C, 48.9; H, 2.8%; M^+, 222. $C_9H_6F_4S$ requires C, 48.65; H, 2.70%; M, 222). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed four signals of equal intensity at 140.0, 141.4. 157.4 and 161.5 ppm upfield from internal $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a doublet at δ 1.48 (CH_3), a broad multiplet from 3.01 to 3.46 (CH_2), and a multiplet at 4.12 (CH). The isolated yields of (109) and (110) are 40% and 30% respectively.

2.10 Detailed investigation of reaction of Pentafluorophenyl Prop-2-enyl Thioether (101) in N,N'-diethylaniline

The thioether (101) (24.1g) and N,N'-diethylaniline (240 ml) were refluxed under nitrogen for 23 hours. The mixture was treated with excess hydrochloric acid (4M), polymeric perfluoropoly(phenylene sulphide) (114) (1.37g) was filtered off and identified by i.r., and the filtrate was extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue containing at least fourteen components by g.l.c. (2-cyanoethylmethylsilicone at 200°C) and this was distilled in vacuo through a 15 cm concentric tube fractionating column. This gave fourteen fractions: (i) Fractions 1 to 3 (8.23g) b.p. 76 - 81.5°C at 13 mm Hg was ca. 75% thioether (101) and another component identified in a further experiment as pentafluorophenyl ethyl thioether (115); (ii) Fractions 4 to 11 (5.91g) b.p. 19 - 80°C at 0.05 mm Hg; the components of fractions 4 to 6 (1.91g) were partially separated by thick layer chromatography on silica (light petroleum b.p. 40 - 60°C as eluent) to give (2H,3H)-2-methyl-4,5,6,7-tetrafluorobenzo(b)thiophene (110) (0.33g) identified by i.r.; the components of fractions 9 and 10 (3.1g) were partially separated by repeated preparative g.l.c. (2-cyanoethylmethylsilicone at 210°C) to give 2-(prop-2-enyl)-3,4,5,6-tetrafluorophenyl prop-2-enyl thioether (116) (0.39g) identified by i.r.; (iii) Fractions 12 to 14 (0.82g) b.p. 44 - 95°C at 0.001 mm Hg; components of fractions 12 and 13 (0.25g) were partially separated by thick layer chromatography on silica (light petroleum b.p. 40 - 60°C as eluent) to give 5,6,7,8-tetrafluorothiachroman (109) (0.043g) identified by i.r.; (iv) a residue (8.4g).

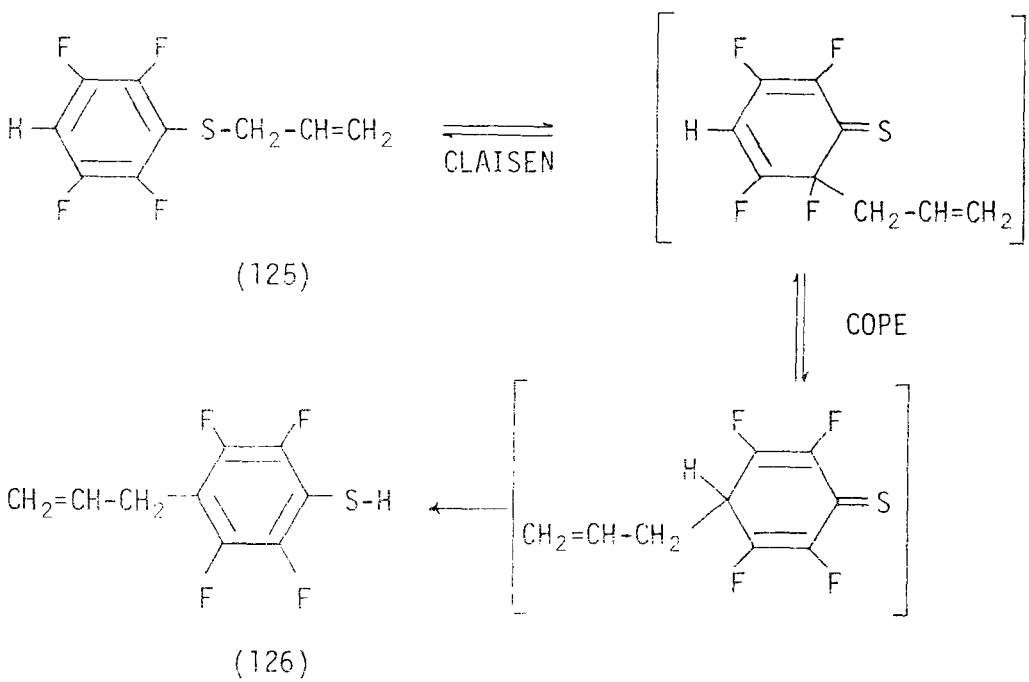
In a separate experiment under identical conditions the thioether (101) (1.23g) gave a volatile material (0.75g) b.p. 25 - 110°C at

0.05 mm Hg. G.l.c. analysis (using a gas density balance with 30% silicone elastomer at 200°C) indicates the presence of unreacted thioether (0.31g) in an eleven component mixture. Compounds (109), (110) and (116) had essentially the same retention times and 0.19g of the distillate (ca. 15% yield). From the fractional distillation it is estimated that this 15% yield is composed of ca. 8% (116), ca.5% (110) and ca. 2% (109).

Chapter 3 Synthesis and Reactions of 2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (125) and Isolation of Pentafluorophenyl Ethyl Thioether (115)

3.1 Introduction

Pentafluorophenyl prop-2-enyl thioether (101) gave a complex mixture with N,N'-diethylaniline when refluxed for 23 hours, whereas 2,3,4,5-tetrafluorophenyl prop-2-enyl thioether (107) underwent a clean thio-Claisen rearrangement under the same conditions. It was expected that 2,3,5,6-tetrafluorophenyl prop-2-enyl thioether (125) would undergo a para thio-Claisen rearrangement to give 4-(prop-2-enyl)-2,3,5,6-tetrafluorothiophenol (126).



(125)

(126)

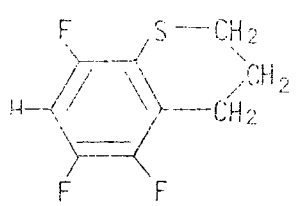
The thioether (125) was synthesised (83% yield) from 2,3,5,6-tetrafluorothiophenol (127) by treatment with n-butyllithium and then prop-2-enyl bromide. Vapour phase thermolysis at 210°C for 22 hours gave no reaction and decomposition occurred in a neat

liquid phase reaction in a sealed tube at 210°C for 22 hours to give a tarry mixture of at least five components by t.l.c.

3.2 Reaction of 2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (125) in N,N-diethylaniline

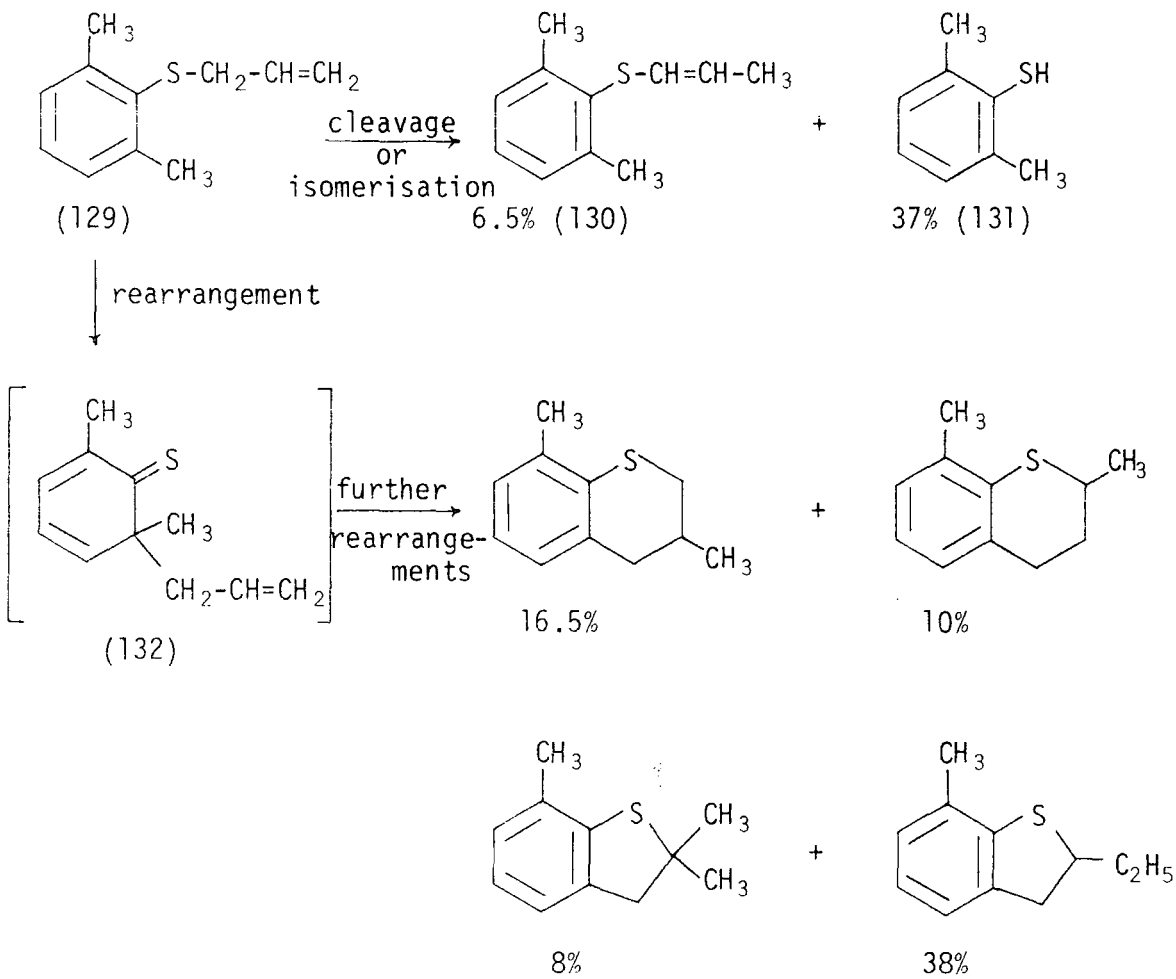
Neat thermolysis of the thioether (125) did not involve rearrangement and so reaction in N,N-diethylaniline was tried to promote thio-Claisen rearrangement. The thioether (125) was refluxed for 22.5 hours in N,N-diethylaniline to give a residue which was distilled up to 100°C at 0.5 mm Hg. The distillate was chromatographed on silica to give material with t.l.c. retention time and infra-red essentially that of unreacted thioether (125) ca. 64% and one other major component in ca. 14% yield plus components in much smaller amounts.

The component obtained in ca. 14% yield was identified as 5,7,8-trifluorothiachroman (128) by spectroscopic data. The mass spectrum had M^+ 204, which is equivalent to starting material (125) minus one fluorine plus one hydrogen atom. The ^{19}F n.m.r. spectrum only showed three signals of equal intensity at 120.6, 139.0 and 144.7 ppm upfield from internal $CFCl_3$. The ^1H n.m.r. spectrum showed multiplets at δ 2.14, δ 2.78, δ 3.01 for three CH_2 groups and a multiplet at δ 6.64 for an aromatic proton.



(128)

When a para-Claisen rearrangement was attempted by refluxing 2,6-dimethylphenyl prop-2-enyl thioether (129) in quinoline no para-substituted thiophenol was obtained[45]. Instead isomerisation of the thioether (129) gave 2,6-dimethylphenyl prop-1-enyl thioether (130) and cleavage produced 2,6-dimethylthiophenol (131). In addition four isomeric bicyclic products were obtained. Their formation was explained by considering a thio-Claisen rearrangement of the thioether (129) to an intermediate ortho-dienethione (132) which subsequently rearranged to the cyclised compounds.

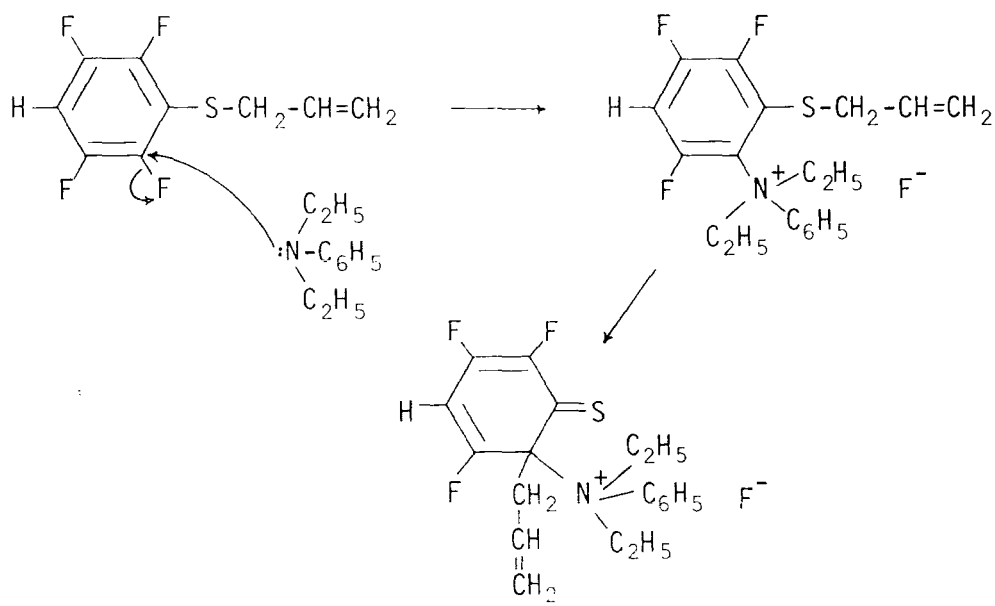


A similar process cannot occur for the thioether (125) because the product formed (128) has lost a fluorine and gained a hydrogen

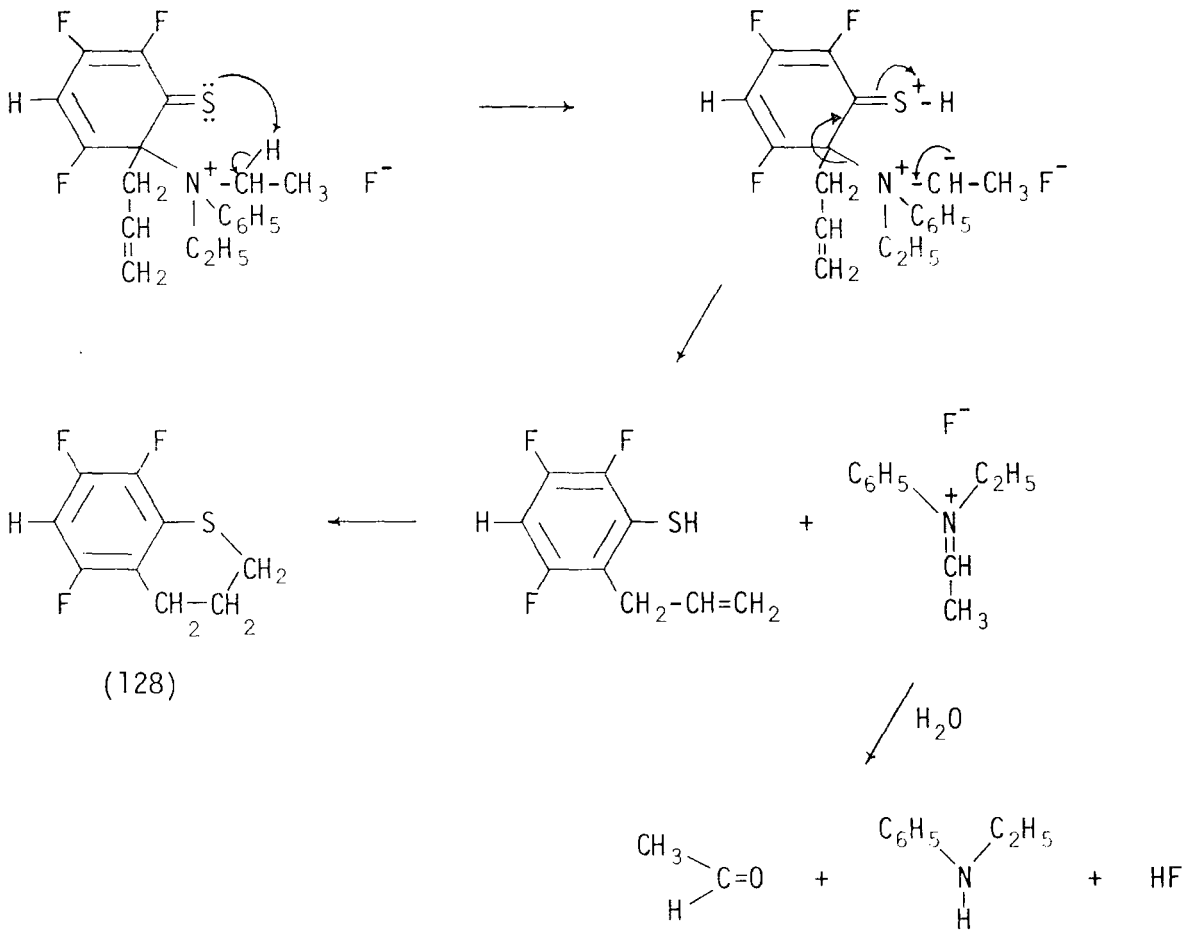
atom. In order to investigate the role of the solvent in the reaction, excess thioether (125) was reacted with N,N-diethylaniline in a sealed tube at 210°C for 22 hours giving a red solid and liquid. The solid was dissolved in aqueous acid to give a solution which was shown to contain fluoride ion. A similar mixture of products was obtained to those from refluxing the thioether (125) in excess diethylaniline with ca. 16% of the thiachroman (128) and ca. 49% of material assumed, on the basis of t.l.c., to be unreacted thioether (125); the yields are based on the N,N-diethylaniline used. In addition a complex mixture of at least eight components was obtained in the amine residue from which N-ethylaniline was isolated as the major component, in ca. 20% yield.

This reaction poses an interesting problem to account for mechanistically. In order to obtain the thiachroman (128) the thioether (125) must lose a fluorine and gain a hydrogen with the solvent playing a direct part, giving N-ethylaniline. Two possible explanations were considered involving either nucleophilic or electrophilic displacement of fluorine.

In the first mechanism, nucleophilic attack occurs by the solvent at C-2 of the thioether (125) followed by thio-Claisen rearrangement with migration of the prop-2-enyl group to C-2.



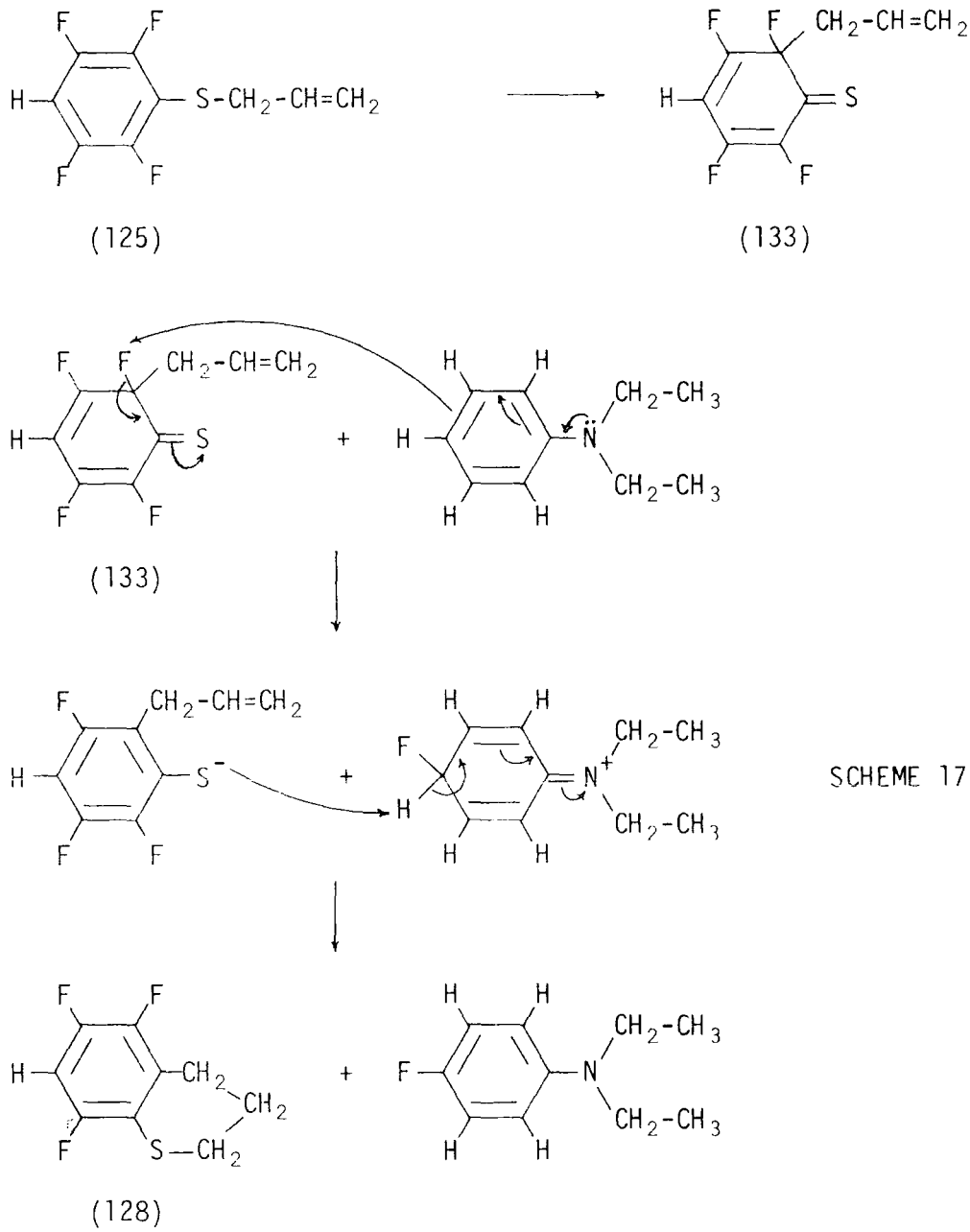
The thiocarbonyl sulphur abstracts a proton from an ethyl group of the amino group to give a nitrogen ylid and an ortho prop-2-enyl thiophenol, which cyclises to the thiachroman (128). Hydrolysis of the ylid should give acetaldehyde and N-ethylaniline (Scheme 16).



(128)

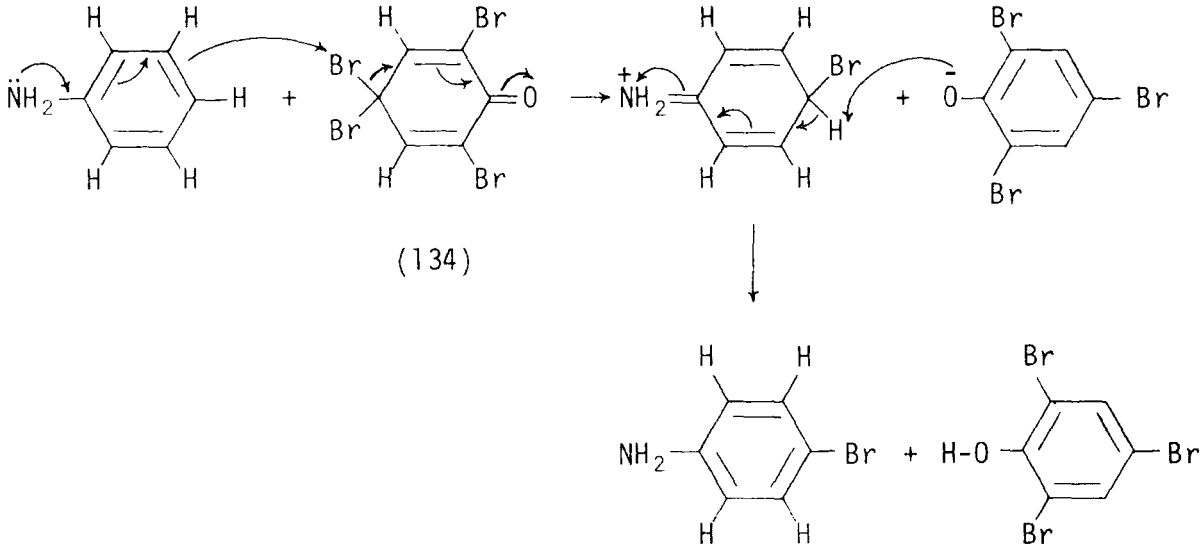
SCHEME 16

The other proposal requires loss of a positive fluorine ion. The thioether (125) rearranges to an ortho-dienethione (133) which is attacked by the solvent. The amine is substituted by electrophilic fluorine in the para-position to give p-fluoro-N,N-diethylaniline, and the ortho-prop-2-enyl thiol formed concurrently then cyclises to give the thiachroman (128) (Scheme 17).



SCHEME 17

The driving force for the loss of fluorine is the aromatisation of the ortho-dienethione. A similar process is illustrated with 2,4,4,6-tetrabromocyclohexa-2,5-dienone (134) which has been used to brominate aromatic amines in the para position[46]. Here the dienone (134) acts as a source of electrophilic bromine and in so doing it aromatises to 2,4,6-tribromophenol.



(134)

3.3 Further Investigation into Mechanism of Reaction of 2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (125) and N,N-diethylaniline: Search for Acetaldehyde

In an attempt to isolate acetaldehyde or para-fluoro-N,N-diethylaniline from the reaction mixture from the thioether (125) and N,N-diethylaniline, a further sealed tube reaction was carried out at 210°C for 22 hours with excess thioether (125) and N,N-diethylaniline. The solid obtained was dissolved in acid and the resulting aqueous solution was shown to contain fluoride ion, but no 2,4-dinitrophenylhydrazone derivative was obtained. Blank solutions of acetaldehyde in dilute acid were made up with concentrations similar to and less than that expected from the tube reaction of (125) and all these gave precipitates on addition of the 2,4-dinitrophenylhydrazine reagent. It is concluded that no acetaldehyde is formed during work up in this reaction which discounts the mechanism outlined in Scheme 16. No fluorine was incorporated into the solvent since no ^{19}F n.m.r. signals were found in recovered amine solvent and this rules out the

electrophilic fluorine displacement given in Scheme 17.

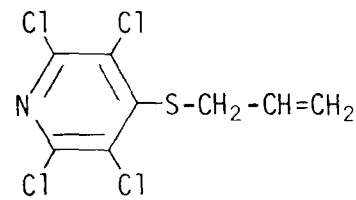
This left the problem of how the thioether (125) did lose a fluorine and gain a hydrogen. In a further investigation of this reaction the thioether (125) was refluxed for 190 hours in N,N-diethylaniline in order to increase the yield of products. The resulting solution was stirred with water for 20 minutes and the aqueous phase was shown to contain fluoride ion but again no carbonyl compound. Addition of base to the aqueous phase allowed N,N-diethylaniline to be isolated from which it was assumed that the salt in the solution was N,N-diethylanilinium fluoride. The organic phase contained four major components as shown by coupled g.l.c.-mass spectrometry. In order of increasing g.l.c. retention time these had masses as follows: (i) M^+ 210, [starting material - 41 (prop-2-enyl) + 29 (ethyl)]; (ii) M^+ 222, starting material (125); (iii) M^+ 204, [starting material - 19 (fluorine) + 1 (hydrogen)]; and (iv) M^+ 204, thiachroman (128). The first three components all had t.l.c. retention times essentially the same and their separation was very difficult.

Chromatography on silica gave material with the t.l.c. retention time of (125) (but what in fact by g.l.c. was a mixture of three components), and the thiachroman (128) in ca. 12% yield. The first material was treated with borane-tetrahydrofuran solution to convert all alkenes to organo-boranes which would be effectively static during chromatography on silica. Chromatography gave a mixture of the components with M^+ 210 and M^+ 204 and these were separated by preparative g.l.c. and identified as 2,3,5,6-tetrafluorophenyl ethyl thioether (135), obtained in ca. 18% yield, and 2H,3H-2-methyl-4,6,7-trifluorobenzo(b)thiophene (136), obtained in ca. 5% yield.

The tetrafluorophenyl ethyl thioether (135), which had a very similar infra-red spectrum to the starting material (125), was

confirmed by an independent synthesis. Treatment of 2,3,5,6-tetrafluorothiophenol (127) with n-butyllithium followed by reaction with ethyl iodide gave the thioether (135) in 76% yield.

The 2H,3H-benzo (b) thiophene (136) had a ^{19}F n.m.r. spectrum with only three signals of equal intensity at 117.9, 136.1 and 143.7 ppm upfield from external $CFCl_3$. The ^{1}H n.m.r. spectrum showed a doublet at δ 1.49 for the CH_3 group, a broad multiplet centred at δ 2.98 and δ 3.41 for the CH_2 group, a signal at δ 4.14 for the aliphatic proton, and a signal at δ 6.57 for the aromatic proton.

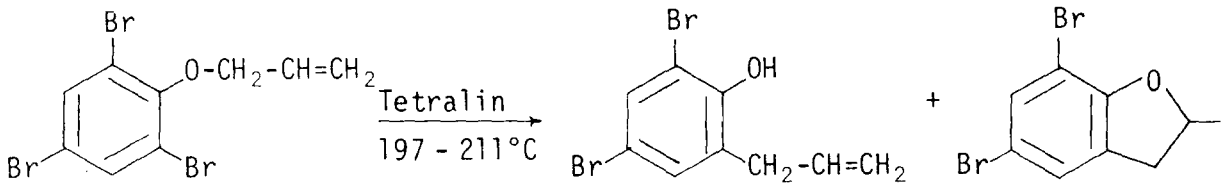


(137)

The only reported rearrangement of an aryl prop-2-enyl thioether with the ortho positions blocked by halogens involves 2,3,5,6-tetrachloro-4-pyridyl prop-2-enyl thioether (137)[47]. However, this produced intractable material on attempted rearrangement.

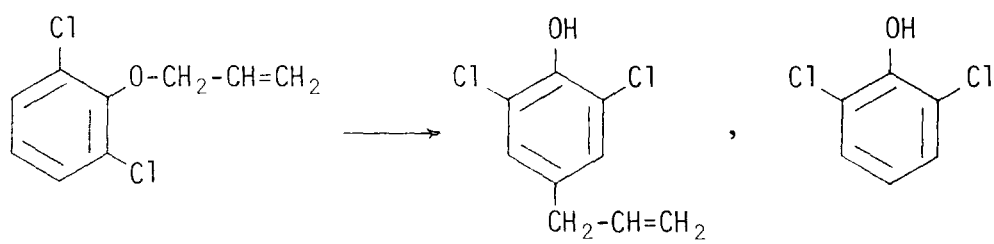
There have been a number of studies with related ethers with the ortho positions blocked by halogens. 2,4,6-Tribromophenyl prop-2-enyl ether (138) reacts in tetralin at 197 - 211°C over 2 hours to give the bromo-displacement products 2-(prop-2-enyl)-4,6-dibromophenol (139) in 68% yield and 2H,3H-2-methyl-5,7-dibromobenzo (b) furan (140) in 17% yield[48]. The bicyclic compound was formed by the cyclisation of the phenol (141) but not in the absence of hydrogen bromide. The phenol formation requires a dehydrogenation of the solvent or reactant so that the ether (138) reacts with two

hydrogen atoms to give the phenol (139) and hydrogen bromide.

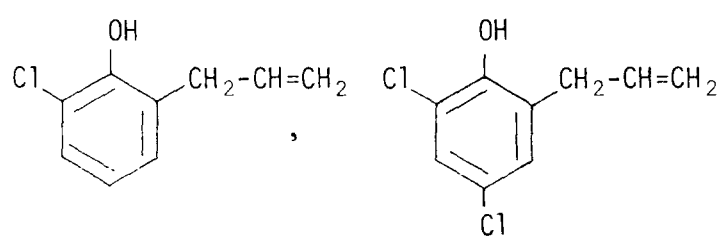


(138) (139) (140)

2,6-Dichlorophenyl prop-2-enyl ether (141) reacts at 180°C - 200°C to give 4-(prop-2-enyl)-2,6-dichlorophenol (142) as the main product by para-Claisen rearrangement[49]. Also formed are 2,6-dichlorophenol (143) by cleavage of the ether function, 2-(prop-2-enyl)-6-chlorophenol (144) by reductive removal of chlorine, and 2-(prop-2-enyl)-4,6-dichlorophenol (145) by chlorine migration, with the amounts varying depending on the solvents used.



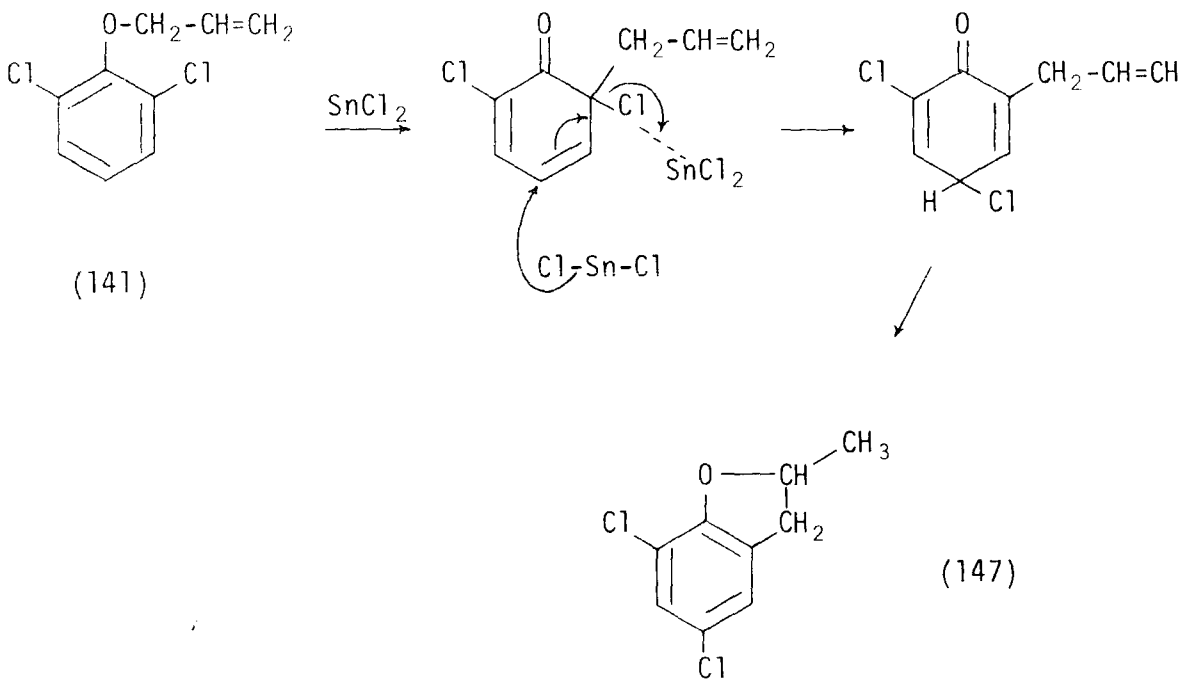
(141) (142) (143)



(144) (145)

No cyclisation occurred under these conditions, but with added

stannous chloride in 1,2-dichlorobenzene as solvent, 2H,3H-2-methyl-7-chlorobenzo (b) furan (146) and 2H,3H-2-methyl-5,7-dichlorobenzo (b) furan (147) were obtained in 8% and 4% yields respectively[50]. The stannous chloride acted as a Lewis acid catalyst. It not only speeded up the rate of reaction but also caused chlorine migration in the intermediate ortho-dienone giving the 2H,3H-benzo (b) furan (147) on cyclisation. The mechanism proposed is shown in Scheme 18.



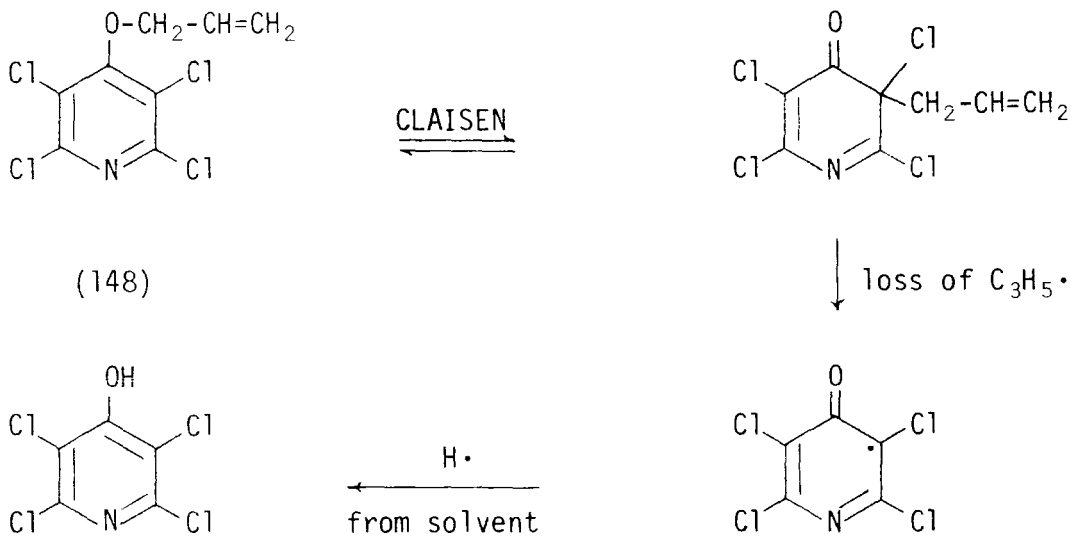
(141)

(147)

SCHEME 18

Recently the results of the thermal rearrangement of 2,3,5,6-tetrachloro-4-pyridyl prop-2-enyl ether (148) in sulpholane have been published[47]. This gives 2,3,5,6-tetrachloro-4-hydroxypyridine (149) in 6% yield and 3-(prop-2-enyl)-2,5,6-trichloro-4-hydroxy-pyridine (150) in 26% yield. In addition two cyclised products are formed: 6% of 4,6,7-trichloro-2,3-dihydro-2-chloromethylfuro[3,2,-c] pyridine (151) and 10.5% of 4,6,7-trichloro-2,3-dihydro-2-methylfuro [3,2,-c]pyridine (152). The formation of all these products was

rationalised in terms of an initial Claisen rearrangement followed by homolytic cleavage at C-3 by loss of a chlorine atom or a prop-2-enyl radical. Subsequent cyclisation was followed by hydrogen abstraction (probably from the solvent) to give (152), or by chlorine abstraction (or reaction with a chlorine atom) to give (151) (Scheme 19).

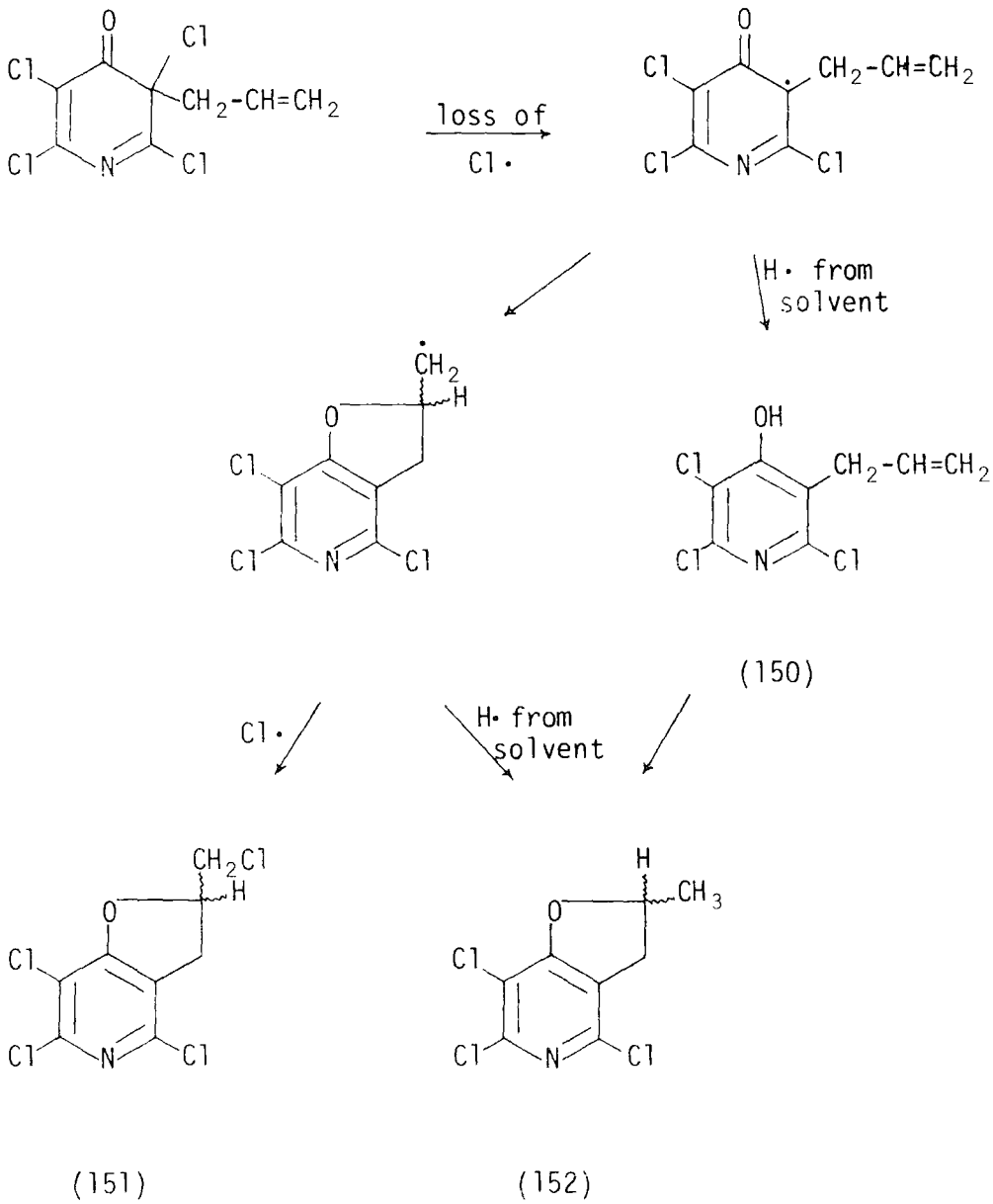


(148)

(149)

The formation of the thiachroman (128) and the 2H,3H-benzo(b)-thiophene (136) from the thioether (125) did not occur with inclusion of fluorine in the heterocyclic rings which contrasts with the isolation of the chloromethyl compound (151) derived from the ether (148)[47].

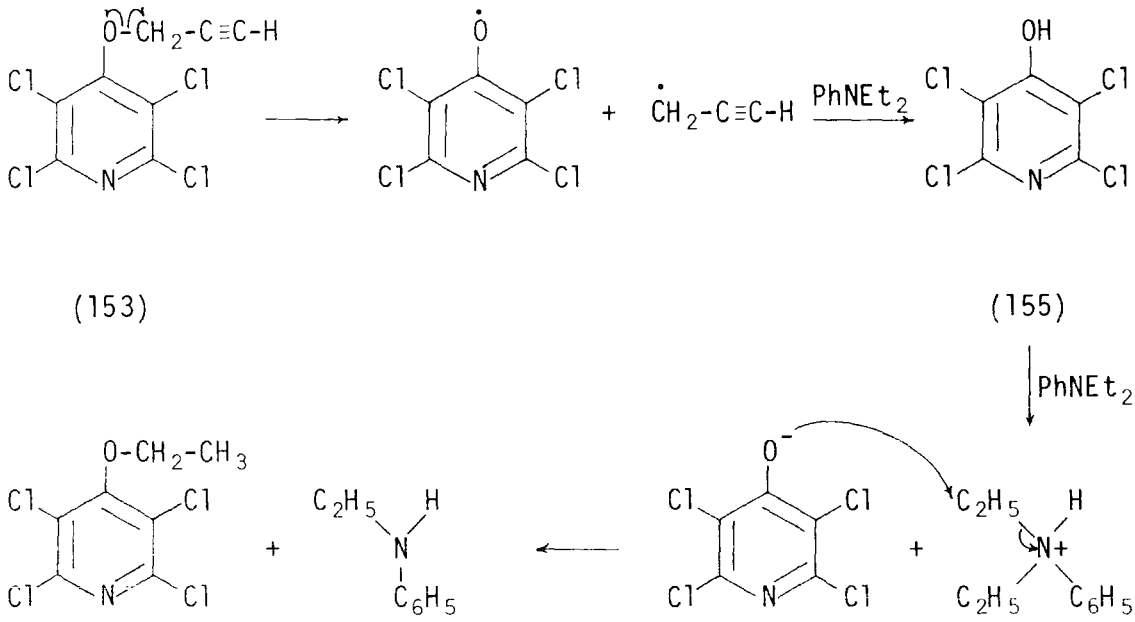
In contrast the reaction of 2,3,5,6-tetrachloro-4-pyridyl prop-2-ynyl ether (153) in N,N-diethylaniline gave ethyl 2,3,5,6-tetrachloro-4-pyridyl ether (154) and 2,3,5,6-tetrachloro-4-hydroxy-pyridine (155) as the only isolable products[47]. In order to explain these results a mechanism was proposed invoking cleavage of the ether (153) leading to the hydroxypyridine (155). Acid-base reaction of (155) with the solvent would give the anion of (155) and this



(151) (152)

SCHEME 19

would attack the protonated amine giving the ethyl ether (154) and N-ethylaniline.



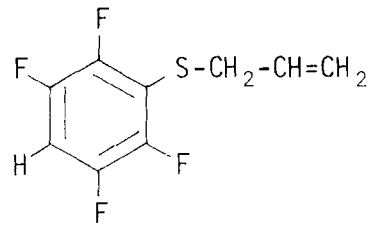
(153) (155)

(154)

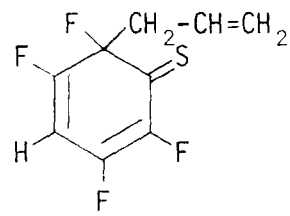
Support for this proposal came from the reaction of (155) with N,N-diethylaniline which in a separate experiment gave the ethyl ether (154).

Up till now the explanations for the formation of the thiachroman (128) from the thioether (125) have involved both thio-Claisen rearrangement and a consideration of either nucleophilic or electrophilic displacement of fluorine. The reactions just discussed set a precedent for considering a free radical mechanism to account for the loss of fluorine. The explanation now postulated involves an initial thio-Claisen rearrangement of the thioether (125) followed by homolytic cleavage at C-2 in the intermediate ortho-dienethione (133).

The ortho-dienethione (133) can either lose a fluorine atom or a prop-2-enyl radical from C-2. If a fluorine atom is lost the radical formed cyclises to two heterocyclic radicals which abstract

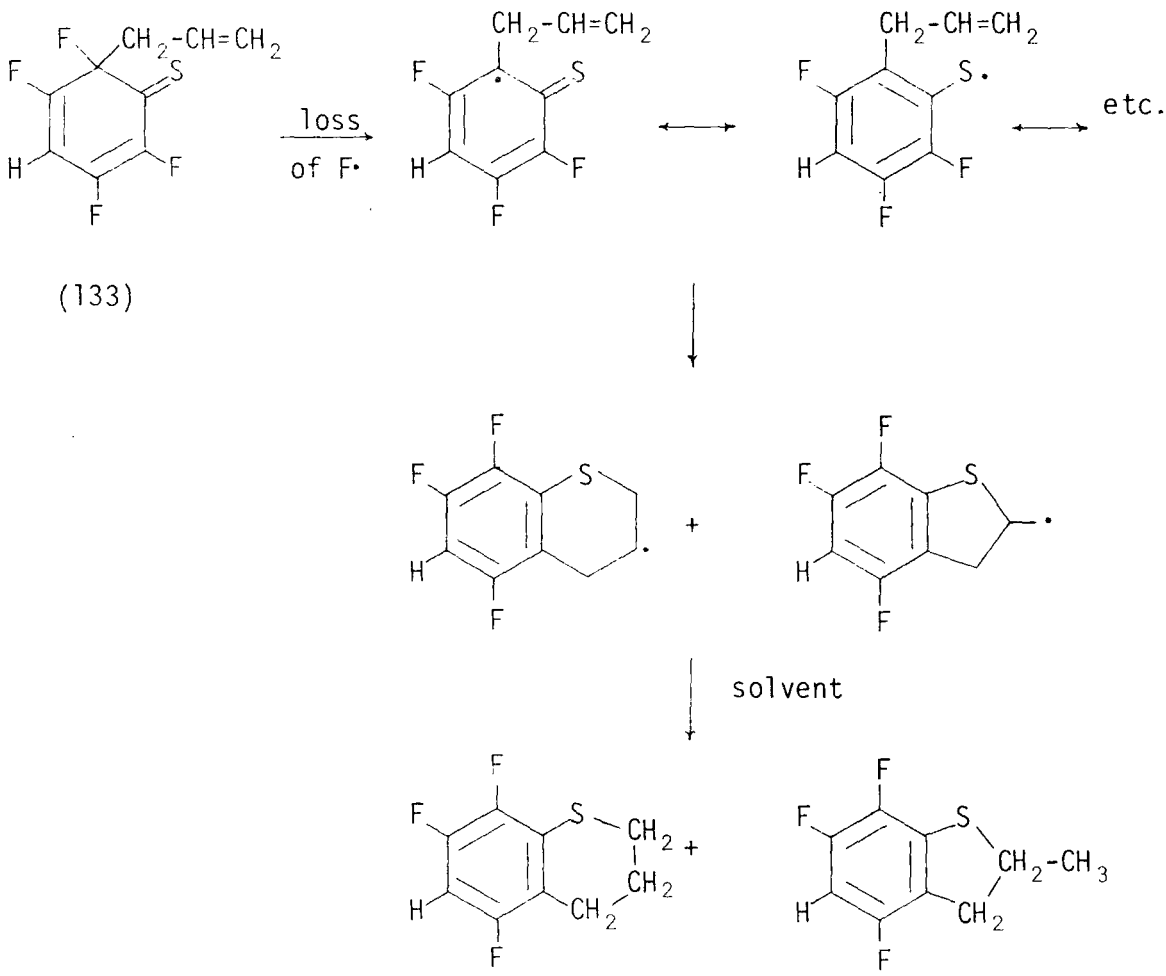


(125)



(133)

hydrogen from the solvent to give the thiachroman (128) and the benzo (b) thiophene (136). The fluorine abstracts a hydrogen from the solvent to give hydrogen fluoride which reacts with more solvent to give N,N-diethylanilinium fluoride.

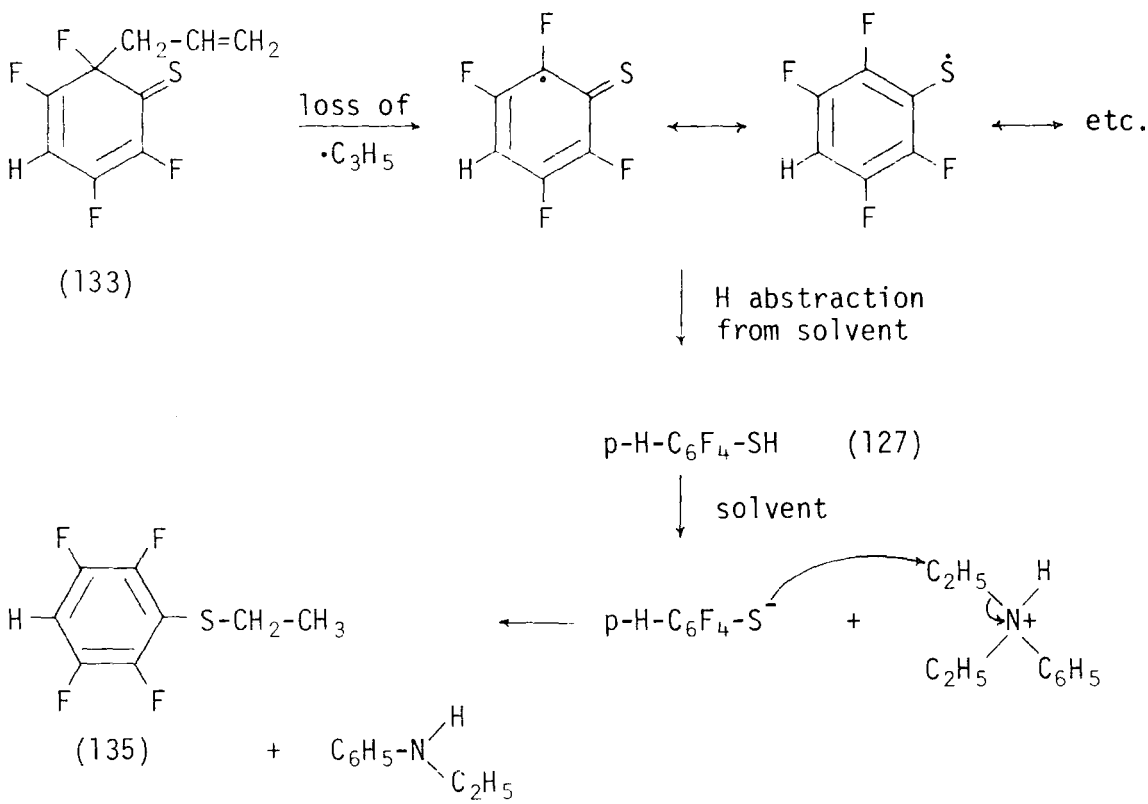


(133)

(128)

(136)

If the ortho-dienethione loses a prop-2-enyl radical, the resulting radical on abstraction of hydrogen from the solvent will give 2,3,5,6-tetrafluorothiophenol (127). Simple acid-base reaction with the solvent yields the thiolate anion and protonated diethylaniline, which leads to 2,3,5,6-tetrafluorophenyl ethyl thioether (135) and N-ethylaniline by nucleophilic displacement of an ethyl group from the amine by the thiolate anion in a manner which is similar to the formation of the ethyl ether (154) from the prop-2-ynyl ether (153) in N,N-diethylaniline.



The unusual proposal in this mechanism is the homolytic cleavage of a bond between fluorine and a sp^3-hybridised carbon in the ortho-dienethione (133). Of all the halogens, fluorine bonds most strongly to carbon and cleavage of a carbon to fluorine bond is energetically difficult (the bond energies for the carbon to halogen bond in the

halomethanes are 108, 84, 70, 56 kcal/mole where the halogens are fluorine, chlorine, bromine and iodine, respectively). A major driving force may be the aromatisation of the ortho-dienethione (133) with the production of a thiyl radical, which will be stabilised by resonance with the aromatic ring. Similar processes will be invoked later to explain the products formed by pentafluorophenyl prop-2-enyl thioether (101) and by pentafluorophenyl- and heptafluoro-2-naphthyl prop-2-ynyl ethers (see Chapters 5 and 6).

3.4 Further Investigation into the Reaction of Pentafluorophenyl Prop-2-enyl Thioether (101) and N,N-diethylaniline: Isolation of Pentafluorophenyl Ethyl Thioether (115)

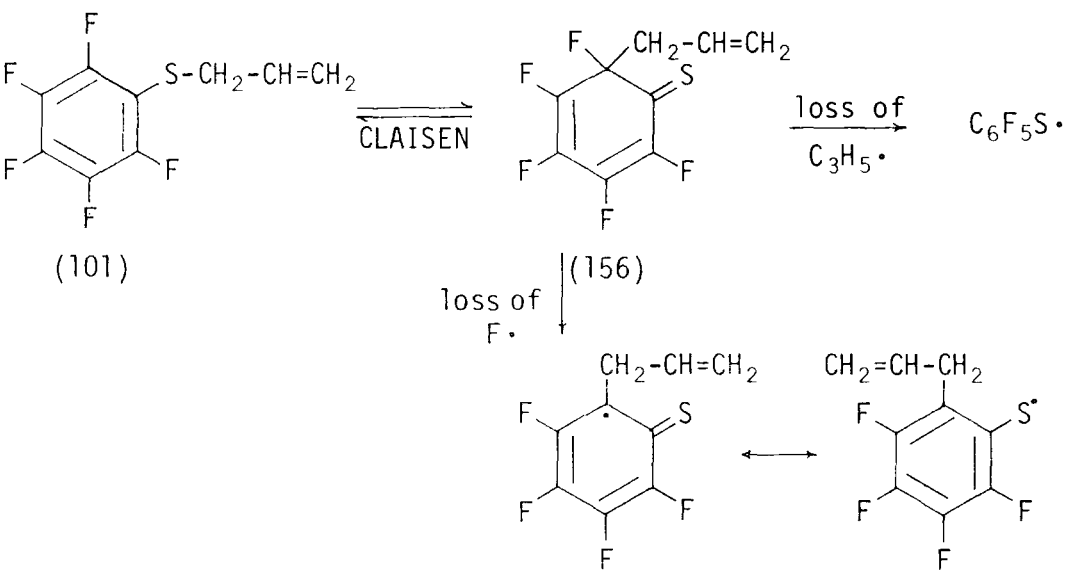
Since 2,3,5,6-tetrafluorophenyl prop-2-enyl thioether (125) reacted in N,N-diethylaniline to give the ethyl thioether (135) amongst its products, pentafluorophenyl prop-2-enyl thioether (101) should behave similarly in N,N-diethylaniline. This should give pentafluorophenyl ethyl thioether (115) amongst its products, and a specific search for this compound has shown that it is present in the complex reaction mixture.

The thioether (101) was refluxed for 23 hours in N,N-diethylaniline and the products were fractionally distilled up to 95°C at 8 mm Hg. The lowest boiling fractions contained unreacted starting material (101) and another component in ca. 6% yield. This other component was separated by preparative g.l.c. and confirmed by independent synthesis as pentafluorophenyl ethyl thioether (115), obtained in 68% yield from pentafluorothiophenol (106) by treatment with n-butyllithium and ethyl iodide.

From the various experiments carried out with the thioether (101)

in N,N-diethylaniline it is now known that perfluoro(polyphenylene-sulphide) (114) is produced in ca. 6% yield along with a fourteen component mixture. The major components of this mixture are pentafluorophenyl ethyl thioether (115) (ca. 6%), starting material (101) (ca. 30%), 5,6,7,8-tetrafluorothiachroman (109) (ca. 2%), 4,5,6,7-tetrafluorobenzo (b) thiophene (110) (ca. 5%) and 2-(prop-2-enyl)-3,4,5,6-tetrafluorophenyl prop-2-enyl thioether (116) (ca. 8%).

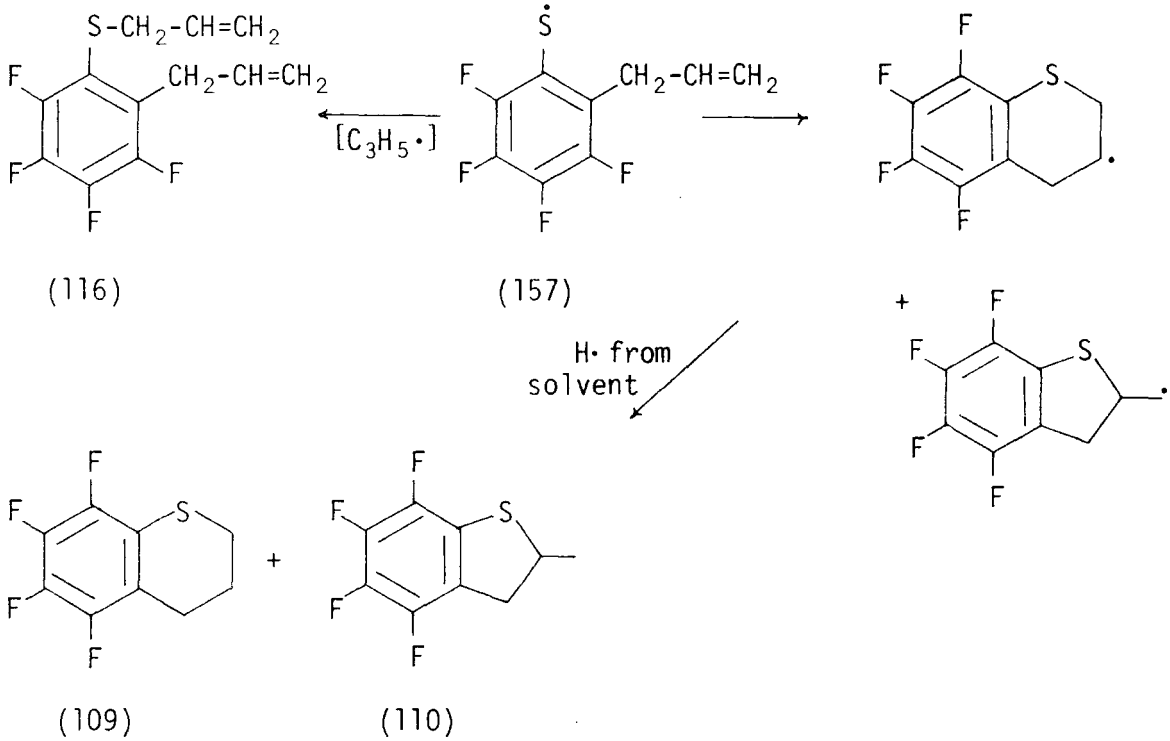
The explanation of the formation of the products from (101) is based on the mechanism proposed for the reaction of the tetrafluorophenyl thioether (125) in N,N-diethylaniline and it also involves homolytic cleavage of a carbon to fluorine bond. Pentafluorophenyl prop-2-enyl thioether (101) rearranges to 2-(prop-2-enyl)-2,3,4,5,6-pentafluorocyclohexa-3,5-dienethione (156) which undergoes homolytic cleavage at C-2 losing either a fluorine atom or a prop-2-enyl radical.



(157)

Loss of a fluorine atom from (156) leads to the radical (157), which can cyclise to two heterocyclic radicals giving the thiachroman

(109) and benzo (b) thiophene (110) by hydrogen abstraction from the solvent. Alternatively the radical (157) can combine with a prop-2-enyl radical to give the thioether (116). The fluorine atom abstracts a hydrogen from the solvent and subsequently ends up in N,N-diethylanilinium fluoride.



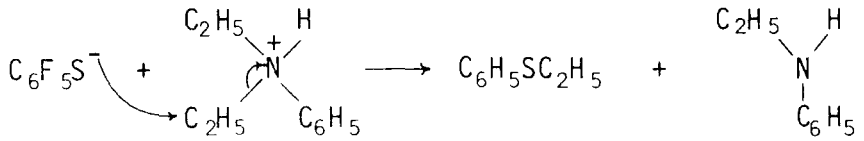
(116) (157) (109) (110)

Loss of a prop-2-enyl radical from (156) followed by hydrogen abstraction from the solvent leads to pentafluorothiophenol (106). This can undergo polymerisation by nucleophilic aromatic substitution to give perfluoro(polyphenylene sulphide)[51] (114).

$$nC_6F_5S\cdot \xrightarrow[\text{solvent}]{\text{H}\cdot\text{ from}} nC_6F_5SH \xrightarrow[\text{solvent}]{\text{basic}} C_6F_5S^- + p\text{-}F\text{-}C_6F_4SH \longrightarrow \{C_6F_4S\}_n$$

(106) (114)

The anion from pentafluorothiophenol (106) can also attack protonated N,N-diethylaniline to give the thioether (115) and N-ethylaniline by nucleophilic displacement of an ethyl group from the amine.

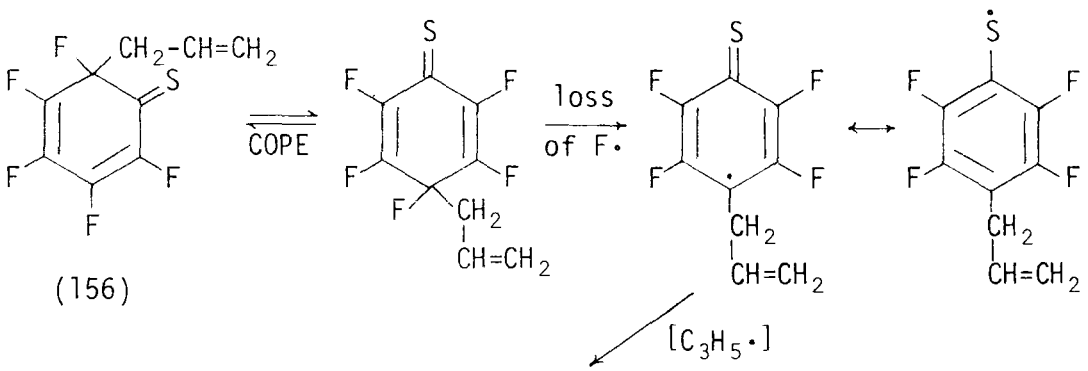


(115)

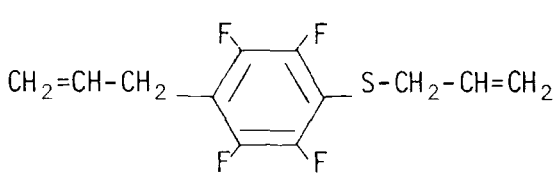
The major difference of the reaction of the thioether (101) compared to (125) in N,N-diethylaniline is in the formation of the 2-(prop-2-enyl) substituted thioether (116); no evidence was found for formation of an analogous thioether in the reaction of (125).

Three other compounds were considered to be likely products 4-(prop-2-enyl)-2,3,5,6-tetrafluorophenyl prop-2-enyl thioether (117), 4H-5,6,7,8-tetrafluorothiochromene (158) and N-ethyl-N-[4-(prop-2-enylthio)-2,3,5,6-tetrafluorophenyl-]aniline (159).

Surprisingly, none of the thioether (117) is obtained in the reaction mixture from (101) in N,N-diethylaniline. This rules out the possibility of a Cope rearrangement of the ortho-dienethione (156) to a para-dienethione which could give the thioether (117) in a process analogous to the formation of (116).

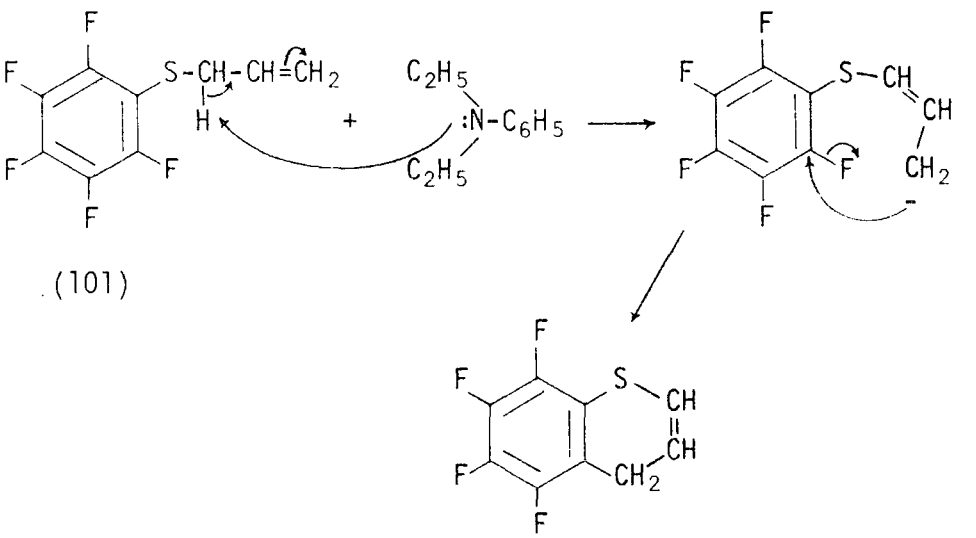


(156)



(117)

Attack of the basic solvent on the thioether (101) could lead to abstraction of a proton from the methylene group adjacent to the sulphur atom giving a carbanion. Cyclisation and displacement of fluoride ion could then occur to give the 4H-thiochromene (158).



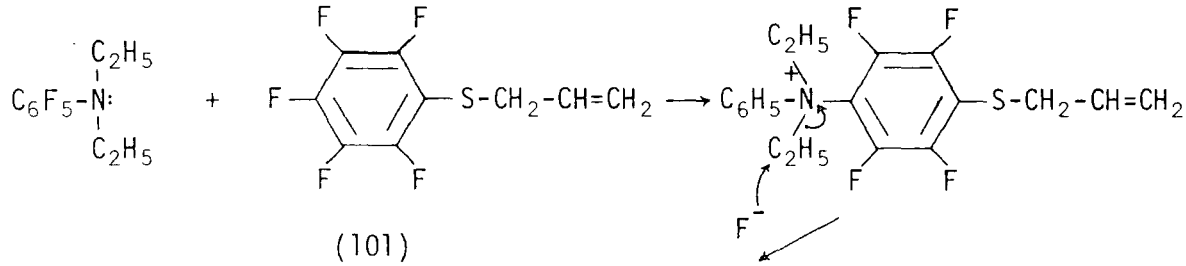
(101)

(158)

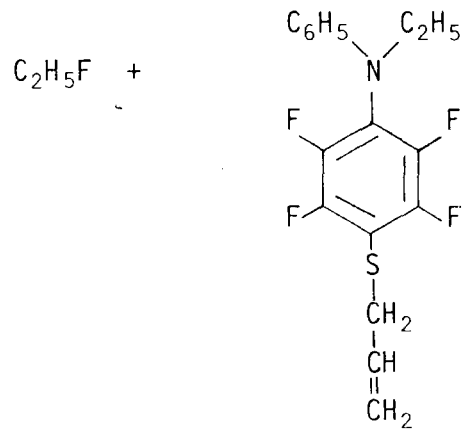
In an attempt to obtain (158) independently, the thioether (101) was refluxed with sodium hydride in tetrahydrofuran for 5 hours. However, no reaction occurred and so it was concluded that (158) would not be produced in any significant amount during the reaction of (101) in N,N-diethylaniline.

Nucleophilic attack on the thioether (101) by the solvent could give an amine salt and fluoride ion. Reaction of the fluoride ion with this salt could then lead to ethyl fluoride and N-ethyl-N-[4-(prop-2-enylthio)-2,3,5,6-tetrafluorophenyl-]aniline (159) (Scheme 20).

However, attempts to synthesise the amine (159) by attack of N-ethylanilide anion on the thioether (101) all failed to give the amine (159)[52] (see Chapter 4). It is unlikely that the process outlined in Scheme 20 would be an easier reaction than the attempted



(101)



(159)

SCHEME 20

syntheses, so the formation of this amine (159) in significant amounts in the reaction of (101) in N,N-diethylaniline is discounted.

Chapter 3 Experimental

3.5 Synthesis of 2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (125)

2,3,5,6-Tetrafluorophenol (127) (31.28g) and dry tetrahydrafuran (220 ml) were cooled to -77°C under nitrogen and n-butyllithium solution (110 ml, 1.32M) was added over 50 minutes keeping the temperature below -65°C. The solution was stirred 30 minutes at -77°C and prop-2-enyl bromide (18.64g) was added and the mixture allowed to warm to room temperature over 2 hours before acidifying with sulphuric acid (2M) and extracting with ether. The extracts were dried ($MgSO_4$) and the solvent removed by distillation through a 60 cm column to give a residue which was distilled in vacuo to give 2,3,5,6-tetrafluorophenyl prop-2-enyl thioether (125) (31.5g) b.p. 86 - 89°C at 12.5 mm Hg. (Found: C, 48.93; H, 2.80%; M^+, 222. $C_9H_6F_4S$ requires C, 48.65; H, 2.70%; M, 222). The ^{19}F n.m.r. spectrum (neat liq.) showed two signals of equal intensity at 133.0 and 138.3 ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum (neat liq.) showed a doublet at δ 3.62 (CH_2), a multiplet at 5.10 (vinylic CH_2), a broad multiplet from 5.62 to 6.18 (vinylic CH), and a multiplet at 7.18 (aromatic CH).

3.6 Static thermolysis of 2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (125)

The thioether (125) (0.25g) was sealed in a 2 litre bulb evacuated to low pressure (0.05 mm Hg) and heated at 210°C for 22 hours. The product was condensed into a side-arm using liquid air, the bulb opened and the contents washed out with diethyl ether. The ether solution was dried ($MgSO_4$) and the solvent evaporated to give

a residue of starting material by i.r. and t.l.c.

The thioether (125) (0.45g) was sealed in a 50 ml tube under reduced pressure (0.05 mm Hg) and heated at 210°C for 22 hours, cooled and the tube opened and the contents washed out with diethyl ether. The ether solution was dried ($MgSO_4$) and the solvent evaporated to give a black residue containing at least five components by t.l.c. which was not examined further.

3.7 Initial investigation of reaction of 2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (125) in N,N'-diethylaniline

The thioether (125) (5.63g) was refluxed under nitrogen with N,N'-diethylaniline (57 ml) for 22.5 hours. The mixture was acidified with hydrochloric acid (4M), extracted with ether and the extracts dried ($MgSO_4$). The solvent was evaporated to give a residue which was distilled in vacuo to give a liquid (4.34g) b.p. 40 - 100°C at 0.5 mm Hg and a residue (1.29g). The distillate was chromatographed on silica (190 cm x 2.4 cm diam.) (light petroleum b.p. 30 - 40°C as eluent) to give material with the t.l.c. retention time of unreacted thioether (125) (3.63g) and a solid (0.73g) which on recrystallisation from light petroleum b.p. 30 - 40°C gave 5,7,8-trifluorothiachroman (128) m.p. 45.5 - 46.5°C. (Found: C, 52.94; H, 3.10%; M^+, 204. $C_9H_7F_3S$ requires C, 52.94; H, 3.43%; M, 204). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed three signals of equal intensity at 120.6, 139.0 and 144.7 ppm upfield from internal $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a multiplet at δ 2.14 (CH_2), a multiplet at 2.78 (CH_2), a multiplet at 3.01 (CH_2), and a multiplet at 6.64 (aromatic CH).

3.8 Reaction of excess 2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (125) with N,N-diethylaniline in a sealed tube

The thioether (125)(4.92g) and N,N'-diethylaniline (1.55g) were sealed in a 50 ml tube under reduced pressure (0.05 mm Hg) and heated at 210°C for 22 hours to give a red liquid and solid on cooling to room temperature. The tube was opened and the contents washed out with dry diethyl ether and the solid filtered off.

The solid was treated with water (10 ml) and it partially dissolved; addition of sulphuric acid (20 ml, 4M) completely dissolved it to give a yellow solution. The solution gave a precipitate with cerous nitrate reagent showing the presence of fluoride ion but no precipitate was obtained with Brady's reagent showing the absence of a carbonyl compound.

The filtrate was washed with excess hydrochloric acid (2M), dried ($MgSO_4$) and the solvent evaporated to give a residue which was chromatographed on silica (190 cm x 2.4 cm diam.) (light petroleum b.p. 30 - 40°C as eluent) to give material with the same t.l.c. retention time as starting material (125) (3.74g) and 5,7,8-trifluorothiachroman (128) (0.34g). The acid washings were basified with sodium hydroxide (2M) and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give an eight component residue which had no ^{19}F n.m.r. signals. The residue was separated by repeated thick layer chromatography on silica (carbon tetrachloride: chloroform, 2:1 as eluent) to give N-ethylaniline (0.25g) identified by i.r.

3.9 Further investigation of the reaction of 2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (125) in N,N-diethylaniline: Isolation of 2,3,5,6-Tetrafluorophenyl Ethyl Thioether (135) and 2H,3H-2-Methyl-4,6,7-Trifluorobenzo(b) thiophene (136)

The thioether (125) (4.91g) was refluxed under nitrogen with N,N'-diethylaniline (50 ml) for 190 hours. The mixture was treated with water (10 ml) and stirred for 20 minutes. A sample of the aqueous layer was removed and treated with cerous nitrate reagent giving a milky white precipitate indicating the presence of fluoride ion. The rest of the aqueous layer was removed and treated with Brady's reagent but no precipitate formed even after acidification with sulphuric acid (2M) and prolonged boiling showing the absence of a carbonyl compound.

The organic reaction mixture was washed with water, and the aqueous extracts were basified with sodium hydroxide (2M), extracted with ether and the extracts dried ($MgSO_4$), the solvent evaporated to give diethylaniline identified by i.r. The organic material was acidified with hydrochloric acid (4M) and extracted with ether. The extracts were dried ($MgSO_4$), and the solvent evaporated to give a residue, which contained material with the t.l.c. retention time apparently of starting material which seemed to indicate only two components: unreacted starting material (125) and the thiachroman (128). Examination of this residue by coupled g.l.c. - mass spectrometry (V.G. Micromass 12B instrument and 2-cyanoethylmethylsilicone at 208°C) however, indicated a mixture with four main components M^+, 210; M^+, 222 the thioether (125); M^+, 204; M^+, 204 the thiachroman (128). The residue was therefore chromatographed on silica (190 cm x 2.4cm diam.) (light petroleum b.p. 40 - 60°C as eluent) to give a mixture of three

components by g.l.c. but with the t.l.c. retention time of starting material (125) (3.58g) and 5,7,8-trifluorothiachroman (128) (0.52g), (the heterocycle (128) was identified with material isolated before). The three-component mixture was treated with excess borane-tetrahydrofuran solution (20 ml, 2M) under nitrogen and left at 20°C for an hour; this procedure was to convert alkene materials to organoboranes which would be immobile on chromatography whilst the other components would be unchanged. The solution was cooled to 0°C and the excess hydride destroyed by adding water. The solution was acidified with hydrochloric acid (2M) and extracted with ether, the extracts dried ($MgSO_4$) and the solvent evaporated to give a residue which was chromatographed on silica (68 cm x 2.4 cm) (light petroleum b.p. 40 - 60°C as eluent) to give a mixture of two components which were separated by preparative g.l.c. (2-cyanoethylmethylsilicone at 185°C). This gave 2,3,5,6-tetrafluorophenyl ethyl thioether (135) (0.84g) distilled in vacuo b.p. 36 - 50°C at 0.05 mm Hg and identified by i.r.; and (2H,3H)-2-methyl-4,6,7-trifluorobenzo (b) thiophene (136) (0.24g), b.p. 44 - 50°C at 0.05 mm Hg. (Found: C, 52.77; H, 3.69%; M^+, 204. $C_9H_7F_3S$ requires C, 52.94; H, 3.43%; M, 204). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed three signals of equal intensity at 117.9, 136.1 and 143.7 ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a doublet at δ 1.49 (CH_3), a broad multiplet centred at 2.98 and 3.41 (CH_2), a multiplet at 4.14 (aliphatic CH), and a multiplet at 6.57 (aromatic CH).

3.10 Further investigation of the reaction of Pentafluorophenyl Prop-2-enyl Thioether (101) and N,N-diethylaniline: Isolation of Pentafluorophenyl Ethyl Thioether (115)

The thioether (101) (20.26g) was refluxed with N,N'-diethylaniline (200 ml) under nitrogen for 23 hours. The mixture was acidified with hydrochloric acid (5M) and extracted with ether. The extracts were dried ($MgSO_4$) and the solvent evaporated to give a residue which was partially distilled in vacuo through a 15 cm concentric tube fractionating column to give eight fractions at 8 mm Hg: (i) Fractions 1 to 4 (3.99g) b.p. 25 - 68°C; Fraction 2 (2.67g) was separated by preparative g.l.c. (2-cyanoethylmethylsilicone at 160°C) to give unreacted thioether (101) (1.34g) and pentafluorophenyl ethyl thioether (115) (0.81g) identified by i.r.; (ii) Fractions 5 to 6 (3.57g) b.p. 66 - 75°C were mainly unreacted thioether (101);(iii) Fractions 7 to 8 (3.92g) b.p. 73 - 95°C contained four components including unreacted thioether (101); (iv) a residue (8.45g). G.l.c. analysis (using a gas density balance and 2-cyanoethylmethylsilicone at 160°C) indicated the proportions of unreacted thioether (101) and thioether (115) in the distillate as ca. 59% and 11% respectively, representing a yield of ca. 6% of the thioether (115).

3.11 Synthesis of 2,3,5,6-Tetrafluorophenyl Ethyl Thioether (135)

2,3,5,6-Tetrafluorothiophenol (127) (4.40g) and dry tetrahydrofuran (100 ml) were cooled to -75°C under nitrogen and n-butyllithium solution (22 ml, 1.1M) added over 20 minutes keeping the temperature below -65°C. The solution was stirred at -75°C for 1 hour and then ethyl iodide (10 ml) was added at -70°C. The mixture was stirred at

-75°C for 1 hour and allowed to warm to room temperature over 1 hour before acidifying with sulphuric acid (2M) and extracting with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue which was distilled in vacuo to give 2,3,5,6-tetrafluorophenyl thioether (135) (3.88g) b.p. 87 - 88°C at 11 mm Hg. (Found: C, 45.46; H, 3.24%; M^+, 210. $C_8H_6F_4S$ requires C, 45.71; H, 2.86%; M, 210).

3.12 Synthesis of Pentafluorophenyl Ethyl Thioether (115)

Pentafluorothiophenol (106) (10.20g) and dry tetrahydrofuran (200 ml) were cooled to -77°C under nitrogen and n-butyllithium solution (47 ml, 1.1M) added over 30 minutes keeping the temperature below -65°C. The solution was stirred for 20 minutes at -75°C before adding ethyl iodide (20 ml), stirring at -75°C for 1 hour and allowing to warm to room temperature over 1 hour. The mixture was acidified with sulphuric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue which was distilled in vacuo to give pentafluorophenyl ethyl thioether (115) (7.95g) b.p. 78 - 79°C at 14 mm Hg. (Found: C, 42.35; H, 2.42%; M^+, 228. $C_8H_5F_5S$ requires C, 42.10; H, 2.19%; M, 228).

3.13 Reaction of Pentafluorophenyl Prop-2-enyl Thioether (101) with sodium hydride

Sodium hydride (0.44g), pentafluorophenyl prop-2-enyl thioether (101) (4.4g) and dry tetrahydrofuran (120 ml) were stirred under nitrogen for 1 hour at 35°C. The mixture was then refluxed for 5 hours before treating with water, which caused a vigorous effervescence to occur. After the reaction had subsided, the solution was acidified with

sulphuric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give unreacted thioether (101).

Chapter 4 Synthesis of Products Obtained from the Reaction of Pentafluorophenyl Prop-2-enyl Thioether (101) in N,N-diethylaniline

4.1 Introduction

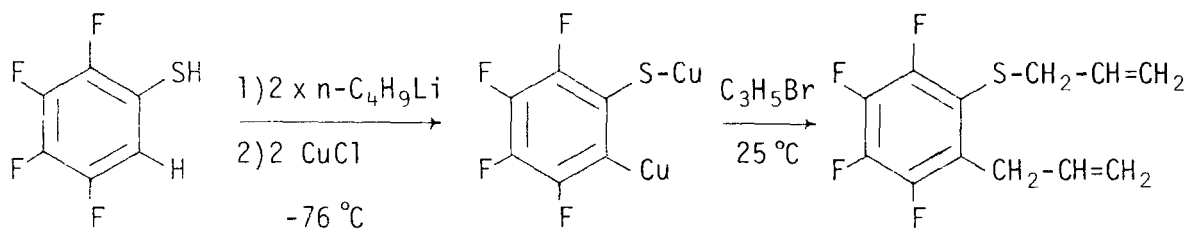
This work is concerned with the independent synthesis of the products arising from the reaction of pentafluorophenyl prop-2-enyl thioether (101) in N,N-diethylaniline. Successful syntheses were achieved for 2-(prop-2-enyl)-3,4,5,6-tetrafluorophenyl- (116) and 4-(prop-2-enyl)-2,3,5,6-tetrafluorophenyl- (117) prop-2-enyl thioethers as well as 5,6,7,8-tetrafluorothiachroman (109). However, attempts to make 2H,3H-2-methyl-4,5,6,7-tetrafluorobenzo(b)thiophene (110) and N-ethyl-N-[4-(prop-2-enylthio)-2,3,5,6-tetrafluorophenyl-]aniline (159) were unsuccessful.

4.2 Synthesis of 2-(Prop-2-enyl)-3,4,5,6-Tetrafluorophenyl- (116) and 4-(Prop-2-enyl)-2,3,5,6-Tetrafluorophenyl- (117) Prop-2-enyl Thioethers

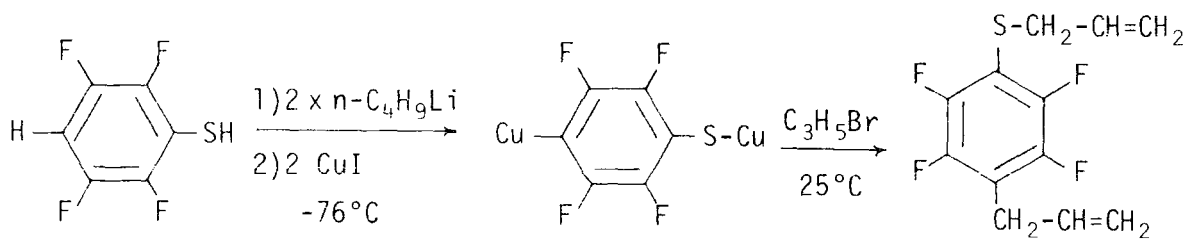
Treatment of 2,3,4,5-tetrafluorothiophenol (108) or 2,3,5,6-tetrafluorothiophenol (127) with two equivalents of n-butyllithium and prop-2-enyl bromide did not lead to the thioethers (116) and (117) but gave complex mixtures. This reaction involves stepwise metallation of the thiophenols (108) and (127). Initially the acidic proton of the thiol function is replaced by lithium but the ring proton takes longer to react with the base. It is probable that the prop-2-enyl bromide was added before complete reaction had occurred between the base and aromatic proton. As a result there would be (107) and (125) in addition to (116) and (117). Excess n-butyllithium present would attack these thioethers abstracting a proton from the prop-2-enyl

groups. The resulting carbanions on reaction with more prop-2-enyl bromide would give a wide variety of products. These processes are illustrated for 2,3,4,5-tetrafluorothiophenol (108) in Scheme 21.

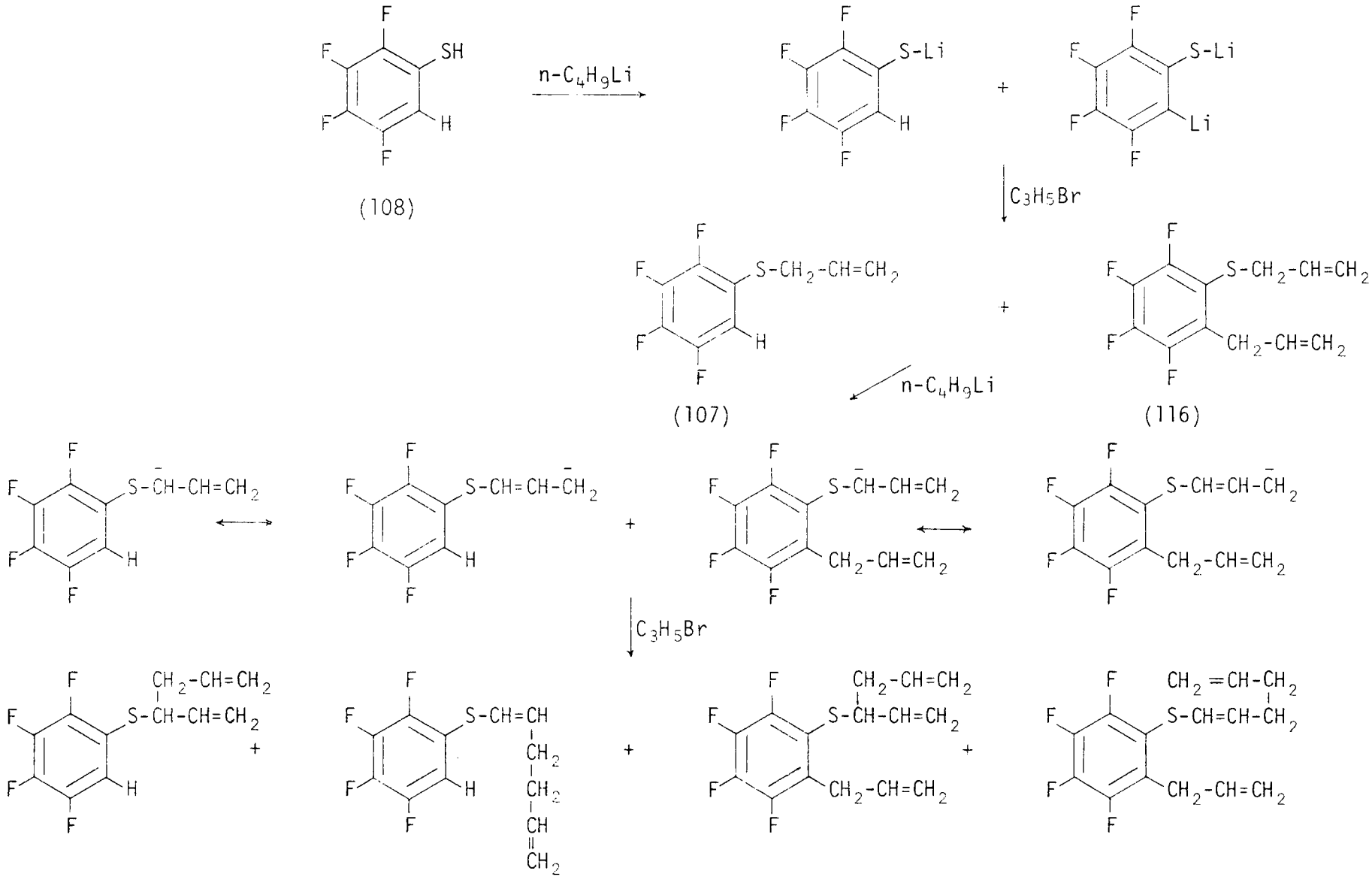
In order to overcome this problem intermediate copper salts were made from the thiophenols (108) and (127) and reacted with prop-2-enyl bromide according to the procedure reported for the preparation of pentafluoro-(prop-2-enyl)-benzene from pentafluorophenylcopper and prop-2-enyl bromide[53]. The thiophenols (108) and (127) were treated with two equivalents of n-butyllithium, then cuprous chloride or iodide and finally prop-2-enyl bromide. This gave 71% of the thioether (117) after distillation, and 60% of the thioether (116) after distillation and preparative g.l.c. purification.



(108) (116)



(127) (117)

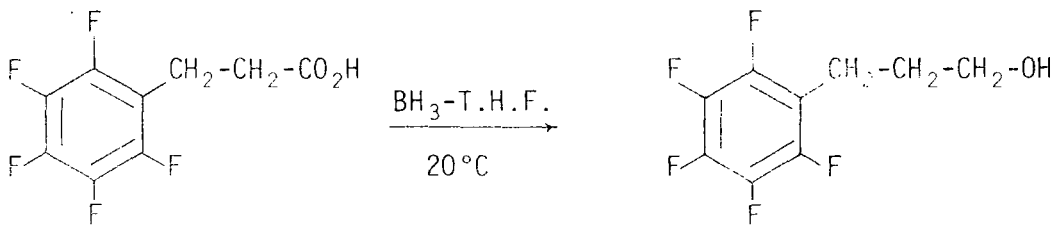


(108) (107) (116)

SCHEME 21

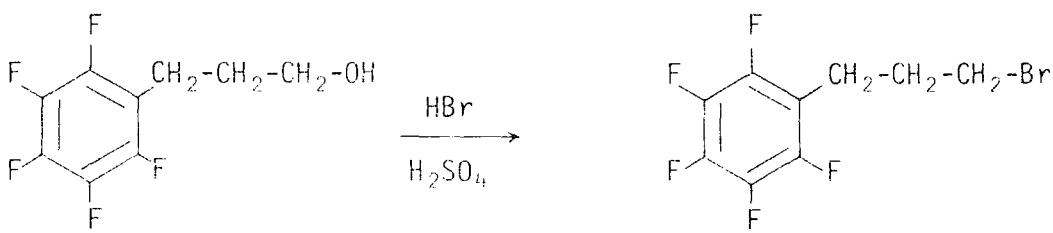
4.3 Synthesis of 5,6,7,8-Tetrafluorothiachroman (109)

3-Pentafluorophenylpropanoic acid (160), prepared in three stages from bromopentafluorobenzene[54], was reduced with borane-tetrahydrofuran, by a modification of Brown's method[55], to give 3-pentafluorophenyl propan-1-ol (161) in 73% yield.



(160) (161)

The alcohol (161) was converted to the corresponding bromide (162) in 81% yield by refluxing 18.5 hours in concentrated hydrobromic acid with added concentrated sulphuric acid.

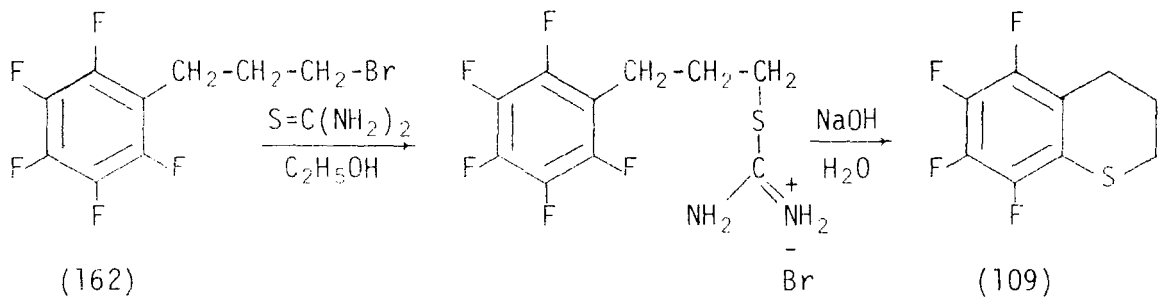


(161) (162)

It was expected that the Grignard reagent of the bromide (162) would react with sulphur to give the thiachroman (109) but in fact it gave several products with none of the heterocycle (109).

Reaction of the bromide (162) with thiourea in ethanol gave an isothiouronium salt. This salt was not isolated but reacted with aqueous base to give the thiol which cyclised to the thiachroman (109)

under the conditions of high dilution. Purification of the products by g.l.c. and preparative t.l.c. gave 16% of the heterocycle (109).

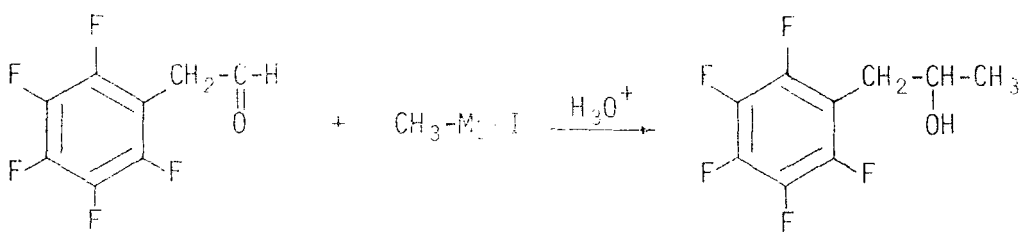


(162) (109)

4.4 Attempted Synthesis of 2H,3H-2-Methyl-4,5,6,7,-Tetrafluorobenzo (b) thiophene (110)

Reaction of thiourea with 2-bromo-3-pentafluorophenylpropane (163) should give the benzo (b) thiophene (110). However, all attempts to make the bromide (163) failed.

2-Pentafluorophenylacetaldehyde (164) has been reacted with a Grignard reagent to give α-(2,3,4,5,6-pentafluorobenzyl)-benzyl alcohol[56]. Reaction of the aldehyde (164) with methylmagnesium iodide on hydrolysis gave 3-pentafluorophenyl propan-2-ol (165)[57].



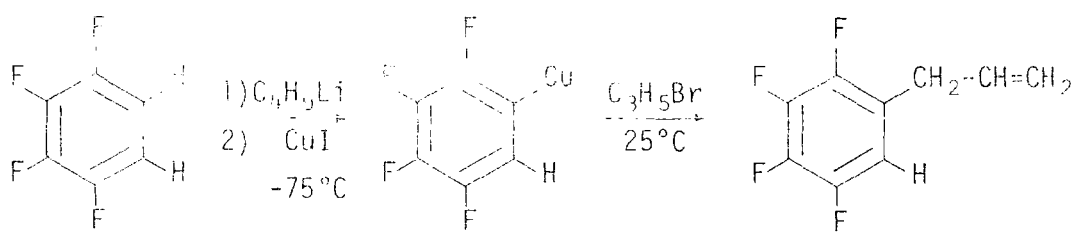
(164) (165)

Refluxing the alcohol (165) with concentrated hydrobromic acid with concentrated sulphuric acid gave a complex mixture. Triphenyl-

phosphine dibromide is reported to brominate secondary alcohols[58] but this reagent also gave many components on reaction with the alcohol (165)[57]. Equally para-toluenesulphonate derivatives of secondary alcohols are reported to give secondary bromides on reaction with sodium bromide in dimethylsulphoxide[59]. However, 3-pentafluorophenyl-2-propyl-para-toluenesulphonate (166), prepared from the alcohol (165) and para-toluenesulphonyl chloride in pyridine, did not react under the conditions reported. Heating the mixture led to complex mixtures.

The pentafluorothiophenoxide anion (167) reacts with diethylbut-2-yn-1,4-dioate to give a benzo (b) thiophene derivative[60]. An attempt was made to react the anion (167) similarly with ethylbut-2-enoate to give a 2-methylbenzo (b) thiophene derivative which could be converted to (110). However, this reaction gave at least seven components and was not investigated further.

Cyclisation of 2-(prop-2-enyl)-3,4,5,6-tetrafluorothiophenol (111) in N,N-diethylaniline should give the thiachroman (109) and the benzo (b) thiophene (110). This reaction would also serve as confirmation of the pathway postulated for the thio-Claisen rearrangement of the thioether (107). The first stage in one possible synthesis of the thiophenol (111) involved reaction of 1,2,3,4-tetrafluorobenzene (168) with n-butyllithium and cuprous iodide and then prop-2-enyl bromide. Fractional distillation of the products gave 64% of 2,3,4,5-tetrafluoro-prop-2-enylbenzene (169).

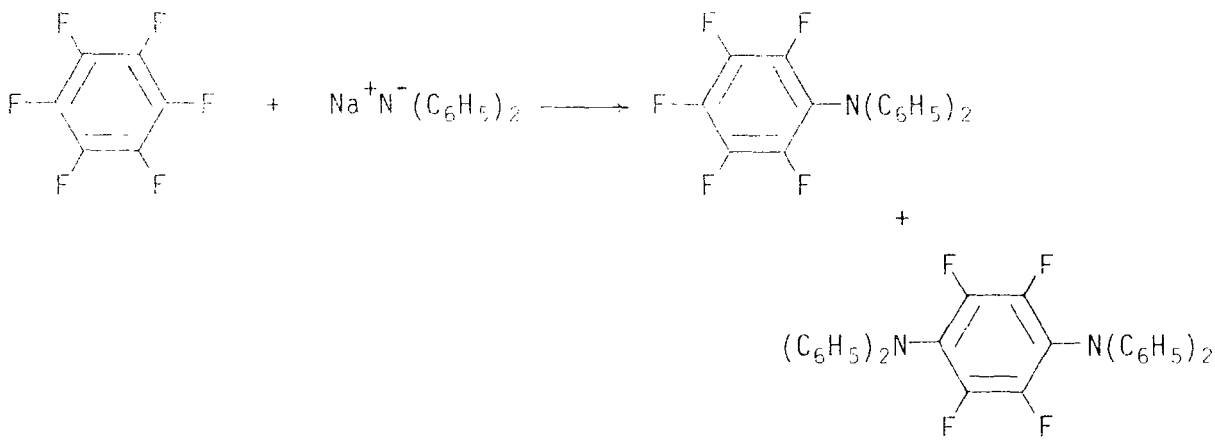


(168) (169)

Reaction of the compound (169) with n-butyllithium and sulphur however gave at least six products but no thiophenol (111).

4.5 Attempted Synthesis of N-Ethyl-N-[4-(Prop-2-enylthio)-2,3,5,6-Tetrafluorophenyl-]Aniline (159)

The sodium salt formed by reaction of sodium hydride and diphenylamine has been shown to react with hexafluorobenzene to give monosubstitution and some disubstitution of fluorines[52].



A similar nucleophilic aromatic substitution by the sodium salt of N-ethylaniline on pentafluorophenyl prop-2-enyl thioether (101) should give the amine (159). Reaction of sodium hydride and N-ethylaniline in diglyme followed by reaction with the thioether (101) by refluxing for 14.75 hours gave at least five products. Similarly, refluxing the sodium salt of N-ethylaniline with the thioether (101) for 2 hours in 1,4-dioxan also gave at least five products. In sharp contrast from treatment of N-ethylaniline with n-butyllithium in 1,4-dioxan followed by refluxing for 5 hours with the thioether (101) only the thioether (101) and N-ethylaniline were recovered unchanged after work up.

Chapter 4 Experimental

4.6 Attempted synthesis of 2-(Prop-2-enyl)-3,4,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (116)

2,3,4,5-Tetrafluorothiophenol (108) (4.66g) and dry tetrahydrofuran (100 ml) were cooled to -77°C under nitrogen and n-butyllithium solution (41 ml, 1.32M) was added over 40 minutes keeping the temperature below -65°C. The solution was stirred for 50 minutes at -77°C and then prop-2-enyl bromide (9.9g) was added. The mixture was stirred at -76°C for 15 minutes, allowed to warm to room temperature over 2.5 hours, acidified with hydrochloric acid (2M) and was extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated and the residue thus obtained was analysed by g.l.c. (2-cyanoethylmethylsilicone at 200°C) which showed at least seven components.

4.7 Successful synthesis of 2-(Prop-2-enyl)-3,4,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (116)

2,3,4,5-Tetrafluorothiophenol (108) (4.92g) and dry tetrahydrofuran (200 ml) were cooled to -76°C under nitrogen and n-butyllithium solution (42 ml, 1.32M) was added over 30 minutes keeping the temperature below -70°C. The solution was stirred 200 minutes at -76°C before adding cuprous chloride (5.79g) and stirring a further 5 hours at -76°C. The mixture was warmed to 0°C and prop-2-enyl bromide (10.25g) was added and then the solution was stirred at room temperature for 14.5 hours. Excess aqueous ammonia (2M) was added and the mixture extracted with ether. The extracts were washed with hydrochloric acid (2M), dried ($MgSO_4$) and the solvent evaporated to give a residue.

This was distilled in vacuo to give two fractions at 0.05 mm Hg: (a) (3.02g), b.p. 43 - 57°C, a mixture of the product and an unidentified material; (b) (2.64g), b.p. 57 - 59°C, which was largely the product (by g.l.c.). The pure thioether (116) was obtained by preparative g.l.c. (30% silicone elastomer at 200°C) to give 2-(prop-2-enyl)-3,4,5,6-tetrafluorophenyl prop-2-enyl thioether (116). (Found: C, 55.25; H, 3.98%; M^+, 262. $C_{12}H_{10}F_4S$ requires C, 54.96; H, 3.84%; M, 262). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed four signals of equal intensity at 129.8, 142.3, 156.4 and 159.3 ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a doublet at δ 3.73 (CH_2), a multiplet at 3.96 (CH_2), a multiplet at 5.26 (2 vinylic CH_2), and a broad multiplet from 5.78 to 6.45 (2 vinylic CH).

4.8 Attempted synthesis of 4-(Prop-2-enyl)-2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (117)

2,3,5,6-Tetrafluorothiophenol (127) (5.12g) and dry tetrahydrofuran (110 ml) were cooled to -78°C under nitrogen and n-butyllithium solution (50 ml, 1.34M) added over 60 minutes keeping the temperature below -74°C. The solution was stirred for 25 minutes at -77°C and then prop-2-enyl bromide (8.74g) was added over 10 minutes at -74°C and the mixture was allowed to warm to room temperature over 1.5 hours. The mixture was acidified with sulphuric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue and this was distilled in vacuo to give three fractions at 13 mm Hg: (i) (0.5g) b.p. 86 - 96°C; (ii) (2.85g) b.p. 96 - 120°C; (iii) (0.45g) b.p. 104 - 110°C; and a residue. Each fraction was analysed by g.l.c. (2-cyanoethylmethylsilicone at 190°C) which indicated that each fraction was a mixture of at least seven components.

4.9 Successful synthesis of 4-(Prop-2-enyl)-2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether (117)

2,3,5,6-Tetrafluorothiophenol (127) (6.47g) and dry tetrahydrofuran (150 ml) were cooled to -75°C under nitrogen and n-butyllithium solution (48 ml, 1.55M) was added over 30 minutes keeping the temperature below -70°C. The solution was stirred at -76°C for 200 minutes before adding cuprous iodide (15.02g) and stirring a further 5 hours at -76°C. The mixture was warmed to 10°C and prop-2-enyl bromide (14.24g) was added and the mixture was then stirred at room temperature for 16 hours before treating with excess aqueous ammonia (2M) and extracting with ether. The extracts were dried ($MgSO_4$) and the solvent evaporated to give a residue which was distilled in vacuo giving 4-(prop-2-enyl)-2,3,5,6-tetrafluorophenyl prop-2-enyl thioether (117) (6.65g) b.p. 65 - 70°C at 0.05 mm Hg. (Found: C, 55.10; H, 4.22%; M^+, 262. $C_{12}H_{10}F_4S$ requires C, 54.96; H, 3.84%; M, 262). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed two signals of equal intensity at 151.6 and 161.6 ppm upfield from $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a doublet at δ 4.00 (2 CH_2), a multiplet at 5.55 (2 vinylic CH_2), and a broad multiplet from 6.0 to 6.63 (2 vinylic CH).

4.10 Synthesis of 3-Pentafluorophenyl Propan-1-ol (161)

3-Pentafluorophenyl propanoic acid (160) (14.45g) in dry tetrahydrofuran (150 ml) was treated at 20°C with borane-tetrahydrofuran solution (90 ml, 0.86M) under nitrogen over 30 minutes. The mixture was kept at room temperature for 3 hours, the excess hydride destroyed by adding water, and after acidification with hydrochloric acid (2M), the solution was extracted with ether. The extracts were

dried ($MgSO_4$), the solvent evaporated to give a residue which was distilled in vacuo to give 3-pentafluorophenyl propan-1-ol (161) (9.96g) b.p. 113°C at 12 mm Hg. (Found: C, 48.03; H, 3.26%. $C_9H_7F_5O$ requires C, 47.79; H, 3.13%).

4.11 Synthesis of 1-Bromo-3-Pentafluorophenylpropane (162)

The alcohol (161) (9.96g) was refluxed with hydrobromic acid (25 ml, 46% w/w) and sulphuric acid (5 ml, 18M) for 18.5 hours, and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated and the residue was distilled in vacuo to give 1-bromo-3-pentafluorophenylpropane (162) (10.39g) b.p. 102 - 104°C at 11 mm Hg. (Found: C, 37.55; H, 2.32%. $C_9H_6BrF_5$ requires C, 37.39; H, 2.09%).

4.12 Attempted synthesis of 5,6,7,8-Tetrafluorothiachroman (109)

The bromide (162) (2.52g) was added at 0°C to a stirring mixture of activated magnesium (1.26g) in dry tetrahydrofuran (30 ml). The mixture was kept at 0°C for 1 hour before adding sulphur (0.28g) at -6°C and stirring below 0°C for 25 minutes. The solution was hydrolysed with excess sulphuric acid (2M), extracted with ether and the extracts dried ($MgSO_4$). The solvent was evaporated to give a residue which was distilled in vacuo to give two fractions at 13 mm Hg: (i) (0.075g) b.p. 55 - 60°C; (ii) (0.26g) b.p. 70 - 73°C; and a residue (1.45g). Analysis of these fractions and residue by g.l.c. (2-cyanoethylmethylsilicone at 210°C) showed the presence of at least three components but no thiachroman (109).

4.13 Synthesis of 5,6,7,8-Tetrafluorothiachroman (109)

The bromide (162) (4.14g), thiourea (1.71g) and ethanol (30 ml) were refluxed under nitrogen for 64 hours. The ethanol was evaporated and water (20 ml) added, and the solution poured into aqueous sodium hydroxide (1.2g in 300 ml water). The mixture was refluxed for 5 hours, extracted with ether, the extracts dried ($MgSO_4$) and the solvent evaporated. Distillation of the residue in vacuo gave a mixture (0.95g) b.p. 34 - 72°C at 0.05 mm Hg which consisted of the thiachroman (109) (ca. 70% by g.l.c.) and an unidentified compound. Preparative g.l.c. (30% silicone elastomer at 200°C) of this mixture, followed by thick layer chromatography on silica (light petroleum b.p. 40 - 60°C as eluent) on the enriched material gave the pure 5,6,7,8-tetrafluorothiachroman (109) (0.174g) b.p. 42 - 56°C at 0.05 mm Hg. (Found: C, 48.92; H, 2.85%; M^+, 222. $C_9H_6F_4S$ requires C, 48.65; H, 2.70%; M, 222). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed four signals of equal intensity at 143.6, 145.8, 162.5 and 165.5 ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a doublet at δ 2.14 (CH_2) and a multiplet centred at 2.74 and 2.96 (2 CH_2).

4.14 Synthesis of 3-Pentafluorophenyl-2-Propyl-p-Toluenesulphonate (166)

3- Pentafluorophenyl propan-2-ol (165) (4.2g) and dry pyridine (30 ml) were cooled to 0°C and p-toluenesulphonyl chloride (3.93g) was added and the mixture kept at 0°C for 16 hours. The mixture was acidified with hydrochloric acid (2M) and extracted with ether, the extracts dried ($MgSO_4$) and the solvent evaporated to give a solid (8.5g). This gave, after recrystallisation from light petroleum (b.p. 60 - 80°C), 3-pentafluorophenyl-2-propyl-p-toluenesulphonate (166) m.p. 96 - 97°C.

(Found: C, 50.81; H, 3.39%; M^+, 380. $C_{16}H_{13}F_5SO_3$ requires C, 50.52; H, 3.42%; M,380).

4.15 Reaction of 3-Pentafluorophenyl-2-Propyl-p-Toluenesulphonate (166) with sodium bromide in dimethylsulphoxide

The ester (166) (0.54g) and sodium bromide (0.19g) were stirred under nitrogen in dry dimethylsulphoxide (3 ml) at room temperature for 68.4 hours. The mixture was treated with excess sulphuric acid (2M), extracted with ether, the extracts dried ($MgSO_4$) and the solvent evaporated to give unreacted ester (166).

Similar experiments were carried out with more ester (166) (0.44g), sodium bromide (0.14g) in dimethylsulphoxide (2 ml), heating under nitrogen and analysing by t.l.c. Thus heating at 50°C for 3 hours gave no reaction; heating at 85°C for 15 hours gave three components; and heating at 110°C for 16 hours gave seven components.

4.16 Reaction of Lithium Pentafluorothiophenoxide (167) with ethyl crotonate

Pentafluorothiophenol (106) (5.46g) and dry tetrahydrofuran (100 ml) were cooled to -75°C under nitrogen and n-butyllithium solution (19 ml, 1.5M) was added over 20 minutes keeping the temperature below -70°C. The mixture was stirred for 30 minutes at -75°C and then ethyl crotonate (4.16g) was added. The mixture was warmed to room temperature over 30 minutes and was then refluxed for four hours, acidified with sulphuric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue which was distilled in vacuo to give two fractions at 0.3 mm Hg: (i) (0.10g) b.p. 26 - 34°C; (ii) (1.69g) b.p. 87 - 90°C; and a residue.

Analysis by g.l.c. (2-cyanoethylmethylsilicone at 190°C) showed the first fraction was a mixture of starting materials; the second fraction and residue contained two major components in a mixture of at least seven components.

4.17 Synthesis of Prop-2-enyl-2,3,4,5-Tetrafluorobenzene (169)

1,2,3,4-Tetrafluorobenzene (168) (14.15g) and dry tetrahydrofuran (200 ml) were cooled to -77°C under nitrogen and n-butyllithium solution (63 ml, 1.5M) was added over 15 minutes keeping the temperature below -73°C, the last traces being washed in with more dry tetrahydrofuran (40 ml). The solution was stirred 1.5 hours at -75°C and then cuprous iodide (18.36g) was added and the mixture was stirred for 5 hours at -75°C. The mixture was warmed to 15°C over 1 hour and prop-2-enyl bromide (12.12g) added over 10 minutes keeping the temperature below 25°C. The solution was stirred at room temperature for 15.5 hours and then treated with excess aqueous ammonia (2M) and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue, and this was distilled at atmospheric pressure to give five fractions: (i) (4.39g) b.p. 72 - 76°C, a mixture of tetrahydrofuran and unidentified material; (ii) (3.71g) b.p. 76°C, as fraction (i); (iii) (3.42g) b.p. 72 - 100°C, a mixture of tetrahydrofuran and two unidentified components; (iv) (9.51g) b.p. 118 - 150°C, a mixture of product and two unidentified components; (v) (6.10g) b.p. 146 - 158°C, mainly product; and a residue. These were all analysed by g.l.c. (2-cyanoethylmethylsilicone at 150°C). The material from fractions (iv) and (v) was combined and redistilled through a 15 cm concentric tube fractionating column to give eight fractions, each of which was analysed by g.l.c.: (a) Fractions 1 to 3

(0.95g) b.p. 64 - 151°C were unidentified materials; (b) Fractions 4 to 5 (3.46g) b.p. 151 - 159°C, mainly product; (c) Fractions 6 to 8 (8.01g) b.p. 158 - 159°C, were all product. Analysis by g.l.c. indicated a total of 11.5g of prop-2-enyl-2,3,4,5-tetrafluorobenzene (169). (Found: C, 56.68; H, 3.54%; M^+, 190. $C_9H_6F_4$ requires C, 56.84; H, 3.16%; M, 190). The ^{19}F n.m.r. spectrum (neat liq.) showed four signals of equal intensity at 141.8, 145.6, 158.5 and 161.2 ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum (neat liq.) showed a doublet at δ 3.43 (CH_2), a multiplet at 5.17 (vinylic CH_2), a broad multiplet from 5.68 to 6.33 (vinylic CH), and a multiplet at 6.83 (aromatic CH).

4.18 Attempted synthesis of 2-(Prop-2-enyl)-3,4,5,6-Tetrafluorothiophenol (111)

Compound (169) (2.61g) and dry tetrahydrofuran (50 ml) were cooled to -75°C under nitrogen and n-butyllithium solution (9.5 ml, 1.5M) was added over 10 minutes keeping the temperature below -70°C. The solution was stirred at -77°C for 2 hours before adding sulphur (0.49g). The mixture was stirred 40 minutes at -77°C and then poured into excess sulphuric acid (2M) at room temperature and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue and this was distilled in vacuo to give two fractions at 7 mm Hg: (i) (0.51g) b.p. 42 - 44°C, unreacted starting material (169); (ii) (0.07g) b.p. 62 - 67°C, a mixture of four components by t.l.c.; and a residue containing at least six components by t.l.c.

4.19 Attempted synthesis of N-Ethyl-N'-[4-(Prop-2-enylthio)-2,3,5,6-Tetrafluorophenyl]Aniline (159)

Method 1

Sodium hydride (4.65g, oil dispersion ca. 70% w/w), N-ethylaniline (3.25g) and dry diglyme (100 ml) were refluxed under nitrogen for 20 minutes. The thioether (101) (4.86g) was added and the mixture refluxed for 14.75 hours and acidified with hydrochloric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$) and the solvent evaporated to give a residue which was a mixture of at least five components by t.l.c.

Method 2

Sodium hydride (0.55g, oil dispersion ca. 70% w/w), N-ethylaniline (1.91g) and dry 1,4-dioxan (70 ml) were refluxed under nitrogen for 3 hours. The thioether (101) (3.75g) was added and the mixture was refluxed for 2 hours, diluted with water and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated to give a residue and this was analysed by t.l.c. which showed at least five components.

Method 3

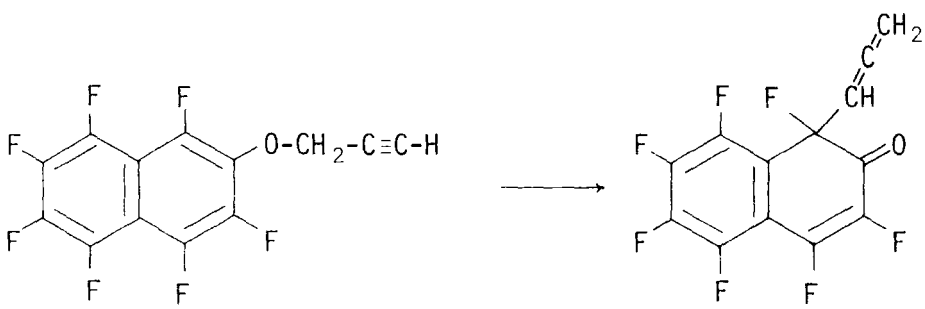
N-Ethylaniline (1.72g) and 1,4-dioxan (100 ml) were cooled to 15°C under nitrogen and n-butyllithium solution (9.3 ml, 1.54M) was added over ten minutes keeping the temperature below 20°C. The mixture was stirred at 20°C for 1 hour and then the thioether (101) (3.46g) was added and the mixture was refluxed for 5 hours. The mixture was diluted with water and extracted with ether, the extracts dried ($MgSO_4$) and the solvent evaporated to give a residue of unreacted

thioether (101) and N-ethylaniline.

Chapter 5 Synthesis of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (170) and its Reactions in Hydrocarbon Solvents

5.1 Introduction

1,3,4,5,6,7,8-Heptafluoro-2-naphthyl prop-2-ynyl ether (170) was synthesised as part of an attempt to obtain a stable naphthalenone (171) to parallel the reaction of the naphthyl prop-2-enyl ether (36).

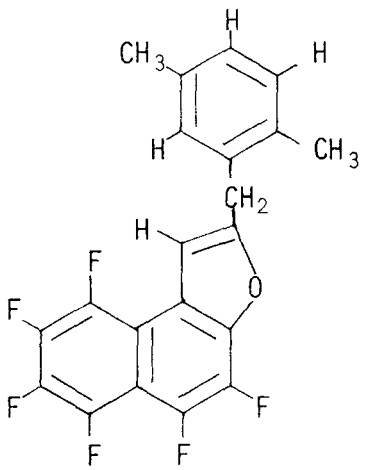


(170) (171)

Refluxing 1,3,4,5,6,7,8-heptafluoro-2-naphthol (172) with potassium carbonate and prop-2-ynyl bromide in acetone for 22 hours gave the ether (170) in 83% yield. Reaction of the ether with n-decane over 80 minutes or with n-nonane over 150 minutes gave hydrogen fluoride and complex mixtures (which were not investigated further). The ether (170) was then refluxed for 17 hours in the mixture of xylenes which was used as the solvent in the rearrangement of the naphthyl prop-2-enyl ether (36). Although this gave one major only, according to t.l.c., the solution was not worked up further because reaction with the mixture of xylenes would have caused isolation difficulties with isomeric products. Further work on this reaction was carried out with pure p-xylene.

5.2 The Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (170) with p-Xylene and Benzene

The ether (170) was refluxed for 20 hours with p-xylene and reaction occurred to give a solid which was designated 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan (173) (obtained in 75% crude yield as shown by ^{1}H n.m.r.). The ^{1}H n.m.r. spectrum showed a singlet at δ 2.32 for six methyl protons, a singlet at δ 4.17 for two methylene protons, a multiplet at δ 6.83 for a vinylic proton and a multiplet at δ 7.05 for three aromatic protons. The ^{19}F n.m.r. spectrum showed three signals in the ratio 2:1:3 at 145.5 to 146.5 ppm, 151.4 ppm and 158.0 to 158.9 ppm upfield from internal $CFCl_3$, respectively.



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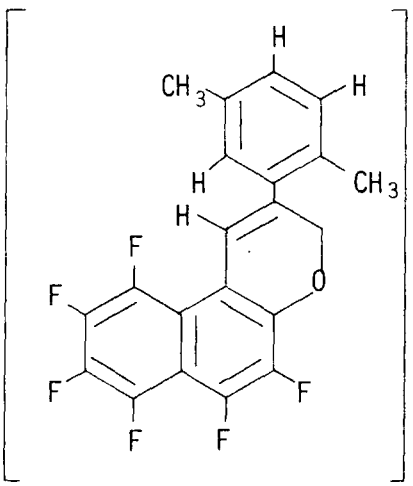
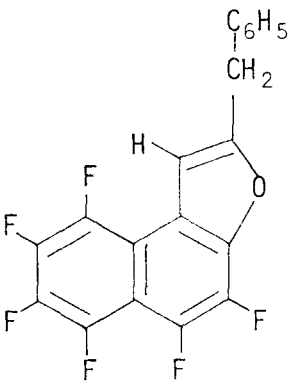


(174)

The n.m.r. data did not distinguish between a naphtho[2,1-b]furan with the structure (173) or the naphtho[2,1-b]pyran isomer with the structure (174) as no models were available to make a comparison. However, the reaction of pentafluorophenyl prop-2-ynyl ether (175) and benzene gave a benzyl benzo(b)furan which was confirmed by independent synthesis (see Chapter 6). The ^{1}H n.m.r. spectrum of the benzo(b)furan compound was very similar to that obtained for

the product from p-xylene and (170), and so the solid obtained from (170) was assumed to have the naphtho[2,1-b]furan structure (173).

A solution phase reaction of the ether (170) and benzene in a sealed tube at 140°C for 21 hours gave a solid. The ^{1}H n.m.r. spectrum showed a singlet at δ 4.21 for two methylene protons, a multiplet at δ 6.95 for a vinylic proton and a singlet at δ 7.34 for five aromatic protons. The ^{19}F n.m.r. spectrum showed three signals in the ratio 2:1:3 at 146.6 to 147.4 ppm, 151.9 ppm and 158.8 to 159.7 ppm, upfield from external $CFCl_3$, respectively.



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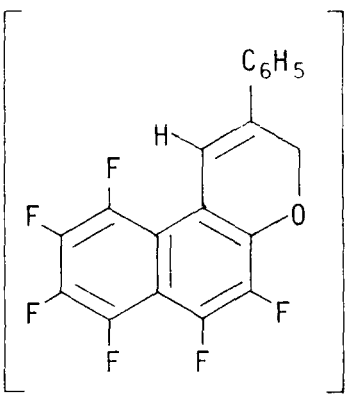
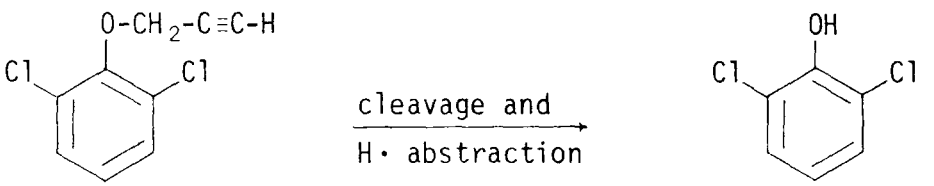


(177)

Again two possible structures could be fitted to the n.m.r. data: a naphtho[2,1-b]furan (176) or its naphtho[2,1-b]pyran isomer (177). This product also had a similar ^{1}H n.m.r. spectrum to that of the benzyl benzo(b)furan obtained from (175) and benzene. Consequently the product from (170) was designated 2-benzyl-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan (176), obtained in 66% crude yield according to ^{1}H n.m.r.

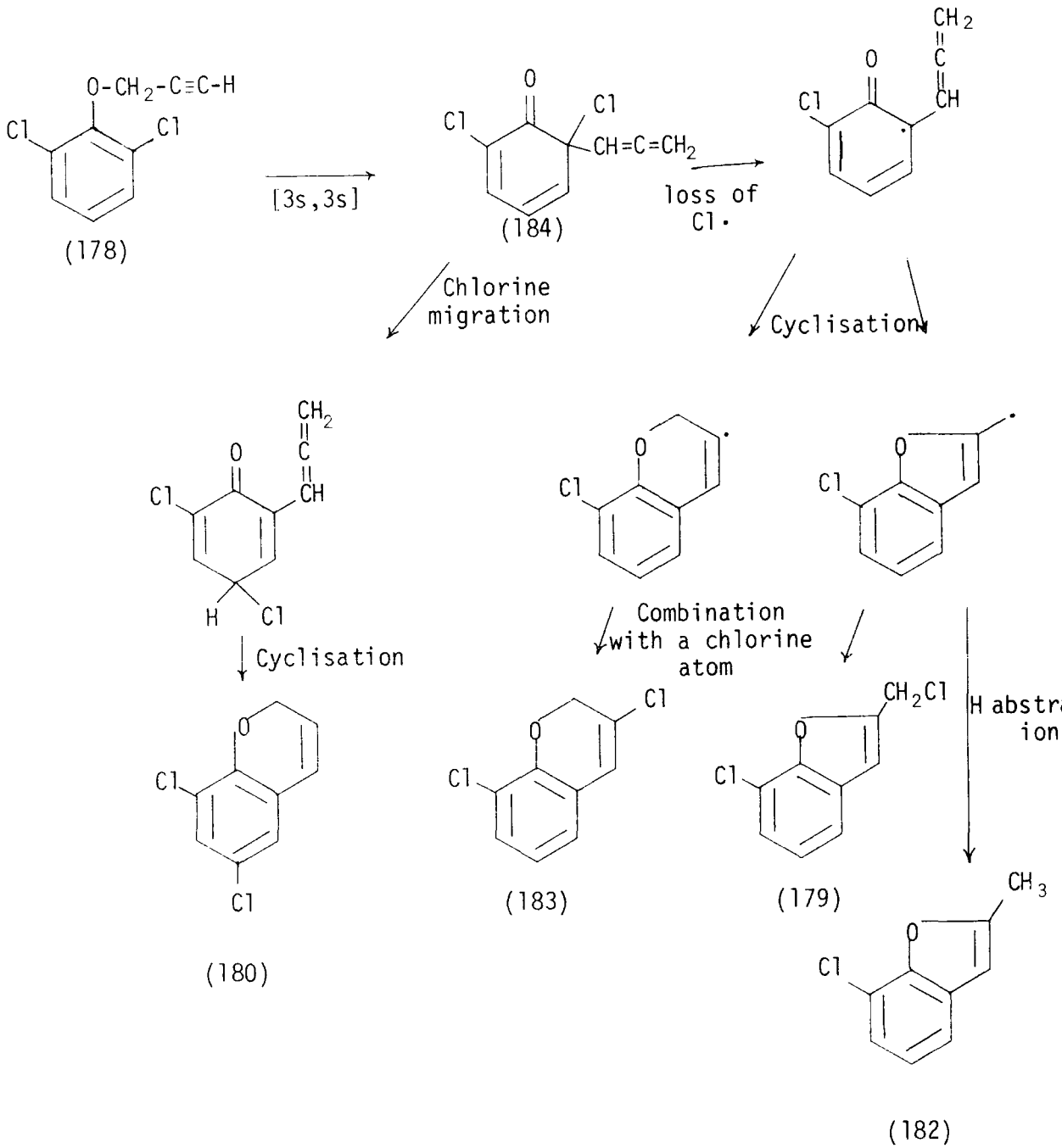
2,6-Dichlorophenyl prop-2-ynyl ether (178) rearranges in decane at 230°C to give mainly 2-chloromethyl-7-chlorobenzo(b)furan (179) and 2H-6,8-dichlorochromene (180)[61]. Other products formed are

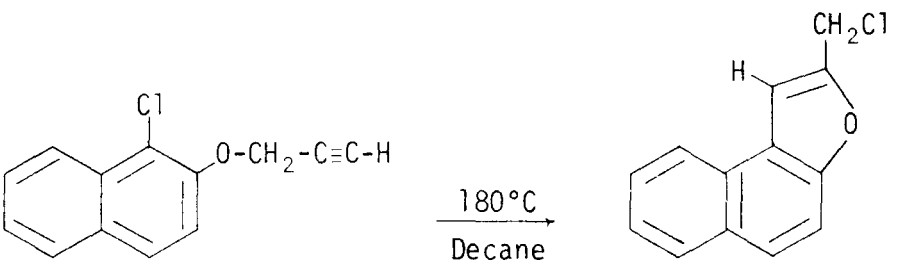
2,6-dichlorophenol (181), 2-methyl-7-chlorobenzo(b) furan (182) and 2H-3,8-dichlorochromene (183). The phenol (181) is obtained by homolytic cleavage of the ether linkage in (178), whereas the other products arise from an initial Claisen rearrangement to an ortho-dienone (184). Homolysis of the ortho-dienone (184) at C-2 with loss of a chlorine atom gives a radical which can cyclise to a benzo(b) furan or a chromene. The benzo(b) furan radical can combine with a chlorine atom to give (179) or it can abstract a hydrogen to give (182). The chromene radical on combination with a chlorine atom will lead to (183). Chlorine migration in the ortho-dienone (184) followed by cyclisation leads to (180).



(178) (181)

The reaction of 1-chloro-2-naphthyl prop-2-ynyl ether (185) in decane makes an interesting comparison with the phenyl ether (178)[61]. The temperature for rearrangement of (185) is 180°C whereas the phenyl ether (178) is harder to rearrange requiring a higher temperature; this fits in with the general pattern observed for Claisen rearrangements in the naphthalene and benzene series. The only product from the reaction of the naphthyl ether (185), 2-chloromethylnaphtho[2,1-b]furan (186), is obtained by initial Claisen rearrangement to a naphthalenone which undergoes homolysis at C-1 and loss of a chlorine atom followed by cyclisation and recombination with the chlorine atom.


O-CH2-C≡C-H
Cl
Cl
(178)
[3s,3s]
O
Cl
Cl
CH=C=CH2
(184)
loss of Cl·
CH2
C
CH
O
Cl
Chlorine migration
Cyclisation
CH2
C
CH
O
Cl
H
Cl
Cyclisation
O
Cl
Cl
(180)
O
Cl
Combination with a chlorine atom
O
Cl
Cl
(183)
O
Cl
CH2Cl
(179)
H abstr
ion
CH3
O
Cl
(182)

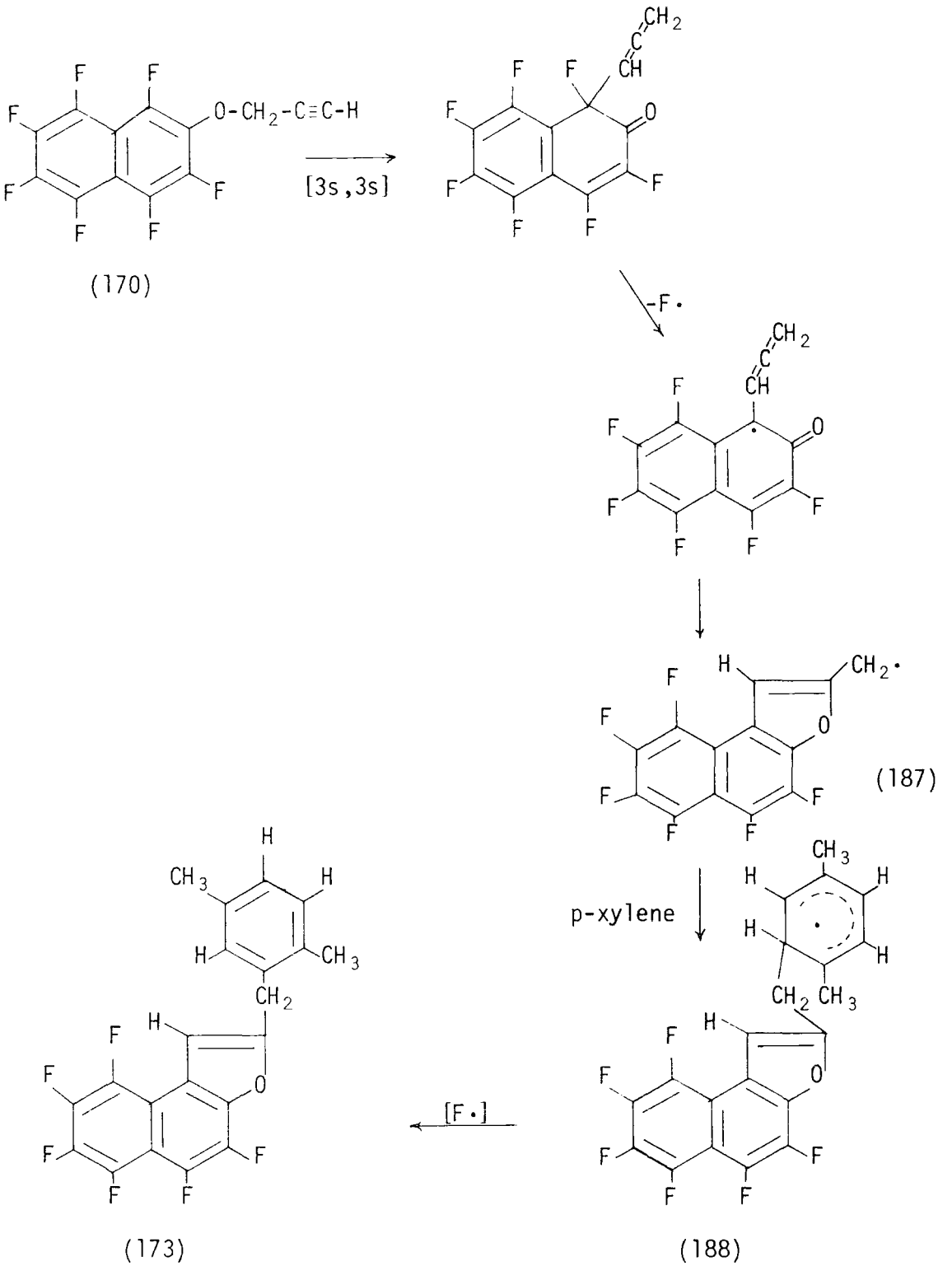


(185) (186)

The mechanism postulated to explain the formation of the aryl naphtho[2,1-b]furan products from the ether (170) requires an initial Claisen rearrangement to an ortho-dienone which then undergoes homolytic cleavage at C-1 with loss of a fluorine atom. The radical formed cyclises to a naphtho[2,1-b]furan (187) and the product is obtained by homolytic aromatic substitution of the solvent by this radical (187), via an intermediate aromatic radical complex (188). Termination by a fluorine atom leads to the product and hydrogen fluoride (this process is illustrated for the p-xylene adduct (173) in Scheme 22).

This reaction raises several mechanistic points of interest as a result of the proposal of homolysis of a carbon to fluorine bond. Although this process has already been postulated in connection with the reaction of the thioethers (101) and (125) in N,N-diethylaniline (see Chapter 3), it remains an unusual step because cleavage of a carbon to fluorine bond should be energetically difficult. Complications could arise in this reaction because the homolysis at C-1 of the intermediate ortho-dienone gives two radicals each of which could attack the aromatic solvent: the heterocyclic radical (187) and a fluorine atom.

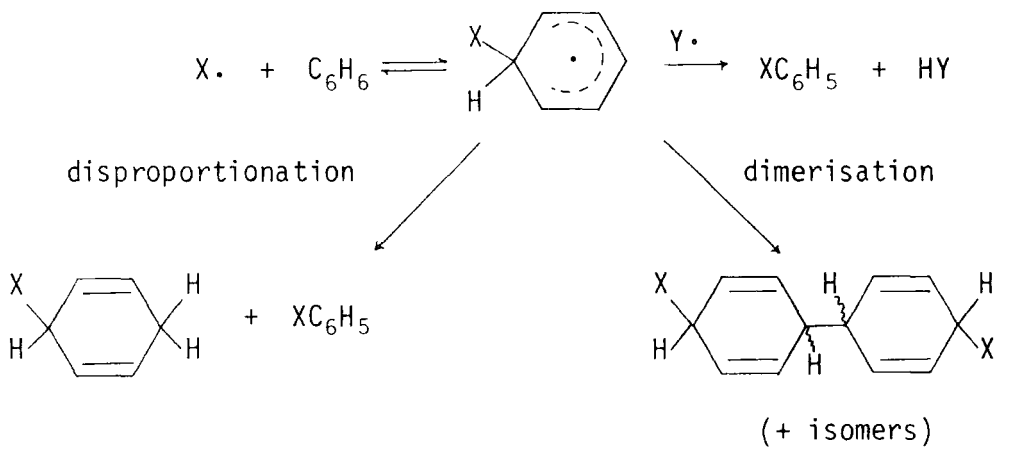
Despite the difficulty of working with fluorine a few studies


F
F
F
F
F
F
O-CH2-C≡C-H
[3s,3s]
CH2
C
CH
O
-F·
H
CH2·
O
(187)
p-xylene
CH3
CH2
CH3
[F·]
(170)
(173)
(188)

SCHEME 22

on fluorine atom chemistry have been carried out[62]. These have shown that a fluorine atom abstracts a hydrogen from a saturated hydrocarbon but it adds to an aromatic hydrocarbon to form a radical complex which loses a substituent other than fluorine to give an aryl fluoride.

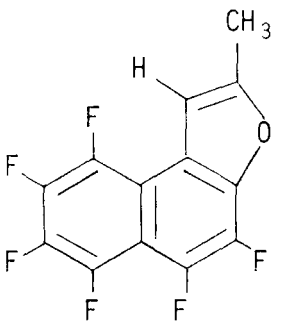
The general process of homolytic attack on benzene is shown in Scheme 23 where X· is the substituting radical and Y· is another radical present which terminates the process by abstracting a hydrogen from the intermediate radical complex.



SCHEME 23

In the mechanism given to explain the behaviour of the ether (170), X· will represent the heterocyclic radical (187), Y· a fluorine atom and XC_6H_5 will be the product (176). If a fluorine atom attacked the solvent then in Scheme 23 X· will now represent the fluorine atom, Y· the radical (187), HY a methylnaphtho[2,1-b]furan (189) and XC_6H_5 will be an aryl fluoride. However, no product corresponding to (189) has been isolated and neither have any cyclohexadienyl derivatives. As a result it is concluded the probable reaction pathway involves substitution by the heterocyclic radical (187) alone

with a fluorine atom abstracting a hydrogen from the radical complex as the only termination process.



(189)

Chapter 5 Experimental

5.3 Synthesis of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (170)

1,3,4,5,6,7,8-Heptafluoro-2-naphthol (172) (14.02g), anhydrous potassium carbonate (15.70g), prop-2-ynyl bromide (15.65g, 80% solution in toluene w/w) and dry acetone (150 ml) were refluxed under nitrogen for 22 hours. The mixture was acidified with hydrochloric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$), the solvent evaporated and the residue distilled in vacuo to give 1,3,4,5,6,7,8-heptafluoro-2-naphthyl prop-2-ynyl ether (170) (13.31g) b.p. 94 - 97°C at 0.05 mm Hg. (Found: C, 50.77; H, 0.69%; M^+, 308. $C_{13}H_3F_7O$ requires C, 50.65; H, 0.97%;M, 308). The ^{19}F n.m.r. spectrum (neat liq.) showed a multiplet at 139.4, a broad multiplet from 147.5 to 149.4, and a multiplet at 157.9 ppm, in the ratio 1:4:2, upfield from external $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a triplet at δ 2.58 (acetylenic CH) and a doublet at 4.99 (CH_2).

5.4 Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (170) in various hydrocarbon solvents

The ether (170) (3.44g) and n-decane (50 ml) were refluxed for 80 minutes under nitrogen during which time hydrogen fluoride was evolved. The solvent was evaporated to give a tarry residue containing at least seven components by t.l.c. and this was not worked up further.

The ether (170) (2.92g) and n-nonane (50 ml) were refluxed for 2.5 hours under nitrogen and hydrogen fluoride was evolved again. The solvent was evaporated to give a residue containing at least five components by g.l.c. and this was not investigated further.

The ether (170) (3.17g) and xylene (commercial blend of isomers, 60 ml) were refluxed for 17 hours under nitrogen. The solvent was evaporated to give a residue with one major component by t.l.c. but this was not worked up further.

5.5 Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (170) with p-xylene

The ether (170) (2.86g) and p-xylene (50 ml) were refluxed under nitrogen for 20 hours. The solvent was evaporated to give a residue which was chromatographed on silica (88 cm x 2.4 cm diam.) (carbon tetrachloride as eluent) to give a solid (2.98g, 92% pure by ^{1}H n.m.r. spectroscopy). On recrystallisation from ethanol this gave 2-(2,5-dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan (173) m.p. 116 - 117°C. (Found: C, 64.00; H, 3.25%; M^{+}, 394. $C_{21}H_{12}F_{6}O$ requires C, 63.96; H, 3.05%; M, 394). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed a broad multiplet from 145.5 to 146.5, a multiplet at 151.4, a broad multiplet from 158.0 to 158.9 ppm upfield from internal $CFCl_3$ in the ratio 2:1:3, respectively. The ^{1}H n.m.r. spectrum ($CDCl_3$) showed a singlet at δ 2.32 ($2CH_3$), a singlet at 4.17 (CH_2), a multiplet at 6.83 (vinylic CH) and a multiplet at 7.05 (aromatic C_6H_3).

5.6 Reaction of 1,3,4,5,6,7,8-Heptafluoro-2-Naphthyl Prop-2-ynyl Ether (170) with benzene

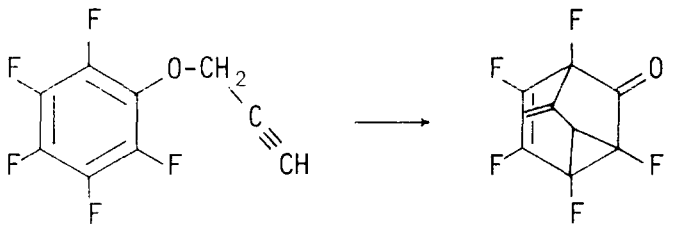
The ether (170) (2.12g) and benzene (20 ml) were sealed in a 50 ml tube under reduced pressure (0.05 mm Hg) and heated at 140°C for 21 hours to give a black solution which evolved hydrogen fluoride

on opening the tube. The solvent was evaporated to give a residue which was chromatographed on silica (88 cm x 2.4 cm diam.) (carbon tetrachloride as eluent) to give a solid (1.70g, 95% pure by ^{1}H n.m.r. spectroscopy), which after sublimation at 100°C at 0.05 mm Hg followed by recrystallisation from ethanol gave 2-benzyl-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan (176) m.p. 98.5 - 100.0°C. (Found: C, 62.39; H, 2.10%; M^{+}, 366. $C_{19}H_8F_6O$ requires C, 62.3; H, 2.19%; M, 366). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed a broad multiplet from 146.6 to 147.4, a multiplet at 151.9, and a broad multiplet from 158.8 to 159.7 ppm upfield from internal $CFCl_3$ in the ratio 2:1:3, respectively. The ^{1}H n.m.r. spectrum ($CDCl_3$) showed a singlet at δ 4.21 (CH_2), a multiplet at 6.95 (vinylic CH) and a singlet at 7.34 (aromatic C_6H_5).

Chapter 6 The Thermal Chemistry of Pentafluorophenyl Prop-2-ynyl Ether (175)

6.1 Introduction

The synthesis of pentafluorophenyl prop-2-ynyl ether (175) from pentafluorophenol has been reported in the literature[24]. The ether (175) was expected to give a stable tricyclic ketone by Claisen rearrangement and internal Diels-Alder addition and to achieve this vapour-phase and solution-phase experiments were carried out with the ether (175).



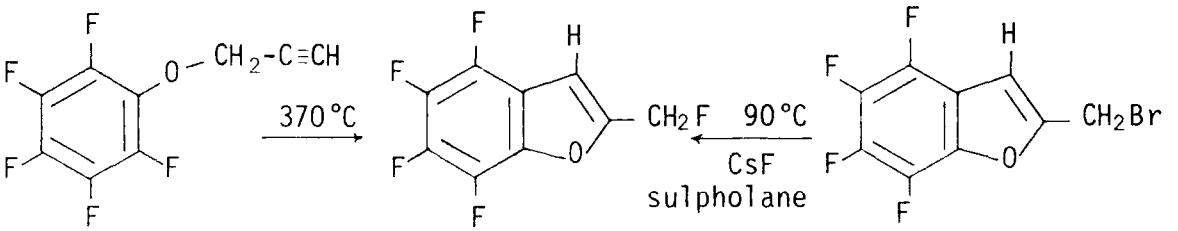
(175)

6.2 Vapour-phase Reactions of Pentafluorophenyl Prop-2-ynyl Ether (175)

Static thermolysis of the ether (175) at 148°C for 17.5 hours only gave unchanged starting material (175), whereas heating at 138 - 140°C for 95.5 hours gave a black residue containing at least four components according to t.l.c. and this was not investigated further. Thermolysis at 178°C for 5 hours resulted in a black residue which was insoluble in diethyl ether.

Since the thermolysis experiments were not particularly promising, the ether was subjected to flow pyrolysis at 370°C through a silica tube packed with quartz wool. The tarry residue obtained was chromatographed on silica followed by preparative

thick layer chromatography on silica to give ca. 8% of a liquid confirmed by independent synthesis as 2-fluoromethyl-4,5,6,7-tetrafluorobenzo (b) furan (190). Stirring the known compound, 2-bromomethyl-4,5,6,7-tetrafluorobenzo (b) furan (191) in sulpholane at 90°C with excess anhydrous caesium fluoride for 3 hours gave (190) in 72.5% yield.



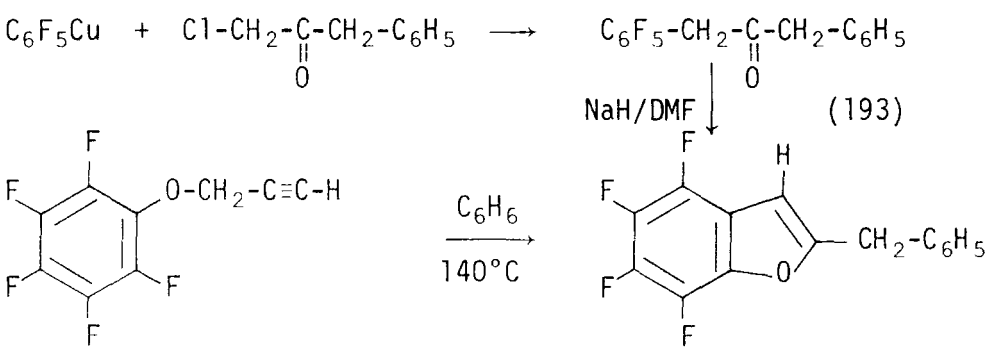
(175) (190) (191)

The ^{1}H n.m.r. spectrum showed a doublet at δ 5.42 for two methylene protons and a multiplet at δ 7.02 for a vinylic proton. The ^{19}F n.m.r. spectrum showed five signals of equal intensity at 147.3, 160.3, 161.7, 164.1 and 211.4 ppm upfield from internal $CFCl_3$. The coupling constant between the fluorine and two protons on the fluoromethyl group was 48.0 Hz.

6.3 Reaction of Pentafluorophenyl Prop-2-ynyl Ether (175) with benzene and p-xylene

The phenyl ether (175) was reacted with benzene and p-xylene in an attempt to parallel the reactions of the naphthyl ether (170). The reaction of the ether (175) with benzene in a solution-phase experiment heating at 140°C in a sealed tube for 116 hours gave a solution which evolved hydrogen fluoride. Chromatography on silica of the residue followed by preparative thick layer chromatography

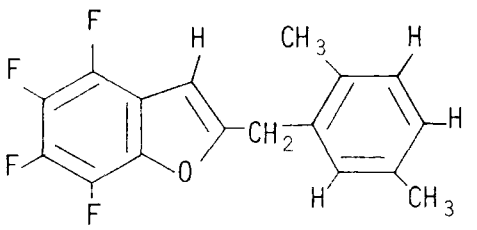
on silica gave 2-benzyl-4,5,6,7-tetrafluorobenzo (b) furan (192) in 28% crude yield. The product was confirmed by independent synthesis. The reaction of pentafluorophenylcopper, prepared from bromopentafluorobenzene[53], and chloromethylbenzylketone gave benzyl pentafluorobenzylketone (193) which was cyclised to the benzo (b) furan (192) on refluxing with sodium hydride in dimethylformamide[57].



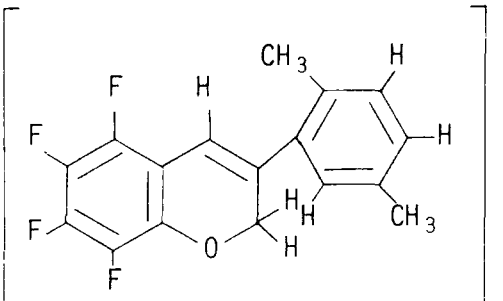
(175) (192)

The ^{1}H n.m.r. spectrum of (192) showed a singlet at δ 4.08 for two methylene protons, a multiplet at δ 6.42 for a vinylic proton and a singlet at δ 7.3 for five aromatic protons. The ^{19}F n.m.r. spectrum showed four signals of equal intensity at 148.5, 162.4, 163.4 and 165.4 ppm upfield from internal $CFCl_3$.

Refluxing the phenyl ether (175) for 118 hours with p-xylene gave a black solution evolving hydrogen fluoride. Chromatography on silica of the residue followed by preparative thick layer chromatography on silica gave as a viscous liquid 2-(2,5-dimethyl-benzyl)-4,5,6,7-tetrafluorobenzo (b) furan (194) in 21.5% crude yield. The ^{1}H n.m.r. spectrum showed a singlet at δ 2.33 for six methyl protons, a multiplet at δ 4.07 for two methylene protons, a multiplet at δ 6.38 for a vinylic proton and a multiplet at δ 7.10 for three aromatic protons.



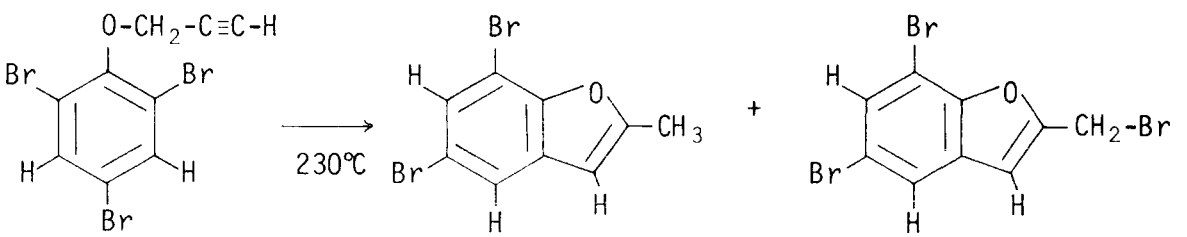
(194)



(195)

Two structures could be fitted to the n.m.r. data: a benzo (b) furan (194) or a benzo (b) pyran (195) but the structure with a five-membered ring (194) was chosen by comparison with the ^1H n.m.r. data of the product obtained from (175) and benzene.

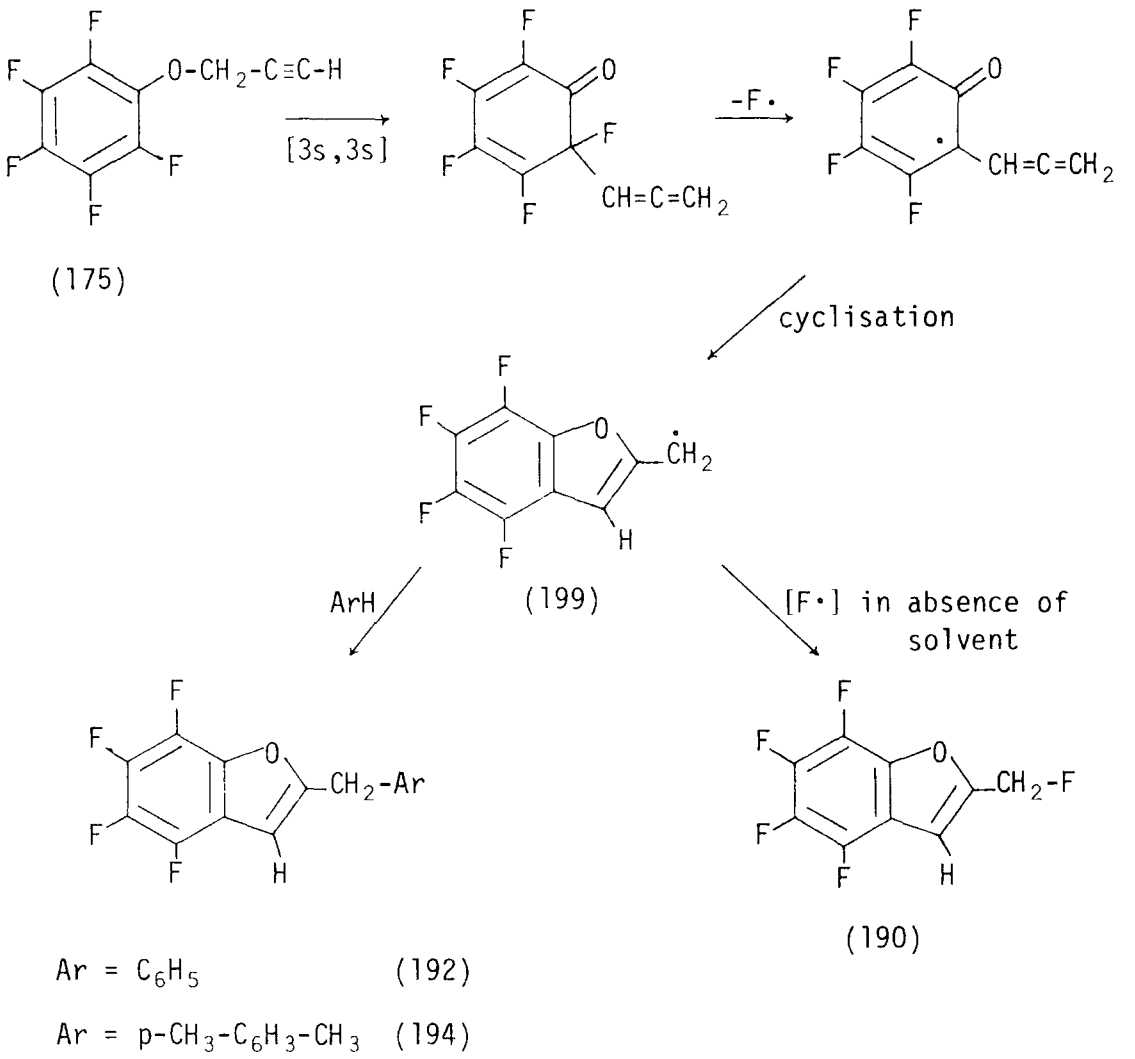
The reaction of 2,4,6-tribromophenyl prop-2-ynyl ether (196) in decane at 230°C has been shown previously to give 2-methyl-5,7-dibromobenzo (b) furan (197) and 2-bromomethyl-5,7-dibromobenzo (b) furan (198)[61]. Initial Claisen rearrangement of (196) to an ortho-dienone is followed by homolysis at C-2 with loss of a bromine atom. The radical formed cyclises to a benzo (b) furan radical which either abstracts a hydrogen to give (197) or combines with a bromine atom to give (198)



(196) (197) (198)

The mechanism proposed to explain the behaviour of (175) is essentially based on the above reaction of (196). Thus the phenyl ether (175) undergoes initial Claisen rearrangement to an ortho-dienone followed by homolytic cleavage at C-2 with loss of a fluorine atom. The radical formed cyclises to a benzo (b) furan radical

(199) which combines with a fluorine atom in the absence of solvent or it attacks the aromatic solvent leading to the products (192) and (194) by homolytic aromatic substitution.



Ar = C_6H_5 (192)

Ar = p-CH_3-C_6H_3-CH_3 (194)

Parallel to the reaction of the naphthyl ether (170) the mechanism proposed to explain the formation of the observed products requires homolysis of a carbon to fluorine bond. The radical formed by loss of a fluorine atom cyclises to a heterocyclic radical (199) and this combines with the fluorine atom in the absence of solvent. It is necessary to propose again when an aromatic solvent is present

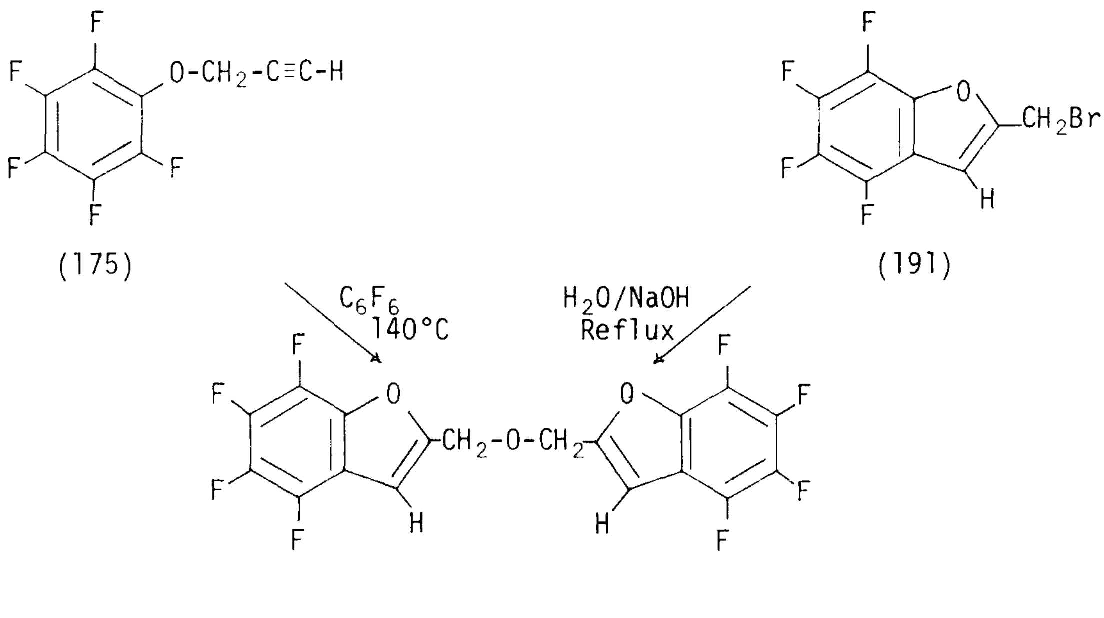
that the heterocyclic radical adds to it first and then a fluorine atom abstracts a hydrogen from the radical complex formed to give the observed products.

6.4 Reaction of Pentafluorophenyl Prop-2-ynyl Ether (175) with hexafluorobenzene

In an attempt to obtain the benzo (b) furan (190) in a solution-phase experiment parallel to the flow pyrolysis reaction, the ether (175) was heated at 140°C for 118 hours in a sealed tube with hexafluorobenzene. This solvent was chosen because of the absence of any hydrogens which could be abstracted; this was expected to make this solvent inert with respect to this reaction. A black solution which evolved hydrogen fluoride was obtained from this reaction. Chromatography on silica of the residue gave a viscous liquid which quickly changed to a solid with a different infra-red spectrum. The solid, obtained in ca. 8% yield, was confirmed by independent synthesis as di-(4,5,6,7-tetrafluorobenzo (b) furan-2-yl) methyl ether (200). 2-Bromomethyl-4,5,6,7-tetrafluorobenzo (b) furan (191) and 2.5M sodium hydroxide were refluxed for 18.5 hours. Chromatography on silica of the residue gave a liquid which quickly solidified with the same change in infra-red spectrum as seen for the product from (175) and hexafluorobenzene. The solid, obtained in ca. 33% crude yield, was sublimed and recrystallised to give the ether (200).

The ^{1}H n.m.r. spectrum showed a multiplet at δ 4.74 and a multiplet at δ 6.89 in the ratio 2:1, respectively. The ^{19}F n.m.r. spectrum showed three signals in the ratio 1:2:1 at 147.3 ppm, 160.5 to 161.8 ppm, and 164.1 ppm, repectively.

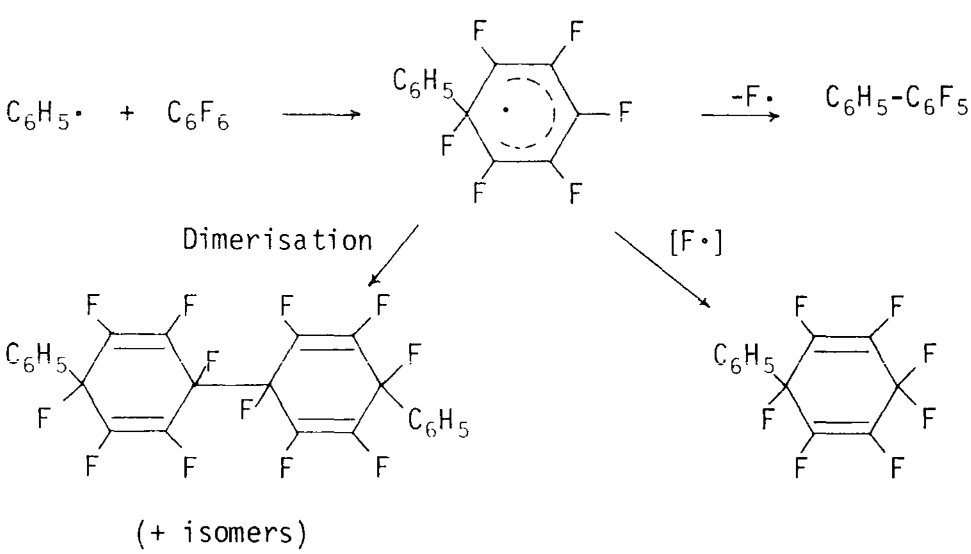
The reaction of the phenyl ether (175) with aromatic



(175) (191)

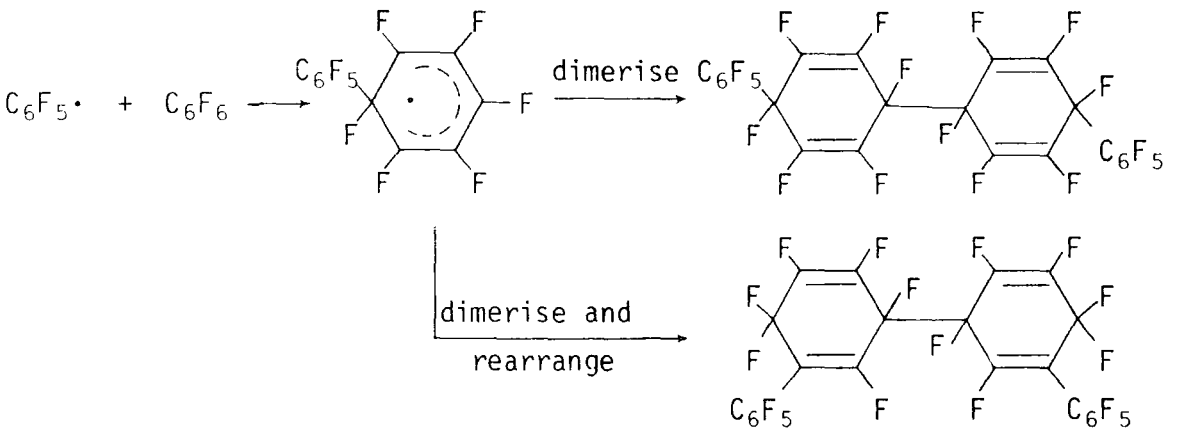
(200)

hydrocarbon solvents suggested the involvement of the heterocyclic radical (199) in this reaction with hexafluorobenzene. However, only a few radical reactions involving hexafluorobenzene have been reported and this makes the behaviour of (199) with this solvent hard to predict. Phenyl radicals, obtained by decomposition of benzoyl peroxide, add to hexafluorobenzene to give a radical complex[63]. This complex then dimerises or loses fluorine to give a biphenyl or adds fluorine to give an arylcyclohexadiene.



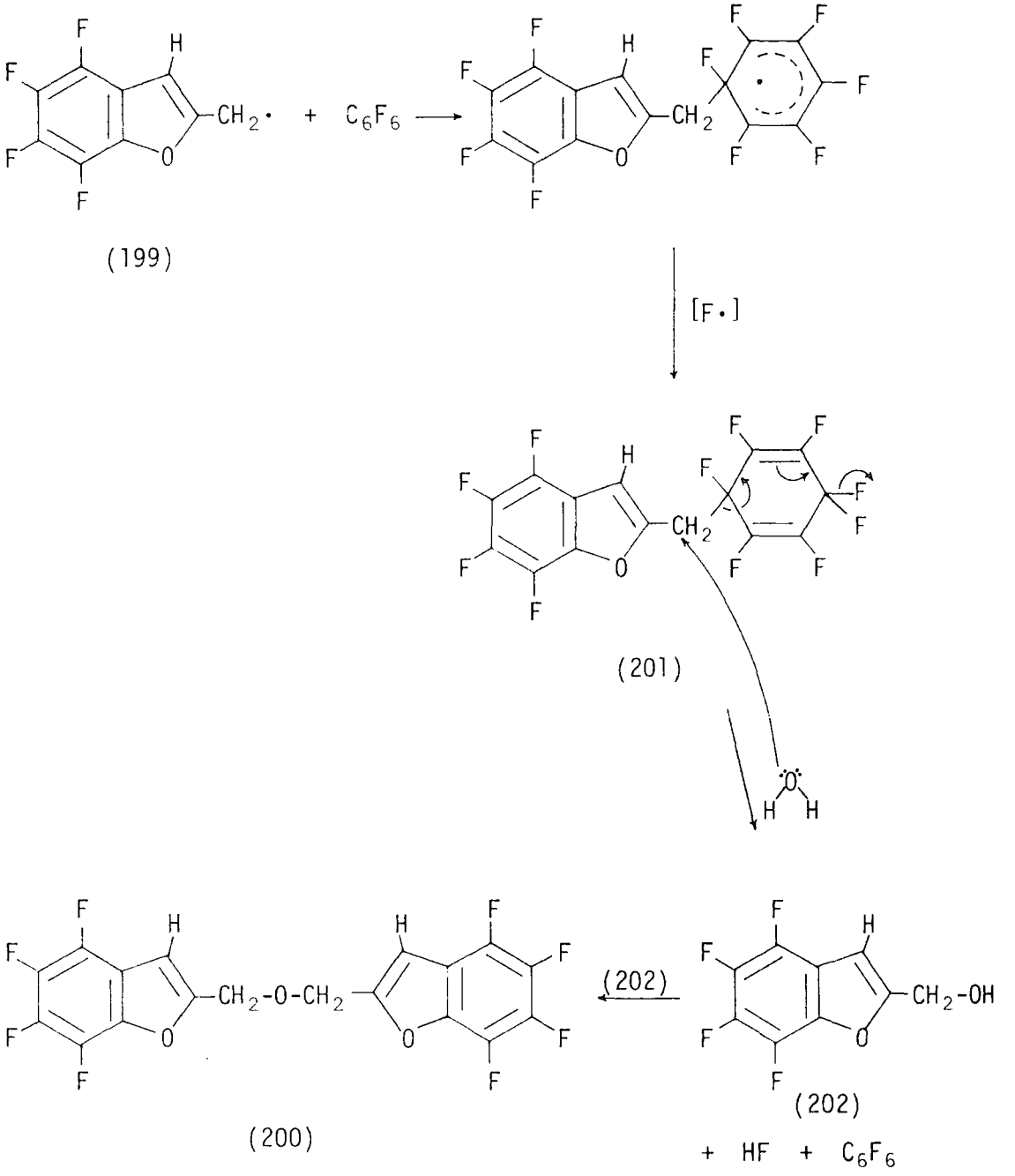
(+ isomers)

Oxidation of pentafluorophenylhydrazine with silver oxide in hexafluorobenzene gave pentafluorophenyl radicals[64]. The main reaction of these radicals was abstraction of hydrogen from the hydrazine to give pentafluorobenzene. However, attack on the aromatic ring of hexafluorobenzene did occur to give several rearranged and unrearranged dimers. Rearrangement of the addition complex took place with migration of fluorine from a sp^3-hybridised carbon to the neighbouring position.



Considering the reaction of the ether (175) with hexafluorobenzene, the mechanism proposes formation of the heterocyclic radical (199) again by homolysis of a carbon to fluorine bond. The radical (199) adds to the solvent and the complex formed can then add a fluorine atom to give a heptafluorocyclohexadiene derivative (201). Hydrolysis of this compound (201) by the adventitious presence of water gives an alcohol (202) which can then attack more of the adduct (201) to give the symmetrical ether (200).

Surprisingly, none of the expected benzo (b) furan (190) was obtained although it may be argued that it is hydrolysed during the reaction to give the ether (200). However, it was found that refluxing the benzo (b) furan (190) with aqueous sodium hydroxide for 16 hours gave no reaction which tends to rule out the suggestion



that the ether (200) arises out of hydrolysis of (190). In order to investigate the mechanism further, and to try and explain the observation that (200) is obtained as a liquid which changes its infra-red spectrum on solidifying, more work should be carried out on this reaction.

Chapter 6 Experimental

6.5 Static Thermolysis of Pentafluorophenyl Prop-2-ynyl Ether (175)

The ether (175) (1.28g) was sealed in a 2 litre bulb evacuated to low pressure (0.01 mm Hg) and then heated at 148°C for 17.5 hours. On condensing the contents into a side-arm using liquid air, the bulb was opened and the liquid analysed by g.l.c. (2-cyanoethyl-methylsilicone at 200°C) which only showed unchanged ether (175).

The ether (175) (1.28g) was again sealed in a 2 litre bulb as before and then heated at 178°C for 5 hours. This gave a black residue which was insoluble in ether.

In a further experiment the ether (175) (1.32g) was heated at 138 - 140°C for 95.5 hours. This gave a brown residue in the bulb on cooling. It was washed out with diethyl ether, dried ($MgSO_4$) and the solvent was evaporated to give a black residue which contained at least four components by t.l.c. and this was not worked up further.

6.6 Flow Pyrolysis of Pentafluorophenyl Prop-2-ynyl Ether (175)

The ether (175) (5.42g) was distilled from a vessel through a silica tube (58 cm x 1.4 cm diam.) packed with quartz wool, heated at 370°C, over 10 minutes into a trap cooled by liquid air, connected to a high vacuum system (0.001 mm Hg). The products collected in the trap (4.24g) were chromatographed on silica (120 cm x 3.4 cm diam.) (light petroleum b.p. 40 - 60°C as eluent), followed by preparative thick layer chromatography on silica (light petroleum b.p. 40 - 60°C as eluent) on the enriched product to give 2-fluoromethyl-4,5,6,7-

tetrafluorobenzo(b) furan (190) (0.41g) b.p. 28 - 29°C at 0.05 mm Hg. (Found: C, 48.39; H, 1.67%; M^+, 222. $C_9H_3F_5O$ requires C, 48.65; H, 1.35%; M, 222). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed five signals of equal intensity at 147.3, 160.3, 161.7, 164.1 and 211.4 (triplet for CH_2F group) ppm upfield from internal $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a doublet centred at δ 5.42 (CH_2F group) and a multiplet at 7.02 (vinylic CH). [J(F, CH_2) for CH_2F group was 48.0 Hz].

6.7 Synthesis of 2-Fluoromethyl-4,5,6,7-Tetrafluorobenzo (b) furan (190)

2-Bromomethyl-4,5,6,7-tetrafluorobenzo (b) furan (191) (1.35g) and dry caesium fluoride (2.9g) were stirred in dry sulpholane (10 ml) under nitrogen at 90°C for 3 hours. The mixture was diluted with water and extracted with ether. The extracts were dried ($MgSO_4$) and the solvent evaporated to give a residue which was distilled in vacuo to give 2-fluoromethyl-4,5,6,7-tetrafluorobenzo (b) furan (190) (0.77g) b.p. 28 - 29°C at 0.05 mm Hg, identified by i.r.

6.8 Reaction of Pentafluorophenyl Prop-2-ynyl Ether (175) with benzene

The ether (175) and benzene (20 ml) were sealed in a 50 ml tube under reduced pressure (0.05 mm Hg) and heated at 140°C for 116 hours. On opening the tube hydrogen fluoride was evolved. The solvent was evaporated and the residue was chromatographed on silica (118 cm x 3.4 cm diam.) (carbon tetrachloride as eluent) to give crude product (1.08g). This was purified by thick layer chromatography on silica (carbon tetrachloride as eluent) to give 2-benzyl-4,5,6,7-tetrafluorobenzo (b) furan (192) b.p. 103 - 105°C

at 0.05 mm Hg, confirmed by comparison of the infra-red spectrum with that of material synthesised unambiguously. (Found: C, 64.00; H, 2.89%; M^+, 280. $C_{15}H_8F_4O$ requires C, 64.29; H, 2.86%; M, 280). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed four signals of equal intensity at 148.5, 162.4, 163.4 and 165.4 ppm upfield from internal $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a singlet at δ 4.08 (CH_2), a multiplet at 6.42 (vinylic CH) and a singlet at 7.3 (aromatic C_6H_5).

6.9 Reaction of Pentafluorophenyl Prop-2-ynyl Ether (175) with p-xylene

The ether (175) (5.63g) and p-xylene (100 ml) were refluxed under nitrogen for 118 hours evolving hydrogen fluoride to give a black solution. Evaporation of the solvent gave a residue which was chromatographed on silica (114 cm x 3.4 cm diam.)(carbon tetrachloride as eluent), followed by thick layer chromatography on silica on the enriched material (carbon tetrachloride as eluent) (1.68g) to give 2-(2,5-dimethylbenzyl-)4,5,6,7-tetrafluorobenzo(b)-furan (194) b.p. 120 - 126°C at 0.05 mm Hg. (Found: C, 66.08; H, 4.07%; M^+, 308. $C_{17}H_{12}F_4O$ requires C, 66.23; H, 3.9%; M, 308). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed four signals of equal intensity at 148.3, 162.0, 163.2 and 165.1 ppm upfield from external $CFCl_3$. The ^1H n.m.r. spectrum ($CDCl_3$) showed a singlet at δ 2.33 ($2CH_3$), a multiplet at 4.07 (CH_2), a multiplet at 6.38 (vinylic CH) and a multiplet at 7.10 (aromatic C_6H_3).

6.10 Reaction of Pentafluorophenyl Prop-2-ynyl Ether (175) with Hexafluorobenzene

The ether (175) (4.18g) and hexafluorobenzene (20 ml) were sealed in a 50 ml tube under reduced pressure (0.05 mm Hg) and

heated at 140°C for 118 hours. On opening the tube, the black solution evolved hydrogen fluoride. The volatile material was evaporated (g.l.c. only showed hexafluorobenzene), to give a residue which was chromatographed on silica (90 cm x 2.4 cm diam.) (carbon tetrachloride as eluent) to give a liquid (0.65g) which rapidly changed to a solid with a different infra-red spectrum. The solid was confirmed as di-(4,5,6,7-tetrafluorobenzo (b) furan-2-yl)methyl ether (200) by comparison of the infra-red spectrum with authentic material synthesised independently.

6.11 Reaction of 2-Fluoromethyl-4,5,6,7-Tetrafluorobenzo (b) furan (190) with aqueous sodium hydroxide

The benzo (b) furan (190) (0.73g) and aqueous sodium hydroxide (32.4 ml, 0.1M) were refluxed for 18 hours. The mixture was acidified with hydrochloric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$) and the solvent evaporated to give unchanged benzo (b) furan (190).

In a further experiment the benzo (b) furan (190) (0.73g) and aqueous sodium hydroxide (20 ml, 2.5M) were refluxed for 16 hours, acidified with hydrochloric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$) and the solvent evaporated to give unchanged starting material (190).

6.12 Reaction of 2-Bromomethyl-4,5,6,7-Tetrafluorobenzo (b) furan (191) with aqueous sodium hydroxide

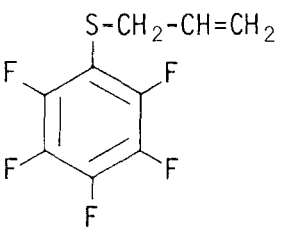
The benzo (b) furan (191) (1.45g) and aqueous sodium hydroxide (20 ml, 2.5M) were refluxed for 18.5 hours. The solution was acidified

with hydrochloric acid (2M) and extracted with ether. The extracts were dried ($MgSO_4$), and the solvent was evaporated to give a residue which was chromatographed on silica (40 cm x 2.4 cm diam.) (carbon tetrachloride:chloroform 1:1 as eluent) to give crude product (0.75g). The infra-red spectrum of this liquid at this time was the same as that observed for the liquid product initially obtained from the reaction of (175) and hexafluorobenzene. Again this material rapidly changed to a solid with a different i.r. After sublimation at 80 - 90°C at 0.05 mm Hg and then recrystallisation from light petroleum (b.p. 30 - 40°C), this gave di-(4,5,6,7-tetrafluorobenzo (b) furan-2-yl)methyl ether (200) m.p. 55.5 - 56.5°C. (Found: C, 51.46; H, 1.21%; M^+, 422. $C_{18}H_6F_8O_3$ requires C, 51.19; H, 1.42%; M, 422). The ^{19}F n.m.r. spectrum ($CDCl_3$) showed a multiplet at 147.3, a broad multiplet from 160.5 to 161.8, and a multiplet at 164.1 ppm upfield from external $CFCl_3$ in the ratio 1:2:1, respectively. The ^1H n.m.r. spectrum ($CDCl_3$) showed a multiplet at δ 4.74 (2 equivalent CH_2) and a multiplet at 6.89 (2 equivalent vinylic CH).

General Conclusions

Homolytic cleavage of a carbon to fluorine bond should be a difficult process because of the large bond energy of this bond, which is greater than the bond energy of most other bonds involving carbon. This is borne out by the scarcity of reported reactions in which this process is believed to occur. The loss of fluorine atoms from polyfluoroaromatic compounds is extremely uncommon and very few reports have been published proposing this idea. The examples known include the electrochemical oxidation of pentafluoroaniline to give 1,2,3,4,6,7,8,9-octafluorophenazine[65], the pyrolysis of 3-pentafluorophenylanthranil to give 1,2,3,4-tetrafluoroacridinone[66], and the reaction of hexafluorobenzene with aryl radicals to give fluorinated biaryls[63].

The evidence from the reactions of the thioethers (101) and (125) as well as the ethers (170) and (175) strongly suggests that homolysis of a carbon to fluorine bond has occurred under quite mild conditions. Presumably one of the driving forces for this



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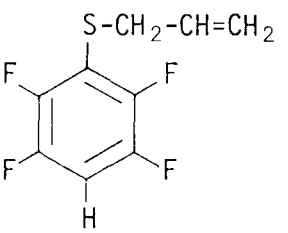

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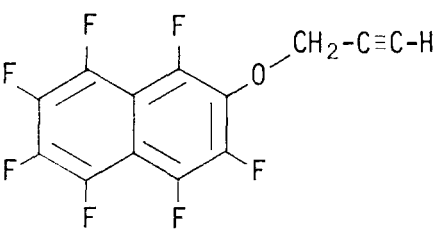

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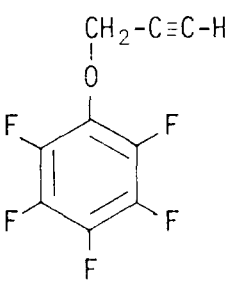
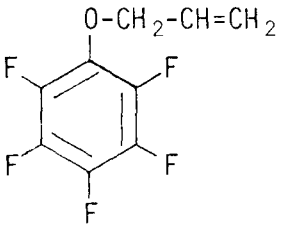


(175)

cleavage is the aromatisation of the ortho-dienone or ortho-dienethione after the fluorine atom is lost.

From this study and the related work on the prop-2-enyl ethers (55) and (36) it is possible to see a certain pattern for Claisen rearrangement in polyfluoroaromatic systems[19,25,26]. The



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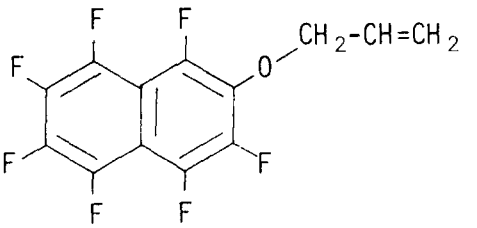


(36)

prop-2-enyl ethers (55) and (36) undergo Claisen rearrangement to an ortho-dienone stable to homolytic loss of fluorine and actually isolable for (36)[19]. Replacing the prop-2-enyl group by a prop-2-ynyl to give (170) and (175) now renders the ortho-dienone unstable with respect to homolytic loss of fluorine. Similarly replacing the oxygen atom of the prop-2-enyl ether (55) by sulphur gives (101) and this together with (125) rearrange to ortho-dienethiones which undergo homolysis of a carbon to fluorine bond.

Work on the pyridine system shows that the behaviour of the prop-2-enyl ethers is similar to the phenyl ether (55)[27]. It is therefore not unreasonable to assume that the corresponding prop-2-ynyl ether or prop-2-enyl thioether derivatives in the polyfluoropyridine system would also involve rearrangement to an intermediate unstable to homolytic loss of fluorine.

Since a prop-2-ynyl group and a sulphur atom in the rearranging group both appear to favour the homolysis process in

the rearrangement product then combining these to give a prop-2-ynyl thioether should promote this cleavage considerably, with a naphthyl derivative more easily undergoing this reaction than a phenyl derivative. Related to this would be a study to find out the mildest conditions necessary for the homolytic process to occur.

It would also be of interest to carry out this reaction in the presence of a series of unsaturated substrates in an attempt to study the addition of a carbon to fluorine bond across the site of unsaturation.

Appendix A Apparatus and Instrumentation

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

Fractional distillation of product mixtures was carried out using a small concentric tube - a Fischer-Spaltrohr MS 200 system.

Analytical gas liquid chromatography (g.l.c.) was carried out using a Varian Aerograph Model 920 Gas Density Balance, or a PYE GCD Chromatograph, using a flame ionisation detector, or a PYE 104 Chromatograph, also using a flame ionisation detector. The columns used were either packed with 30% silicone elastomer SE-30 on chromosorb P or with 17% 2-cyanoethylmethylsilicone on chromosorb P. Preparative-scale g.l.c. was carried out on a Varian Aerograph Model 920 or "Autoprep" instrument.

Infra-red spectra were recorded with either a Perkin-Elmer 127 or 457 Grating Infra-red Spectrophotometer using conventional methods.

Carbon, hydrogen and nitrogen analyses were obtained using a Perkin-Elmer 240 Elemental Analyser.

Mass spectra were recorded on an A.E.I. M.S. 9 Spectrometer, or on a V.G. Micromass 12B Spectrometer fitted with a PYE series 104 gas chromatograph. Latterly both spectrometers were linked to a V.G. Datasystem 2000.

Proton (^{1}H) and fluorine (^{19}F) nuclear magnetic resonance spectra were recorded either on a Varian A 56/60D spectrometer, operating at 60.0 and 56.46 MHz respectively with an ambient probe temperature of 40°C or on a Brüker HX 90 E spectrometer operating at 90.0 and 84.67 MHz respectively with an ambient probe temperature of 22°C.

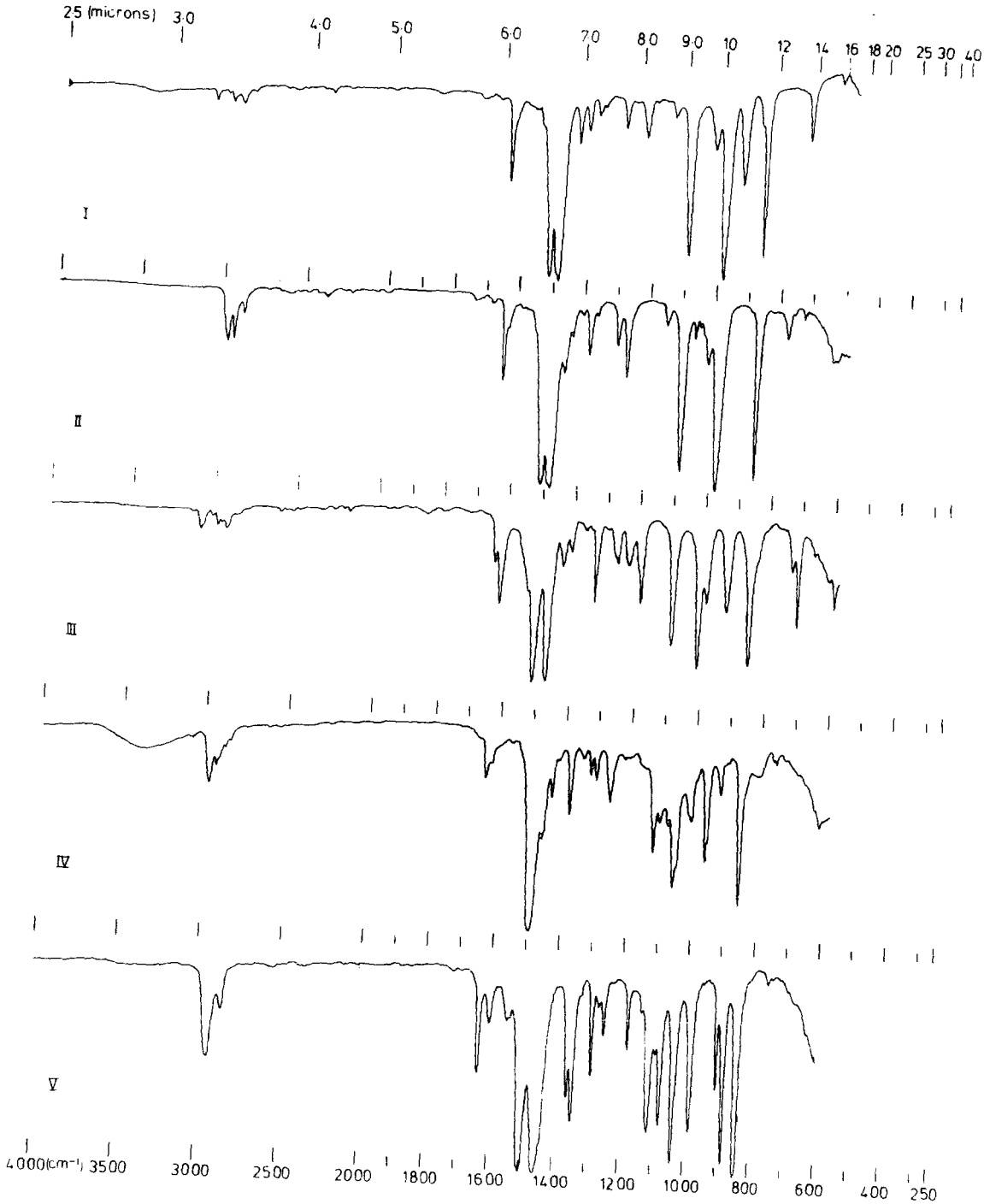
Appendix B Infra-red Spectra

The spectra were obtained using sodium chloride cells and were run as liquids unless denoted by (M) which designates that the spectrum was obtained as a Nujol mull. [The exception being compound (200) whose spectrum, in the solid form, was obtained as a potassium bromide disc (D) .]

Compound Number	Name of Compound		
I	Pentafluorophenyl Prop-2-enyl Thioether		(101)
II	Pentafluorophenyl Ethyl Thioether		(115)
III	2,3,4,5-Tetrafluorophenyl Prop-2-enyl Thioether		(107)
IV	2H,3H-2-Methyl-4,5,6,7-Tetrafluorobenzo (b) - thiophene		(110)
V	5,6,7,8-Tetrafluorothiachroman		(109)
VI	2,3,5,6-Tetrafluorophenyl Prop-2-enyl Thioether		(125)
VII	2,3,5,6-Tetrafluorophenyl Ethyl Thioether		(135)
VIII	2H,3H-2-Methyl-4,6,7-Trifluorobenzo (b) - thiophene		(136)
IX	5,7,8-Trifluorothiachroman	(M)	(128)

Compound Number	Name of Compound		
X	2-Prop-2-enyl-3,4,5,6-tetrafluorophenyl Prop-2-enyl Thioether		(116)
XI	4-Prop-2-enyl-2,3,5,6-tetrafluorophenyl Prop-2-enyl Thioether		(117)
XII	3-Pentafluorophenyl-propan-1-ol		(161)
XIII	3-Pentafluorophenyl-1-bromopropane		(162)
XIV	1-Pentafluorophenyl-2-propyl-p-toluene sulphonate	(M)	(166)
XV	2,3,4,5-Tetrafluoro-prop-2-enyl-benzene		(169)
XVI	1,3,4,5,6,7,8-Heptafluoro-2-naphthyl Prop-2-ynyl Ether		(170)
XVII	2-(2,5-Dimethylbenzyl)-4,5,6,7,8,9-hexafluoronaphtho[2,1-b]furan	(M)	(173)
XVIII	2-Benzyl-4,5,6,7,8,9-hexafluoronaphtho-[2,1-b]furan	(M)	(176)
XIX	2-Fluoromethyl-4,5,6,7-tetrafluoro-benzo (b) furan		(190)
XX	2-Benzyl-4,5,6,7-tetrafluorobenzo (b) furan		(192)
XXI	2-(2,5-Dimethylbenzyl)-4,5,6,7-tetrafluoro-benzo (b) furan		(194)

Compound Number	Name of Compound		
XXII	Initial liquid form of Di-(4,5,6,7-tetrafluorobenzo (b) furan-2-yl) methyl Ether		(200)
XXIII	Final solid form of Di-(4,5,6,7-tetrafluorobenzo (b) furan-2-yl) methyl Ether	(D)	(200)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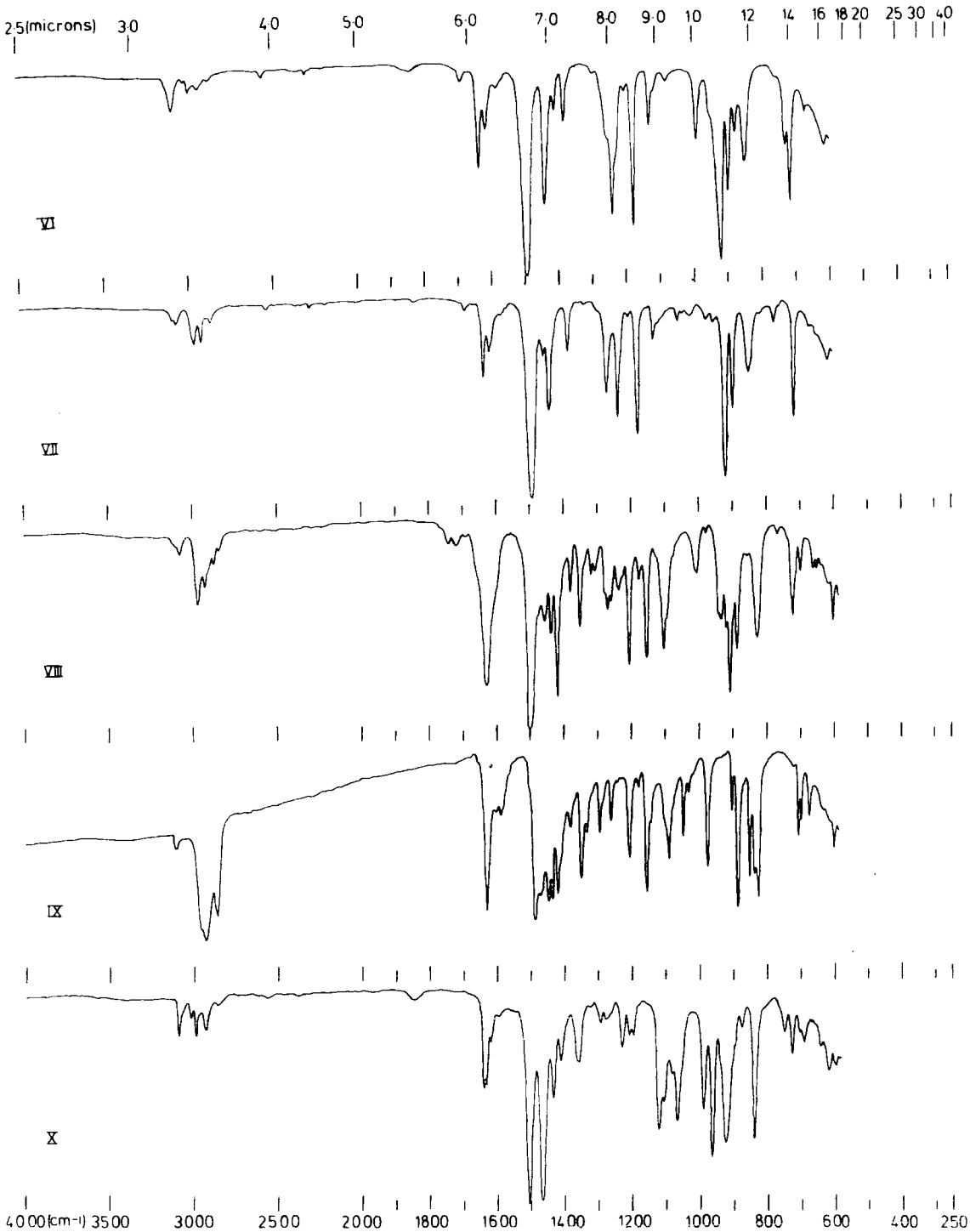
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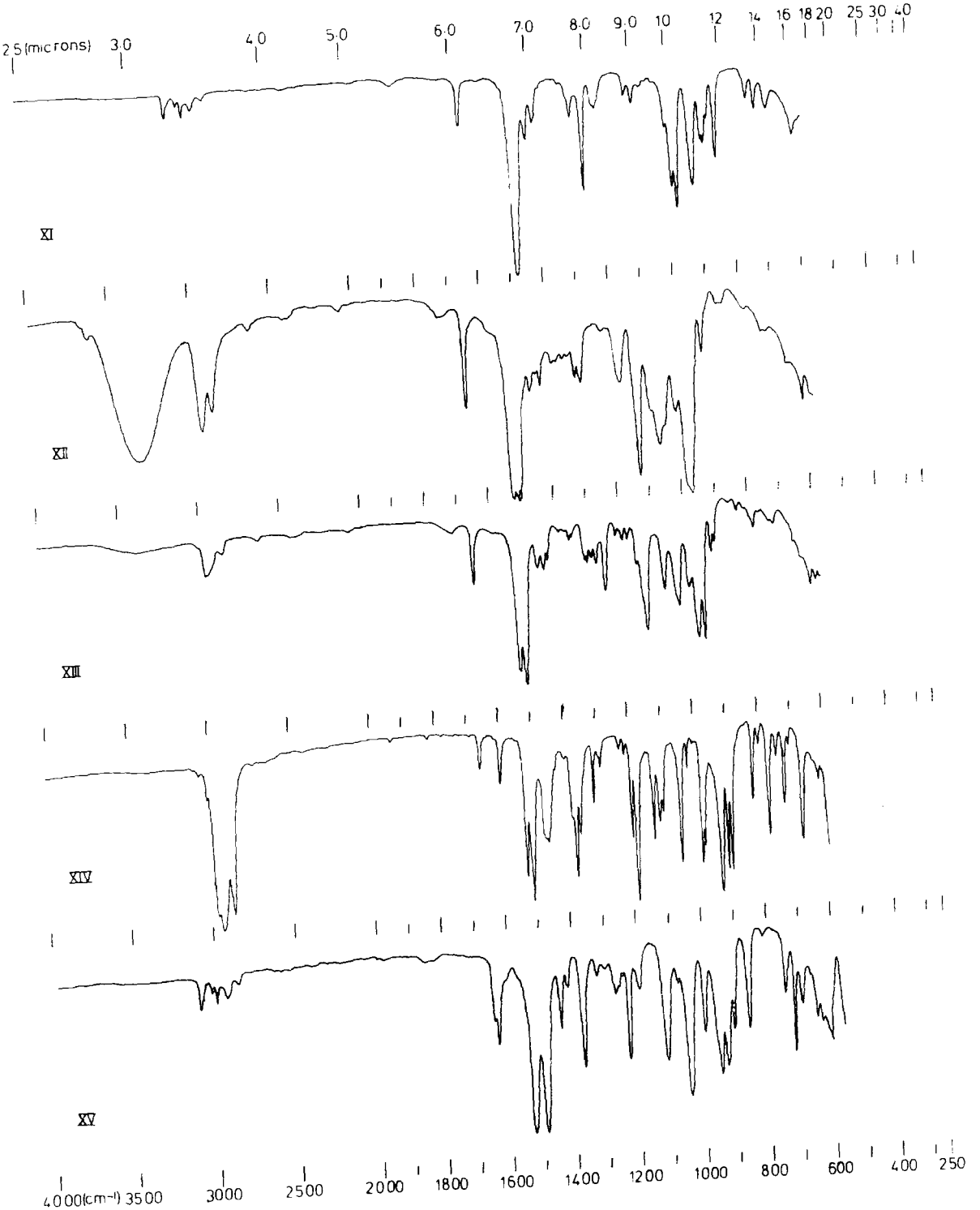
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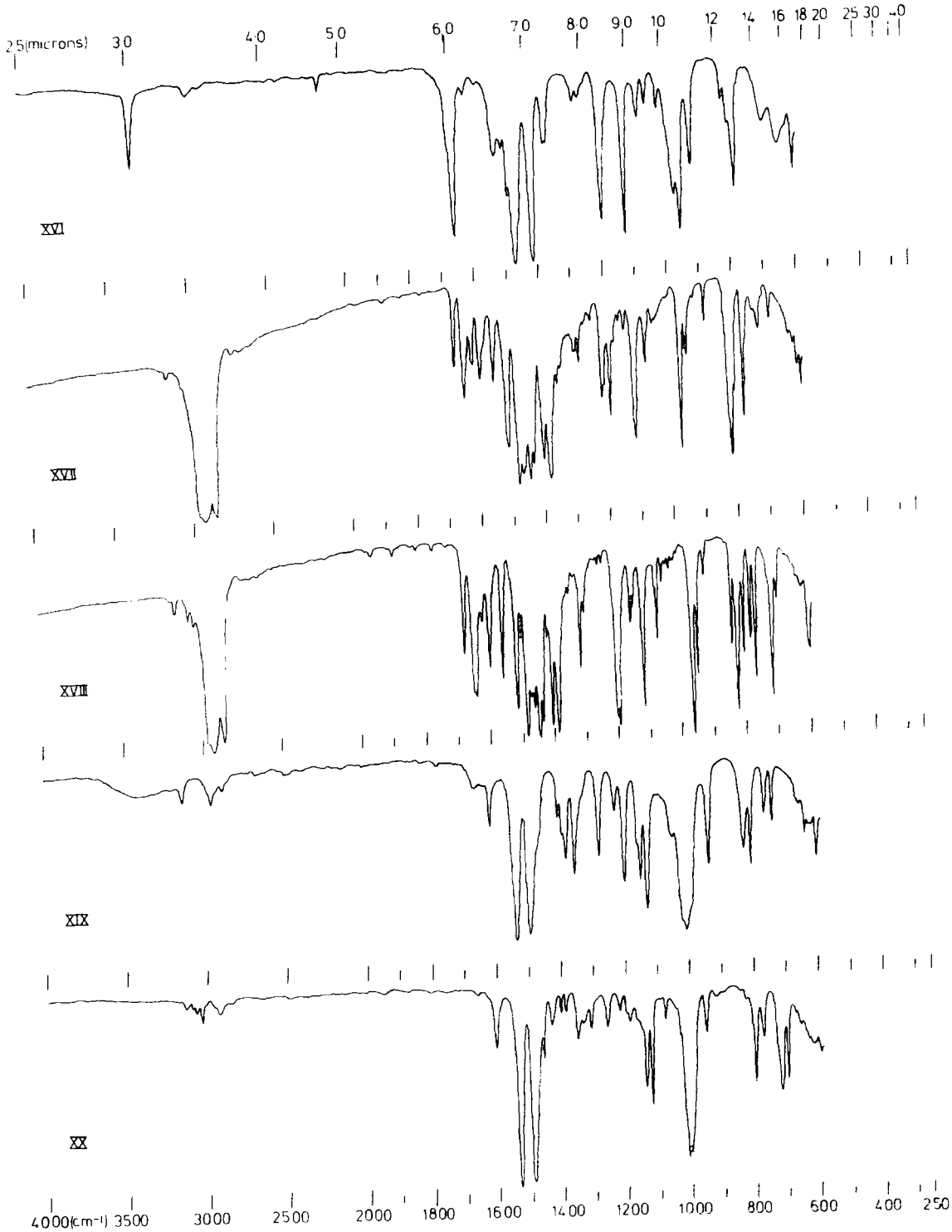
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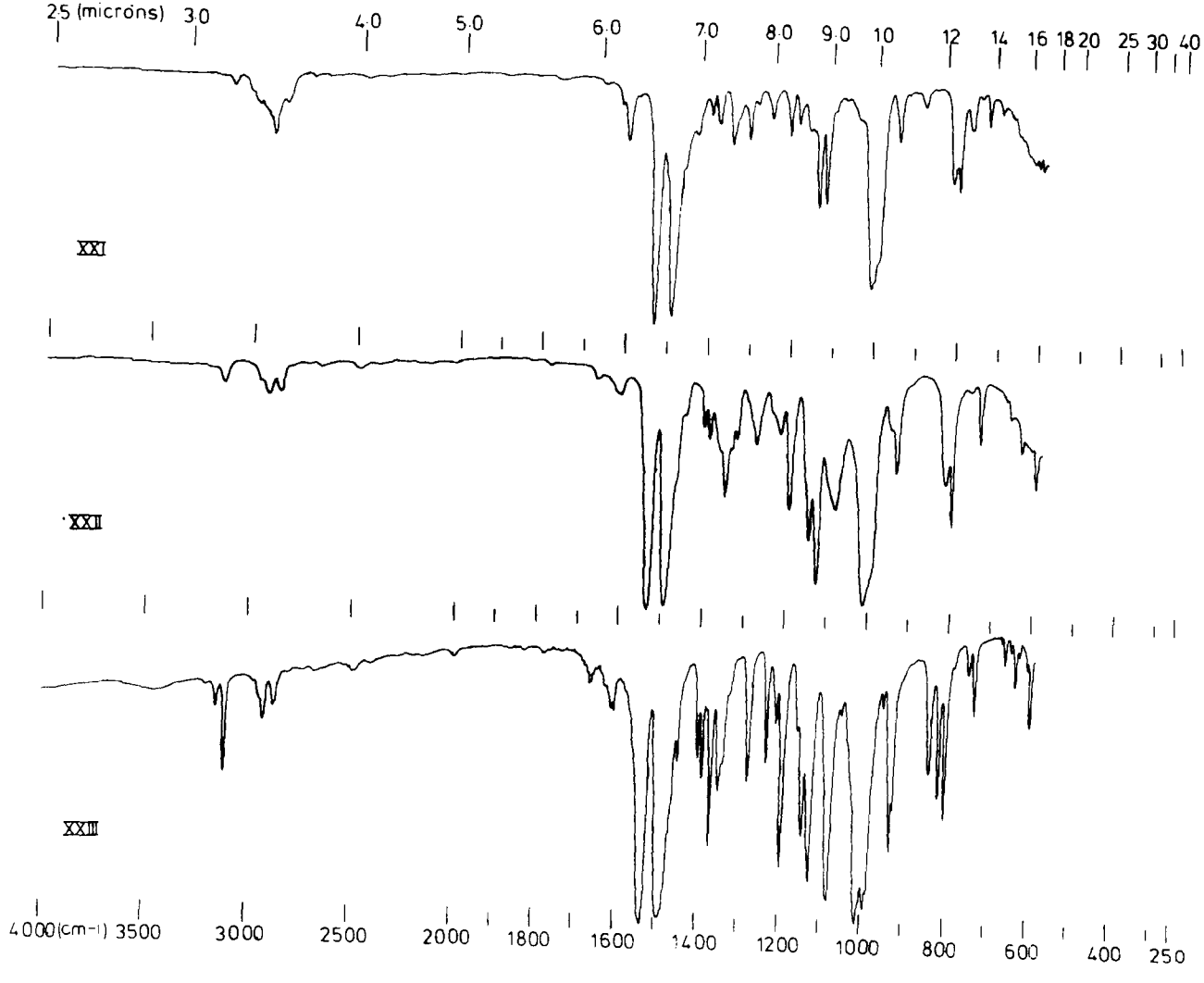
2.5 (microns) 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10 12 14 16 18 20 25 30 40
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Appendix C Departmental Colloquia and First-Year Induction Course for Post-Graduates

The Board of Studies in Chemistry requires that each postgraduate research thesis contains an appendix listing

(a) all research colloquia, research seminars and lectures arranged by the Department of Chemistry during the period of the writer's residence as a postgraduate student;

(b) all research conferences attended and papers read out by the writer of the thesis, during the period when the research for the thesis was carried out; and

(c) details of the first-year induction course.

Events in (a) which were attended are marked *.

Research Colloquia, Seminars and Lectures

1. University of Durham Chemistry Colloquia

Academic Year 1977 - 1978

* 19 Oct. Dr. B. Heyn (U. of Jena, D.D.R.), "Sigma-organo molybdenum complexes as alkene polymerisation catalysts".

* 27 Oct. Professor R.A. Filler (Illinois Institute of Technology, U.S.A.), "Reactions of organic compounds with xenon fluorides".

2 Nov. Dr. N. Boden (U. of Leeds), "N.m.r. spin-echo experiments for studying structure and dynamical properties of materials containing interacting spin-Y_2 pairs".

* 9 Nov. Dr. A.R. Butler (U. of St. Andrews), "Why I lost faith in linear free energy relationships".

7 Dec. Dr. P.A. Madden (U. of Cambridge), "Raman studies of molecular motions in liquids".

* 14 Dec. Dr. R.O. Gould (U. of Edinburgh), "Crystallography to the rescue in ruthenium chemistry".

* 25 Jan. Dr. G. Richards (U. of Oxford). "Quantum pharmacology".

* 1 Feb. Professor K.J. Ivin (Queens U., Belfast), "The olefin metathesis reaction, mechanism of ring opening polymerisation of cycloalkenes".

* 3 Feb. Dr. A. Hartog (Free U., Amsterdam), "Surprising recent studies in organo-magnesium chemistry".

* 22 Feb. Professor J.D. Birchall (Mond Division, I.C.I.), "Silicon in the biosphere".

* 1 Mar. Dr. A. Williams (U. of Kent), "Acyl group transfer reactions".

3 Mar. Dr. G. van Koten (U. of Amsterdam), "Structure and reactivity of arylcopper cluster compounds".

15 Mar. Professor G. Scott (U. of Aston), "Fashioning plastics to match the environment".

22 Mar. Professor H. Vahrenkamp (U. of Freiburg, Germany), "Metal-metal bonds in organometallic complexes".

19 Apr. Dr. M. Barber (UMIST), "Secondary ion mass spectra of surfaces and adsorbed species".

16 May Dr. P. Ferguson (C.N.R.S., Grenoble), "Surface plasma waves and adsorbed species on metals".

18 May Professor M. Gordon (U. of Essex) , "Three critical points in polymer chemistry".

22 May Professor D. Tuck (U. of Windsor, Ontario), "Electrochemical synthesis of inorganic and organometallic compounds".

24 & 25 May Professor P. von R. Schleyer (U. of Erlangen, Nürnberg)

* I "Planar tetra-coordinate methanes, perpendicular ethenes and planar allenes".

* II "Aromaticity in three dimensions".

* III "Non-classical carbo-cations".

21 June Dr. S.K. Tyrlik (Acad. of Sci., Warsaw), "Dimethylglyoxime-cobalt complexes - catalytic black boxes".

23 June Professor G. Mteescu (Case Western Reserve U., Ohio), "A concerted spectroscopy approach to the characterisation of ion and ion-pairs: facts, plans and dreams".

8 Sept. Dr. A. Diaz (I.B.M., San Jose, California), "Chemical behaviour of electrode surface bonded molecules".

15 Sept. Professor W. Siebert (Marburg, W. Germany), "Boron heterocycles".

22 Sept. Professor T. Fehlner (Notre Dame, U.S.A.), "Ferraboranes: synthesis and photochemistry".

Academic Year 1978 - 1979

* 12 Dec. Professor C.J.M. Stirling (U. of Bangor), "Parting is such sweet sorrow - the leaving group in organic chemistry".

* 31 Jan. Professor P.D.B. de la Mare (U. of Auckland, New Zealand), "Some pathways leading to electrophilic substitution".

14 Feb. Professor B. Dunnel (U. of British Columbia), "The application of n.m.r. to the study of motions of molecules in solids".

* 14 Mar. Dr. J. C. Walton (U. of St. Andrews), "Pentadienyl radicals".

* 28 Mar. Dr. A. Reiser (Kodak Ltd.), "Polymer photography and the mechanism of cross-link formation in solid polymer matrices".

* 25 Apr. Dr. C.R. Patrick (U. of Birmingham), "Chlorofluorocarbons and stratospheric ozone: an appraisal of the environmental problem".

* 1 May Dr. G. Wyman (European Research Office, U.S. Army), "Excited state chemistry of indigoid dyes".

* 2 May Dr. J.D. Hobson (U. of Birmingham), "Nitrogen-centred reactive intermediates".

8 May Professor A. Schmidpeter (Inst. of Inorg. Chem., Munich U.), "Five-membered phosphorus heterocycles containing dicoordinate phosphorus".

* 9 May Professor G. Maier (Lahn Giessen U.), "Tetra-tert-butyltetrahedrane".

9 May Dr. A.J. Kirkby (U. of Cambridge), "Structure and reactivity in intramolecular and enzymic catalysis".

16 May Dr. J.F. Nixon (U. of Sussex), "Some recent developments in platinum-metal phosphine complexes".

* 23 May Dr. B. Wakefield (U. of Salford), "Electron transfer in reaction of metals and organometallic compounds with polychloropyridine derivatives".

* 13 June Professor I. Ugi (U. of Munich), "Synthetic uses of super nucleophiles".

* 25 Sept.Professor R. Soulen (Southwestern U., Texas), "Applications of HSAB theory to vinylic halogen substitution reactions and a few copper coupling reactions".

Academic Year 1979 - 1980

* 21 Nov. Dr. J. Müller (U. of Bergen), "Photochemical reactions of ammonia".

28 Nov. Dr. B. Cox (U. of Stirling), "Macrobicyclic cryptate complexes: dynamics and selectivity".

* 5 Dec. Dr. G.C. Eastmand (U. of Liverpool), "synthesis and properties of some multicomponent polymers".

12 Dec. Dr. C.I. Ratcliffe, "Rotor motions in solids."

18 Dec. Dr. K.E. Newman (U. of Lausanne), "High pressure multinuclear n.m.r. in the elucidation of mechanism of fast simple inorganic reactions".

30 Jan. Dr. M.J. Barrow (U. of Edinburgh), "The structures of some simple inorganic compounds of silicon and germanium - pointers to structural trends in group IV".

* 6 Feb. Dr. J.M.E. Quirke (U. of Durham, "Degradation of chlorophyll - a in sediments".

* 23 Apr. B. Grievson B.Sc. (U. of Durham), "Halogen radio-pharmaceuticals".

* 14 May Dr. R. Hutton (Waters Associates), "Recent developments in multi-milligram and multi-gram scale preparative high performance liquid chromatography".

21 May Dr. T.W. Bentley (U. of Swansea), "Medium and structural effects on solvolytic reactions".

* 10 July Professor D. Des Marteau (U. of Heidelberg), "New developments in organonitrogen fluorine chemistry".

2. Durham University Chemical Society

Academic Year 1977 - 1978

13 Oct. Dr. J.C. Young and Mr. A.J.S. Williams (U. of Aberystwyth), "Experiments and considerations touching colour".

* 20 Oct. Dr. R.L. Williams (Metropolitan Police Forensic Science Dept.), "Science and Crime".

* 3 Nov. Dr. G.W. Gray (U. of Hull), "Liquid crystals - their origins and applications".

24 Nov. Mr. G. Russell (Alcan), "Designing for social acceptability".

1 Dec. Dr. B.F.G. Johnson (U. of Cambridge), "Chemistry of binary metal carbonyls".

* 2 Feb. Professor R.A. Raphael (U. of Cambridge), "Bizarre reactions of acetylenic compounds".

* 16 Feb. Professor G.W.A. Foules (U. of Reading), "Home winemaking".

2 Mar. Professor M.W. Roberts (U. of Bradford), "The discovery of molecular events at solid surfaces".

* 9 Mar. Professor H. Suschitzky (U. of Salford), "Fruitful fissions of benzofuroxans".

4 May Professor J. Chatt (U. of Sussex), "Reactions of coordinated dinitrogen".

* 9 May Professor G.A. Olah (Case Western Reserve U., Ohio), "Electrophilic reactions of hydrocarbons".

Academic Year 1978 - 1979

* 10 Oct. Professor H.C. Brown (Purdue U.), "The tool of increasing electron demand in the study of cationic processes".

* 19 Oct. Mr. F.C. Shenton (Public Analyst, Co. Durham), "There is death in the pot".

* 26 Oct. Professor W.J. Albery (Imperial College, London), "Photogalvanic cells for solar energy conversion".

* 9 Nov. Professor A.R. Katritsky (U. of East Anglia), "Some adventures in heterocyclics".

* 16 Nov. Dr. H.C. Fielding (Mond Division, I.C.I.), "Fluorochemical surfactants and textile finishes".

23 Nov. Dr. C. White (Sheffield U.), "The magic of chemistry".

18 Jan. Professor J.C. Robb (Birmingham U.), "The plastics revolution".

8 Feb. Mr. C.G. Dennis (Vaux Ltd.), "The art and science of brewing".

* 1 Mar. Professor R. Mason (Govt. Scientific Advisor), "The Scientist in defence policy".

10 May Professor G. Allen (Chairman SRC), "Neutron scattering for polymer structures".

Academic Year 1979 - 1980

18 Oct. Dr. G. Cameron (U. of Aberdeen), "Synthetic polymers - twentieth century polymers".

25 Oct. Professor P. Gray (U. of Leeds), "Oscillatory combustion reactions".

* 1 Nov. Dr. J. Ashby (I.C.I. Toxicological Laboratory), "Does chemically-induced cancer make chemical sense?".

* 8 Nov. Professor J.H. Turnbull (R.M.C. Shrivenham), "Luminescence of drugs".

* 15 Nov. Professor E.A.V. Ebsworth (U. of Edinburgh), "Stay still, you brute: the shape of simple silyl complexes".

* 24 Jan. Professor R.J.P. Williams (U. of Oxford), "On first looking into biology's chemistry".

14 Feb. Professor G. Gamlen (U. of Salford), "A yarn with a new twist - fibres and their uses".

* 21 Feb. Dr. M.L.H. Green (U. of Oxford), "Synthesis of highly reactive organic compounds using metal vapours".

28 Feb. Professor S.F.A. Kettle (U. of E. Anglia), "Molecular shape, structure and chemical blindness".

* 6 Mar. Professor W.D. Ollis (U. of Sheffield), "Novel molecular rearrangements".

Research Conference Attended

3rd Annual Congress of the Chemical Society, Durham, 9th - 11th April, 1980.

First Year Induction Course

In each part of the course, the use and limitations of the various services available are explained by the people responsible for them.

Departmental organisation	Dr. E.J.F. Ross
Safety matters	Dr. M.R. Crampton
Electrical appliances and infra-red spectroscopy	Mr. R.N. Brown
Chromatography and microanalysis	Mr. T.F. Holmes
Library facilities	Mr. W.B. Woodward (Keeper of scien books)
Atomic absorptiometry and inorganic analysis	Mr. R. Coult
Mass spectrometry	Dr. M. Jones
N.m.r. spectroscopy	Dr. R.S. Matthews
Glassblowing techniques	Mr. W.H. Fettis and Mr. R. Hart

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