Fluoride ion-initiated reactions of acetylenes

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FLUORIDE ION-INITIATED REACTIONS OF ACETYLENES

submitted by

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TO

CHRISTINE

MEMORANDUM

The work described in this thesis was carried out in the University of Durham between November 1968 and December 1971. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

Part of this work has been the subject of the following publication:

R.D. Chambers, W.K.R. Musgrave, and S. Partington, J.Chem.Soc.(D), 1970, 1050.

SUMMARY

This work is concerned with the development of an important technique which has enabled reactions involving polyfluoroalkenyl anions, generated by attack of fluoride ion on a suitable acetylene, and perfluoroheterocyclic compounds, to be carried out. Thus trans-perfluoro-4-(alkenyl)- and perfluoro-4-(polyalkenyl)-pyridines were formed by the reaction of perfluorobut-2-yne and perfluoropyridine, in the presence of caesium fluoride and sulpholan at atmospheric pressure. Using diethylacetylene dicarboxylate, under similar reaction conditions, the corresponding polyfluoro-4-(alkenyl)pyridine was isolated. The use of atmospheric pressure reaction conditions is essential to minimise the fluoride ion-intiated polymerisation of the acetylenes.

Treatment of trans-perfluoro-4-(alkenyl)pyridine with sodium methoxide in methanol, gave the corresponding cis monomethoxy derivative; with concentrated ammonia, an enamine was formed. In both cases, substitution occurred in the alkenyl side chain and not in the perfluoroheterocyclic ring. In a separate fluoride ion experiment, perfluorobut-2-yne did not react with perfluoro-4-(alkenyl)pyridine to form the higher perfluoro-4-(polyalkenyl) derivatives.

An atmospheric pressure polyfluoroalkylation reaction, involving trifluoroethylene and pentafluoropyridine in the presence of caesium fluoride and sulpholan, gave a perfluoro-1,1-bipyridylethane in low yield. Under similar conditions trans-2H-heptafluorobut-2-ene gave trans-perfluoro-4-(2'-butenyl)-pyridine instead of the expected perfluorobipyridylethane.

The atmospheric pressure polyfluoroalkenylation reaction was extended further to the more reactive perfluoropyridazine. Using perfluorobut-2-yne, trans-perfluoro-4-(2'-butenyl)pyridazine and perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene were isolated, the latter in good yield.

Trans-perfluoro-4-(2'-butenyl)pyridazine reacted with methoxide ion to form a cis:trans mixture of the monomethoxy derivative; with ammonia an enamine

was formed. Perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene was hydrolysed with sulphuric acid to give a mono- and di-pyridazone. Treatment of the former with sodium methoxide and two equivalents of perfluorophenyl lithium gave the monomethoxy and perfluorobiphenyl derivatives respectively. Photolysis and pyrrolysis reactions involving perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene were unsuccessful. In a separate fluoride ion experiment, *trans*-perfluoro-4-(2'-butenyl)pyridazine was reacted with perfluorobut-2-yne and perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene isolated.

Using reported conditions, perfluorobut-2-ene was reacted with perfluoropyridine to form perfluoro-4-sec.butyl- and perfluoro-2,4-di-sec.butyl-pyridines respectively. Subsequent defluorination, using an iron catalyst at elevated temperatures, of perfluoro-4-sec.butylpyridine, gave *trans*-perfluoro-4-(2'butenyl)pyridine in good yield. Defluorination of the di-substituted derivative gave complex mixtures. With perfluoropyridazine and perfluorobut-2-ene under fluoride ion reaction conditions, the perfluoro-4-sec.butyl- and perfluoro-3,5-di-sec.butyl-derivatives were isolated. Again, defluorination of perfluoro-4-sec.butylpyridazine using an iron catalyst, gave *trans*-perfluoro-4-(2'-butenyl)pyridazine; the disubstituted derivative gave a complex mixture. Using perfluoropyrazine under similar conditions perfluoro-2,5-di-sec.butylpyrazine was formed in high yield. A complex mixture was formed on defluorination of this derivative.

An attempt to prepare *trans*-perfluoro-4-(2'-butenyl)-pyridine and -pyridazine by reaction of the lithio derivatives derived from *trans*-2H-heptafluorobut-2-ene and the corresponding heterocycle, were unsuccessful.

Attempts to prepare perfluoropolyethers using hexafluoroacetone and perfluoro-pyridine, -pyridazine and -pyrazine, under fluoride ion conditions were unsuccessful. Similar results were obtained when the hexafluoroacetone was replaced with hexafluoropropene epoxide.

In reactions involving sodium chlorodifluoroacetate and perfluoro-pyridine and -pyridazine, the corresponding 4-chloro- and not the expected 4-trifluoromethyl-derivatives were obtained.

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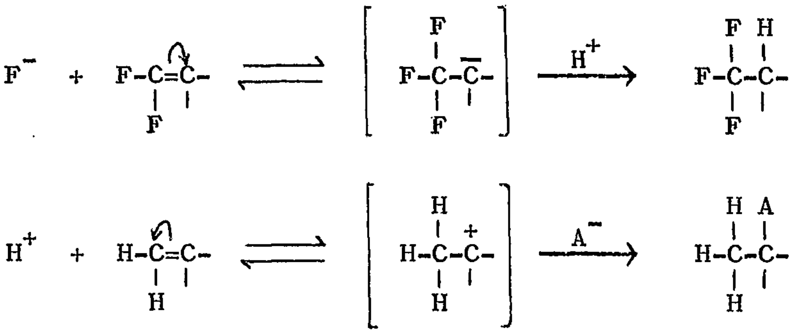
INTRODUCTION

CHAPTER 1

Reactions Involving Fluoride Ion

Introduction

Miller, in a study of reactions of fluoride and other halide ions with fluoro-olefins, formed the basis on which much of the present day interest in fluoride ion chemistry is laid. Further, he underlined the fact that for unsaturated fluorocarbons, fluoride ion occupies a position as a nucleophile which is analogous to that of a proton as an electrophile for unsaturated hydrocarbons.



Suitable sources of fluoride ion, the choice of solvent, the reaction conditions and some of the more important reactions involving fluoride ion will be discussed.

1.1 Experimental conditions

The selection of suitable conditions for studying the reactions of fluoride ion with unsaturated fluorocarbons presents some difficulty. Indeed the choice of solvent, the source of fluoride ion and the reaction temperature and pressure, are often specific for a particular reaction. In order to form a fluorocarbanion by addition of fluoride ion, for example,

$$R_f\cdot CF{=}CF_2 + F^- \rightleftharpoons R_f\bar{C}FCF_3$$

$$\text{or} \quad R_f\cdot C{\equiv}C\cdot R_f' + F^- \rightleftharpoons R_fCF{=}\bar{C}{-}R_f'$$

R_f, R_f' are perfluoro-alkyl groups an equilibrium must exist between the perfluorocarbanion, fluoride ion, and the perfluoro-alkene or -alkyne.

In order to displace the reaction to favour the carbanion formation, an increase in the concentration of fluoride ion is required. Inorganic fluorides tend to restrict this displacement due to their limited solubility in inert aprotic organic solvents, such as saturated hydrocarbons, while in protogenic solvents, for example, alcohols and ethers, proton extraction by the carbanion occurs. Dipolar-aprotic solvents however, have been found to be particularly useful in fluoride ion reactions, giving a compromise between the solubility of the reactants, the products and a tendency to minimise unwanted side reactions.

1.1.1 Dipolar-aprotic solvents

Dipolar-aprotic solvents, although they contain hydrogen atoms, cannot donate suitably labile hydrogen atoms to form hydrogen bonds with appropriate species.[1,1a] In general they are high boiling liquids possessing a large liquid range, and have large dielectric constants and dipole moments. Many examples of this class of solvent exist including acetonitrile, tetramethylene sulphone and the glymes.

The solvation of anions in dipolar-aprotic solvents is poor, although it is found that solvation increases slightly, with increasing anion size.[2]

$$F^- \ll Cl^- < N_3 < Br^- < SCN^- < I^-$$

From the above series, it is evident that as F^- is the smallest anion, it is least solvated and hence is the strongest nucleophile. In protic solvents, for example, CH_3OH, $HCONH_2$, fluoride ion is a weaker nucleophile as a high degree of solvation occurs with the unshielded protons.

In contrast to the low solvation of anions by dipolar-aprotic solvents, cations are highly solvated, and this is the major reason for the solubility of electrolytes in these solvents. Zaugg[3] has shown that cations are strongly solvated in highly polar solvents having a region of high electron density localised on a bare oxygen atom.

An alternative would be to avoid the use of solvent altogether. This technique obviously eliminates proton abstraction by the carbanion; however, a solventless system is definitely less reactive.[3]

1.1.2 Sources of fluoride ion

The alkali metal fluorides, in particular those of potassium and caesium, are the most widely used sources of fluoride ion. Their observed order of reactivity, $LiF < NaF < KF < RbF < CsF$[4], has been shown to resemble their crystal lattice energies. Thus, with a decrease in lattice energy, an increase in reactivity of the metal fluoride is observed. Further, in exchange reactions involving hexafluoropropene and alkali metal fluorides, to determine the relative reactivities of the metal fluorides, a similar order was observed.[5]

Other sources of fluoride ion which have been used include potassium bifluoride, KHF_2,[6] potassium fluorosulphite, KSO_2F[7], but these have only limited applicability because of their low solubility in aprotic solvents. Tetraethylammonium fluoride[8] has also been used as a source of fluoride ion although despite the fact that it is hygroscopic and thermally unstable. In chlorinated solvents, solutions of tetraethylammonium fluoride undergo partial decomposition at room temperature. Proton abstraction by the fluorocarbanion from the reagent also occurs.[8]

1.1.3 Solvent-initiator systems

Potassium[8,8a] and sodium fluoride in formamide solutions and tetraethylammonium fluoride in chlorinated solvents, such as chloroform and methylene chloride[8], were used by Miller in his initial studies involving fluoride ion and unsaturated fluorocarbons. These systems however had several inherent disadvantages, for although formamide will dissolve potassium fluoride readily, it is a poor solvent for fluoro-olefins. Further, proton abstraction by the perfluorocarbanion and reactions involving the olefin and solvent occur at elevated temperatures. Nevertheless, despite these limitations, Miller was able to show the potential that existed in reactions involving fluoride ion and unsaturated fluorocarbons.

Graham and co-workers[9,10] found that 'glymes', dialkyl ethers of ethylene glycol or polyethylene glycol, were effective solvents. They found that substitution of diglyme for monoglyme, caused a 10-fold rate increase in the self-condensation of tetrafluoroethylene, while tri- and tetra-glyme increased the reaction rates still further.[10] However reaction between the solvent and tetrafluoroethylene also occurred. Other solvents which have been used successfully include acetonitrile[11], glycols[11,12] and N-methyl-2-pyrrolidone[13].

Recent work carried out at the University of Durham has shown that combinations of caesium and potassium fluoride with sulpholan[14,15,16] and tetraglyme[17], are particularly useful in the polyfluoroalkylation of heterocyclic compounds.

1.2 Reactions of fluoro-olefins with fluoride ion

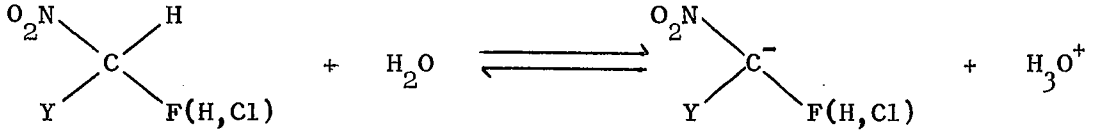
Before discussing some of the more important fluoride ion reactions, it is relevant to briefly consider the effects substituents have on the stability of perfluorocarbanions, since the relative stability of the carbanion will ultimately determine the direction of nucleophilic attack. Much of the work involving stabilities of carbanions has been concerned with the effects of α- and β-substituents, in particular halogens, on the rates of base-catalysed hydrogen-deuterium exchanges.

1.2.1 α-Halogen substituents

The effect of structure on the reactivity of haloforms in their ability to form carbanions has been studied by Hine and co-workers, who measured the rates of hydroxide-ion catalysed transformations of deuterated haloforms, for example, $CDBr_3$, CDI_3, $CDBrCl$, to the corresponding protium compounds in homogeneous aqueous solutions[18]. They observed that α-halogen substituents facilitate carbanion formation in the order,

$$I \sim Br > Cl > F$$

and they postulated that the order was a combination of the inductive effect, polarisability and d-orbital resonance. In contrast, the ionisation constants for a series of fluoronitromethanes, for example,



Y= Cl, $-COOC_2H_5$, $-CONH_2$, NO_2

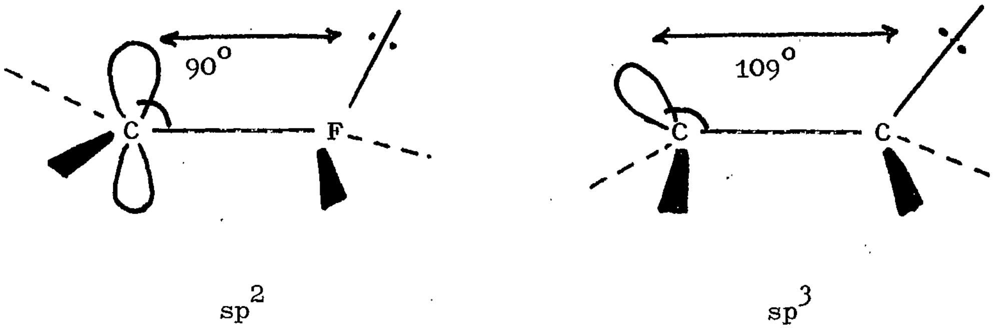
have been measured[19] and observed pKa values were in the order,

$$F > H > Cl$$

for a given Y group, except where Y = NO_2; where Cl ≃ H.

Hine[20] and Kaplan[21] explained the difference in terms of carbanion conformation. Carbanions having α-substituents which are able to exert strong mesomeric effects, for example $-NO_2$, tend towards sp^2 hybridisation i.e. planar. Fluorine however has a strong de-stabilising effect, relative to hydrogen, when sp^2 hybridised but a strong stabilising effect when sp^3 hybridised. Hine has suggested[20] that the halogen bond to sp^2 carbon is weaker than the bond to sp^3 carbon, since the former is more electronegative. This effect, which depends on the square of the electronegativity difference between the atoms involved, is greatest for fluorine.

In a planar carbanion, coulombic repulsions[22] between the electron pair in a p-orbital on the carbon atom and the electrons in a filled p-orbital on the fluorine are possible. This effect (Iπ interaction) will be at a maximum for an sp^2 carbon and offers an alternative explanation.



The order of Iπ repulsion effects for halogens has been shown to be,

$$I < Br < Cl < F$$

and hence Iπ interaction is greatest for fluorine and non-existent for hydrogen as there are no p electrons.

1.2.2 β-Halogen substituents

Monohydrofluorocarbons have been found to readily undergo base-catalysed deuterium exchange according to the following equation:

$$R_fH + CH_3OD \underset{}{\overset{NaOCH_3}{\rightleftharpoons}} R_fD + CH_3OH$$

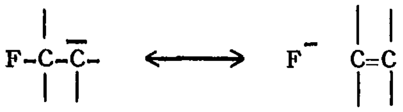
In a series of experiments, where $R_f = CF_3-$, $CF_3(CF_2)_5CF_2-$, $(CF_3)_2CF-$ and $(CF_3)_3C-$, the rates of exchange in both forward (k_H) and reverse (k_D) directions has been measured. From these results Andreades concluded[23] that fluorine exerted a strong stabilising effect on the carbanion when in a β-position.

Compound	CF_3H	$CF_3(CF_2)_5CF_2H$	$(CF_3)_2CFH$	$(CF_3)_3CH$
Relative reactivities	1·0	6·0	2 x 10^5	10^9
Ka	31	30	20	11

Analogous results have been obtained by Hine[24] who found that the kinetic acidity of CF_3CCl_2H was approximately 40 times that of $CFCl_2H$.

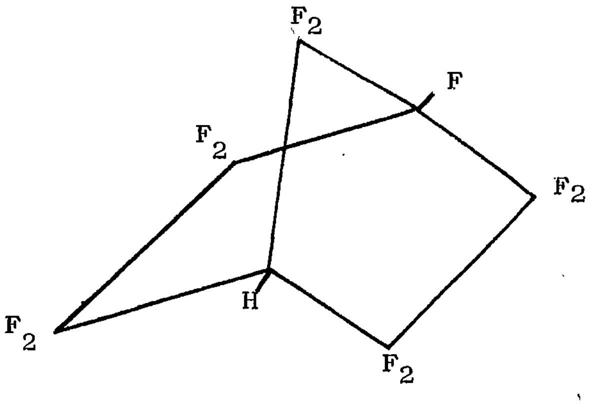
In a comparison of the acid strengths of nitroethanes, Knunyants[24] observed that Ka for $CF_3CH_2NO_2$ and $CH_3CH_2NO_2$ were $4{\cdot}0 \times 10^{-8}$ and $6{\cdot}1 \times 10^{-11}$ respectively.

The stabilization of a carbanion by a β-fluorine atom, was attributed[23] to a negative hyperconjugation effect.



$$\mathrm{F{-}C{-}\bar{C}{-}} \longleftrightarrow \mathrm{F^{-}\quad C{=}C}$$

However in reactions involving base-catalyzed hydrogen/tritium exchanges in 1-H-undecafluorobicyclo[2.2.1]heptane[25], the intermediate carbanion will have a pyramidal structure which precludes stabilization by negative hyperconjugation according to Bredt's rule.



Thus, stabilization of a carbanion by β-fluorine has been explained in terms of the inductive effect[25], and the order of ability to stabilize a carbanion shown to be[23] β-fluorine > α-fluorine > hydrogen.

1.3 Rearrangements catalyzed by fluoride ion

1.3.1 Perfluoro-olefin rearrangements

Terminal perfluoro-olefins are more susceptible to nucleophilic attack than internal olefins and so there is a tendency for a rearrangement from a terminal to an internal olefin to occur via an S_N2' process.[26-28]

$$n\text{-}C_5F_{11}CF{=}CF_2 \xrightleftharpoons[(C_2H_5)_4NF/CHCl_3]{F^-} n\text{-}C_4F_9CF{=}CF\cdot CF_3$$

$$n\text{-}C_4F_9CF{=}CF\cdot CF_3 \rightleftharpoons n\text{-}C_3F_7CF{=}CFC_2F_5$$

Miller and co-workers have shown[28a] that perfluorodienes can be rearranged, in the absence of solvents, to perfluoroacetylenes, indicating that the perfluoroacetylenes are more thermodynamically stable than their isomeric dienes.

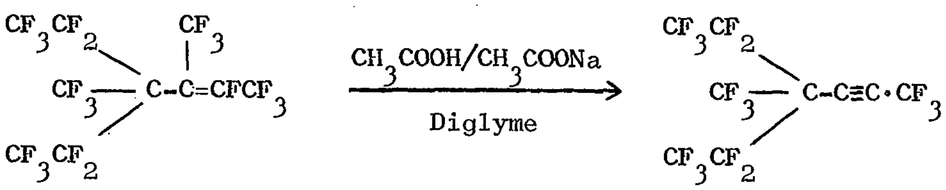
$$F_2C{=}CF\text{-}C{=}CF_2 \xrightarrow[100^o]{F^-/30\ min.} CF_3\cdot C{\equiv}C\cdot CF_3 \qquad 83\%$$

Similarly, with perfluoro-1,4-pentadiene the corresponding acetylene is formed.

$$CF_3\cdot CF{=}CFCF{=}CF_2 \xrightarrow{F^-} CF_3CF{=}C{=}CFCF_3$$

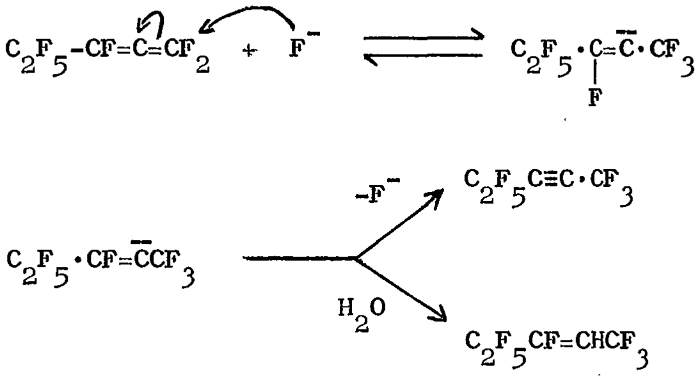
$$CF_3CF{=}C{=}CFCF_3 \longrightarrow CF_3CF_2C{\equiv}C\cdot CF_3$$

An acetylene is also formed when tetrafluoroethylene pentamer, $(C_2F_4)_5$, is refluxed with glacial acetic acid and sodium acetate in a dipolar aprotic solvent.[28b]



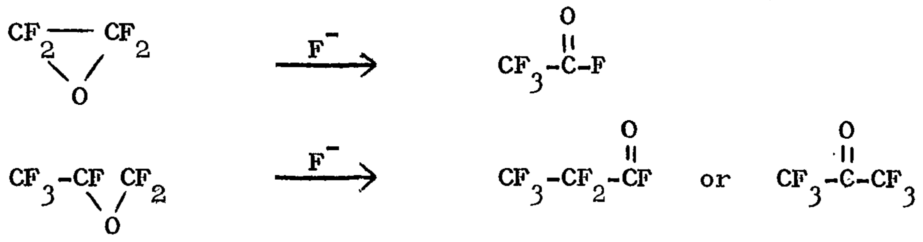
Evidence for transient perfluorocarbanion intermediates in rearrangement reactions has been suggested by Banks[29], who studied reactions involving perfluoropenta-1,2-diene in flow systems.

$$C_2F_5CF{=}C{=}CF_2 \xrightarrow[10^{-1}\ \text{mm}]{CsF/100^{o}} C_2F_5\cdot C{\equiv}C\cdot CF_3 + C_2F_5CF{=}CHCF_3$$

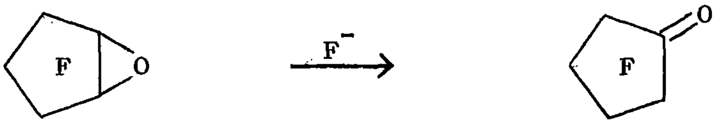


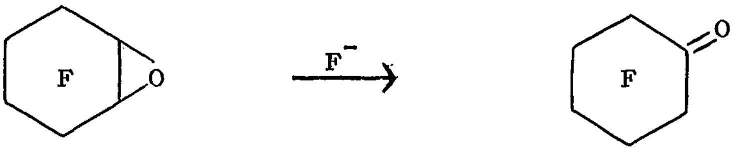
The formation of 2-H-nonafluoropent-2-ene presumably occurs through traces of moisture in the system.[29]

Perfluoro epoxides are rearranged by a variety of catalysts, including potassium and caesium fluoride, in either the gas or liquid phase or in inert polar solvents. The product, however, depends on the symmetry of the epoxide concerned. Thus tetrafluoroethylene epoxide rearranges to give only the corresponding perfluoroacetyl fluoride whereas unsymmetrical epoxides, such as hexafluoropropene epoxide, give either an acid fluoride or the isomeric ketone.[30]



However the acid fluoride is usually formed with an alkali fluoride. Symmetrically substituted cyclic fluoro-epoxides rearrange to form the corresponding perfluoroketone.



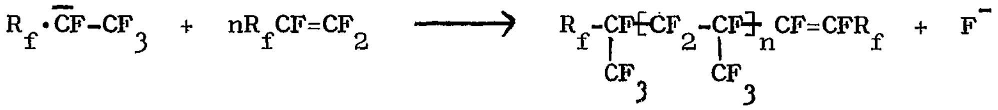


1.4 Oligomerisations and polymerisations catalyzed by fluoride ion

1.4.1 Acyclic olefins

The fluoride ion catalyzed polymerisation of perfluoro-olefins to yield high molecular weight polymers, according to the scheme annexed below, is prevented by several inherent factors.

$$R_f\cdot CF{=}CF_2 \xrightarrow{F^-} R_f\cdot\bar{C}F-CF_3$$

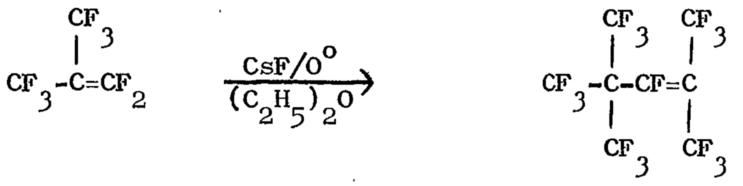


$$R_f\cdot\bar{C}F-CF_3 + nR_fCF{=}CF_2 \longrightarrow R_f-\underset{CF_3}{CF}[CF_2-\underset{CF_3}{CF}]_n CF{=}CFR_f + F^-$$

For linear olefins containing greater than three carbon atoms, double-bond migration occurs with elimination of fluoride ion, rather than self-condensation.

$$R_f\cdot CF_2CF{=}CF_2 \xrightarrow{F^-} R_fCF_2\bar{C}FCF_3 \xrightarrow{-F^-} R_fCF{=}CFCF_3$$

Where structural factors prevent the elimination of fluoride ion then highly branched, internally unsaturated polymers of low molecular weight are formed. Thus perfluoroisobutene and perfluoropropene cannot re-arrange to internal olefins by double-bond migration and although they are prone to nucleophilic attack, they do not polymerise. They can, however, be dimerised.



$$(CF_3)_2C{=}CF_2 \xrightarrow[(C_2H_5)_2O]{CsF/0^\circ} (CF_3)_3C{-}CF{=}C(CF_3)_2$$

31

and $$CF_3{\cdot}CF{=}CF_2 \overset{F^-/\text{Solvent}}{\rightleftharpoons} (CF_3)_2\bar{C}F$$

$$(CF_3)_2CF^- + CF_3{\cdot}CF{=}CF_2 \overset{F^-}{\rightleftharpoons} (CF_3)_2CFCF_2\bar{C}FCF_3$$

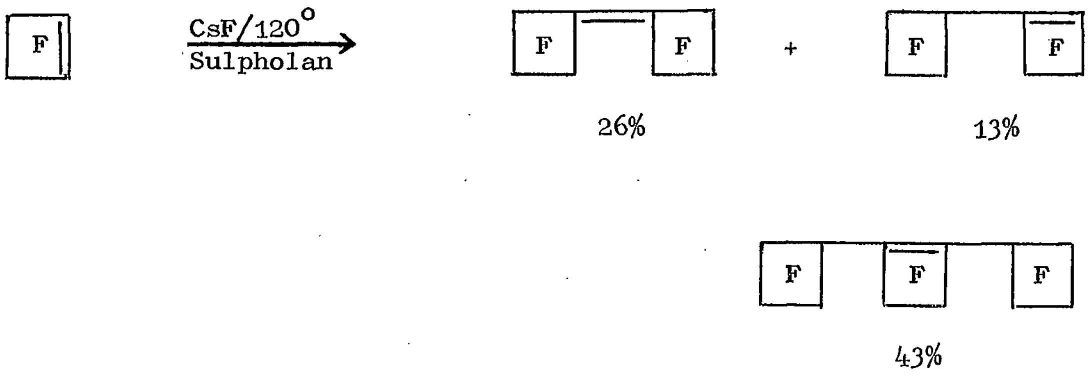
3,14,32-36

$$(CF_3)_2CFCF_2\bar{C}FCF_3 \xrightarrow{-F^-} (CF_3)_2CFCF{=}CFCF_3$$

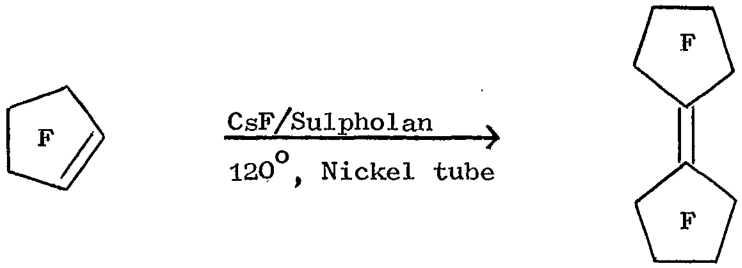
Trimers of hexafluoropropene have also been reported[14,34,35] and treatment of the individual trimers with fluoride ion leads to isomerisation.[35]

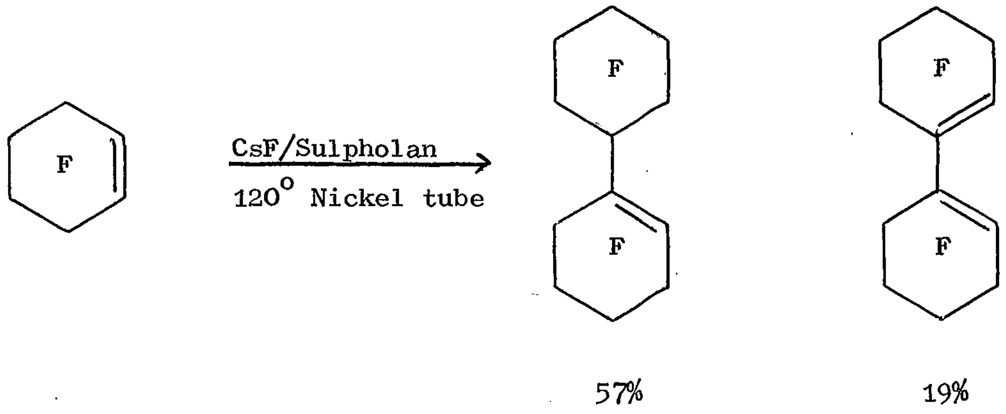
1.4.2 Cyclic olefins

In fluoride ion catalyzed reactions of perfluorocyclobutene, dimers and a trimer have been reported.[34,37]



More recently[37] other cyclic olefins, for example, perfluorocyclopentene and perfluorocyclohexene, have been dimerized.



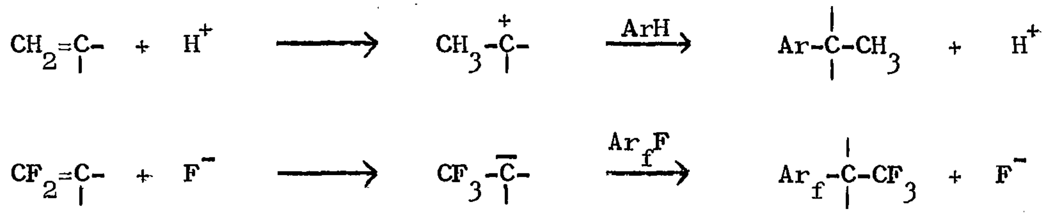


1.4.3 Perfluoro acetylenes

The polymerisation of perfluorobut-2-yne occurs readily with a variety of catalysts including fluoride ion. The formation of this polymer, under fluoride ion conditions, and its structure will be discussed in Chapter 4.

1.5 Perfluoroalkylation of aromatic compounds

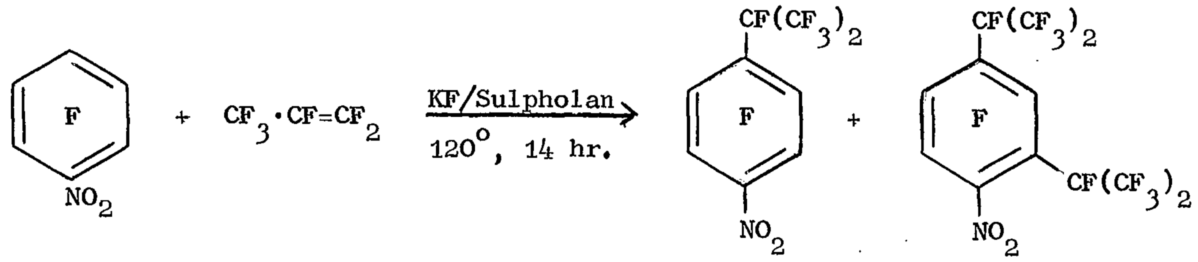
The reactions of polyfluorocarbanions, generated by reaction of polyfluoro-olefins with fluoride ion, have been studied by Chambers and co-workers who were first to report[38] the preparation of polyfluoroalkyl-nitrobenzenes and pyridines in a process which may be considered as the nucleophilic equivalent of the Friedel-Crafts reaction in hydrocarbon chemistry.



$$CH_2{=}\underset{|}{C}- \;+\; H^+ \longrightarrow CH_3-\overset{+}{\underset{|}{C}}- \xrightarrow{ArH} Ar-\overset{|}{\underset{|}{C}}-CH_3 \;+\; H^+$$

$$CF_2{=}\underset{|}{C}- \;+\; F^- \longrightarrow CF_3-\overset{-}{\underset{|}{C}}- \xrightarrow{Ar_fF} Ar_f-\overset{|}{\underset{|}{C}}-CF_3 \;+\; F^-$$

i.e.



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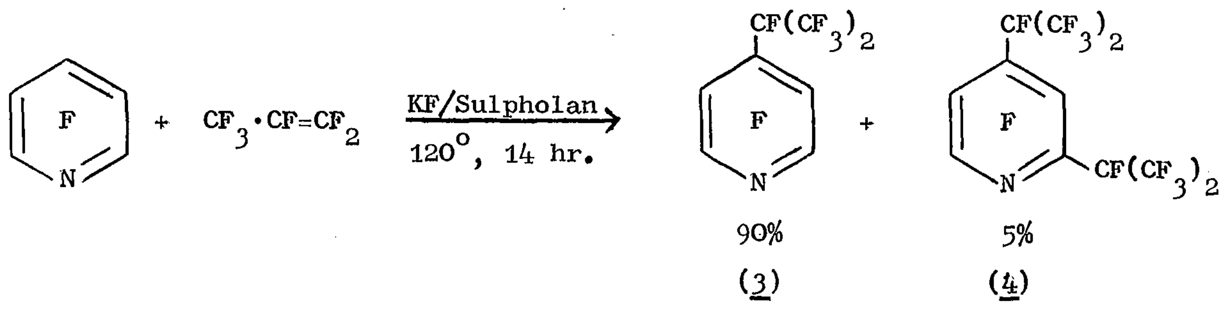
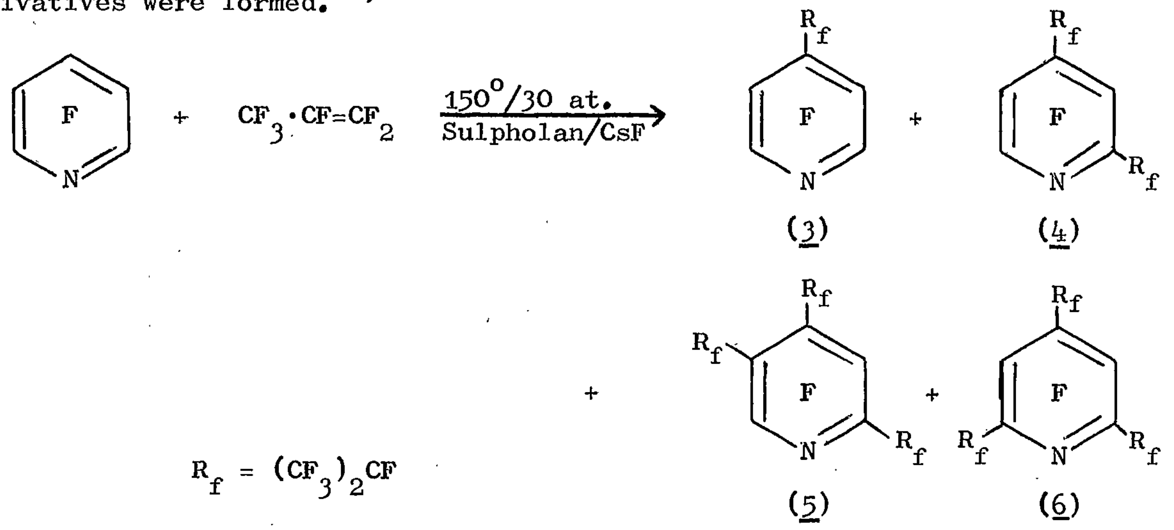
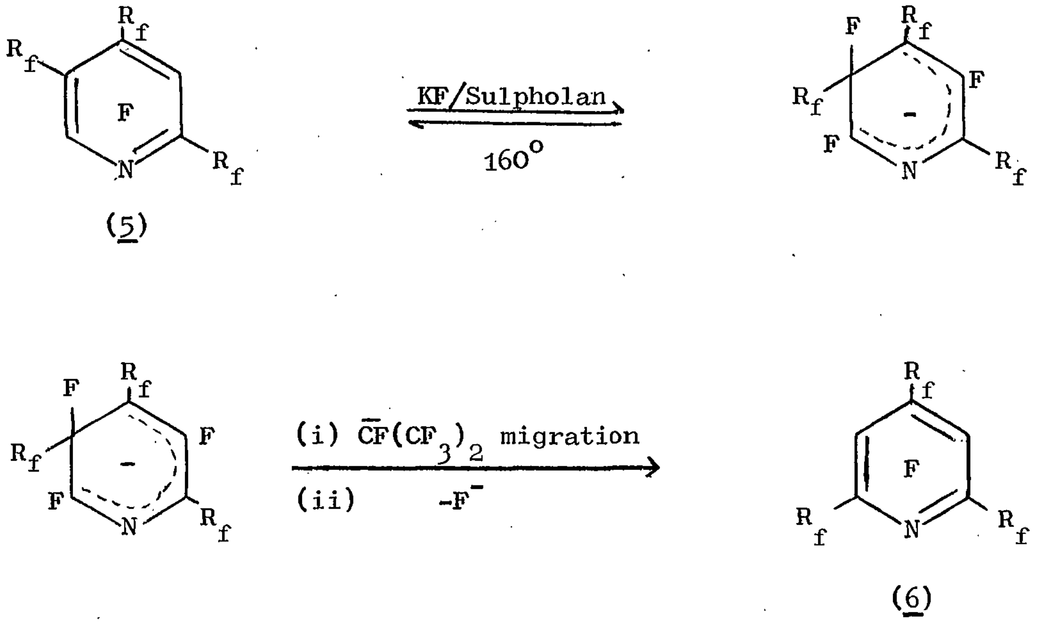


Further substitution of the perfluoropyridine nucleus was not achieved by increasing the amount of perfluoro-olefin, since oligomerisation of the olefin occurs. However, the high yield of the monosubstituted pyridine (3) was explained[39] by the low concentration of the perfluoro-olefin at the site of reaction; when this was increased by performing the reaction under more forcing conditions, 4-, 2,4-bis, and 2,4,5-, 2,4,6-tris-(heptafluoroisopropyl) derivatives were formed.[39,40]



$R_f = (CF_3)_2CF$

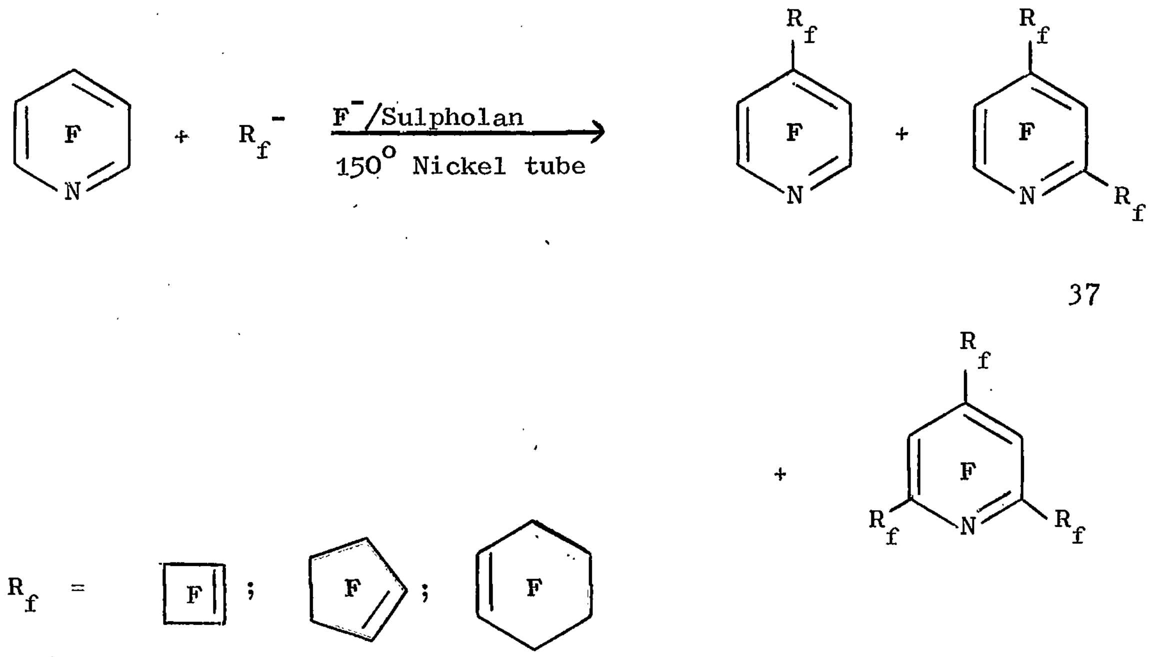
The formation of (5) and (6) has been explained in terms of kinetic and thermodynamic control.[15] Further, it has been shown that (5), the kinetically controlled product, will rearrange to (6), the thermodynamically controlled product under fluoride ion conditions.[15]



Cross-over products observed when the rearrangement is carried out in the presence of excess perfluoroquinoline, which is known to readily polyfluoroalkylate, indicate that rearrangement occurs via an intermolecular process.

In contrast, when tetrafluoroethylene was used instead of hexafluoropropene, a mixture of mono- to pentakis-pentafluoroethyl derivatives was obtained.[40] Andreades[23] demonstrated the greater stability of a secondary polyfluorocarbanion, $(CF_3)_2\bar{C}F$, than a primary anion, $-\bar{C}F_2$. Hence the ion, $CF_3{\cdot}\bar{C}F_2$ would be expected to be a much more effective nucleophile than $(CF_3)_2\bar{C}F$. The greater steric requirements of the latter also inhibit polysubstitution.

Although initial polyfluoroalkylation reactions involved pentafluoropyridine and hexafluoropropene, the scope of the reaction has been extended to include cyclic olefins[37] and acetylenes[16], the use of a more reactive substrate, for example, tetrafluoropyridazine,[16,41,42] and the use of atmospheric pressure reactions.[16,42]



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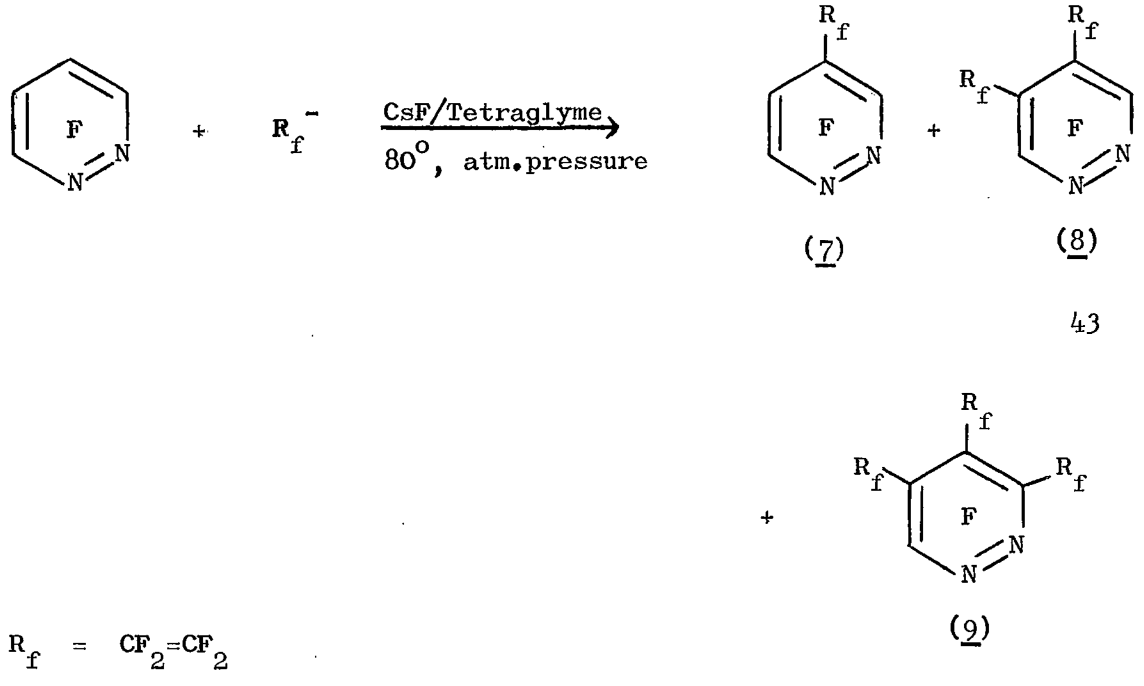


(7) (8)

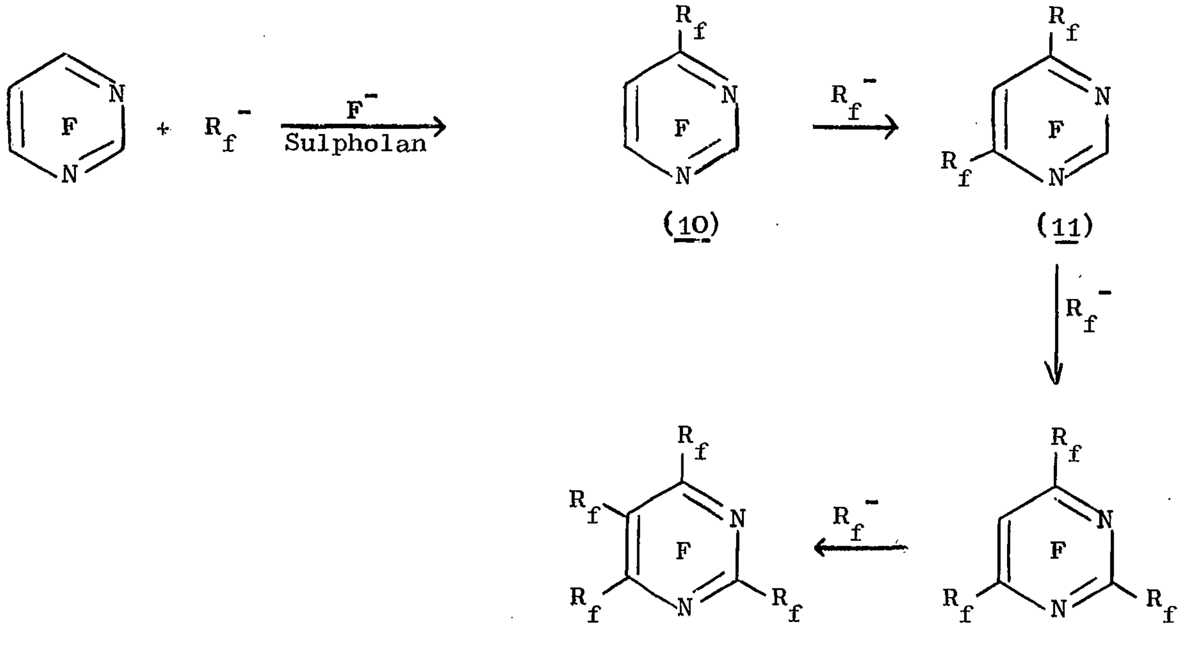
43

(9)

No evidence for the formation of either the tetra-substituted pyridazine, which has been isolated from reactions involving bromotrifluoroethylene and tetrafluoropyridazine, or the thermodynamically controlled product, 3,4,6-tris-(pentafluoroethyl)pyridazine, was observed.[42] The thermodynamically controlled tri-substituted product has, however, been reported in a recent patent.[43]

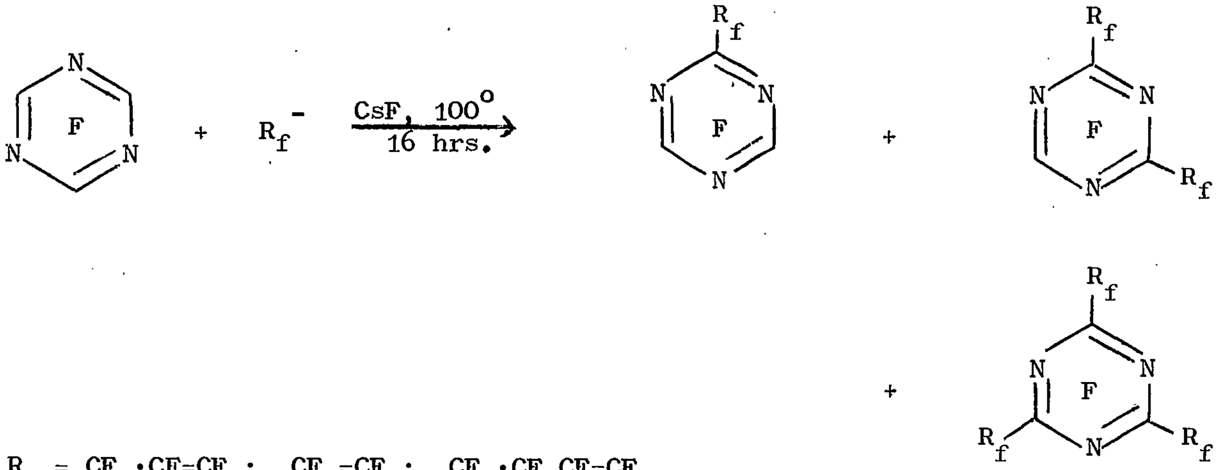
The development of atmospheric pressure reaction techniques and their current application to fluoride ion initiated reactions of acetylenes, will be discussed in Chapter 4.

Fluoride ion-initiated reactions of perfluoro-olefins involving tetrafluoropyrimidine[44] and 2,4,6-trifluoro-1,3,5-s-triazine (cyanuric fluoride) have also been reported.[45-47]



(10) (11) (12) (13)

$R_f = CF_3 \cdot CF{=}CF_2$



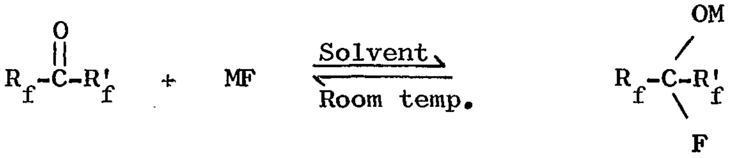
$R_f = CF_3 \cdot CF{=}CF_2$; $CF_2{=}CF_2$; $CF_3 \cdot CF_2CF{=}CF_2$

Reaction conditions could be adjusted to favour any one of the three substituted products.

1.6 Fluoroanions other than carbanions

1.6.1 Perfluoro-oxyanions

The ease with which hydrogen fluoride is eliminated from compounds having a fluorine atom α to a hydroxyl group, precludes the existence of primary and secondary perfluorinated alcohols. Nevertheless, the preparation of perfluorinated alkoxides of the heavier alkali metal fluorides have been reported[48] by addition of an alkali metal fluoride to the corresponding polyfluorocarbonyl compound in a solvent such as diglyme, acetonitrile or sulpholan.[48,49]



$$R_f\text{-}\overset{\overset{O}{\|}}{C}\text{-}R'_f \; + \; MF \;\underset{\text{Room temp.}}{\overset{\text{Solvent}}{\rightleftharpoons}}\; R_f\text{-}\underset{F}{\overset{OM}{C}}\text{-}R'_f$$

R_f = CF_3, F, CF_2Cl $\qquad R_f = R'_f = CF_3$; (14)

R'_f = CF_3, F, CF_2Cl

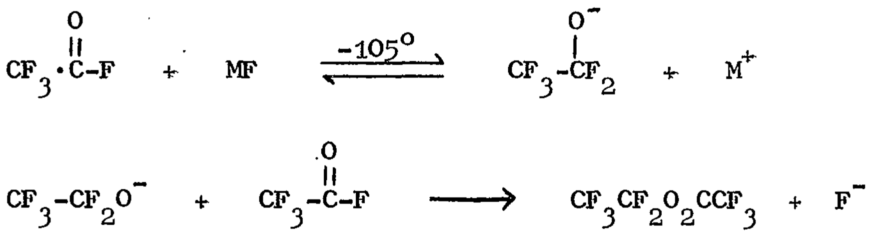
M = K, Rb, Cs

It should be noted however that although the complexes undergo reactions which formally result from a fluoroalkoxide structure, the structure of the complex (14) has still to be fully characterised.

Much of the published work concerns the complexes formed from hexafluoroacetone and potassium or caesium fluoride, which, although it is a relatively weak nucleophile,[49,50] will undergo nucleophilic displacement reactions. Cyclic ketones, for example, perfluorocyclopentanone and perfluorocyclohexanone, will only form complexes in acetonitrile with caesium fluoride.[52]

(a) Ester formation

Shreeve and co-workers[51], in a study of the reactions of HNF_2KF with perfluoroacyl fluorides, have found that dimerisation of trifluoroacetyl fluoride occurs at low temperatures. Although the role of HNF_2 in this dimerisation is not fully understood, the overall reaction is described by the following equation.

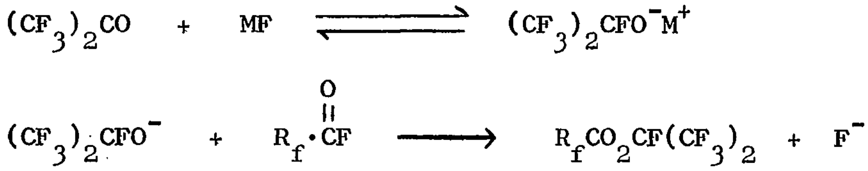


$$CF_3\cdot\overset{O}{\overset{\|}{C}}\text{-}F \;+\; MF \;\overset{-105^o}{\rightleftharpoons}\; CF_3\text{-}\overset{O^-}{\overset{|}{C}}F_2 \;+\; M^+$$

$$CF_3\text{-}CF_2O^- \;+\; CF_3\text{-}\overset{O}{\overset{\|}{C}}\text{-}F \;\longrightarrow\; CF_3CF_2O_2CCF_3 \;+\; F^-$$

M = K, Cs

At higher temperatures, products involving HNF_2 are formed. However, the reaction between perfluoroacyl fluorides and hexafluoroacetone in the presence of metal fluoride, proceeds without HNF_2 at -105^o and, in the case of the higher acid fluorides, at -78^o.[51]

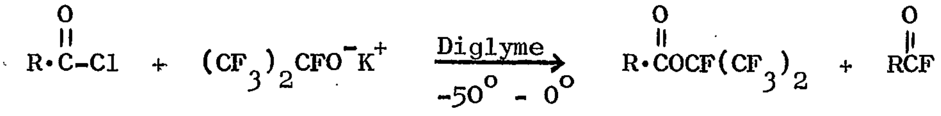


$$(CF_3)_2CO \;+\; MF \;\rightleftharpoons\; (CF_3)_2CFO^-M^+$$

$$(CF_3)_2CFO^- \;+\; R_f\cdot\overset{O}{\overset{\|}{C}}F \;\longrightarrow\; R_fCO_2CF(CF_3)_2 \;+\; F^-$$

R_f = F, CF_3, C_2F_5 and C_3F_7

Similarly, mixed esters have also been prepared.[50]



$$R\cdot\overset{O}{\overset{\|}{C}}\text{-}Cl \;+\; (CF_3)_2CFO^-K^+ \;\xrightarrow[-50^o\ -\ 0^o]{\text{Diglyme}}\; R\cdot\overset{O}{\overset{\|}{C}}OCF(CF_3)_2 \;+\; R\overset{O}{\overset{\|}{C}}F$$

85%   15%

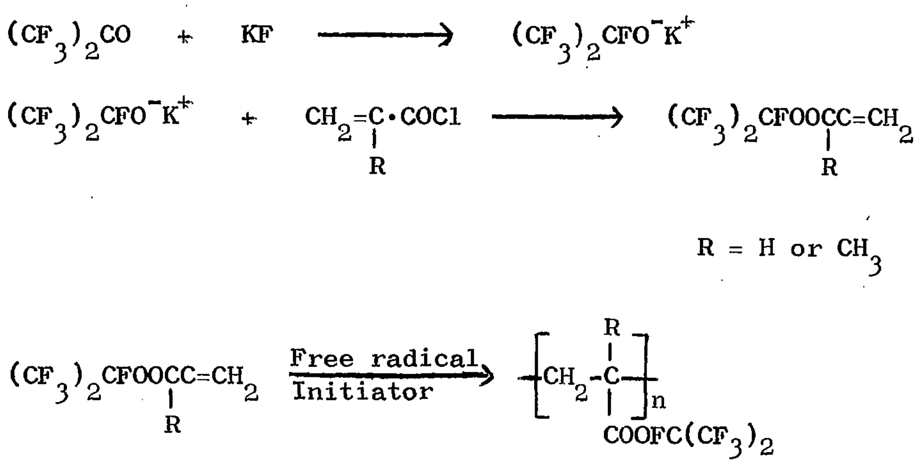
R = C_6H_5, CH_3

and $$R\cdot SO_2Cl \;+\; (CF_3)_2CFO^-K^+ \;\longrightarrow\; R\cdot SO_2OCF(CF_3)_2 \;+\; RSO_2F$$

70%	40%	R = C_6H_5
30%	60%	R = CH_3

At room temperature, extensive replacement of the acyl halogen by fluorine occurs.[50]

Pittman and co-workers have shown[53-55] that the complex (<u>14</u>) will react with, for example, acryloyl and methacryloyl chloride, to form esters which are capable of being polymerised to form thermally stable, high molecular weight, polymeric materials.



$$(CF_3)_2CO + KF \longrightarrow (CF_3)_2CFO^-K^+$$

$$(CF_3)_2CFO^-K^+ + \underset{\displaystyle R}{CH_2{=}C{\cdot}COCl} \longrightarrow \underset{\displaystyle R}{(CF_3)_2CFOOCC{=}CH_2}$$

R = H or CH_3

$$\underset{\displaystyle R}{(CF_3)_2CFOOCC{=}CH_2} \xrightarrow[\text{Initiator}]{\text{Free radical}} \left[CH_2-\overset{\displaystyle R}{\underset{\displaystyle COOFC(CF_3)_2}{C}} \right]_n$$

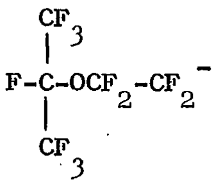
(b) Ether formation

The heptafluoroisopropoxide ion is a relatively weak nucleophile and as such, it will not attack olefins to form the corresponding ether. Thus, only the perfluorinated alcohol is formed with tetrafluoroethylene.[54]

$$CF_2{=}CF_2 + F^- \rightleftharpoons CF_3CF_2^-$$

$$CF_3CF_2^- + (CF_3)_2CO \longrightarrow CF_3CF_2C(CF_3)_2O^- \xrightarrow{H^+} CF_3CF_2C(CF_3)_2OH$$

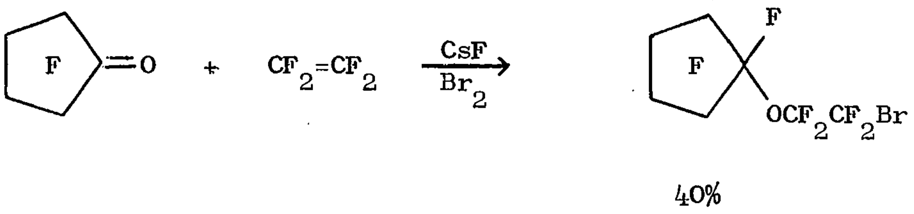
No evidence for the formation of the ether:



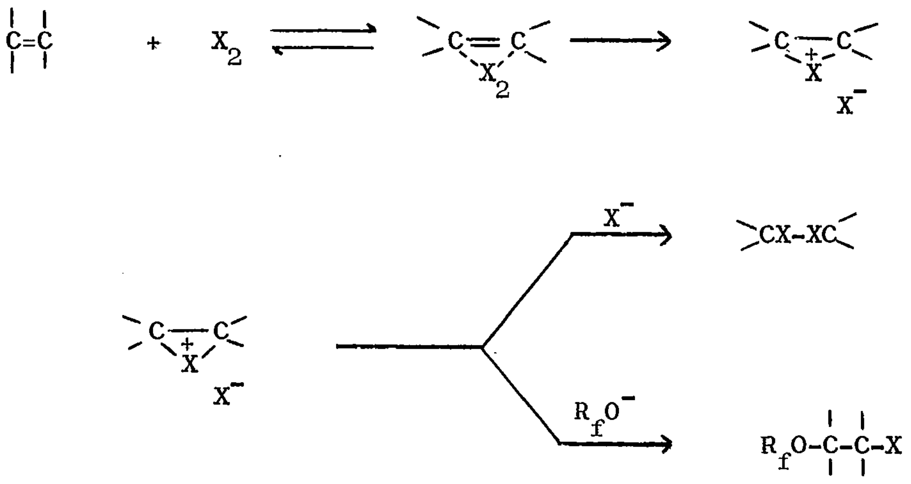
$$F-\overset{\displaystyle CF_3}{\underset{\displaystyle CF_3}{C}}-OCF_2-CF_2^-$$

was observed, indicating that the anion related to the ketone-caesium fluoride complex is too feeble a nucleophile to attack tetrafluoroethylene.

However, a variety of polyfluorocarbonyl-metal fluoride adducts have been reacted with perfluoro-olefin to form the corresponding ether, in the presence of halogen.[56]

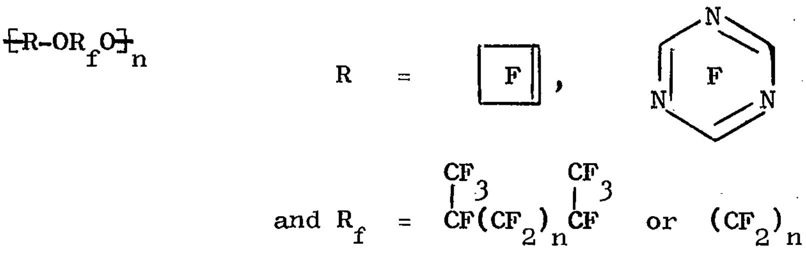


The suggested mechanism involves the formation of a halogen-olefin complex.



Other polyfluorocarbonyl compounds used in this reaction included perfluorocyclohexanone, CF_3COCF_2Cl, and $CF_2ClCOCFCl_2$.

Polyfluoro ethers have also been obtained by reaction of (14) with alkyl halides[50], allyl bromide[49], cyanuric chloride[50] and polyhalobutenes[50]. The formation of ethers from cyanuric chloride and polyhalocyclobutenes are of interest[50] in that they are precursors for polymers of the type

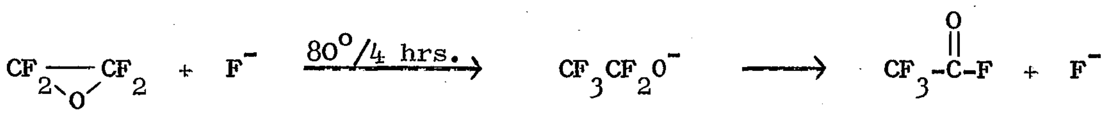


$\{R\text{-}OR_fO\}_n$

and $R_f = CF(CF_3)(CF_2)_nCF(CF_3)$ or $(CF_2)_n$.

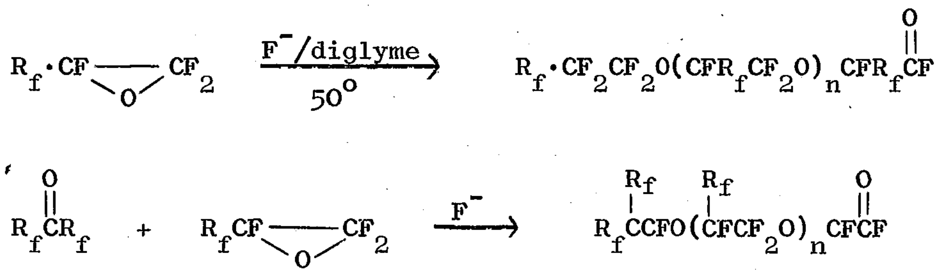
Similarly, other polyethers have been formed by reaction of the hexafluoroacetone-metal fluoride complex (<u>14</u>) with 1,4-dichlorobut-2-ene or epoxides to form products which can be subsequently polymerised using free radical initiators.[55,58]

Gozza and Camaggi[59] reported that tetrafluoroethylene epoxide reacts with fluoride ion to form trifluoroacetyl fluoride.



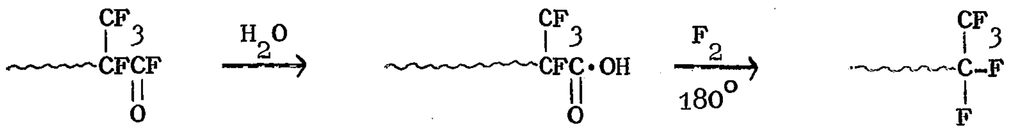
Hexafluoropropene epoxide, which has been the subject of considerably more research[60] than tetrafluoroethylene epoxide, reacts with fluoride ion to give perfluoropropionyl fluoride which, in turn reacts further to give $CF_3CF_2CF_2OCF(CF_3)COF$: this product can be obtained directly from caesium fluoride and 2 moles of the epoxide.[61]

Fluorocarbon epoxides have been converted to high molecular weight products in the presence of fluoride ion, alone[61,62] or in conjunction with a perfluoro-acid fluoride[63] or perfluoroketone[64].



$R_f = F,\ CF_3,\ C_2F_5$

In the case of hexafluoropropylene epoxide, n has been varied from 0 to about 35. The reactive acid fluoride end group, however, must be converted to an inert structure. In one such transformation[65,66] the acid fluoride group is replaced by fluorine to give the fluorocarbon polyether.



1.6.2 Perfluoroanions containing nitrogen or sulphur

Nucleophilic displacement reactions on fluoro-nitrogen and -sulphur compounds occur in an analogous manner to the formation of fluoro- and fluoroxy-carbanions discussed previously.

Perfluoro-2-azapropene, an analogue of hexafluoropropene undergoes a fluoride ion-catalysed reaction to form an anion which may be dimerised[67] or reacted with, for example, carbonyl fluoride.[68]

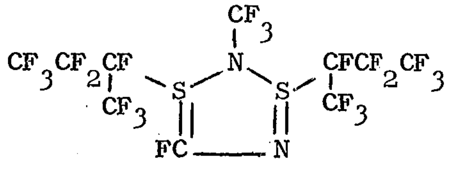
$$CF_3{\cdot}N{=}CF_2 \xrightleftharpoons{CsF} (CF_3)_2N^- \xrightarrow{CF_3{\cdot}N{=}CF_2} (CF_3)_2NCF{=}NCF_3$$

$$(CF_3)_2N^- \xrightarrow[150^{\circ}/CH_3CN]{COF_2} (CF_3)_2NCOF$$

Perfluoroalkyl sulphur derivatives have been obtained by the fluoride ion-catalysed addition of various sulphur fluorides to perfluoro-acetylenes and -olefins.[69]

$$C_2F_5N{=}SF_2 + CF_3{\cdot}C{\equiv}C{\cdot}CF_3 \xrightarrow[150^{\circ}/72\text{ hr.}]{CsF} C_2F_5N{=}S(F){\cdot}C(CF_3){=}CFCF_3 + C_3F_7N{=}S(F){\cdot}C(CF_3){=}CFCF_3$$

In the reaction involving $CF_3{\cdot}N{=}SF_2$, the main product was thought to have the following structure,



When a mixture of hexafluoropropene and iminosulphur difluoride was treated with powdered caesium fluoride at 83°, the perfluoroisopropyl carbanion generated, complexed with the sulphur atom and fluoride ion was eliminated.

$$CF_3{\cdot}CF{=}CF_2 + CF_3{\cdot}N{=}SF_2 \xrightarrow[83^{\circ}/115\text{ hr.}]{CsF} CF_3N{=}SF{-}CF(CF_3)_2$$

CHAPTER 2

Acetylenes

Introduction

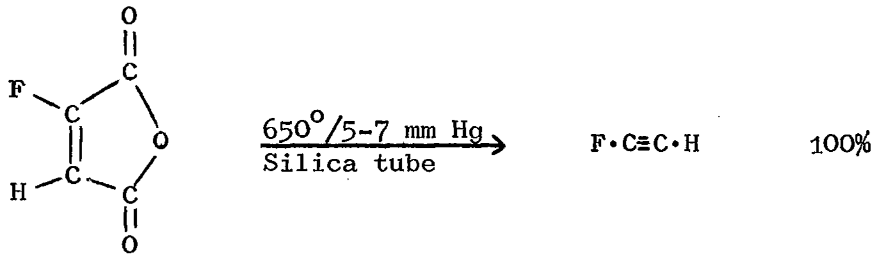
Hydrocarbon acetylenic compounds have been of great industrial and commerical interest for many years and their chemistry has been extensively reviewed.[70,71] In contrast, relatively little is known about the chemistry of the corresponding fluorocarbon analogues and much of the published work concerns perfluoroalkyl acetylenes, in particular hexafluorobut-2-yne, the simplest readily available perfluoroalkyne. A recent article[72] deals comprehensively with the chemistry of perfluoroacetylenes and only a brief account of their preparation and reactions will be dealt with here.

2.1 Methods of preparation of fluorocarbon acetylenes

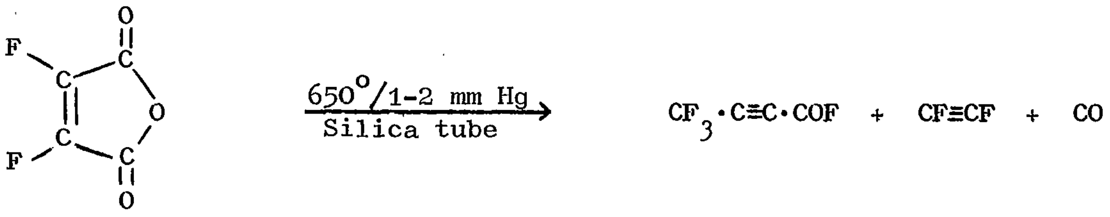
Perfluoroacetylenes are difficult to prepare and only the more stable perfluoroalkyl acetylenes, in particular hexafluorobut-2-yne, are readily available. It is therefore relevant to consider some of the more important methods of their synthesis.

2.1.1 Mono- and di-fluoroacetylenes

Monofluoroacetylene, $F\cdot C\equiv C\cdot H$, has been prepared[73] by dehalogenation of 1,2-dibromo-1-fluoroethylene, but a quantitative yield of the acetylene is reported[74] when fluoromaleic anhydride is pyrolysed at 650°.



Difluoroacetylene, $CF\equiv CF$, however, has never been isolated although it has been suggested as a product of several pyrolitic[75,76] or photolytic reactions.[77] Thus, pyrolysis of difluoromaleic anhydride has been reported[78] to yield difluoroacetylene: its formation being deduced from mass spectrometric analysis.



2.1.2 Perfluoroalkyl acetylenes

Perfluoropropyne, $CF_3{\cdot}C{\equiv}C{\cdot}F$, can be prepared from vinylidine fluoride by a multistage process, but a more convenient synthesis involves the formation of a zinc acetylide intermediate, which can be decomposed by water to form the alkyne[79,80]

$$CF_3{\cdot}CCl{=}CCl_2 + Zn \longrightarrow [(CF_3{\cdot}C{\equiv}C)_2Zn] \xrightarrow{H_2O} CF_3{\cdot}C{\equiv}CH$$

Several general methods are available for the preparation of polyfluoroalkynes involving elimination of hydrogen halide or halogen from an appropriate olefin. Removal of two halogen atoms from adjacent carbon atoms, $CF_3{\cdot}CX{=}CX{-} \xrightarrow{-X_2} CF_3{\cdot}C{\equiv}C{-}$, rather than hydrogen halide, $CF_3{\cdot}CX{=}CH{-}$ or $CF_3{\cdot}CH{=}CX{-} \xrightarrow{-HX} CF_3{\cdot}C{\equiv}C{-}$, is preferred[81]. Thus, perfluorobut-2-yne is usually prepared from perchlorobutadiene:

$$CCl_2{=}CClCCl{=}CCl_2 \xrightarrow[SbF_3/Cl_2]{SbF_3/155^\circ} CF_3{\cdot}CCl{=}CCl{\cdot}CF_3 \qquad (85\%)$$

$$CF_3{\cdot}CCl{=}CClCF_3 \xrightarrow[Heat]{Zn/C_2H_5OH} CF_3{\cdot}C{\equiv}C{\cdot}CF_3 \qquad (50\%)$$

For the preparation of unsymmetrical alkynes of the type $R_fC{\equiv}CR'_f$, where R_f and R'_f are different perfluoroalkyl groups, routes involving the elimination of hydrogen halide are used.

$$R_fI + CH{\equiv}CH \xrightarrow{\text{heat}} R_f\cdot CH{=}CHI \xrightarrow{KOH} R_fC{\equiv}C\cdot H$$

$$R_fC{\equiv}CH \xrightarrow[\text{Heat or u.v. light}]{R'_fI} R_fCI{=}CHR'_f \xrightarrow{\text{Alc. KOH}} R_fC{\equiv}CR'_f$$

$R = CH_3$, $R_f = CF_3$ [82,83]

$R = C_6H_5$, $R_f = CF_3$ [84]

Of academic interest is the isomerisation of perfluorobuta-1,3-diene to perfluorobut-2-yne in 83% yield, under the influence of anhydrous caesium fluoride at 100° in a sealed tube.[28a]

$$F_2C{=}CF{-}FC{=}CF_2 \xrightarrow[\text{30 mins.}]{100^\circ\ \text{CsF}} CF_3\cdot C{\equiv}C\cdot CF_3 \qquad (83\%)$$

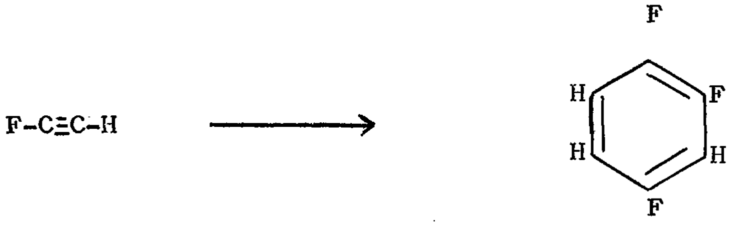
Perfluorobut-2-yne can also be prepared by fluorination of acetylene dicarboxylic acid with sulphur tetrafluoride, which is a specific reagent for the conversion of carbonyl and carboxyl groups into difluoromethylene and trifluoromethyl groups respectively.[85]

$$HO_2C\cdot C{\equiv}C\cdot CO_2H + SF_4 \xrightarrow[\substack{\text{Autoclave} \\ TiF_4\ \text{catalyst}}]{SF_4,\ 170^\circ} CF_3\cdot C{\equiv}C\cdot CF_3 \qquad 80\%$$

2.2 Reactions of acetylenes

2.2.1 Oligomerisation and polymerisation of fluoroacetylenes

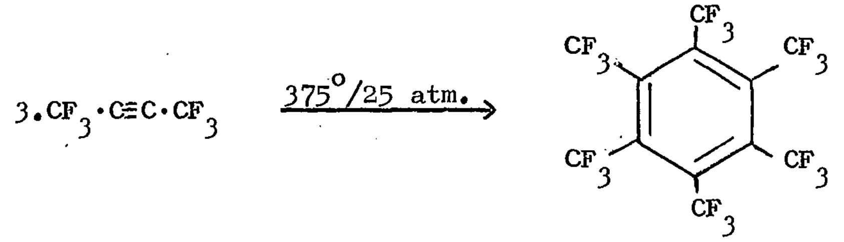
Polymerisation of mono- and di-fluoroacetylene occurs spontaneously at room temperature to yield yellow-brown solids.[74] Monofluoroacetylene will also undergo slow condensation to give 1,2,4-trifluorobenzene (14).



(14)

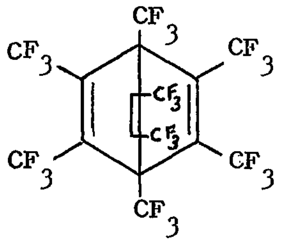
Inorganic catalysts, commonly used to polymerise acetylenes[86], polymerise $CF_3 \cdot C \equiv C \cdot H$ to an oil.

When perfluorobut-2-yne is heated under pressure, either alone or in the presence of catalytic amounts of iodine, trifluoroiodomethane or triphenylphosphine nickel carbonyl, it trimerizes to hexakis(trifluoromethyl)benzene in good yield.[87-89]

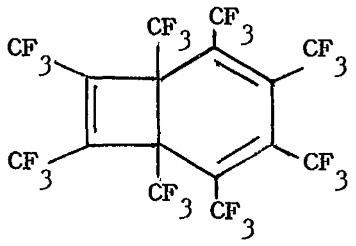


(15) (69%)

It is claimed[89] that a tetramer, believed to have structure (16) or (17) is also formed in the reaction.



(16)



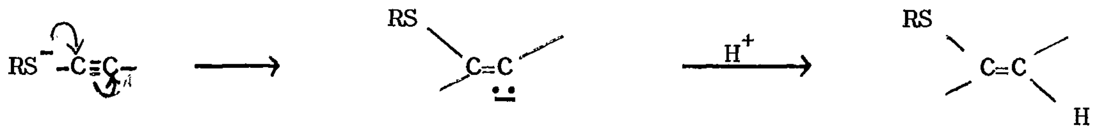
(17)

The polymerisation of hexafluorobut-2-yne will be discussed in Chapter 4.

2.2.2 Nucleophilic addition reactions of acetylenes

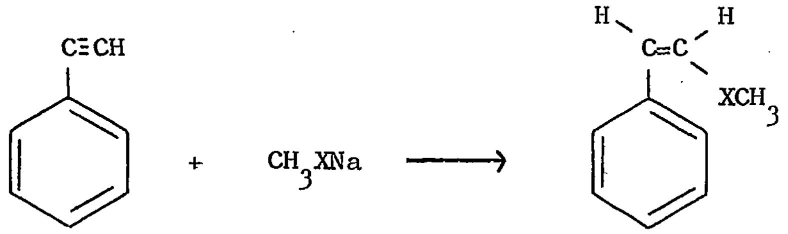
(a) Addition of thiols

Nucleophilic reaction of thiols to acetylenes have been known for many years.[90] Reppe and co-workers initially studied the reaction with acetylene itself while Truce[91] extended the investigation to the base-catalysed addition of thiols to substituted acetylenes. In an extensive study of these additions, to a variety of acetylenes including phenylacetylene and but-2-yne[92,93], it was observed that the thiolates usually reacted with the triple bond to give products by an overall *anti*-addition.



In all cases, high yields of the *anti*-addition product were formed. This lead to a general rule of an "*anti*-addition of nucleophiles to acetylenes" being postulated by Truce and Sims[92] and independently by Miller.[94]

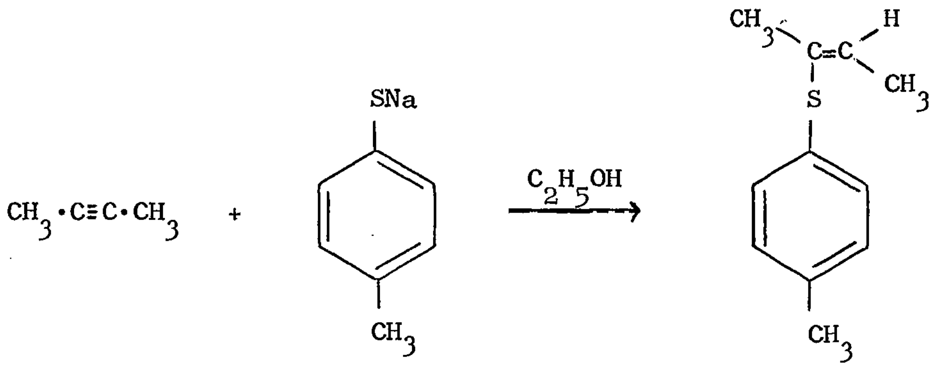
The addition of methane thiol and sodium methoxide gave the corresponding *cis* product, i.e. *anti*-addition.



(18) $X = S$ [92]

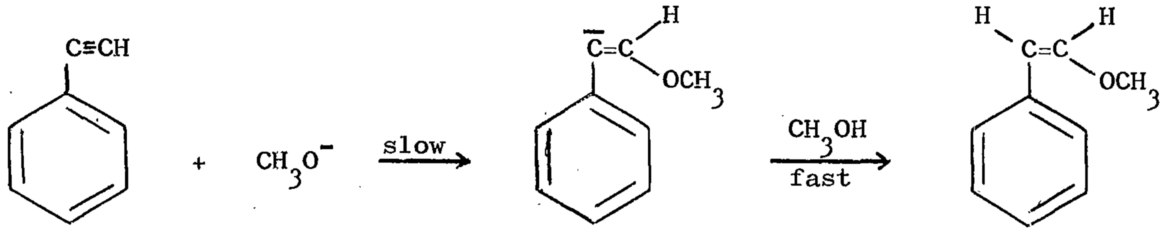
(19) $X = O$ [94]

Similarly, *p*-toluenethiolate reacts with but-2-yne to form 2-*p*-tolylmercapto-*trans*-but-2-ene.[92]



(20)

It is believed[92,94] that *anti*-addition occurs due to the tendency of the electron pair, displaced from the triple bond, to be as far away as possible from the electron pair donated by the nucleophile. The reaction may first involve carbanion formation[92,95], or the addition of a proton (derived from the solvent) may be coincident with the addition of the nucleophile.



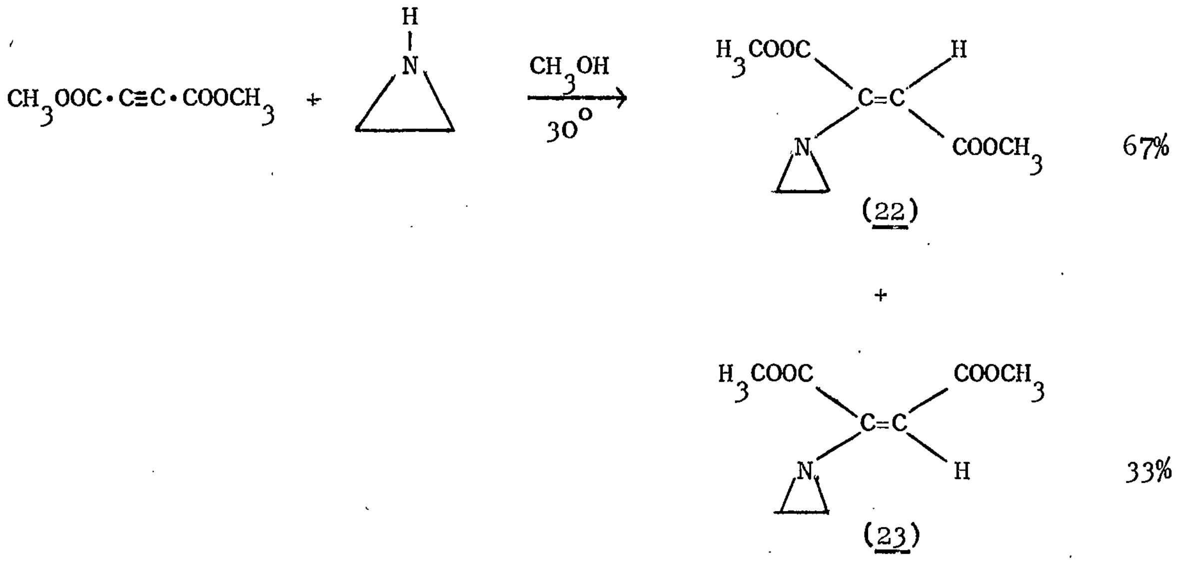
(21)

In a reaction involving mesitylacetylene and sodium mesitylenethiolate[96], it was thought that the size of the substrate and nucleophile would increase steric hindrance to such an extent that _syn_-addition would occur, i.e. the bulky groups would then be in a _trans_ disposition to each other. In fact the _anti_-addition product was again formed, indicating that any steric effects the bulky mesityl groups might have on the course of the addition are insufficient to prevent _anti_-addition.

(b) Addition of amines

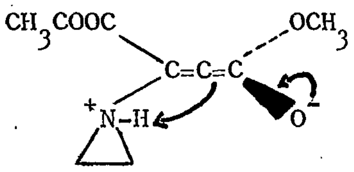
Although Truce et al, has postulated a rule of _anti_-nucleophilic addition to acetylene, evidence that amines react with acetylenic compounds in a _syn_ manner[97-99] has been suggested.

Dolfini[100] and Winterfeldt[101], have independently shown that in fact both _syn_- and _anti_-addition of amines can occur. Further, the addition was found to be solvent dependent. Thus, in reactions involving aziridine and dimethyl acetylenedicarboxylate in methanol, a _cis:trans_ mixture of isomers was obtained in the ratio 33:67.



However, when the reaction was carried out in dimethyl sulfoxide under the same conditions the isomer ratio was 95:5 cis:trans. No isomerisation of the esters under the conditions of reaction could be effected.

Dolfini attributed the difference in the ratio of reaction products to the formation of a zwitterionic intermediate (24).

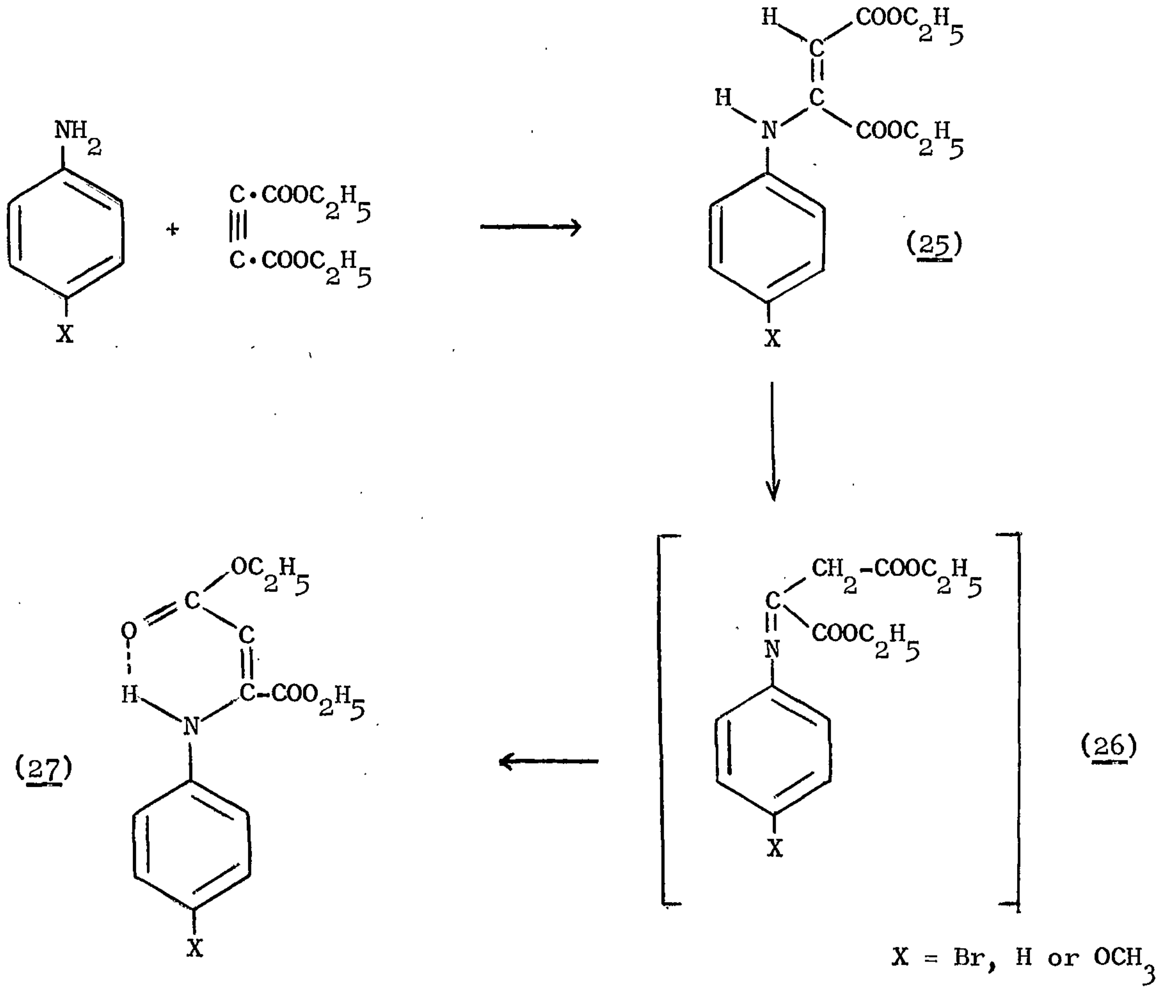


(24)

In the absence of an external proton source, (24) would be expected to undergo a stereospecific collapse via intramolecular protonation, leading to the cis disposition of the ester functions. In hydroxylic solvents, solvation of the incipient anion will be an attenuating factor on such cisoid reactions: protonation of the anion by solvent becomes the favoured path.

Winterfeld and Preuss[101] have studied the reactions of dimethylamine, piperidine and aziridine with dimethyl acetylenedicarboxylate and methyl propiolate in ether. The products obtained were almost extensively those resulting from *syn*-addition of the nucleophile. Only in the reactions with aziridine was a small quantity (≃ 13%) of the *anti*-addition product obtained.

Toppet et al have recently shown[102] that the anilinomaleate (25) formed in the reaction between aniline and diethyl acetylenedicarboxylate, isomerises to the thermodynamically more stable chelated anilinofumarate (27) via the imine (26).



(25)

(26)

(27)

X = Br, H or OCH_3

The isomerisation is slow in neutral medium, but rapid in the presence of trace amounts of acid.[103,104]

2.2.3 Nucleophilic addition reactions of perfluoroacetylenes

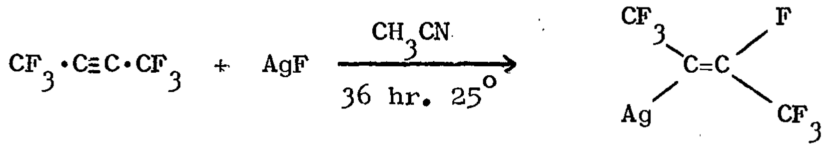
Successive replacements of hydrogen by fluorine in an acetylenic system leads to a lowering of electron density in the π-system due to the electronegativity of fluorine. Thus, bis(polyfluoroalkyl)acetylenes are found to be resistant to electrophilic attack but susceptible to nucleophilic and free radical attack.[105] Perfluorobut-2-yne readily adds halogen, on ultraviolet irradiation, to give the expected olefin[81], but resists attack by anhydrous hydrogen chloride.

$$\begin{array}{llll} CF_3\cdot C\equiv C\cdot CF_3 \xrightarrow{X_2/u.v.} CF_3\cdot CX{=}CX\cdot CF_3 & & X = Cl & 98\% \\ & & X = Br & 98\% \end{array}$$

$$CF_3\cdot C\equiv C\cdot CF_3 \xrightarrow[2\ \text{days}]{HCl/140^{\circ}} \text{No reaction}$$

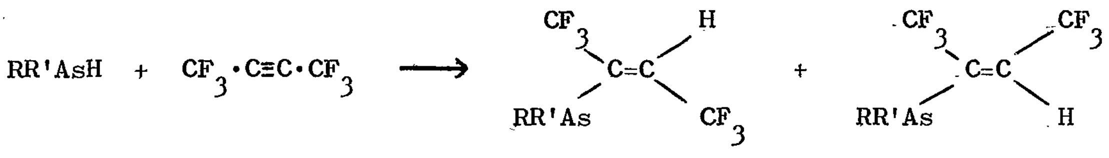
The addition of a suitable catalyst, such as aluminium trichloride, converts the perfluoroacetylene smoothly to the corresponding olefin.[106]

Hexafluorobut-2-yne reacts with silver fluoride to give the thermally stable trans-perfluoro-1-methylpropenylsilver complex. This is reported[107] as being the first example of a perfluorovinylsilver compound and its thermal stability is in marked contrast to the corresponding cis- and trans-1-methylpropenylsilver complexes which are unstable at room temperature.[108]



(28)

Cullen and Leeder have studied the reaction of perfluorobut-2-yne with dialkyl arsines.[109]

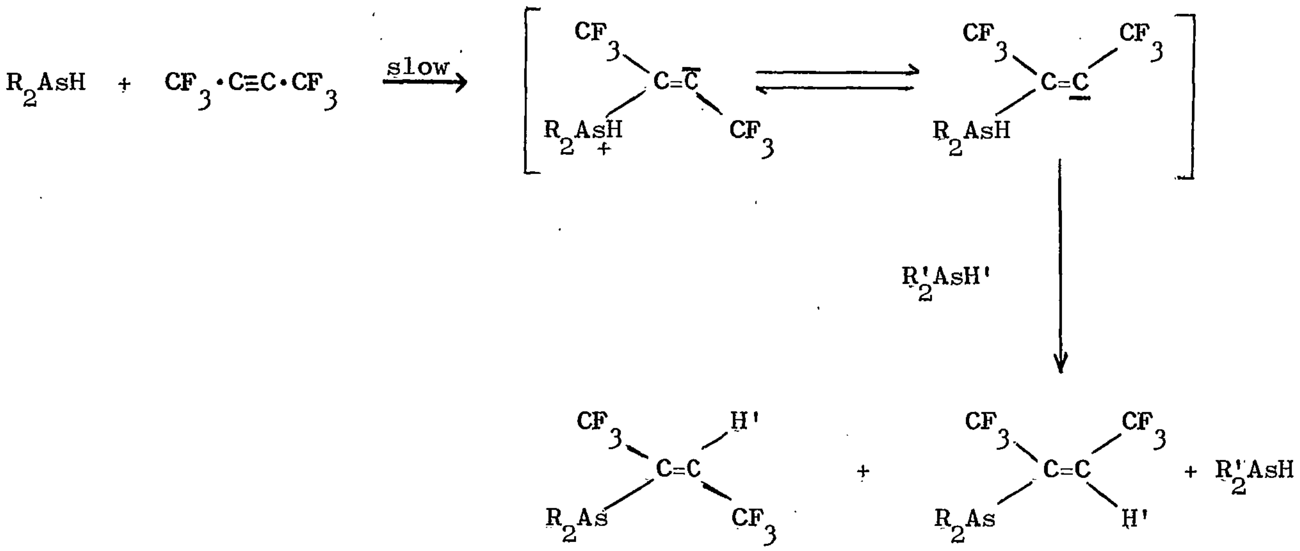


R=R'=CH_3

90-98% (29)

2-10% (30)

This reaction, which is related to the amine additions, was undertaken to establish whether the mechanism of the arsine reaction involved a nucleophilic addition to form both products, and to establish whether the hydrogen atom is transferred inter- or intra-molecularly. They considered several mechanisms and the following mechanism has been suggested.



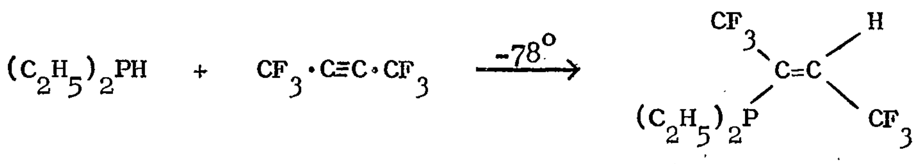
$R_2=R'_2=CH_3$

(31)

(32)

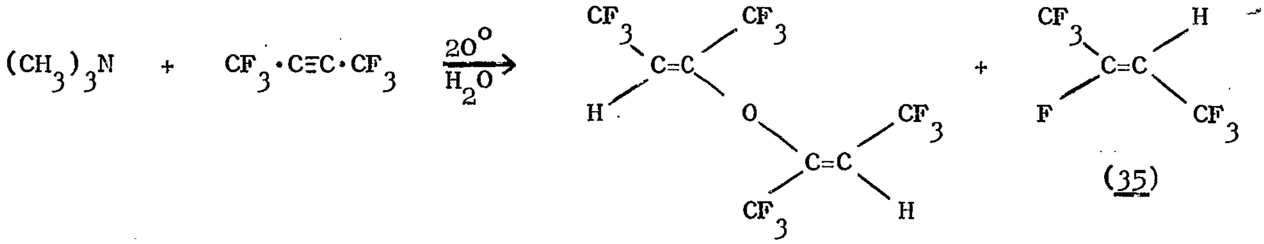
They postulate that the *cis-trans* interconversion could proceed through a hyperconjugated intermediate[110] and that at low concentration, the *cis*-addition does go by an intramolecular process because of the lack of a second arsine molecule to donate its proton.

In reactions involving diethylphosphine and hexafluorobut-2-yne at low temperatures[110], *trans*-2-diethylphosphino-1,1,1,4,4,4-hexafluorobut-2-ene, (26) was isolated.



(33)

With trimethylamine, perfluorobut-2-yne reacts in the presence of water to give a mixture of products, the main product being a bis(butenyl)ether (34). Some trans-2H-heptafluorobut-2-ene (5%) and 1,1,1,4,4,4-hexafluorobutanone (5%) were also isolated.[110]

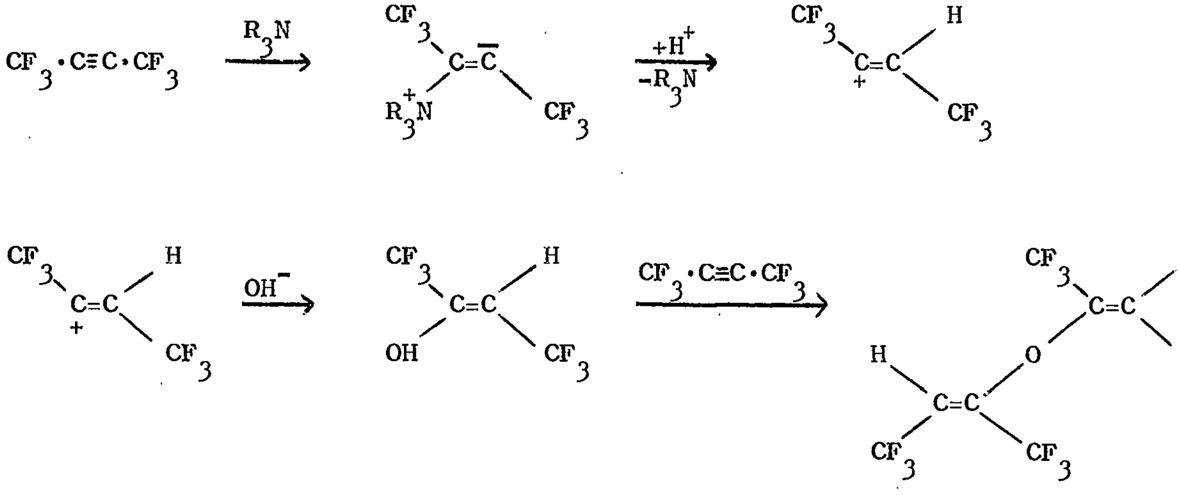


(35)

(34)

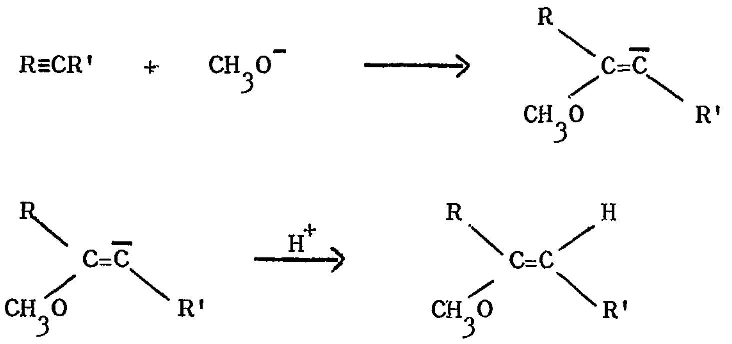
\+ Others

The formation of the bis(butenyl)ether, (34), is regarded[110] as the result of attack of the enol form of 1,1,1,4,4,4-hexafluorobutan-2-one on hexafluorobut-2-yne, possibly by the following mechanism.



(34)

Raunio and Frey[111] have found that the sodium methoxide catalysed addition of methanol to trifluoromethylacetylene and both the sodium methoxide and the triethylamine catalysed additions of methanol to hexafluorobut-2-yne are predominantly anti-addition (> 97%).



$R = H, R' = CF_3$

$R = CF_3, R' = CF_3$

CHAPTER 3

Nucleophilic Aromatic Substitution

Introduction

Nucleophilic aromatic substitution has been extensively studied with particular reference to polyfluoroaromatic systems. The corresponding polyfluoroheterocyclic analogues, have not received the same detailed study, possibly due to the fact that until recently they have not been readily available.

In considering nucleophilic substitution in this chapter, only a brief outline of the polyfluorobenzenoid systems is intended, whilst in the polyfluoroheterocyclic systems, emphasis is placed on the nitrogen derivatives pentafluoropyridine, the tetrafluorodiazines, and perfluoro-quinoline and -isoquinoline.

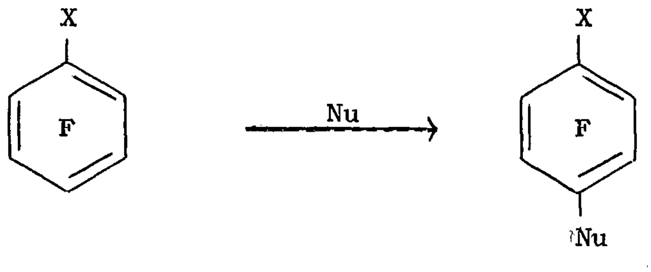
3.1 Nucleophilic substitution in polyfluoro-aromatic and -heterocyclic compounds

Reactions involving displacement of a fluoride ion by a nucleophile in polyfluoroaromatic compounds have been extensively studied. In comparison, much less is known about similar reactions involving polyfluoroheterocyclic compounds.

3.1.1 Benzenoid systems

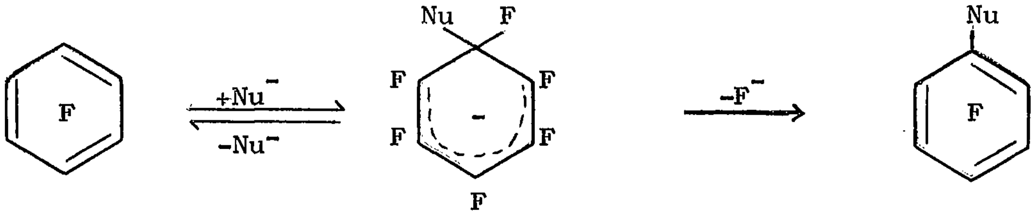
Hexafluorobenzene reacts with a wide variety of nucleophiles, for example, CH_3O^- [112], NH_3 [113], and $C_6H_5^-$ [114] to form, under suitable conditions, the corresponding pentafluorophenyl compound.

Nucleophilic replacement reactions of C_6F_5X compounds however, differ in that different positional isomers can be formed although in most cases the fluorine para to X is replaced, for example, where X = H, CF_3, Br and SCH_3.[115]

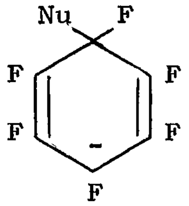


Exceptions to the replacement of para fluorine however, occur where $X = NH_2$[116] and O^-[117] when meta replacement predominates. The solvent[118] and in some cases the nucleophile[119-121] can also determine the position of attack.[118,119]

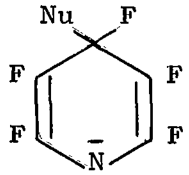
In an attempt to rationalise the orientation of substitution in polyfluoroaromatic compounds, it has been[122] assumed that the substitution reaction involves an addition-elimination mechanism, proceeding through a definite intermediate.



Further, in the transition state, the charge density in benzenoid compounds is assumed to be greatest at the para position:



and for nitrogen heterocyclic systems (see 3.1.2) the highest charge density is assumed to be localised on the ring nitrogen.



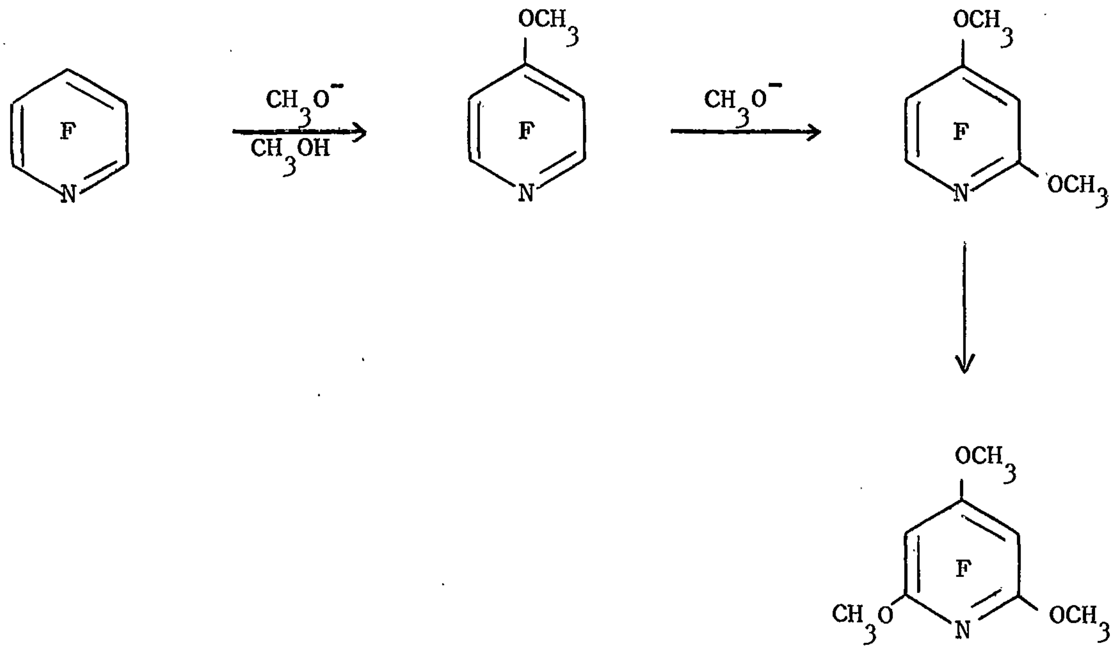
Molecular orbital calculations however do tend to support the assumption in the benzenoid case.[123]

Considering C_6F_5X compounds, the problem of substitution becomes dependent on X. Thus if X is capable of stabilising the carbanion more effectively than fluorine, substitution occurs in the para-, and to a lesser extent, ortho-position. If the substituent destabilises the carbanion with respect to fluorine, then substitution will occur meta to X.

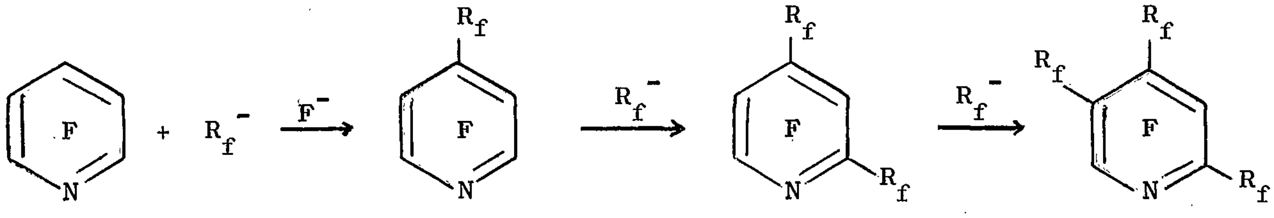
It has been shown (see 1.2.1) that in planar carbanions, halogens stabilise a carbanion in the order: $F < Cl < Br < I < H$. This has been attributed to the Iπ effect and that as the carbanions are planar, due to the effect of the ring, such effects will be maximised.

3.1.2 Nucleophilic substitution in polyfluoroheterocyclic nitrogen compounds

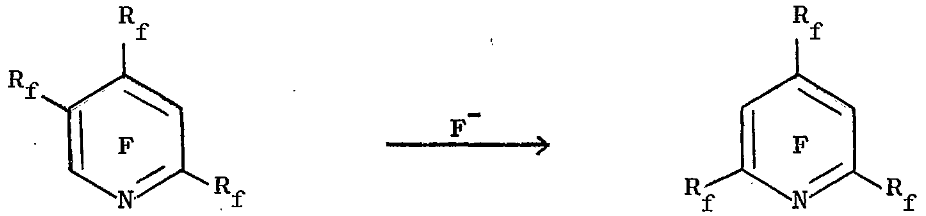
Nucleophilic substitution reactions involving pentafluoropyridine, have shown that the initial attack occurs at the 4-position; further substitution is then governed by the nucleophile. Thus with excess methoxide ion, the thermodynamically controlled 2,4,6-trisubstituted product is obtained.[125,126]



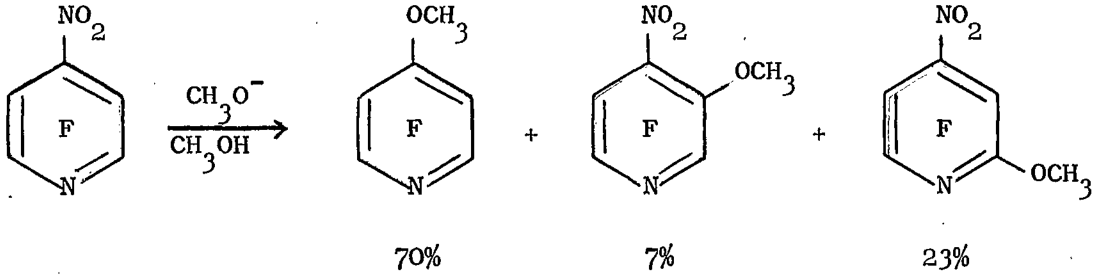
With polyfluoroalkylanions, the kinetically controlled 2,4,5-trisubstituted product is first formed, which can then undergo a fluoride ion-catalysed rearrangement to the thermodynamically controlled 2,4,6-trisubstituted product.[15,42]



Then

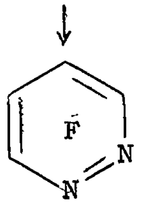


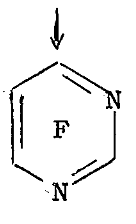
Reactions involving tetrafluoro-4-nitropyridine with for example, methoxide ion, CH_3O^-, gave a mixture of products.[127]

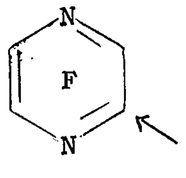


As nitro groups and fluoride ions are comparable in their efficiency as leaving groups in nucleophilic aromatic substitution[128], and because the nitro group is not displaced from pentafluoronitrobenzene or, more significantly, from 2,3,5,6-tetrafluoronitrobenzene, Chambers and co-workers concluded[127] that the ring nitrogen is the greatest factor in determining the orientation of substitution by its activation of the 4-position. The decreased importance of the Iπ effect, is easily understood, since localisation of the negative charge preferentially on the ring nitrogen atom must mean a reduced charge density on the ring carbon atoms compared with the polyfluorobenzene case, hence $I\pi$ interactions are reduced.

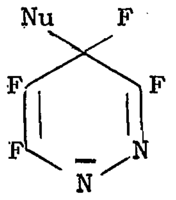
Further evidence for nitrogen determining the orientation of substitution has been provided by the nucleophilic substitution reactions of 1,2-, 1,3- and 1,4-tetrafluorodiazines, which react at the positions indicated.

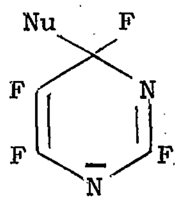


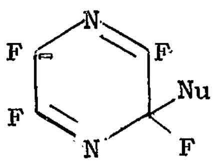




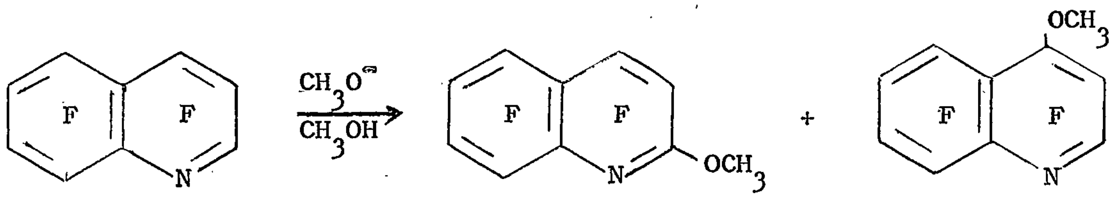
Tetrafluoropyrazine,[139] which has a similar reactivity to pentafluoropyridine, has been shown to be less reactive towards nucleophiles than tetrafluoropyridazine[130,131,131a] and tetrafluoropyrimidine.[132] This can be explained by a consideration of the transition states. In the latter cases, canonical forms result in which the negative charge is localised on a nitrogen atom; in the former, localisation occurs on a carbon bearing a fluorine atom.







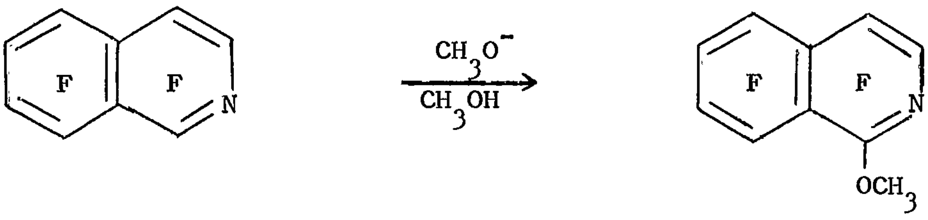
Heptafluoroquinoline reacts with methoxide ion[132] to give a mixture of 2-methoxy (37) and 4-methoxy (38) quinoline in the ratio of 3·4:1, while heptafluoroisoquinoline yields only the 1-methoxyhexafluoroisoquinoline (39).



3·4 1

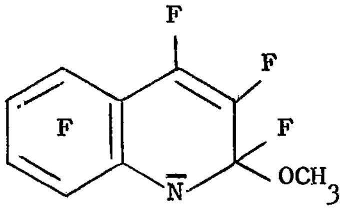
(37) (38)

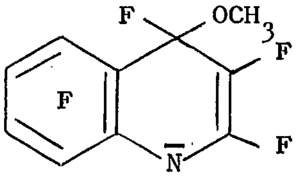
and



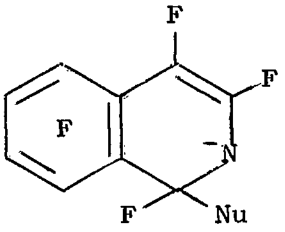
(39)

In the perfluoroquinoline case, the orientation of substitution can be rationalised in terms of localisation of the negative charge in the transition state on the nitrogen atom. The predominance of the 2-substituted isomer is considered to arise due to an increased contribution from an ortho-quinoid type canonical in the transition state.

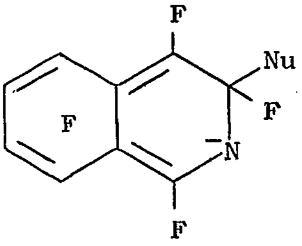




Nucleophilic substitution in perfluoroisoquinoline would be predicted to occur at the 3-position. However the observed 1-substitution[133] can be explained by considering the respective transition state energies



(40)



(41)

Substitution occurs at C1 in preference to C3 because (40) has a lower localisation energy for the transition state than (41) due to the retention of aromaticity by the carbocyclic ring.

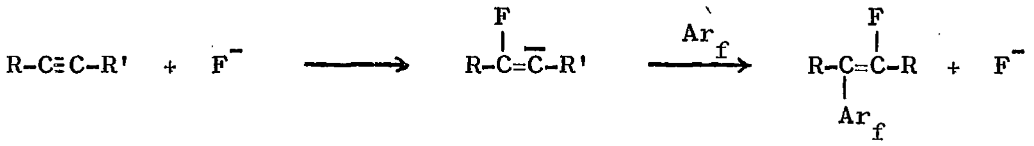
DISCUSSION

CHAPTER 4

Fluoride Ion-initiated Reactions of Acetylenes with Pentafluoropyridine

Introduction

The analogy between polyfluoroalkylation reactions involving polyfluoro-anions and suitably activated polyfluoroaromatic compounds, and Friedel-Crafts reaction in hydrocarbon chemistry has been stated previously. Polyfluoroalkylation of heterocyclic compounds has been successfully achieved with a variety of acyclic olefins, for example, hexafluoropropene, tetrafluoroethylene, as well as cyclic olefins such as perfluorocyclo-butene, -pentene and -hexene. This work has established that it is possible to generate, by a fluoride ion-initiated process, a corresponding polyfluoroalkenyl anion from suitable acetylenes, and react the resultant anion with a reactive perfluoroheterocycle.



$$R{-}C{\equiv}C{-}R' + F^{-} \longrightarrow R{-}\overset{F}{C}{=}\bar{C}{-}R' \xrightarrow{Ar_f} R{-}\underset{Ar_f}{C}{=}\overset{F}{C}{-}R + F^{-}$$

Thus the aim of this work has been to investigate the generation of such anions and their subsequent nucleophilic substitution reactions with perfluoro-N-heterocyclic compounds, in an extension of the polyfluoroalkylation process.

The fluoride ion-initiated reactions of two acetylenes with pentafluoropyridine, and the structure of the products formed, are discussed in this chapter. However it is necessary to consider the methods which were available for polyfluoroalkylation, prior to the development of a new procedure which enabled fluoride ion-initiated reactions of acetylenes to be achieved.

4.1 Polyfluoroalkylation of heterocyclic compounds

Before discussing fluoride ion-initiated reactions of acetylenes, it is relevant to consider the conditions which were available until recently for polyfluoroalkylation reactions, since special conditions were required for the fluoride ion-initiated reactions of hexafluorobut-2-yne with pentafluoropyridine.

4.1.1 The solvent-metal fluoride system

The choice of solvent in polyfluoroalkylation reactions is extremely important. It must be capable of dissolving some of the metal fluoride initiator as well as the reactants; furthermore, side reactions, such as proton abstraction by the carbanion from the solvent, or reaction of the carbanion with the solvent, should be minimised. For these reasons, dipolar aprotic solvents have been successfully utilised.

Storey[134] compared the effectiveness of sulpholan, the glymes and dimethyl formamide in a series of reactions between pentafluoropyridine and hexafluoropropene. His results indicated that sulpholan was the most useful solvent although Jackson[40] later found that tetraglyme was a better solvent in reactions involving hexafluoropropene and octafluorotoluene. However tetraglyme tends to decompose at temperatures greater than 150°, and it is reported[36] that some reaction occurs between tetraglyme and carbanions generated from tetrafluoroethylene.[36]

In contrast, sulpholan is more thermally stable than tetraglyme, minimising solvent-carbanion reactions, and giving good recovery of materials. For these reasons sulpholan has been used extensively in these laboratories.[15,37,40,43]

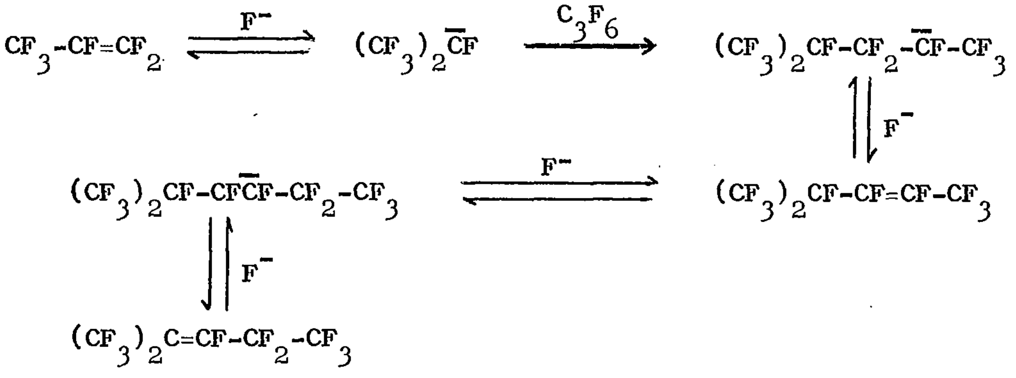
An alternative would be to avoid the use of solvent altogether. This technique would eliminate solvent-carbanion side reactions completely. Jackson reports[40] that solventless systems are definitely less reactive; pentafluoropyridine reacting with hexafluoropropene in the presence of caesium but not potassium fluoride.

Of the alkali metal fluorides, only potassium[15,39] and, in particular, caesium fluoride[37,40,42] have been found to be effective in initiating polyfluoroalkylation reactions at the University of Durham. The ability of caesium rather than potassium fluoride to be a better initiator in these reactions, may be due to the higher solubility of caesium fluoride in dipolar aprotic solvents. This assumes that reaction occurs in solution. Graham and co-workers[36] studying the reaction of the pentafluoroethyl anion with tetrafluoroethylene, found that doubling the amount of caesium fluoride present increased the rate at which tetrafluoroethylene was being used by 50%. As the amount of caesium fluoride present far exceeded its solubility in the solvent, Graham proposed that a surface reaction was occurring.[36]

4.1.2 Reaction conditions

Initially, polyfluoroalkylation reactions involving pentafluoropyridine and perfluoropropene were carried out using Carius tubes at a variety of temperatures.[37,39,40] Attempts to increase the degree of polysubstitution in perfluoropyridine by increasing the perfluoro-olefin to substrate ratio, only led to extensive oligomerisation of the olefin.[39] However polysubstitution was obtained by carrying out the reaction at higher temperatures and pressure using autoclaves.

Thus at the stage when the work being described here began, all polyfluoroalkylation reactions were carried out at elevated temperatures and pressure although extensive decomposition of the solvent at temperatures greater than 150° and extensive oligomerisation of the olefin still occurred.

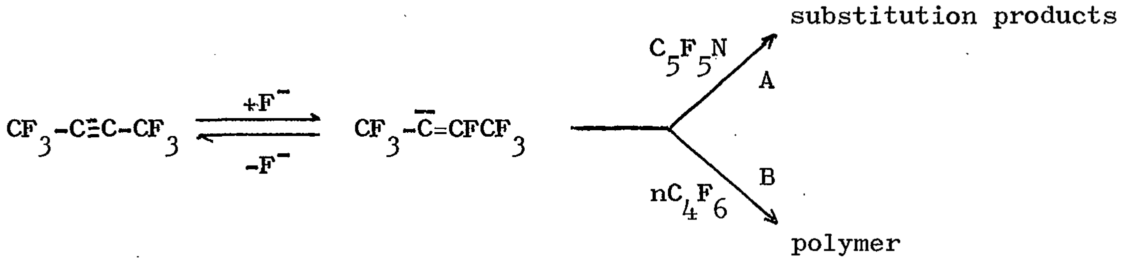


4.1.3 Development of atmospheric pressure techniques

Atmospheric pressure reaction techniques were developed specifically for fluoride ion-initiated reactions of acetylenes. The application of these conditions to perfluoro-olefin chemistry has also had far reaching effects, and reference will be made to these systems later.

Initially, a reaction was carried out involving hexafluorobut-2-yne and pentafluoropyridine using the general experimental conditions outlined in sections 4.1.1 and 4.1.2. However, only a grey-white polymeric solid was obtained with no evidence for the formation of any perfluoroalkenyl pyridine derivatives. Elemental analysis revealed that the polymer was derived solely from the perfluoroacetylene. The structure of the polymer will be discussed in section 4.2.2.

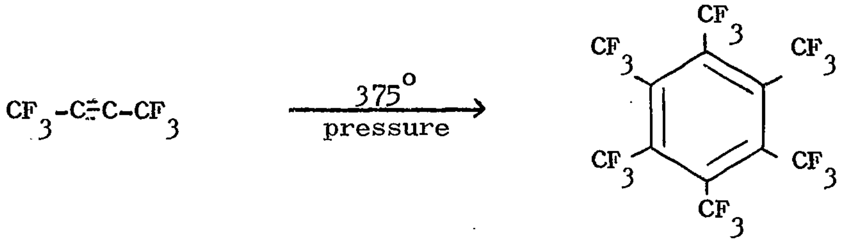
It was obvious, therefore, that competition existed between substitution and polymerisation reactions and that under the conditions employed, the polymerisation reaction (B) was predominating.



i.e. the activation energy $E_A > E_B$.

Thus, in order to enable reaction (A) to compete more favourably than reaction (B), then either the reaction temperature can be increased to make substitution compete more favourably, the concentration of the perfluoroacetylene in solution can be decreased, to inhibit oligomerisation, or a more reactive substrate than pentafluoropyridine could be used, for example, tetrafluoropyridazine.

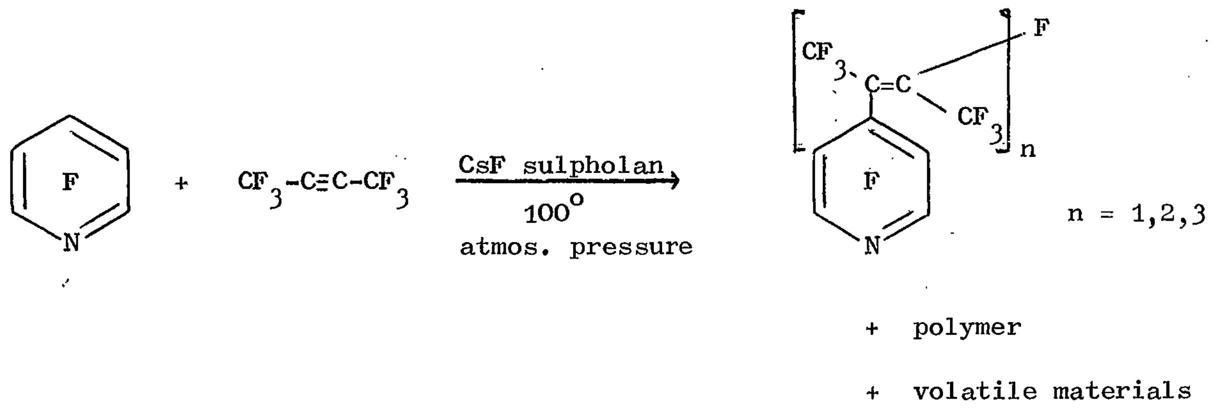
Adopting the first approach, a reaction was carried out using a higher temperature (130°) in a sealed tube but again only polymer was obtained. A modification of this reaction then consisted of mixing the reactants at the reaction temperature. This was accomplished by using two rocking autoclaves, joined together by a stainless steel tube. One autoclave contained sulpholan, caesium fluoride and pentafluoropyridine, the other, hexafluorobut-2-yne. The autoclaves were rocked and heated and on reaching reaction temperature (130°) the reactants were allowed to mix. After only 1 hour, almost complete conversion of the acetylene to polymeric material had occurred. As this approach appeared to enhance the polymerisation reaction, a series of reactions were carried out in which the concentration of the perfluoroacetylene in solution was reduced. Pressure reactions obviously do not favour low concentrations of the acetylene in solution and for this reason, and the fact that hexafluorobut-2-yne is known to form a cyclic trimer when heated alone or with a suitable catalyst[87-89]:



(15); 69%

reactions at atmospheric pressure were carried out.

The first experiment, simply consisted of allowing the perfluorobut-2-yne to bubble slowly through a rapidly stirred suspension of caesium fluoride, pentafluoropyridine and sulpholan at 100°. Although some polymer formation occurred, the complex mixing of volatile products obtained was shown to contain some monosubstituted perfluoroalkenyl pyridine derivatives.



A refinement of this experiment consisted of re-circulating the perfluoroacetylene through the reaction mixture, by means of a small pump (see Diagram 1).

Sulpholan and caesium fluoride were placed into the reaction flask and sections A and B of the system were evacuated separately to avoid 'sucking back'. With the by-pass valve open, hexafluorobut-2-yne was allowed into the system until atmospheric pressure was reached and the flexible reservoir inflated. The reservoir was then isolated from the system and the flask heated to reaction temperature. Pentafluoropyridine was introduced into the system via the septum and the pump started. Too fast a flow rate of hexafluorobut-2-yne through the reaction mixture resulted in complete polymerisation of the acetylene, i.e. the concentration of the acetylene in solution was again too high. Therefore modification to reduce the concentration of the acetylene in solution still further, consisted of diluting the perfluoroacetylene with dry nitrogen. Several reactions were carried out at various dilutions of the acetylene, but the best results were obtained when almost a complete atmosphere of dry nitrogen was circulated through the system with small additions of the acetylene to the nitrogen flow. In this way polymerisation was minimised and higher yields of the perfluoropyridine derivatives were obtained.

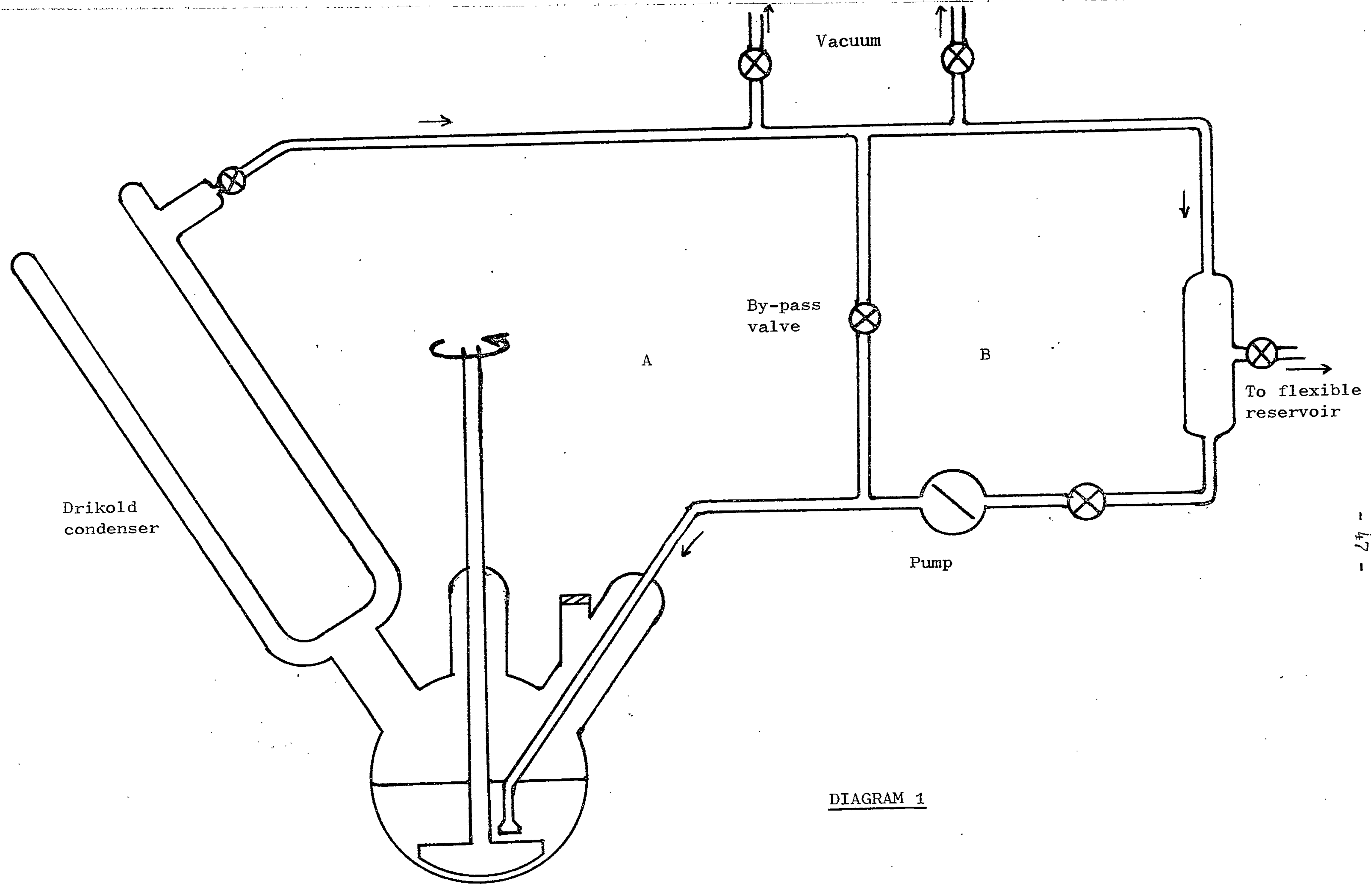
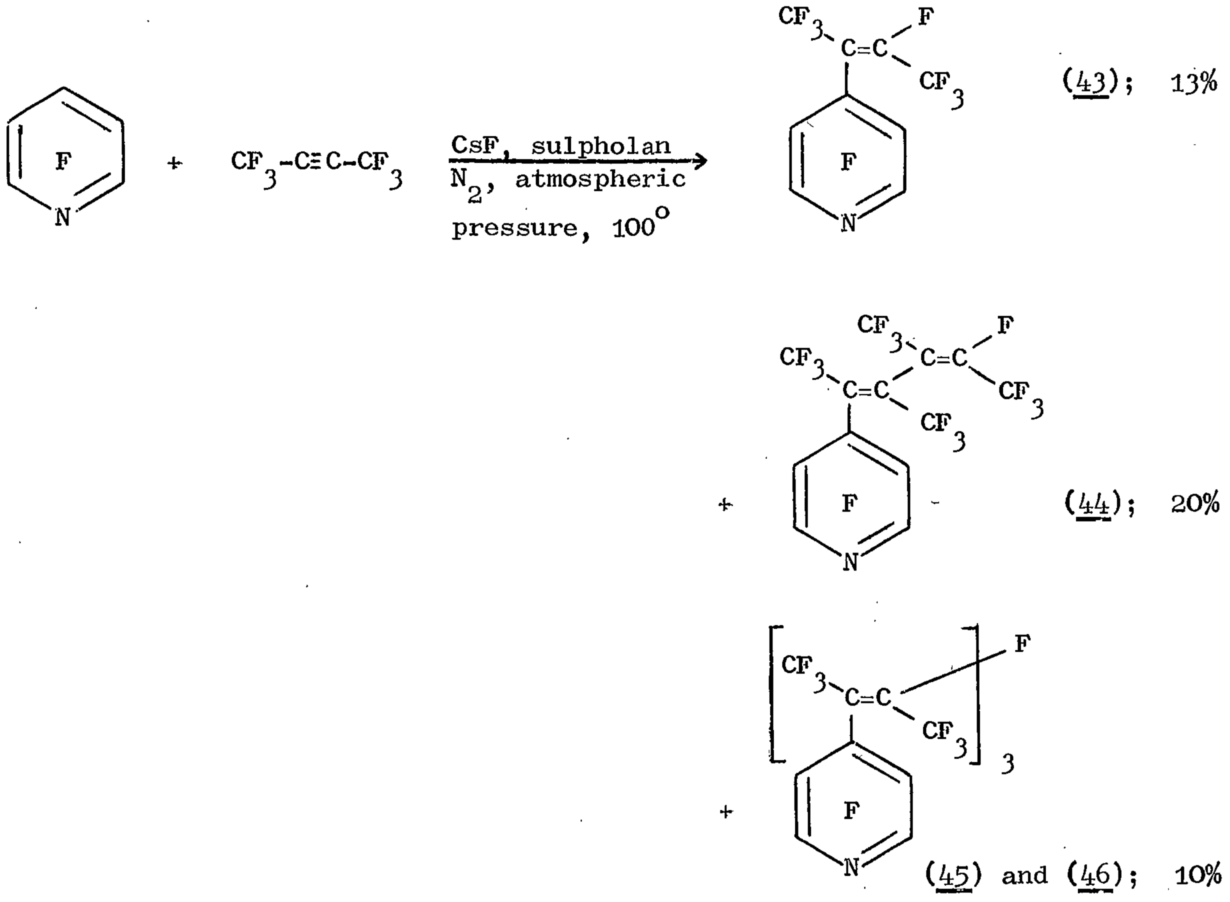

Vacuum
By-pass
valve
A
B
To flexible
reservoir
Pump
Drikold
condenser

DIAGRAM 1



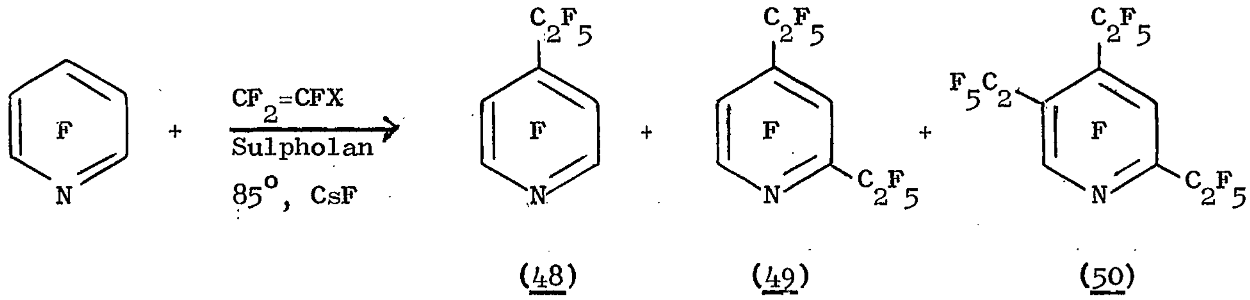
(43); 13%

(44); 20%

(45) and (46); 10%

A disadvantage of this system lies in the fact that materials are being circulated, and as pentafluoropyridine is a reasonably volatile liquid, the concentration of pentafluoropyridine in solution is gradually reduced thus increasing the tendency for polymerisation to occur. This was overcome to some extent by incorporating a dry-ice condenser in the system such that volatile materials were condensed back into the reaction vessel. With both perfluoroacetylenes and perfluoro-olefins[17,42], oligomerisation and polymerisation side reactions have been minimised. Further, the much lower temperatures employed reduced the possibility of any fluoride ion catalysed re-arrangements occurring.[17,42]

A development in atmospheric pressure reactions, a non-circulating system which is used successfully for polyfluoro-olefins[42], consists of evacuating the reaction flask containing the solvent and caesium fluoride and allowing the olefin, for example, tetrafluoroethylene, into the system until atmospheric pressure is reached. The flask is then heated to the reaction temperature and the substrate, for example, pentafluoropyridine, introduced into the system.



X = F, Cl

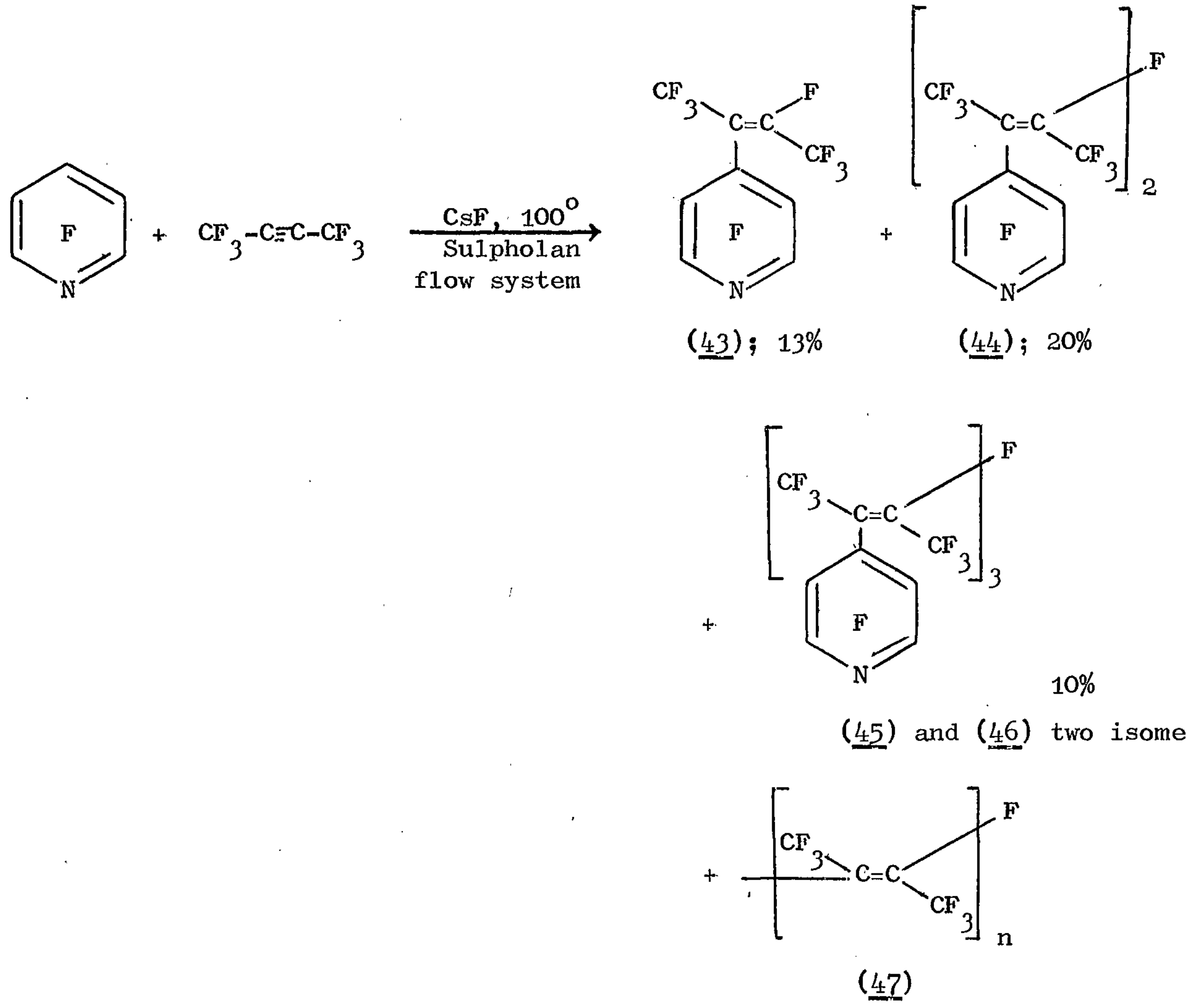
Although the system has been applied successfully to reactions involving hexafluorobut-2-yne and tetrafluoropyridazine (see section 5.1.1), a similar reaction involving pentafluoropyridine led to extensive polymerisation of the perfluoroacetylene.

4.2 Fluoride ion-initiated reactions of acetylenes with pentafluoropyridine

4.2.1 At atmospheric pressure

The reason for, and the subsequent development and modification of atmospheric pressure techniques have been discussed in the previous section.

Thus when hexafluorobut-2-yne, heavily diluted with dry nitrogen, was circulated through a mixture of caesium fluoride, pentafluoropyridine and sulpholan, several perfluoroalkenyl pyridines were obtained.



(43); 13%

(44); 20%

10%

(45) and (46) two isomers

(47)

\+ volatile material

The uptake of hexafluorobut-2-yne was judged by the formation of a slight vacuum in the system.

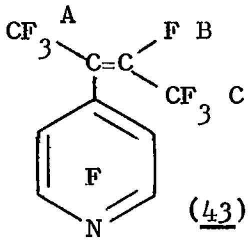
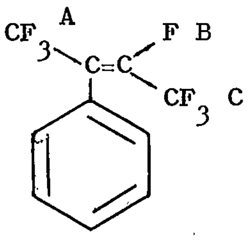
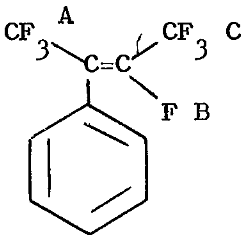
Several reactions were carried out at different temperatures but the highest yields of the products (43), (44), (45) and (46) were obtained at 100°. At temperatures $>$ 100°, polymerisation of the perfluoroacetylene began to increase, presumably due to the decrease in the concentration of pentafluoropyridine in solution. At temperatures $<$ 100°, polymerisation of the perfluoroacetylene again occurred in preference to substitution of the pentafluoropyridine.

(a) Structure of products

All the perfluoroalkenyl derivatives of pentafluoropyridine, separated by v.p.c. had satisfactory elemental analyses, mass and n.m.r. spectra, and were shown to be perfluoro-4-substituted pyridines. These results are in complete agreement with results previously obtained for perfluoromonoalkylation of pentafluoropyridine.[37,40,42]

The structure of perfluoro-4-(2'-butenyl)pyridine, (43) has been determined by ^{19}F n.m.r. spectroscopy. Thus observed chemical shift values for the 3,5 and 2,6 ring fluorine atoms are in close agreement with those for similar compounds.[37,40,42]

Table 1

Compound	Coupling Constants (Hz)		
	J_{AB}	J_{AC}	J_{BC}
 (43)	21	1	7·5
	28	1·5	7
	12	12	7

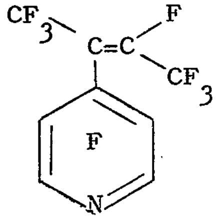
The configuration of the CF_3 groups in the side chain of (**43**), was determined by comparing the observed J values i.e., J_{AB}, J_{AC}, J_{BC}, to those reported[139], for the corresponding *cis* and *trans* phenyl polyfluoro-olefins (Table 1). The preparation of the *cis* and *trans* phenyl polyfluoro-olefins involves reacting phenyl lithium with octafluorobut-2-ene at -80°, and their structures are known to be correct.[139a] As can be seen good agreement was obtained for the *trans* configuration.

Other evidence for (**43**) having the *trans* configuration was obtained from its infrared spectrum. A weak absorption at $5{\cdot}8\mu$, is indicative of a symmetrically substituted *trans* olefin.[138] The presence of an olefinic absorption was confirmed by (**43**) having a strong absorption in the Raman spectrum at 1720 cm^{-1}. E.S.C.A. measurements, carried out in conjunction with Dr. D.T. Clark, confirmed the overall structure of (**43**). The C_{1s} computer simulation is shown, Figure 1, and the assignments are shown in Table 2.

Table 2

Peak	Intensity	C-assignment
A	2	$\underline{C}F_3$ Carbon atoms
B	2	2,6 Ring carbon atoms
C	2	3,5 Ring carbon atoms
D	1	β-Vinylic carbon atoms
E	2	4 Ring carbon atom α-Vinylic carbon atoms

C_{1s} Computer Simulation



(43)

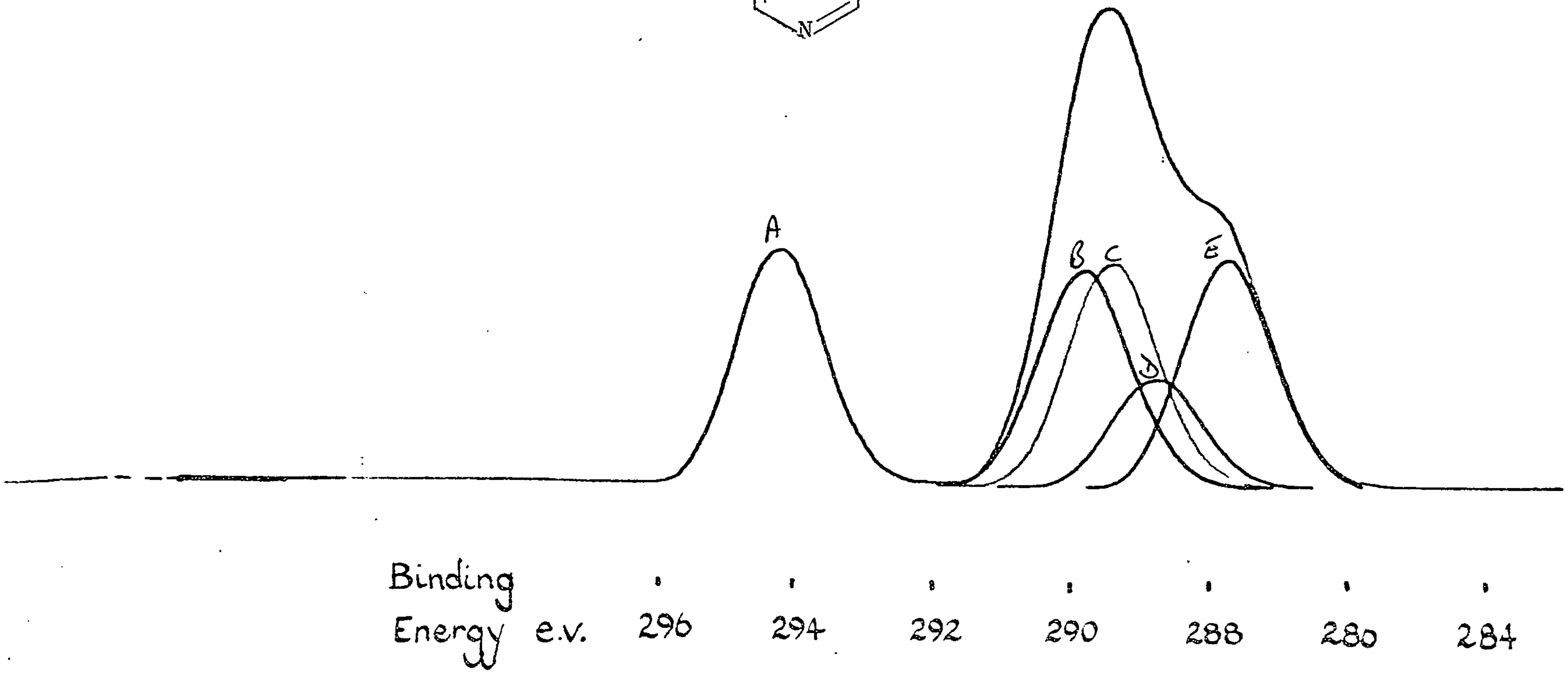
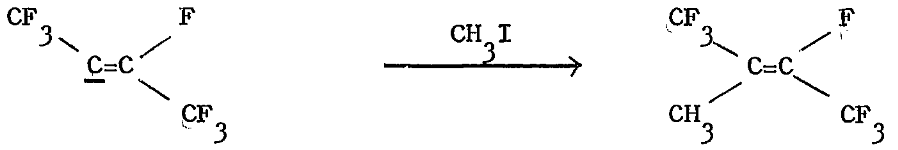


FIGURE 1

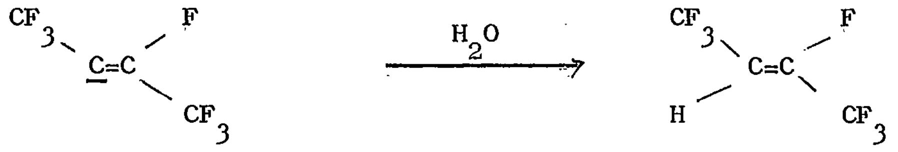
Chemical evidence for the anion (52), derived from hexafluorobut-2-yne retaining its trans configuration has also been reported.[108]



(54)

(52)

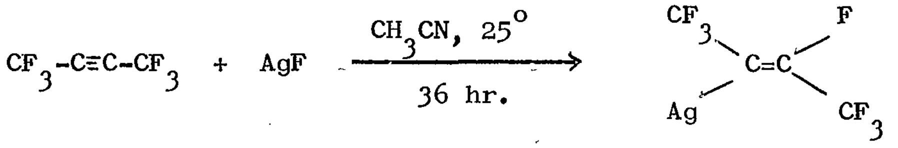
and



(55)

(52)

Miller and co-workers[108] have also isolated trans perfluoro-1-methylpropenylsilver.



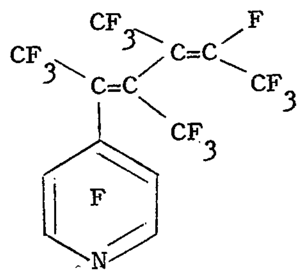
$CF_3-C\equiv C-CF_3 + AgF \xrightarrow[36\ hr.]{CH_3CN,\ 25^o}$

(28)

They also postulate that in reactions involving caesium fluoride and hexafluorobut-2-yne a similar product to (28) is formed, which then reacts further to form the polymer (47).

Only a single isomer of perfluoro-2-(4'-pyridyl)-3,4-dimethylhexa-2,4-diene (44) was detected and its general structure was confirmed by elemental analysis, mass and ^{19}F n.m.r. spectroscopy and E.S.C.A. measurements.[137] Figure 2 shows the C_{1s} computer simulation and Table 3 the assignments.

C_{1s} Computer Simulation



(40)

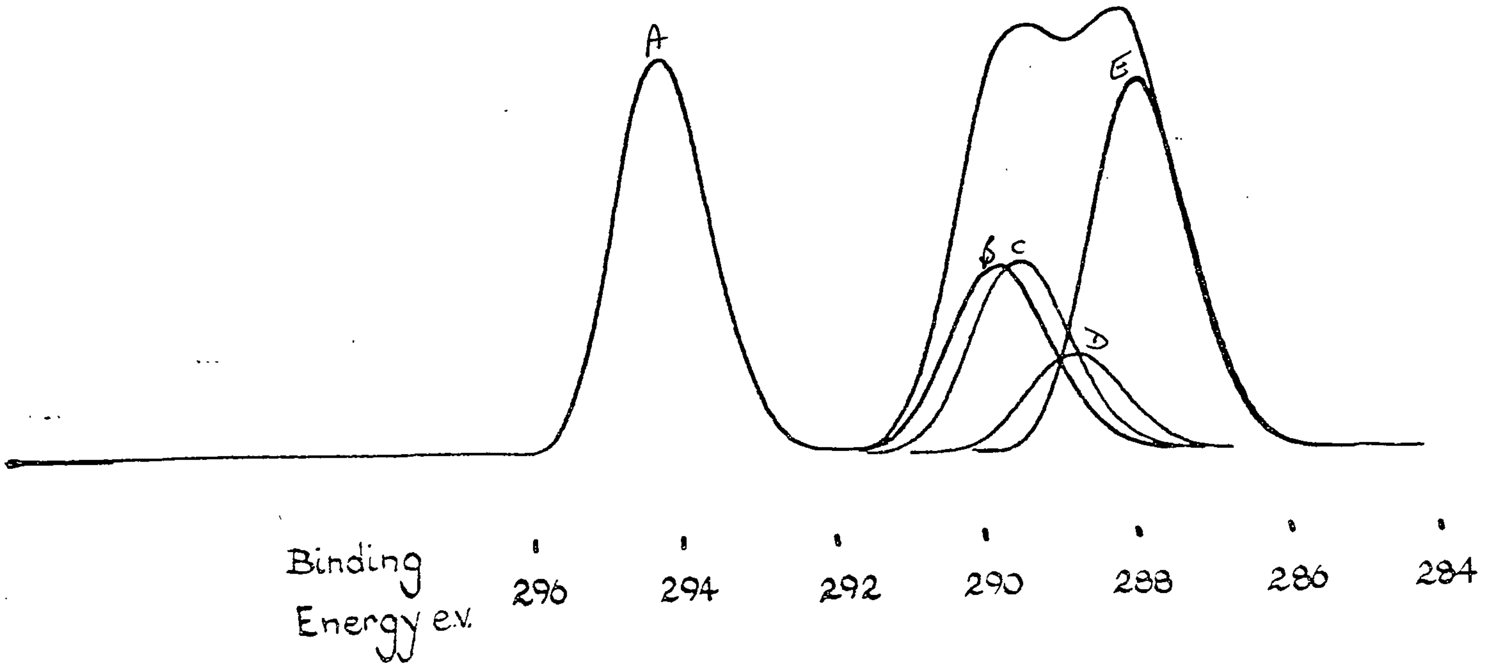
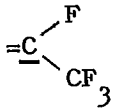
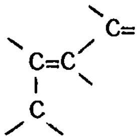


FIGURE 2

Table 3

Peak	Intensity	C-assignment
A	4	$\underline{C}F_3$ Carbon atoms
B	2	2,6 Ring carbon atoms
C	2	3,5 Ring carbon atoms
D	1	
E	4	

The exact configuration of the side chain however, could not be determined from ^{19}F n.m.r. measurements.

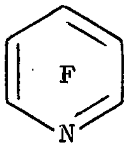
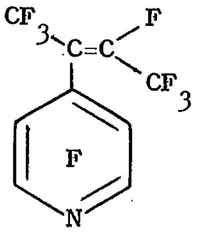
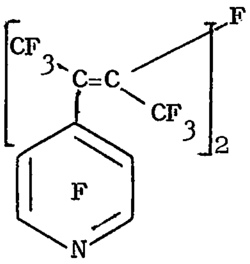
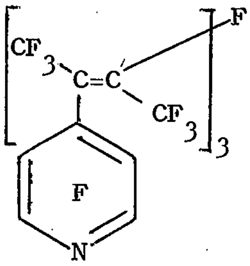
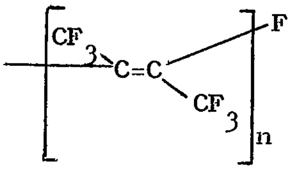
Similarly, the configuration of the two isomeric perfluoro-2-(4'-pyridyl)-3,4,5,6-tetramethylocta-2,4,6-trienes, (45) and (46), could not be determined from their ^{19}F n.m.r. spectra.

The lack of colour in (44), (45) and (46), can be attributed to the severe restriction of configuration in the side chains due to the CF_3 groups (see Section 4.2.2); other evidence is obtained from u.v. data in that no marked increase in λ_{max} or ε is observed on increasing the number of double bonds in the system (see Table 4).

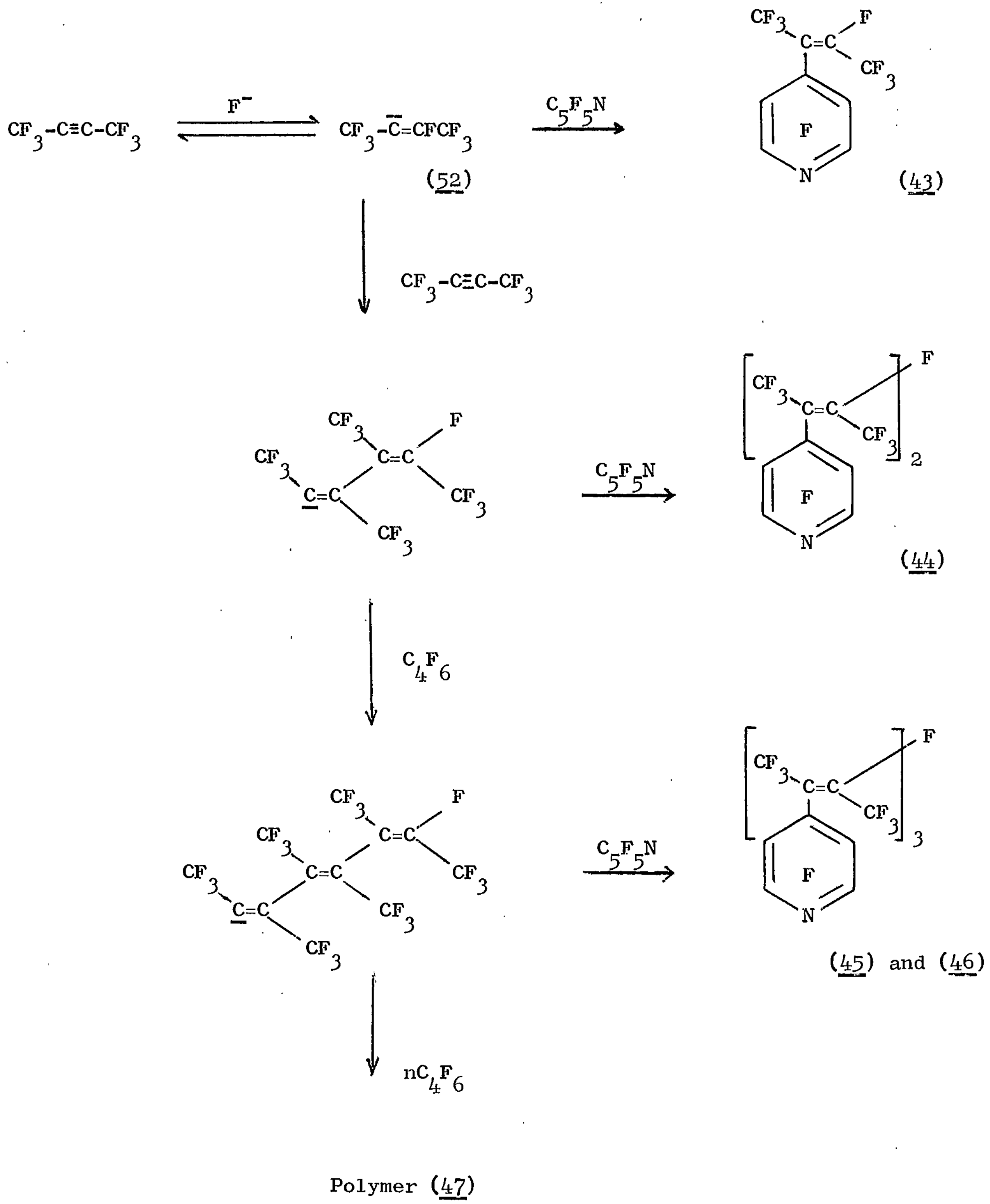
The formation of the perfluoro unsaturated compounds (43), (44), (45) and (46) described, can be accounted for by several mechanisms, involving the initial formation of the perfluoroalkenyl anion (52).

In order to determine whether mechanism (a) or (b) was operating, an atmospheric pressure reaction was carried out using perfluoro-4-(2'-butenyl)-

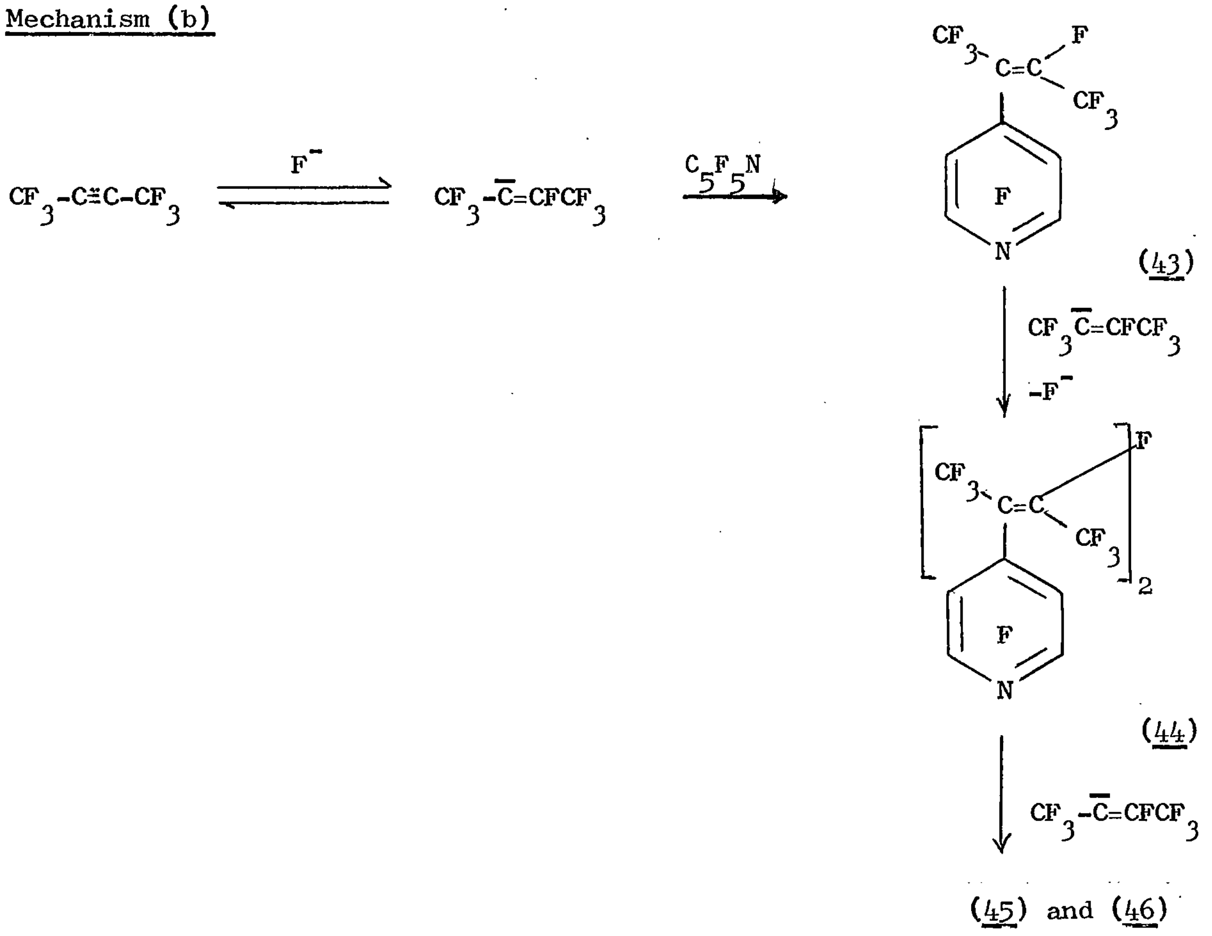
Table 4

Compound	Solvent	λ max mμ	ε
	Ethanol	254	2,700
	Cyclohexane	278	4,180
	Cyclohexane	278	2,682
	Cyclohexane	251 314	6,265 3,324
	Isopropanol	276	-

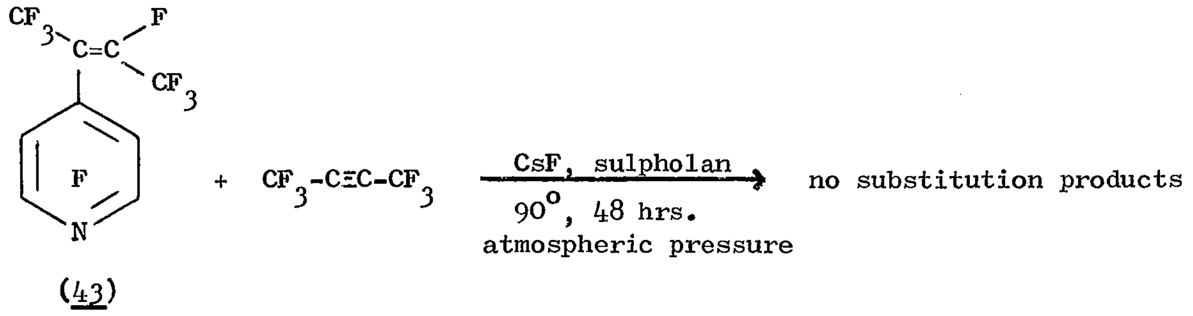
(b) Mechanism (a)



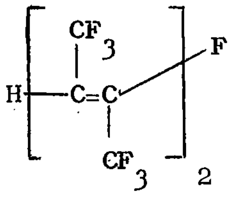
Mechanism (b)



pyridine, hexafluorobut-2-yne and caesium fluoride. After 48 hrs., only polymeric material derived from hexafluorobut-2-yne and fluoride ion and starting materials were recovered.

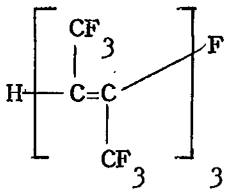


This would suggest, therefore, that the products (43), (44), (45) and (46) are formed by mechanism (a). Further, small quantities of oligomers of hexafluorobut-2-yne (56) and (57) have been isolated and are thought to have the structure:



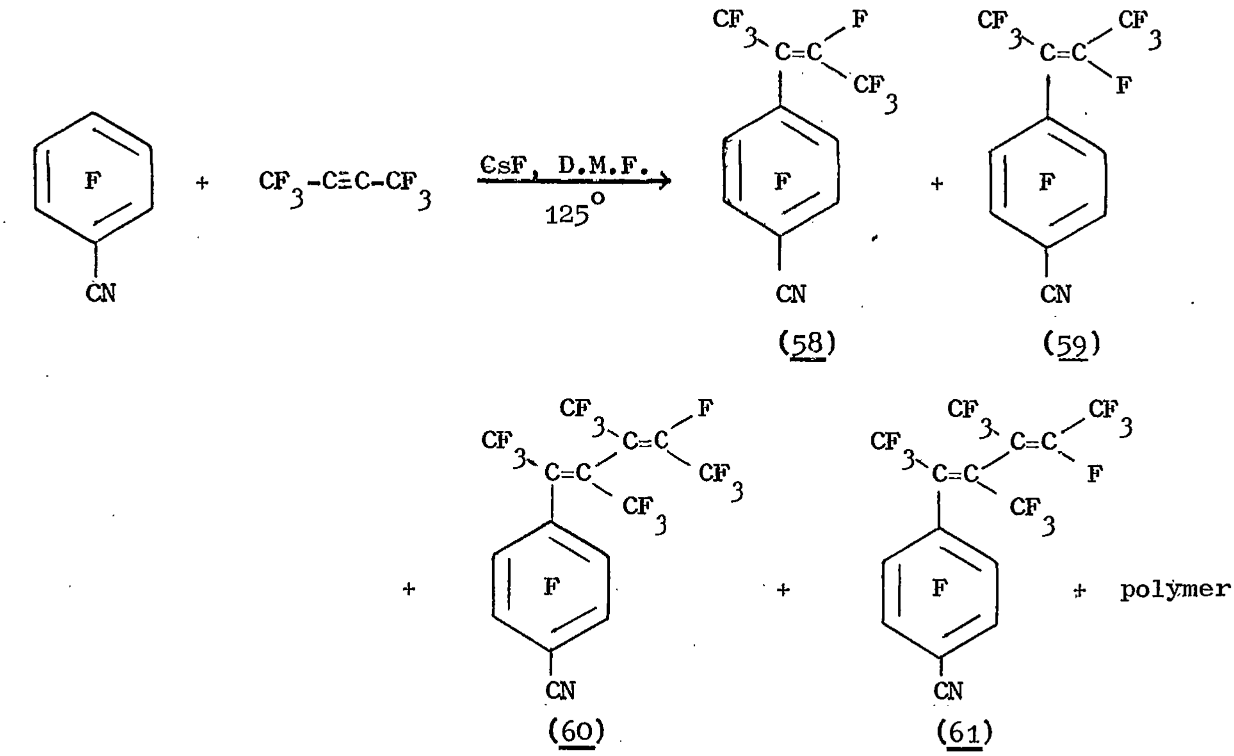
(56)

and



(57)

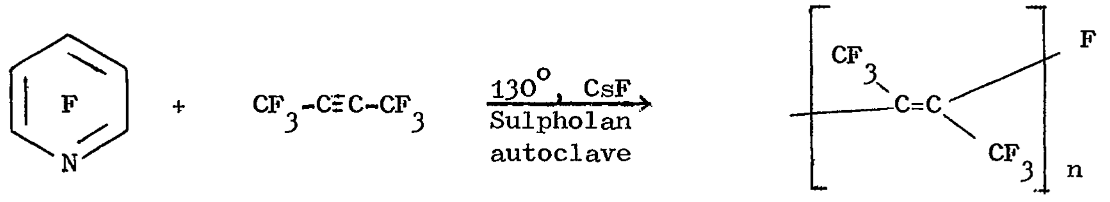
Haszeldine and co-workers[143], have recently reported that a similar series of compounds to (58), (59), (60) and (61) can be formed by a reaction of hexafluorobut-2-yne and perfluorobenzonitrile in the presence of caesium fluoride. Under their reaction conditions, mixtures of isomers were formed.



They also suggest that the dienes, (60) and (61), do not originate from the displacement of the vinylic fluorine of (58) by attack of the perfluoroalkenyl carbanion (52).

4.2.2 In autoclaves

When pentafluoropyridine and a slight excess of hexafluorobut-2-yne were shaken with caesium fluoride and sulpholan in an autoclave at 130° for 33 hrs., a quantitative yield of a polymeric material was produced. Addition of the hexafluorobut-2-yne to the other reactants at the reaction temperature (130°) and reducing the reaction time to 1 hr., still produced a high yield of polymeric material. No evidence for the formation of any substitution products, derived from pentafluoropyridine, were observed.



(47)

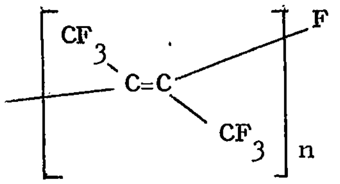
(a) Structure of polymer

Elemental analysis, indicated that the polymer had an empirical formula of C_4F_6, and as nitrogen was absent, the polymer must be derived solely from the hexafluorobut-2-yne. This was confirmed by heating the acetylene with caesium fluoride and sulpholan in a small autoclave at 130° for 5 hrs., and the white solid which was isolated, had an identical infrared spectrum with that of the sample of polymer isolated previously.[40]

Mass spectral analysis gave a molecular weight of ≃ 1500 (max.) but the value varied with probe temperature[135] (e.g. ≃ 1100 at 250°; ≃ 1500 at 270°). The breakdown pattern indicated successive losses of C_4F_6 units from mass no. ∼ 1500 to mass no. ∼ 800. Below ∼ 800 mass units, the breakdown pattern becomes less clear.

The nature of the polymer is extremely interesting in that it has high thermal stability, is only slightly soluble in the usual organic solvents and, more important, it has a white appearance. If a simple, conjugated, polymeric structure was present, then one would expect the polymer to have some colour. It was for this reason and the absence of a double bond absorption in the infrared spectrum, that the polymer was thought to be cross-linked, having a ladder structure.[40,136]

The regular breakdown pattern in the mass spectrum however, is indicative of the more simple structure shown.



(47)

The absence of colour in the polymer is probably due to distortion of the polymer chain by the bulky CF_3 groups.

Although the polymer is insoluble in most solvents, a small amount of material did dissolve in isopropanol enabling a very weak, qualitative, u.v. spectrum to be determined; a value of $\lambda_{max} = 276\mu$ is indicative of the polymer having little or no conjugation.

The absence of a double bond absorption in the infrared spectrum may be due to the fact that double bond absorptions in olefins having a <u>trans</u> configuration are often weak.[138] A Raman analysis, carried out in conjunction with Dr. C.J. Ludman, indicated a weak absorption at 1720 cm^{-1} which could be attributed to a double bond.

E.S.C.A. measurements (Figure 3) were in agreement with the proposed structure; no evidence was found for cross-linking. Although E.S.C.A. involves only the surface of the sample it is reasonable to assume that the results obtained usually apply to the bulk of the sample also.

Recent calculations[137] on a structurally similar compound (see Figure 4):

C_{1s} Computer Simulation

(47)

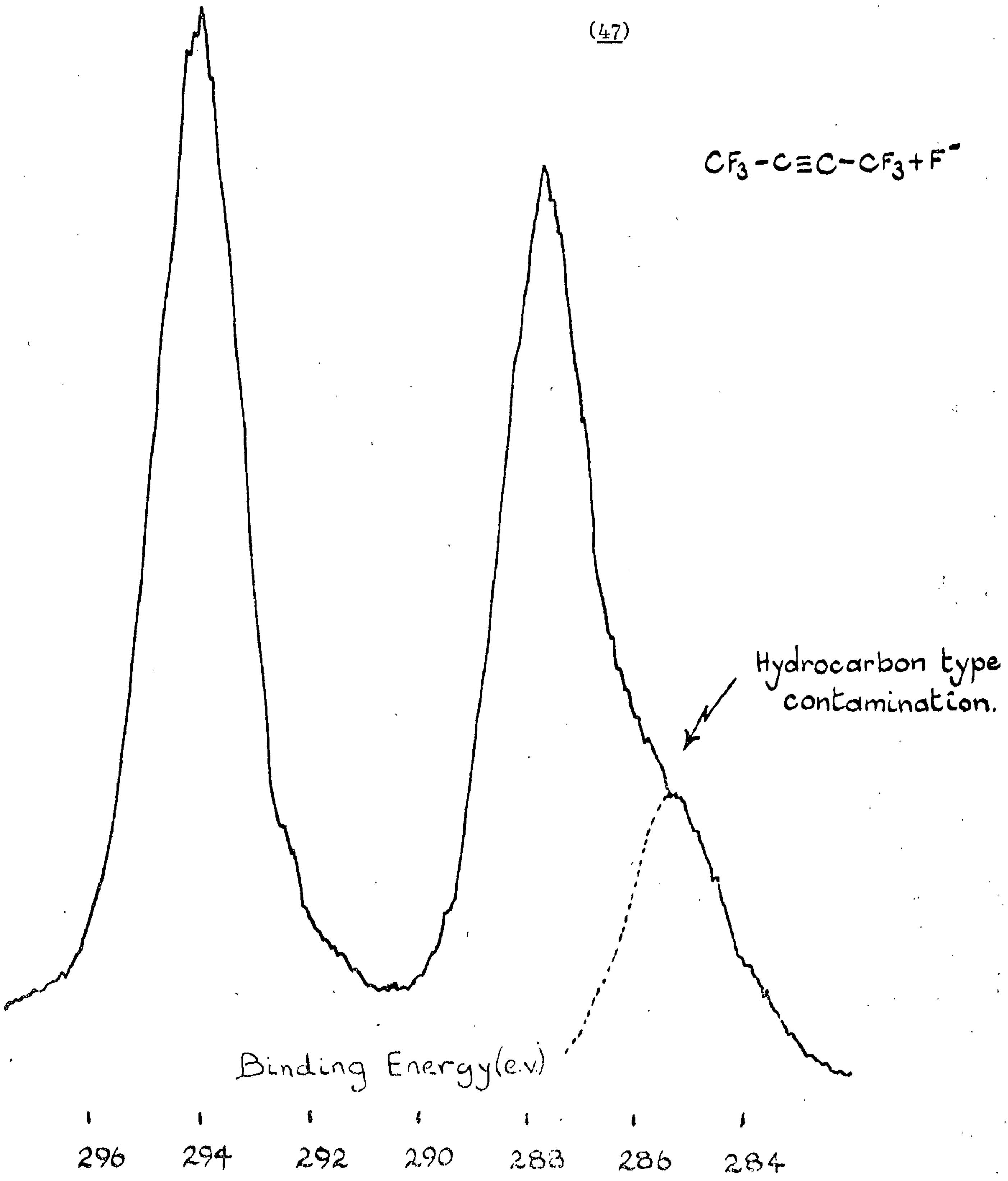


FIGURE 3

Model for charge potential calculations

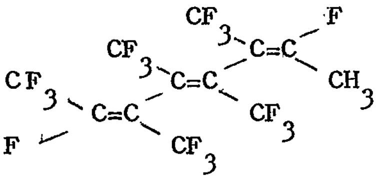
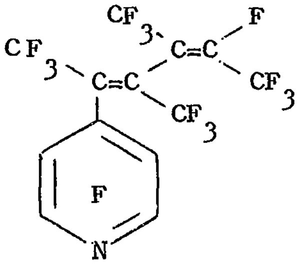
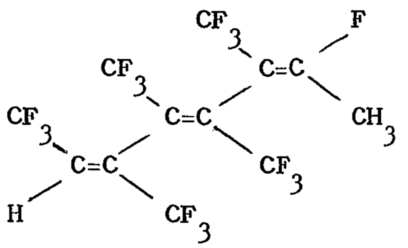
Compound	Atom	Binding Energy (eV)	
		Calculated	Experimental
	$CF_3\text{—}\underline{C}=$	287·8	287·7
	$\underline{C}F_3\text{—}C=$	293·9	294·7
 (44)	$CF_3\text{—}\underline{C}=$	-	287·9
	$\underline{C}F_3\text{—}C=$	-	294·2

FIGURE 4

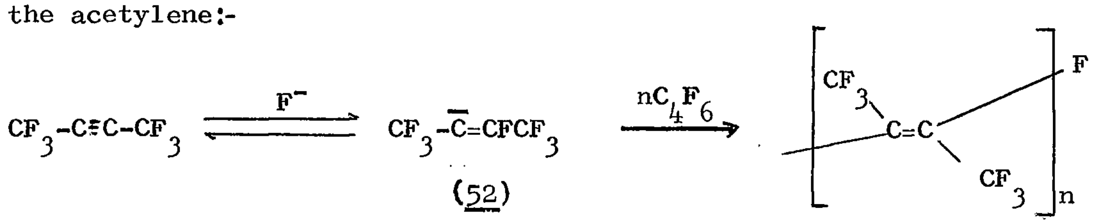


(51)

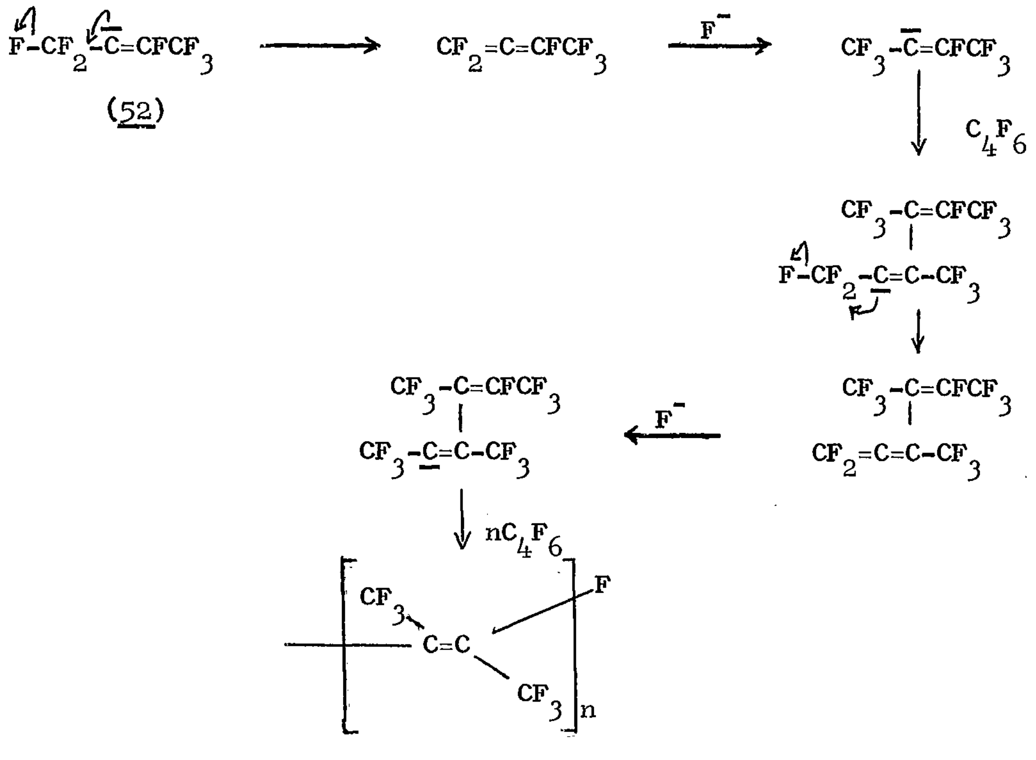
suggests that the double bonds in (51) lie at 90° to each other thus precluding conjugation and causing the polymer chain to spiral. In fact, steric crowding is so great due to the bulky CF_3 groups, that the distance between alternate CF_3 groups is of the order of 1·4Å.

(b) Mechanism

The polymerisation of hexafluorobut-2-yne probably occurs by fluoride ion attack on the acetylene to form the anion (52) which then reacts with an excess of the acetylene:-



or alternatively

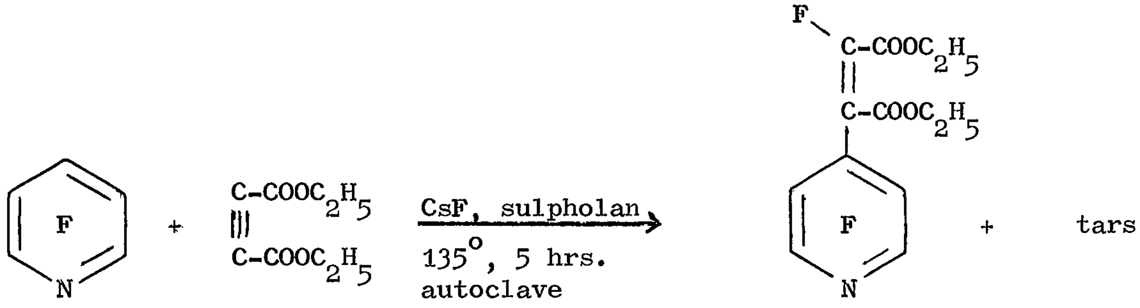


Homopolymers of hexafluorobut-2-yne, of unknown structure, have been reported as being formed on irradiation (^{60}Co source) of the acetylene and also when the acetylene is heated alone or with catalysts such as I_2, $NaOAsF_6$ [87-89], or irradiated with ultraviolet light (254 nm).[140]

4.2.3 Reactions involving diethyl acetylene dicarboxylate

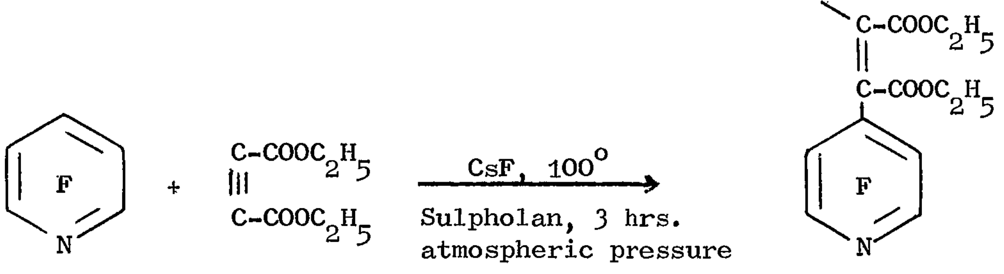
(a) Reaction conditions

Although reactions involving diethyl acetylene dicarboxylate, pentafluoropyridine and caesium fluoride had been shown to give a product thought to be 1-fluoro-1,2-(biscarbethoxy)-2-(2',3',5',6'-tetrafluoropyridyl)ethylene, (42), extensive decomposition of materials occurred.[40]



(42); 20%

It was anticipated that slow addition of the acetylene to the reaction mixture, at a lower temperature and with a shorter reaction time, would increase the yield of (42) and minimise tar formation. Thus adding the acetylene to a rapidly stirred suspension of pentafluoropyridine at 100° over 3 hrs., gave a pale yellow oil which had an identical infrared spectrum with the material isolated previously by Jackson.[40]

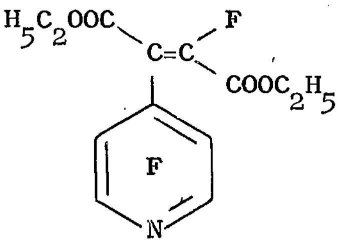
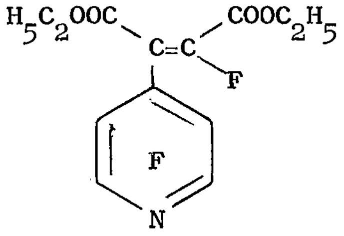


(42); 40%

(b) Structure of product

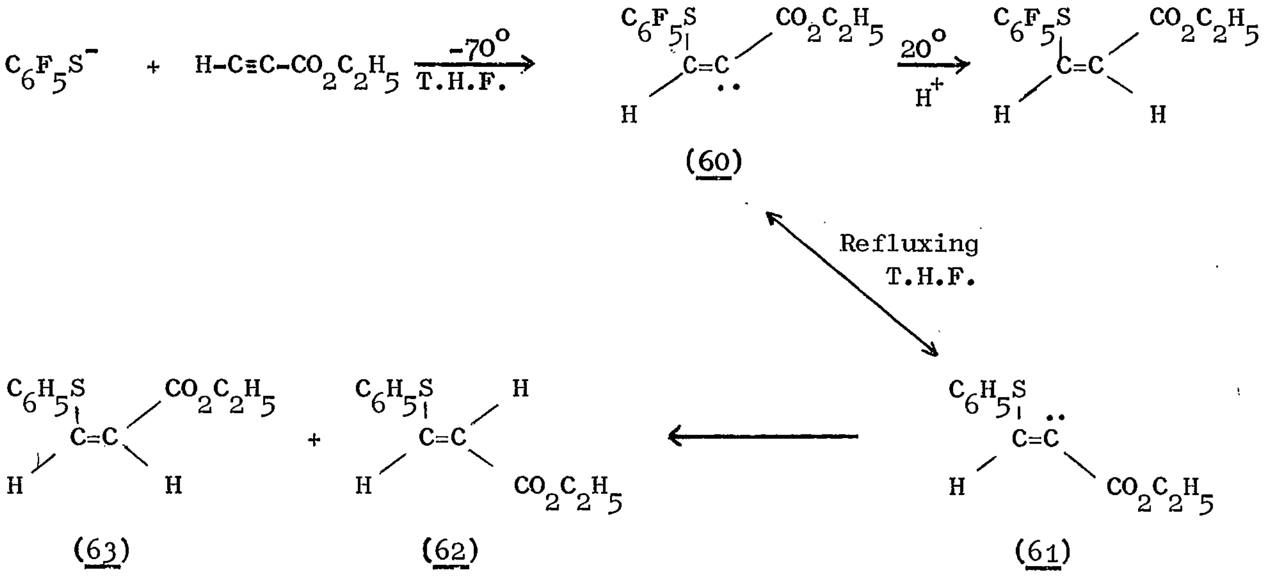
The product, (42), had satisfactory mass spectral and elemental analyses and was shown by ^{19}F n.m.r. studies (Table 5) to be a mixture of *cis* and *trans* isomers in the ratio 50:50.

Table 5

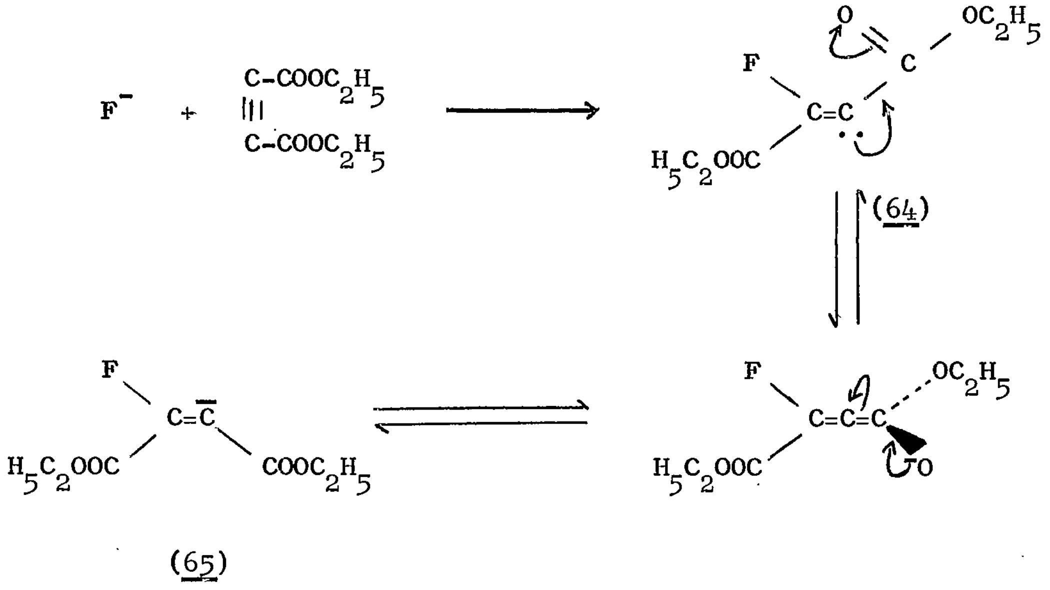
Compound	Chemical Shift	Intensity	Assignment
	83·5	2	2,6 Ring F
	92·2	1	= C$\underline{F}$
	140·6	2	3,5 Ring F
	84·4	2	2,6 Ring F
	92·2	1	= C$\underline{F}$
	142	2	3,5 Ring F

The ratio of isomers was obtained by comparing the ratio of the heights of two similar peaks, in this case the 3,5 ring fluorine resonances. The spectrum was complex and a simple comparison of the vinylic fluorine resonances could not be justified.

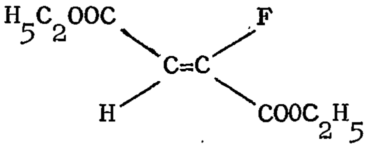
The formation of a mixture of isomers in contrast to the single isomer formed in the reaction between pentafluoropyridine and hexafluorobut-2-yne, can arise through isomerisation of the *trans* carbanion or through a nonstereospecific addition. Quasem[144], observed that additions of lithium pentafluorothiophenate to ethyl propiolate to give the expected cis product, occurred only at -70°. At higher temperatures, for example 65°, cis-trans isomers (50:50) (62), (63) were formed, suggesting that isomerisation of the intermediate carbanion occurs.



Similarly the trans carbanion (64) could under the conditions used, tautomerise by a similar mechanism, thus precluding the specific formation of the trans isomer.



A small quantity of material (66), has been isolated from the reactions and the value of J_{HF} 31 Hz in the ^{19}F n.m.r. spectrum of (66) establishes[138] the trans structure shown.



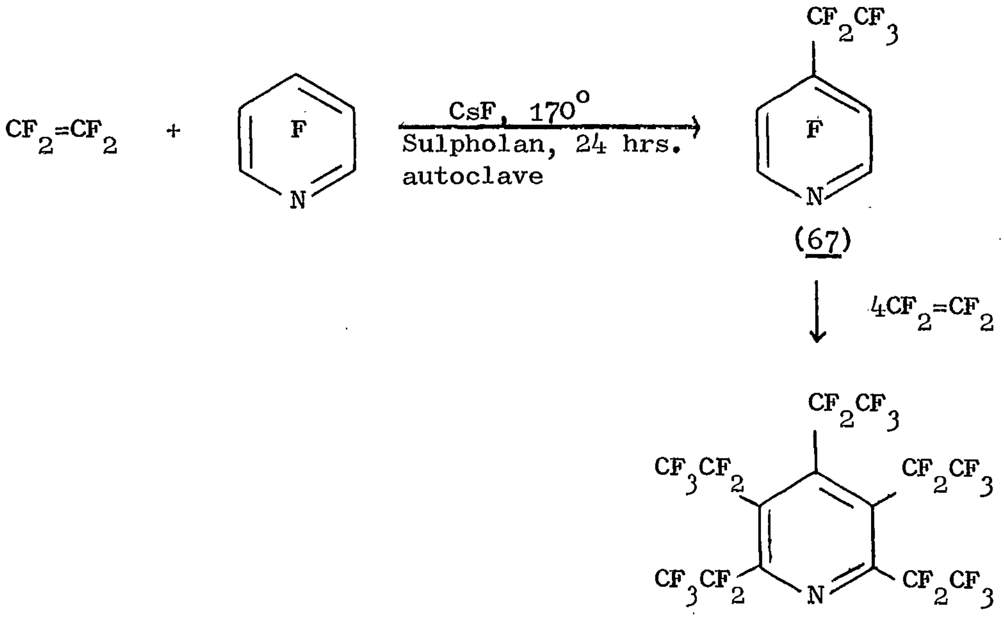
(66)

4.3 Fluoride ion-initiated reactions of polyfluoro-olefins with pentafluoropyridine

Although fluoride ion-induced reactions involving polyfluoro-olefins and pentafluoropyridine form polyfluoroalkyl pyridines, it was thought that a perfluorohydro-olefin, for example trifluoroethylene, $CF_2{=}CFH$, or trans-2H-heptafluorobutene, may undergo hydrogen abstraction by fluoride ion to form the corresponding perfluorovinyl anion; reaction with pentafluoropyridine would then give a perfluorovinyl pyridine.

4.3.1 Reactions involving trifluoroethylene

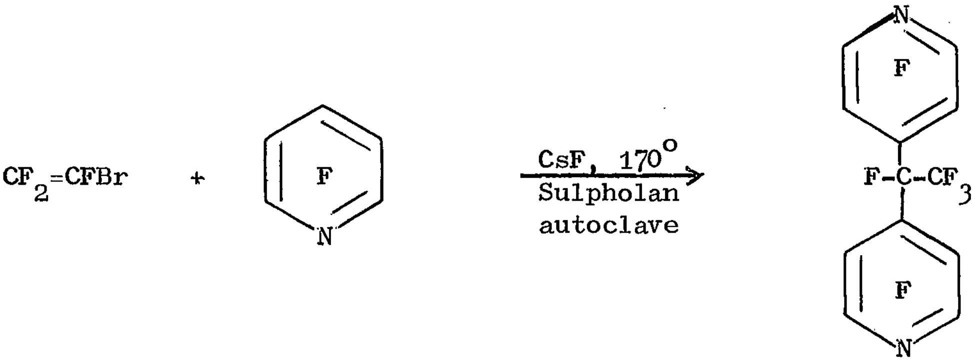
Fluoride ion-initiated reactions of polyfluoro-olefins, $CF_2{=}CFX$, with perfluoroaromatic compounds have been investigated previously using autoclaves.[40] Thus when X=F, a mixture of perfluoromono- to pentakis-pentafluoroethylpyridine was obtained.



(67)

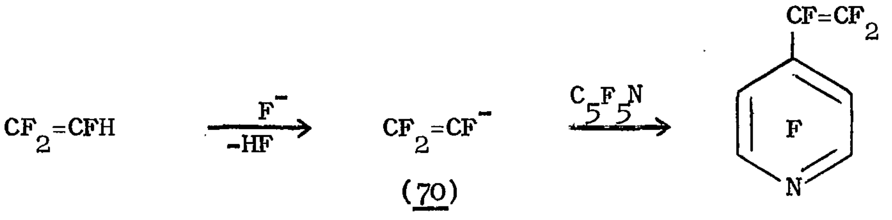
(68)

Using trifluoroethylene, X=H, no reaction occurred at 200°C for 46 hrs., whilst with bromotrifluoroethylene, X=Br, a perfluoro bipyridyl ethane was formed.



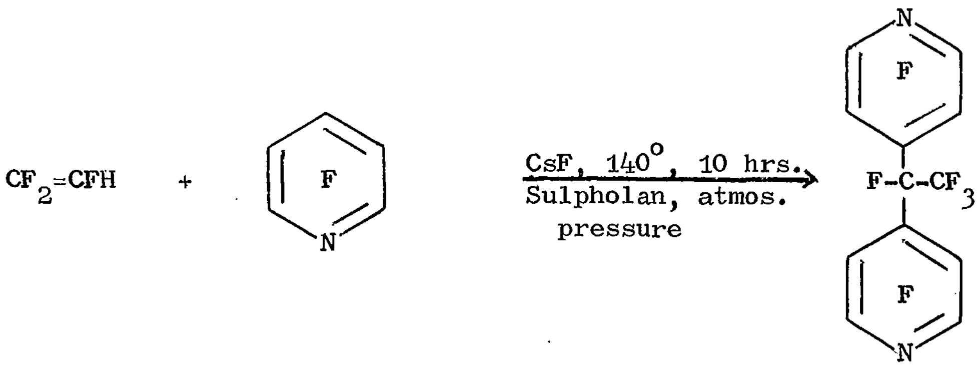
(69)

Under milder conditions, i.e. an atmospheric pressure reaction, trifluoroethylene may undergo hydrogen abstraction and the resulting perfluorovinyl anion, react with pentafluoropyridine thus:



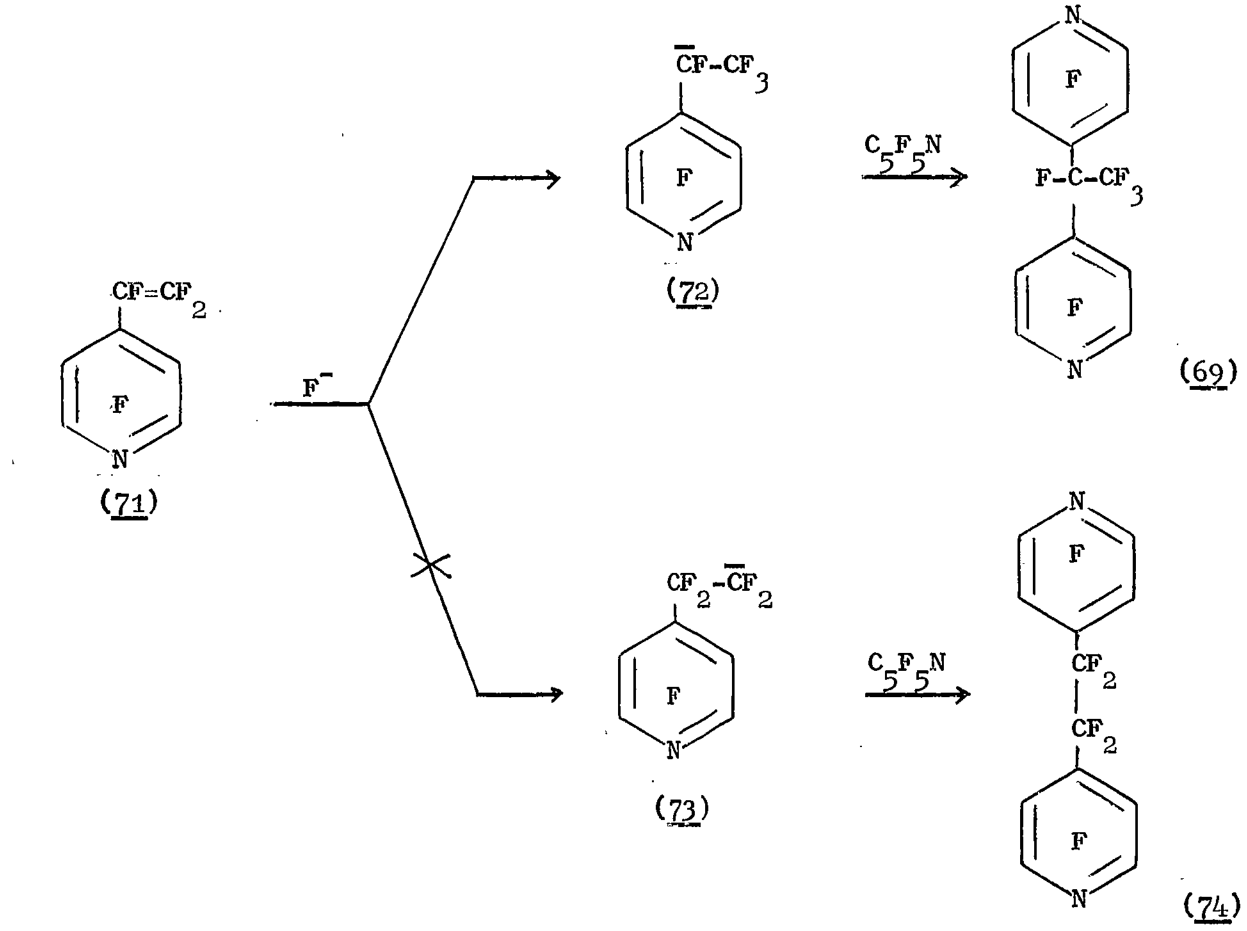
(71)

However, when trifluoroethylene was circulated through a mixture of pentafluoropyridine, caesium fluoride and sulpholan at 140°, a small quantity of white solid was isolated. This was found to have an identical infrared spectrum with that of an authentic sample of (69)



(69); 7%

Thus under the reaction conditions used, any perfluorovinylpyridine formed is reacting further to form a perfluoro bipyridyl ethane.

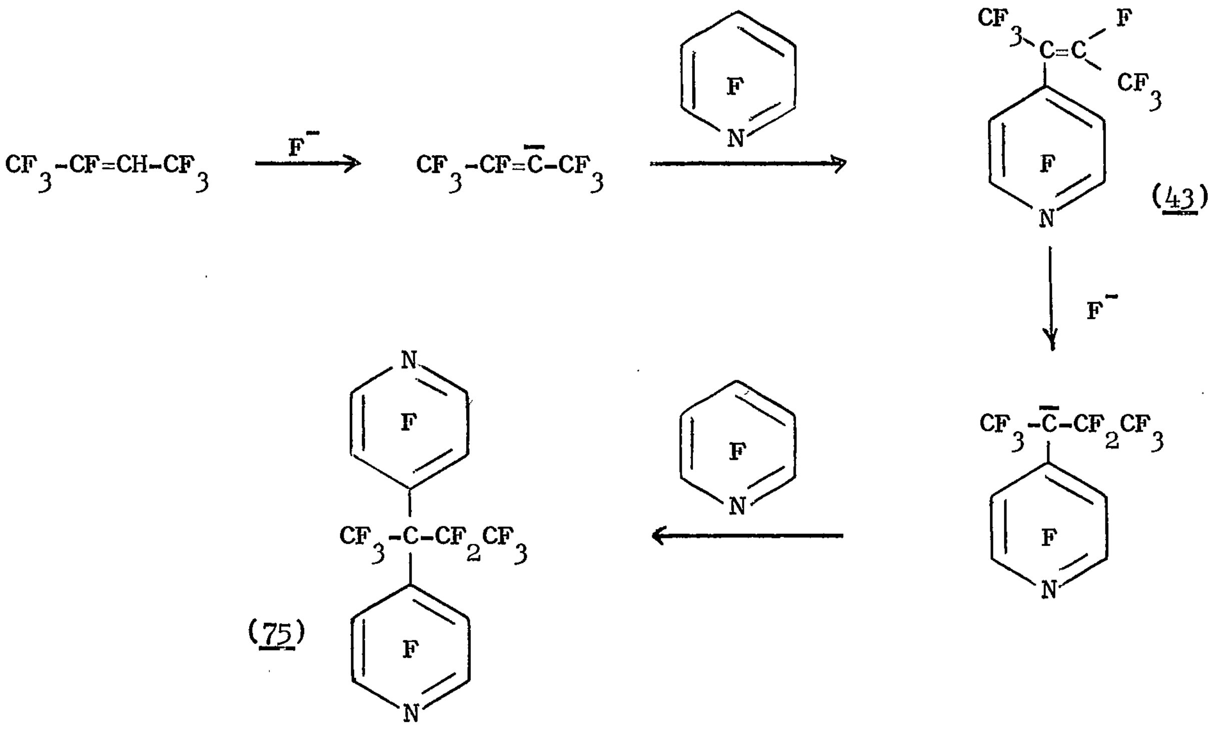


The isolation of perfluoro-1,1-bipyridyl ethane (69), and not perfluoro-1,2-bipyridyl ethane (74), is an indication of the great stability of the anion (72) over (73).

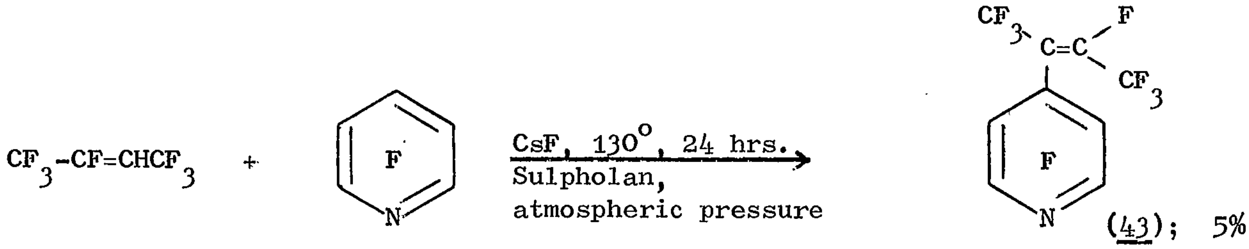
Perfluoro-4-(vinyl)pyridine (71), prepared using defluorination techniques, has been shown[17,42] to readily react with pentafluoropyridine in the presence of caesium fluoride at 40°, indicating that (71) is intermediate in the formation of (69).

4.3.2 Reactions involving trans-2H-heptafluorobut-2-ene

By analogy to the atmospheric pressure reaction of trifluoroethylene and pentafluoropyridine described above, the use of a similar polyfluorohydro-olefin for example, trans-2H-heptafluorobut-2-ene, should give a similar perfluoro-1,1-bipyridyl ethane (75).



An atmospheric pressure reaction involving trans-2H-heptafluorobut-2-ene, and pentafluoropyridine in the presence of caesium fluoride, gave a small amount of a volatile liquid, which was shown (infrared) to be perfluoro-4-(2'-butenyl)-pyridine (43).

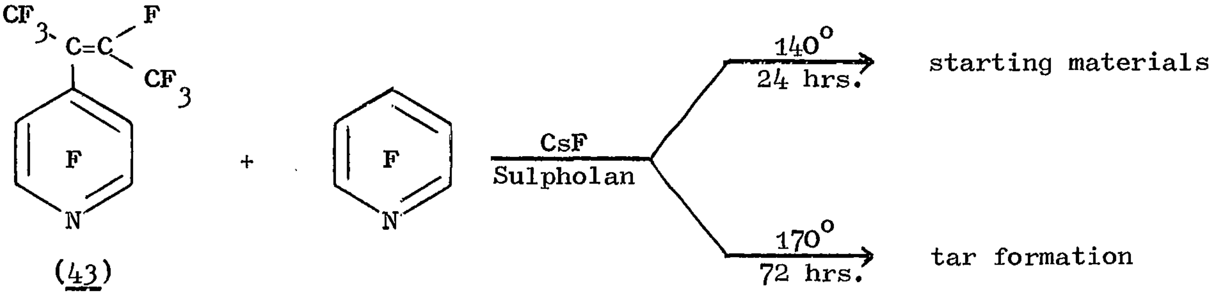


Attempts to force the reaction by using a small nickel autoclave failed to produce (75).

4.4 Reactions involving perfluoro-4-(2'-butenyl)pyridine

4.4.1 With pentafluoropyridine in the presence of caesium fluoride

The reaction of *trans*-2H-heptafluorobut-2-ene and pentafluoropyridine in the presence of caesium fluoride (see section 4.3.2) had only yielded perfluoro-4-(2'-butenyl)pyridine (43). It was anticipated that using perfluoro-4-(2'-butenyl)pyridine, and more forcing conditions i.e. autoclaves, higher reaction temperatures and longer retention times, the corresponding perfluoro-1,1-bipyridyl ethane (75) would be formed. However, a reaction at 140° resulted in an almost quantitative recovery of starting materials, while at a higher temperature (170°) with a longer reaction time, complete breakdown of the starting materials occurred with extensive tar formation.



4.4.2 Nucleophilic substitution with methoxide ion

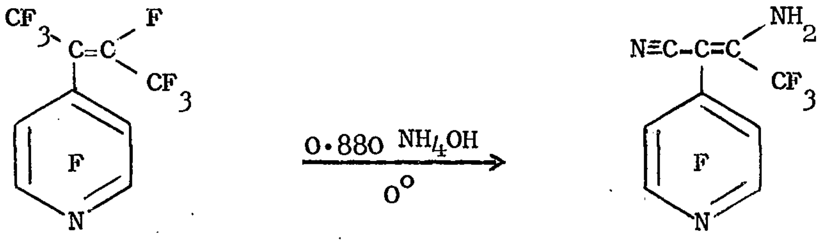
Perfluoroalkyl pyridines have been shown[37,40,42] to react readily with one equivalent of methoxide ion to form a 2-methoxy derivative. It was of interest to determine whether a similar reaction involving perfluoro-4-(2'-butenyl)pyridine (43) would give the corresponding 2-substituted product, or whether replacement of the vinylic fluorine would occur.

A monomethoxy derivative of (43) was prepared by treating a solution of (43) in methanol with methoxide ion at 0°C. The product, (76), had satisfactory elemental analysis and its ^{19}F n.m.r. spectrum indicated that replacement of the vinylic fluorine had occurred in preference to substitution at position 2 in the pentafluoropyridine ring. Further, a comparison of the value of the coupling constant obtained ($J_{CF_3-CF_3}$ 12 Hz), with those in Table 1 , section 4.2.1, indicated that the CF_3 groups were in a cis configuration to each other. The product obtained is therefore cis-perfluoro-2-(2',3',5',6'-tetrafluoropyridyl)-3-methoxy butene (76). A small amount of the corresponding trans compound (< 5%) was also formed. The change of configuration of the side chain can be explained in terms of an initial trans attack by methoxide ion, followed by rotation of the CF_3 groups and elimination of fluoride ion, (Diagram 2).

4.4.3 Nucleophilic substitution with ammonia

(a) Reaction conditions

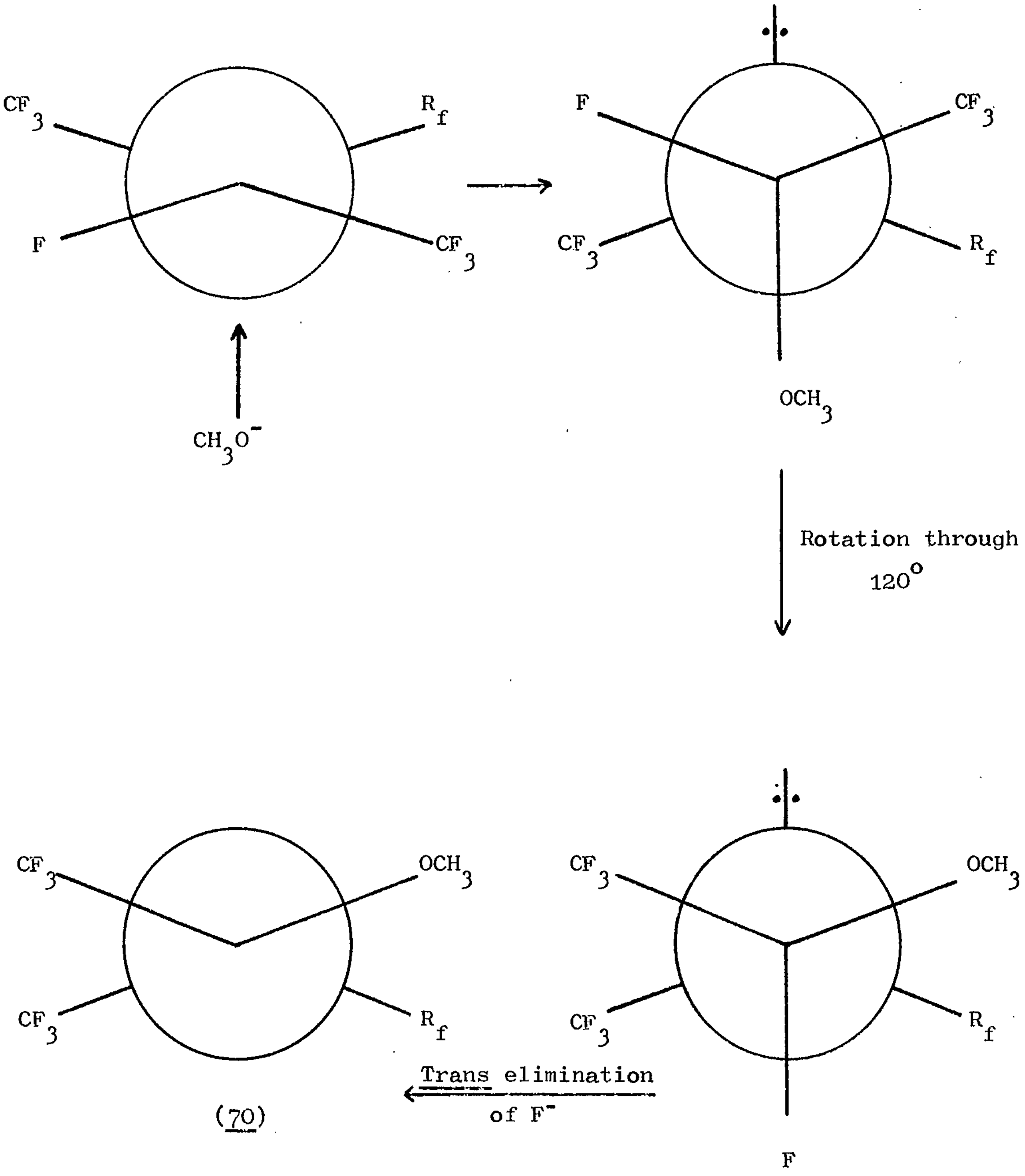
Krespan[145] has shown that terminal fluoro-olefins react with ammonia at low temperatures to form imines. Thus when perfluoro-4-(2'-butenyl)pyridine (43) was reacted with aqueous ammonia at 0° an enamine (77), and not a simple amino derivative, was formed.



(43) (77)

(b) Structural determination

The product (77) has satisfactory elemental and mass spectral analyses. The ^{19}F n.m.r. spectrum of (77) indicated that loss of a CF_3 grouping and the vinylic fluorine had occurred, although 3',5' and 2',6' ring fluorines were still intact i.e. no substitution in the heterocyclic ring had occurred. Further, the remaining CF_3 group appeared as a singlet suggesting that the CF_3

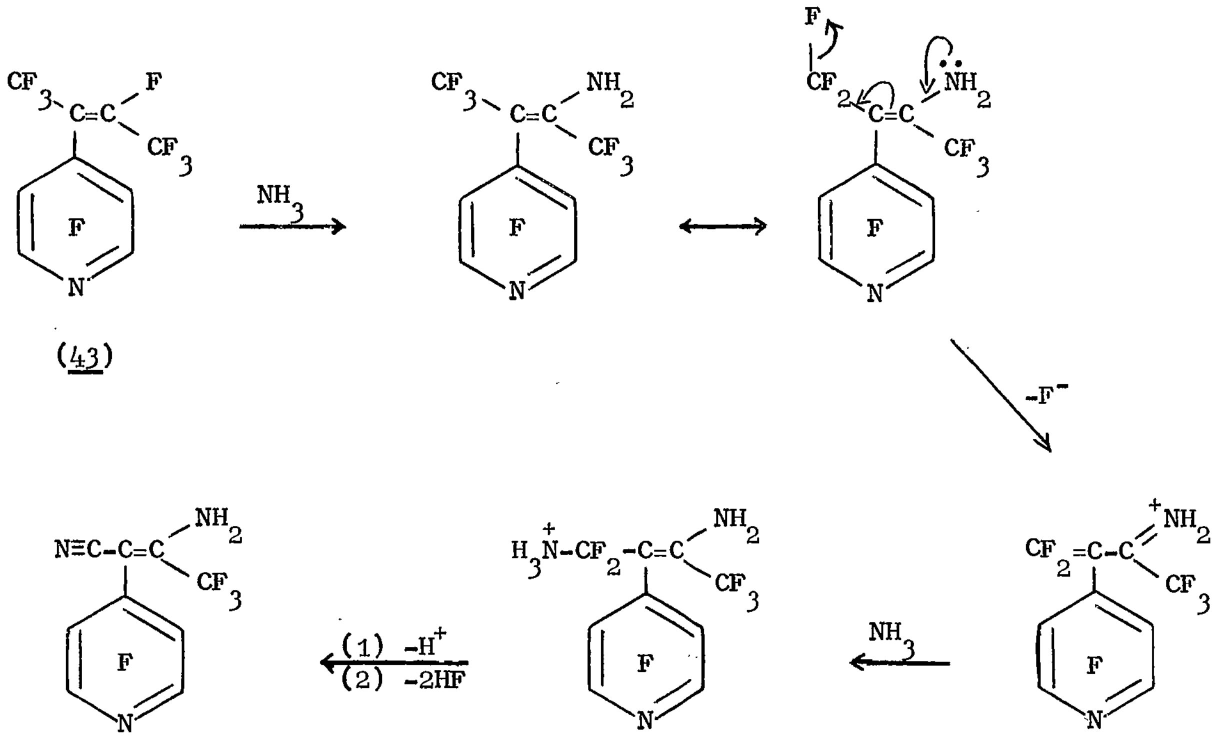

CF3
Rf
F
CF3
CH3O-
F
CF3
CF3
Rf
OCH3
Rotation through 120°
CF3
OCH3
CF3
Rf
CF3
OCH3
CF3
Rf
F
Trans elimination of F-

(70)

DIAGRAM 2

group was in the 3-position in the side chain.

An absorption at 4·5μ in the infrared spectrum of (77) was indicative of a nitrile group.[138] A possible mechanism for the formation of (77) is shown below.



(43)

(77)

CHAPTER 5

Fluoride Ion-initiated Reactions of Acetylenes with Tetrafluoropyridazine

Introduction

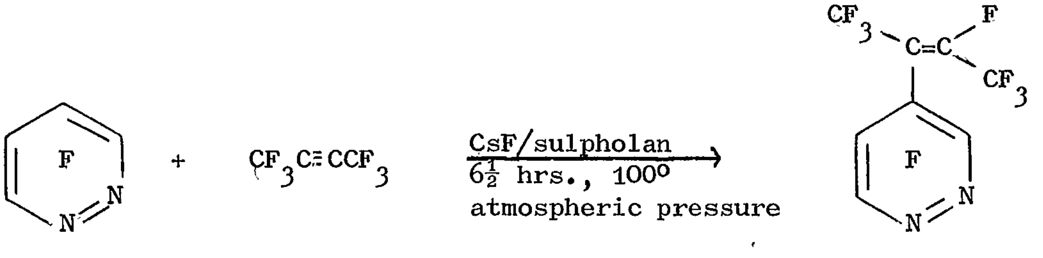
The development of atmospheric pressure techniques in fluoride ion reactions and their important application to pentafluoropyridine and hexafluorobut-2-yne systems, have been discussed in Chapter 4. A different approach to reduce the polymerisation of the acetylene, and hence favour the polyfluoroalkylation reaction, would be to use a more reactive substrate, for example, tetrafluoropyridazine. Tetrafluoropyridazine is known to be one of the most reactive of the fluorinated heterocycles, containing two positions in the heterocyclic ring which are extremely susceptible to nucleophilic attack. Therefore, the possibility of obtaining di-substituted products is apparent. Thus, a preliminary investigation of the fluoride ion-initiated reactions of tetrafluoropyridazine and acetylenes are discussed.

5.1 Fluoride ion-initiated reactions of acetylenes with tetrafluoropyridazine

5.1.1 With hexafluorobut-2-yne

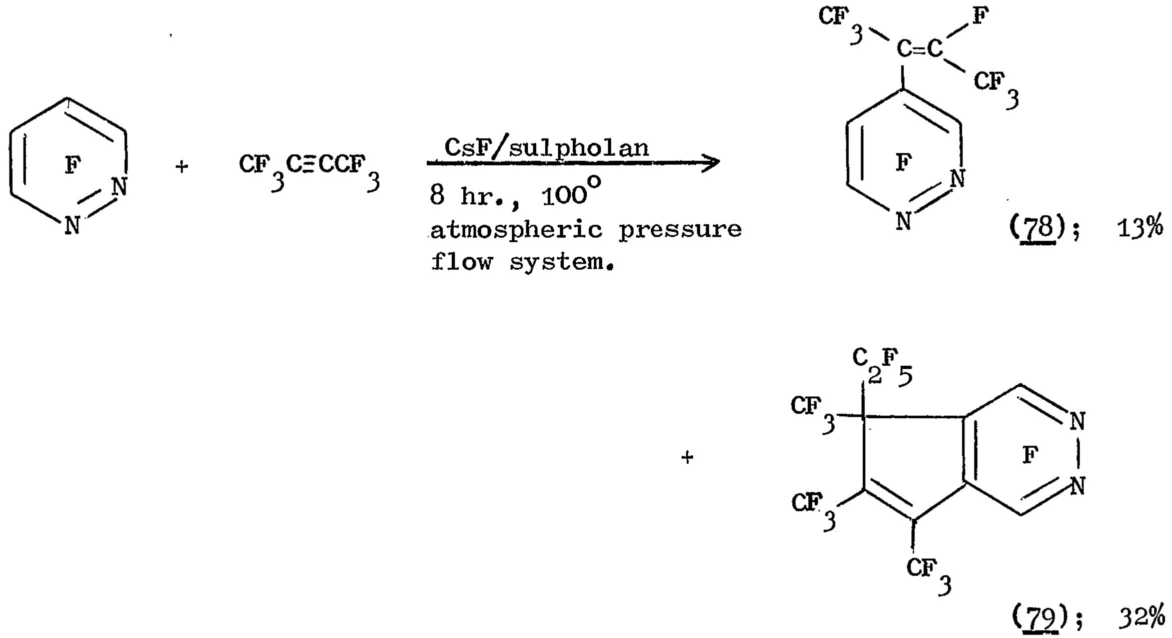
(a) Reaction conditions and products

Initial reactions were carried out using the atmospheric pressure flow system described previously (4.1.3). When hexafluorobut-2-yne, heavily diluted with nitrogen, was circulated through a rapidly stirred suspension of caesium fluoride, tetrafluoropyridazine, and sulpholan at 100°, reaction was extremely slow and, after 6½ hrs., unchanged starting materials were recovered in addition to a small quantity of the monosubstituted pyridazine (78).



(78); 30%

However, polyfluoroalkylation reactions involving tetrafluoropyridazine are known[146] to be inhibited by slight traces of moisture and when a second experiment was carried out, in which extreme care was taken to preclude moisture from the system, a second product (79) was isolated. Oligomers, derived from hexafluorobut-2-yne, and the polymer (47), were not observed.

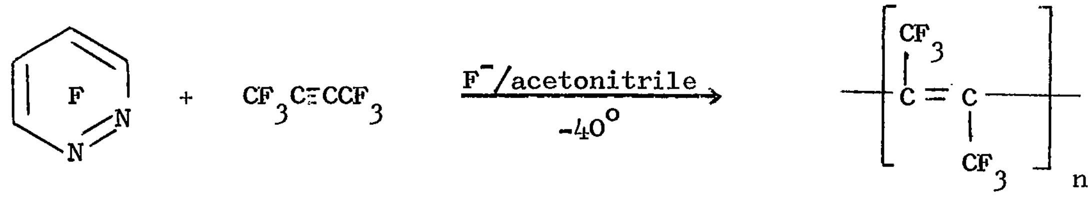


(78); 13%

(79); 32%

Several flow reactions were then carried out at different temperatures in an attempt to optimise the yield of (79); this was achieved (53%) at 80°. In a static system (4.1.3), at 30°, (79) was obtained in 60% yield.

Attempts to increase the yield of (78) by using lower temperatures and acetonitrile as solvent were unsuccessful. Thus when hexafluorobut-2-yne was circulated through a suspension of caesium fluoride, acetonitrile and tetrafluoropyridazine at 0°C, oligomers of hexafluorobut-2-yne were formed. Using even lower temperatures (-40°), polymerisation of the perfluoroacetylene predominated, with no evidence for the formation of (78) or (79).

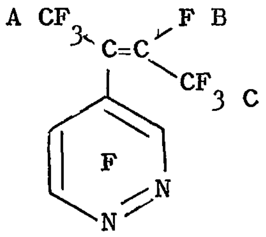
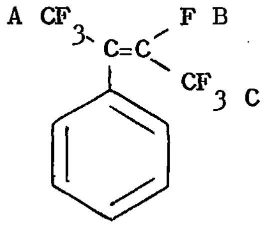
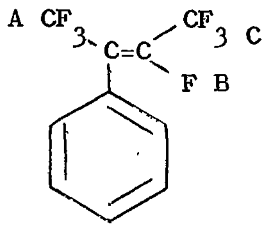


(47)

(b) Structure of the products obtained

The product (78) had satisfactory mass spectral and elemental analyses for a monosubstituted, perfluorobutenyl pyridazine. Resonances, in the ^{19}F n.m.r. spectrum of (78), at 78·4, 97·0 and 121·5 p.p.m., all intensity 1, were attributed to the 3,6 and 5 ring fluorines respectively. Similarly from coupling constant measurements other resonances at 61·5 and 70·5 p.p.m., both intensity 3, and a single resonance at 103·2 p.p.m., intensity 1, were attributed to the two CF_3 groups and the vinylic fluorine. Comparison of the observed couplings $J_{CF_3-CF_3}$ = 1 Hz and J_{CF_3-F} = 21 Hz, in the ^{19}F n.m.r. spectrum of (78) with those in Table 6, indicate a trans-configuration of the CF_3 groups. No coupling constants $J_{CF_3-CF_3}$ = 12 Hz and J_{CF_3-F} = 12 Hz for the corresponding cis arrangement were observed.

Table 6

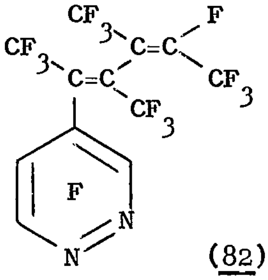
Compound	Coupling Constants Hz		
	J_{AB}	J_{AC}	J_{BC}
 (78)	21	1	7
 (80)	28	1·5	7
 (81)	12	12	7

Other evidence for (78) having the trans-configuration was obtained from the only weak absorption at 5·8μ, which is characteristic of a trans-substituted olefin. Confirmation of the overall structure of (78), was obtained from E.S.C.A. measurements, carried out in conjunction with Dr. D.T. Clark. Figure 5 shows the C_{1s} computer simulation for (78), and the assignments are shown in Table 7.

Table 7

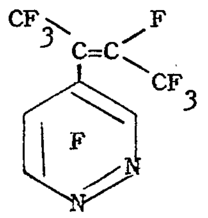
Peak	Intensity	C-assignment
A	2	CF_3 Carbon atoms
B	2	2,6 Ring carbon atoms
C	2	3 Ring carbon atom β-Vinylic carbon atom
D	2	4 Ring carbon atom α-Vinylic carbon atom

The structure of the second product, (79), proved to be more difficult. From mass spectrometry and elemental analysis, a molecular formula $C_{12}F_{16}N_2$ was deduced. Low resolution (60 MHz) ^{19}F n.m.r. measurements did not allow a positive structural assignment of (79) to be made. However, by analogy with the product, (44), obtained from the reaction involving pentafluoropyridine, hexafluorobut-2-yne and caesium fluoride, (4.2.1), an open chain structure, (82) was originally postulated.



(82)

C_{1s} Computer Simulation



(78)

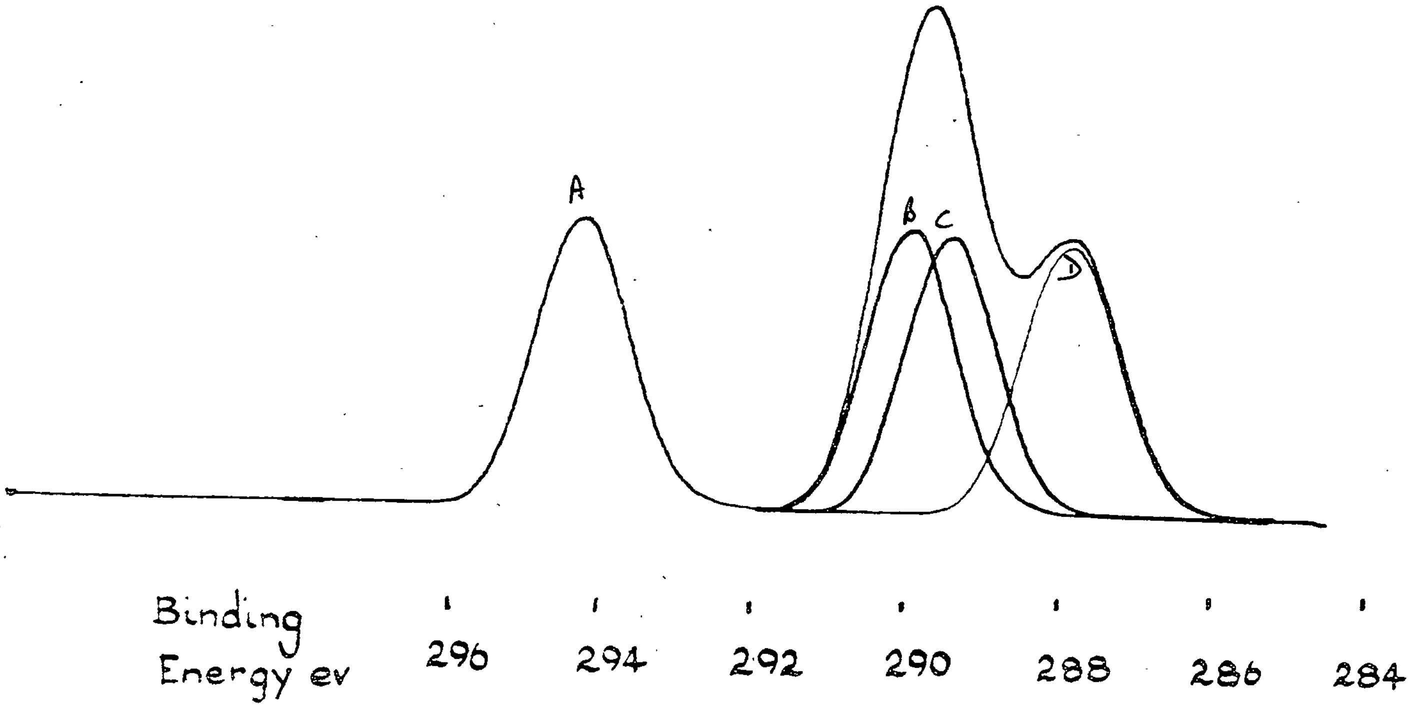
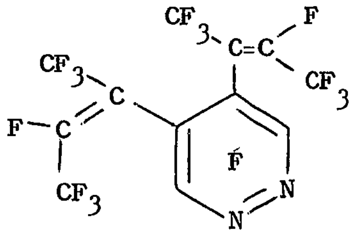


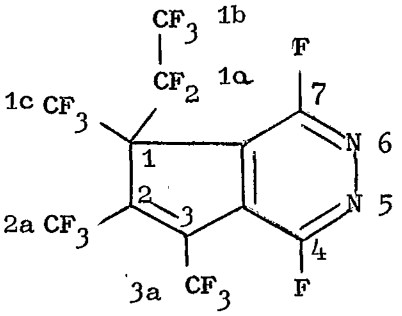
FIGURE 5

Later, using high resolution (100 MHz) ^{19}F n.m.r.[147], a resonance at 78·2 p.p.m. was attributed to the 3,6 ring fluorines. The absence of a resonance at approximately 120 p.p.m., corresponding to a 5 ring fluorine, indicated that (79) was in fact a di-substituted pyridazine. The possibility of a simple di-substituted product of the type (83)



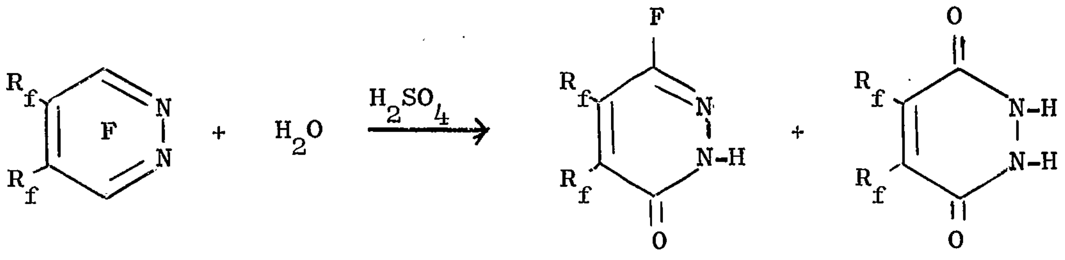
(83)

was eliminated, as the expected resonances in the ^{19}F n.m.r. spectrum did not occur. The possibility of a cyclic structure was then considered. Ultimately, the structure of (79) was shown to be the cyclic compound, perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, and to facilitate easier discussion, the structure and numbering of (79) are given first.



(79)

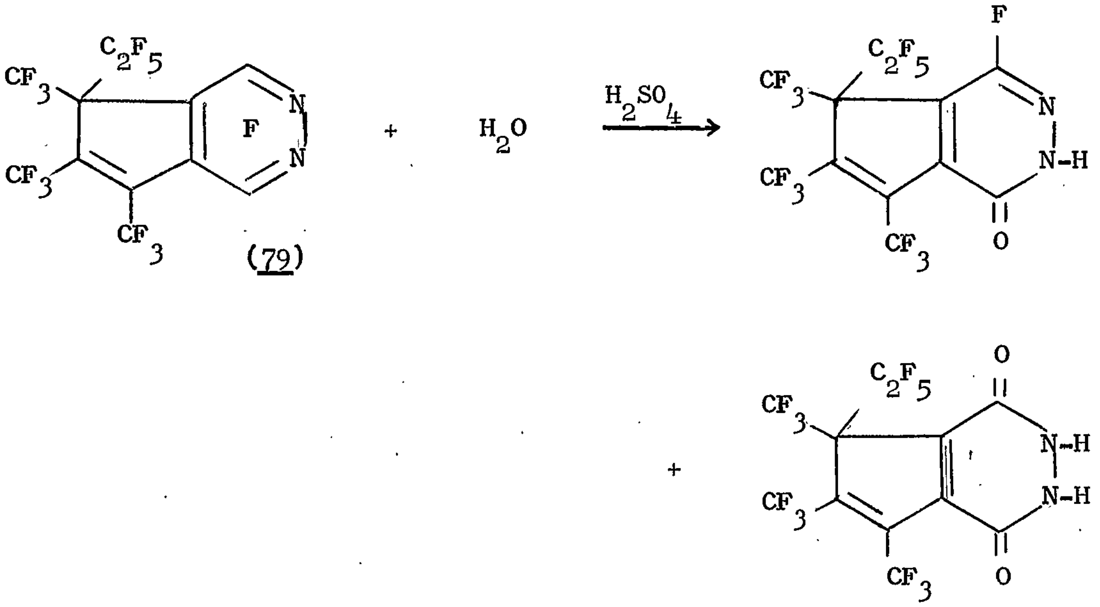
It was anticipated that replacement of the 3,6 ring fluorines by non-fluorinated species, would simplify the ^{19}F n.m.r. spectrum of (79) sufficiently to allow a complete structural analysis to be determined. Use was thus made of perfluoropyridazines ability to give different substitution patterns under different pH conditions. It has been demonstrated that when reactions are carried out under neutral or alkaline conditions, replacement of the 4,5 ring fluorines occurs, while under acidic conditions, replacement of the 3,6 ring fluorines predominates. Perfluoroalkyl pyridazines are known to readily undergo acid hydrolysis to yield the corresponding 3, and 3,6 dihydroxy derivative.[148]



(84) (85)

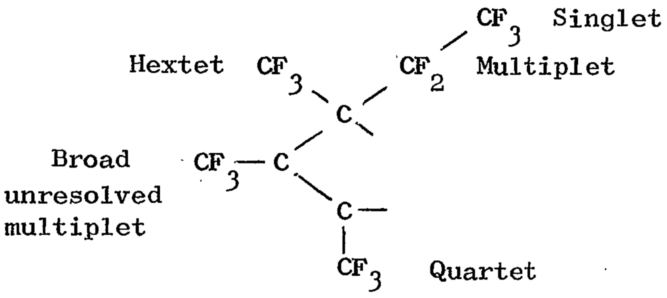
The products (84) and (85), have been shown to exist as pyridazones, rather than the tautomeric hydroxy pyridazines, by the presence of an N-H stretching band and a carbonyl band, in their i.r. spectra.

Thus when (79) was treated with sulphuric acid (5.3.1), two products (86) and (87) were isolated.

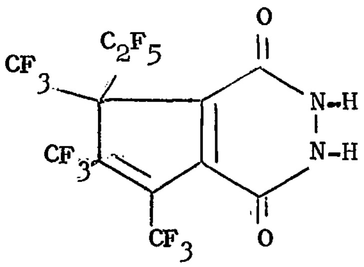


(79) (86) (87)

The ^{19}F n.m.r. spectrum of (87), possessed five separate resonances, integrating to give four CF_3 groups at 56·7, 57·2, 59·6 and 80·5 p.p.m. respectively and one CF_2 group (104·3 p.p.m.). The absence of a resonance at ≃ 78 p.p.m., attributed to the 4,7 ring fluorines in the parent compound (79), confirmed that replacement of these fluorines had occurred. Considering now the CF_3 absorption at 80·5 p.p.m. As this absorption appeared as a singlet at relatively high field with little or no fine structure, a CF_3CF_2-grouping was proposed as $J_{CF_3-CF_2}$ is usually very small. The remaining $3CF_3$ group resonances consisted of a quartet, sextet and a broad multiplet; therefore, assuming that coupling between adjacent CF_3 groups occurs, the configuration shown satisfies the evidence available.



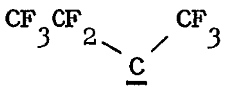
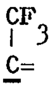
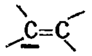
A broad line at 7·72 p.p.m. downfield of an external T.M.S. reference sample in the ^{1}H spectrum was assigned to the NH resonance expected. Therefore, from the ^{19}F and ^{1}H n.m.r. results the structure was shown to be 1,2,3-tris-(trifluoromethyl)-1-pentafluoroethyl-4,7-dihydroxy-5,6-diazaindene, (87).



(87)

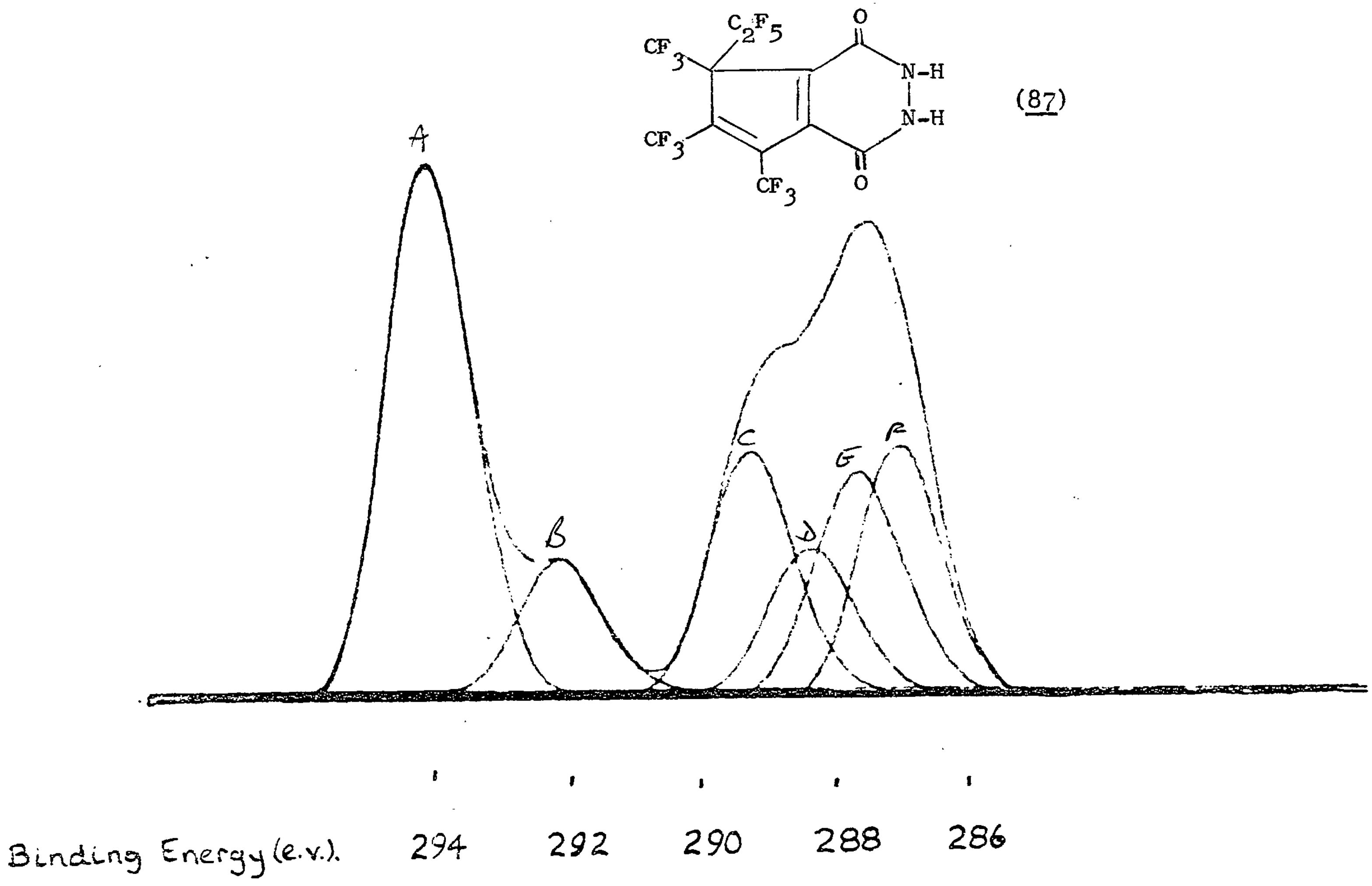
Mass spectral, elemental analysis and E.S.C.A. measurements (Figure 6, Table 8), were consistent with this structure.

Table 8

Peak	Intensity	C-assignment
A	4	$\underline{C}F_3$
B	1	$\underline{C}F_2$
C	2	$\underline{C}=O$
D	1	
E	2	 $\overset{CF_3}{\underline{C}}=$
F	2	 $\underline{C}=C$

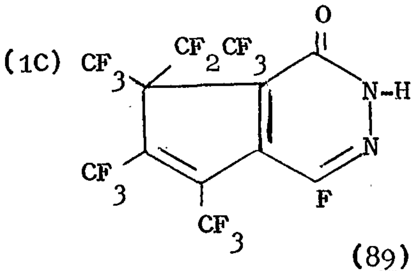
Considering now the structure of (86). The ^{19}F n.m.r. spectrum of (86) closely resembled that of (87), except for the addition of a broad absorption, equivalent to one fluorine and assigned to an aromatic C$\underline{F}$ group, at 94·3 p.p.m. The spectrum still contained a singlet CF_3 (82·0 p.p.m.) and broad multiplet, attributed to a CF_2 at 100·8 p.p.m., i.e. a CF_3CF_2- grouping. The remaining three CF_3 groups consisted of a broad multiplet (55·9 p.p.m.), an octet 60·1 p.p.m. and a quartet at 61·5 p.p.m. suggesting the same type of structure as (87). However, mass spectral and elemental analysis indicated a mono hydroxy derivative, which exists mainly as the amide form, and as such two structures are possible.

C_{1s} Computer Simulation



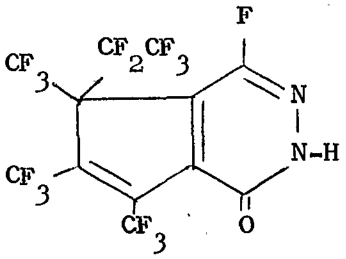
(87)

FIGURE 6



(89)

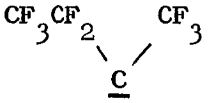
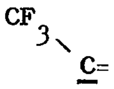
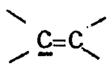
or



(86)

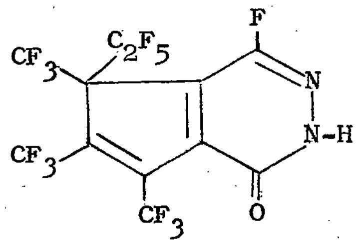
But as the (1C) CF_3 absorption is now an octet due to an additional single spin coupling, the structure was assigned to (86). Further evidence for this structure was obtained from E.S.C.A. measurements (Figure 7, Table 9).

Table 9

Peak	Intensity	C-assignments
A	4	$\underline{C}F_3$
B	1	$\underline{C}F_2$
C	1	$\underline{C}F$
D	2	$\underline{C}{=}O$
E	1	 $CF_3CF_2\diagdown\underline{C}\diagup CF_3$
F	2	 $CF_3\diagdown\underline{C}{=}$
G	2	 $>\underline{C}{=}C<$

The structure of the parent compound (79) now becomes apparent by comparison of ^{19}F n.m.r. spectra. Again CF_3 resonances at 54·9, 58·7, 60·8

C_{1s} Computer Simulation



(86)

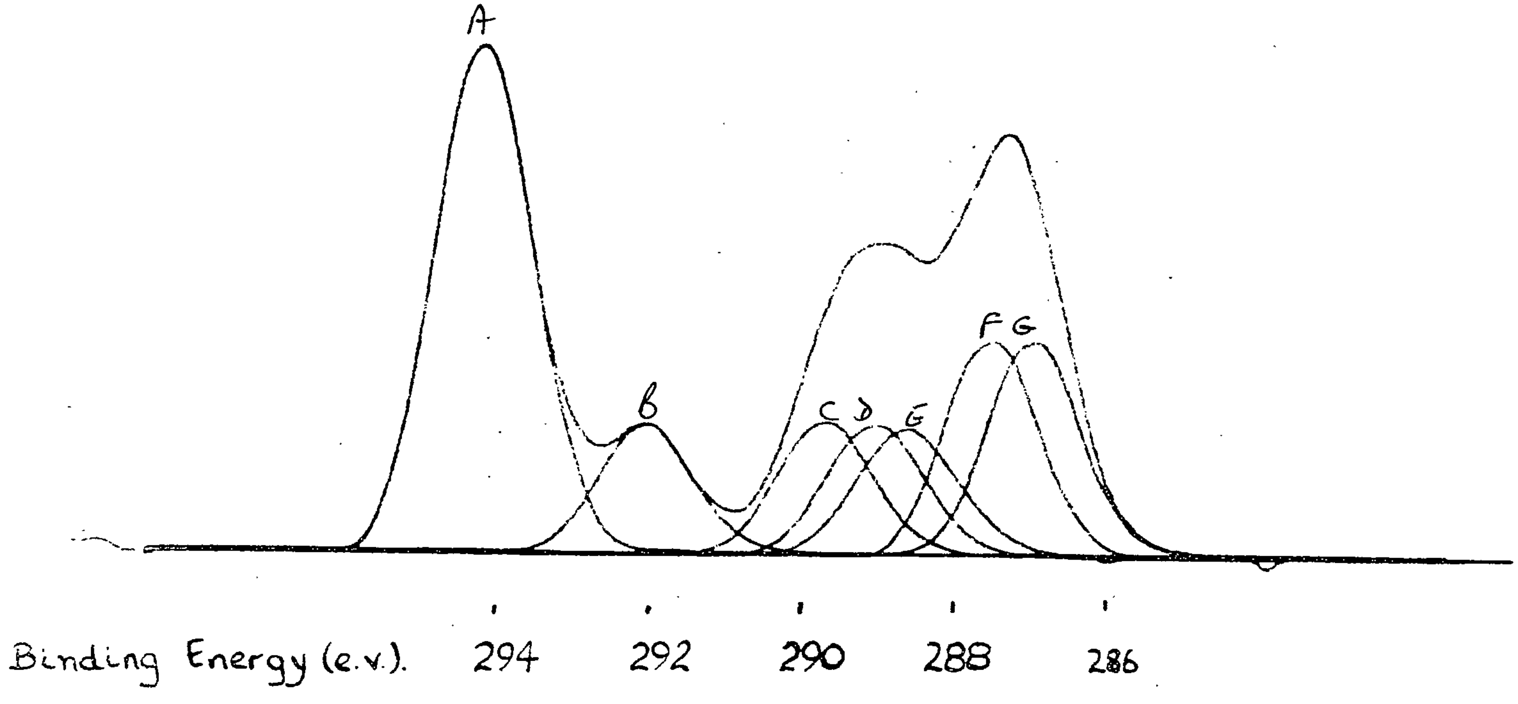
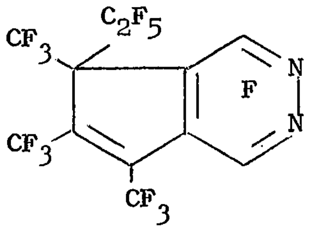


FIGURE 7

and 80·0 p.p.m. were observed and a CF_2 resonance at 106·8 p.p.m. A new resonance, integrating to 2 fluorines, at 78·2 p.p.m. was assigned to the 4,7 ring fluorines. Thus the structure of the parent compound was shown to be



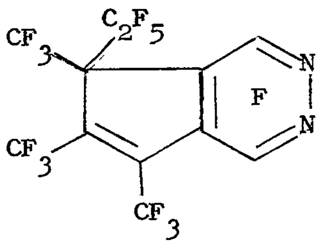
(79)

Again confirmation of the structure was obtained from E.S.C.A. measurements (Figure 8, Table 10).

Table 10

Peak	Intensity	C-assignment
A	4	$\underline{C}F_3$
B	1	$\underline{C}F_2$
C	2	$\underline{C}F$
D	1	$CF_3CF_2\diagdown\underline{C}\diagup CF_3$
E	2	$CF_3\diagdown\underline{C}=$
F	2	$>\underline{C}=C<$

C_{1s} Computer Simulation



(79)

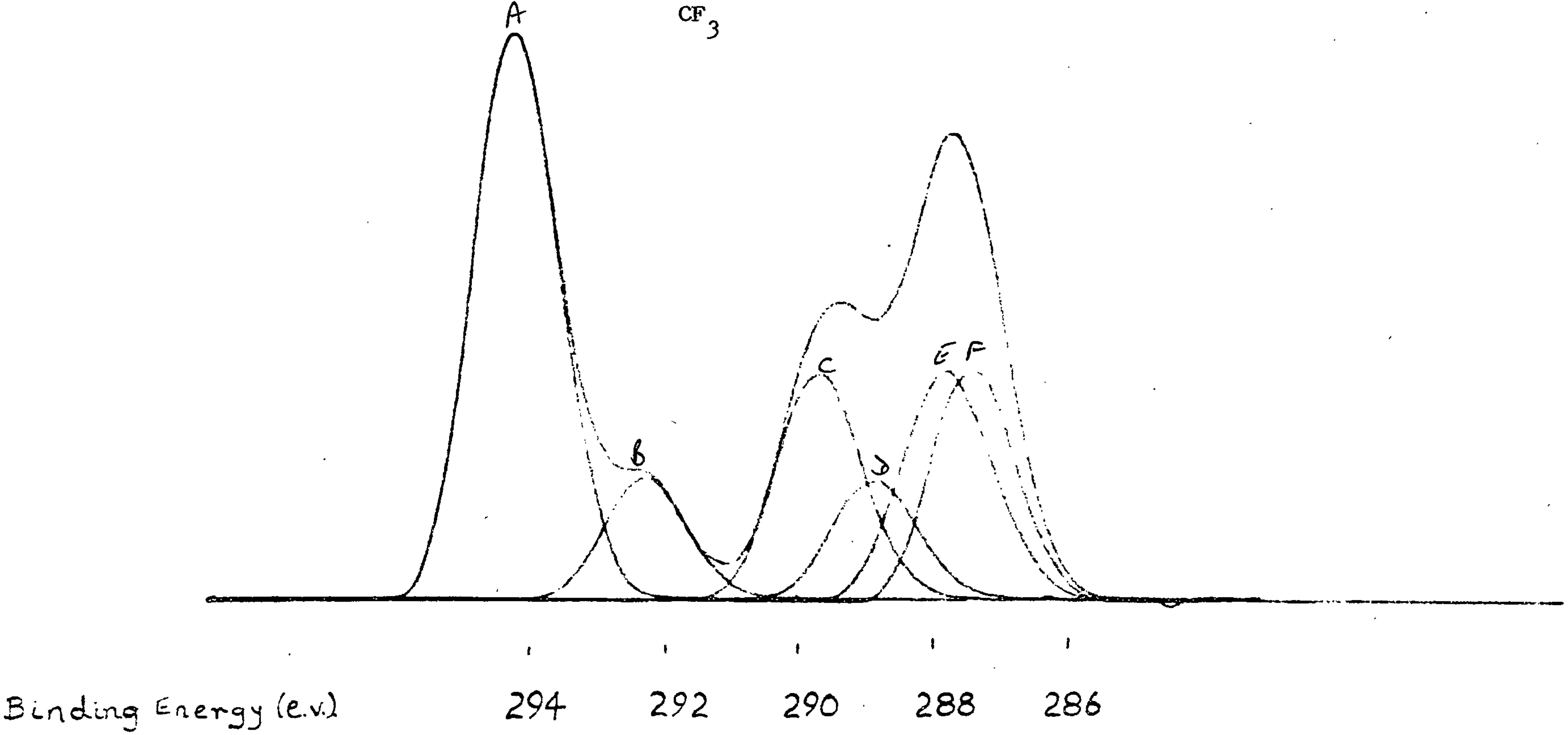
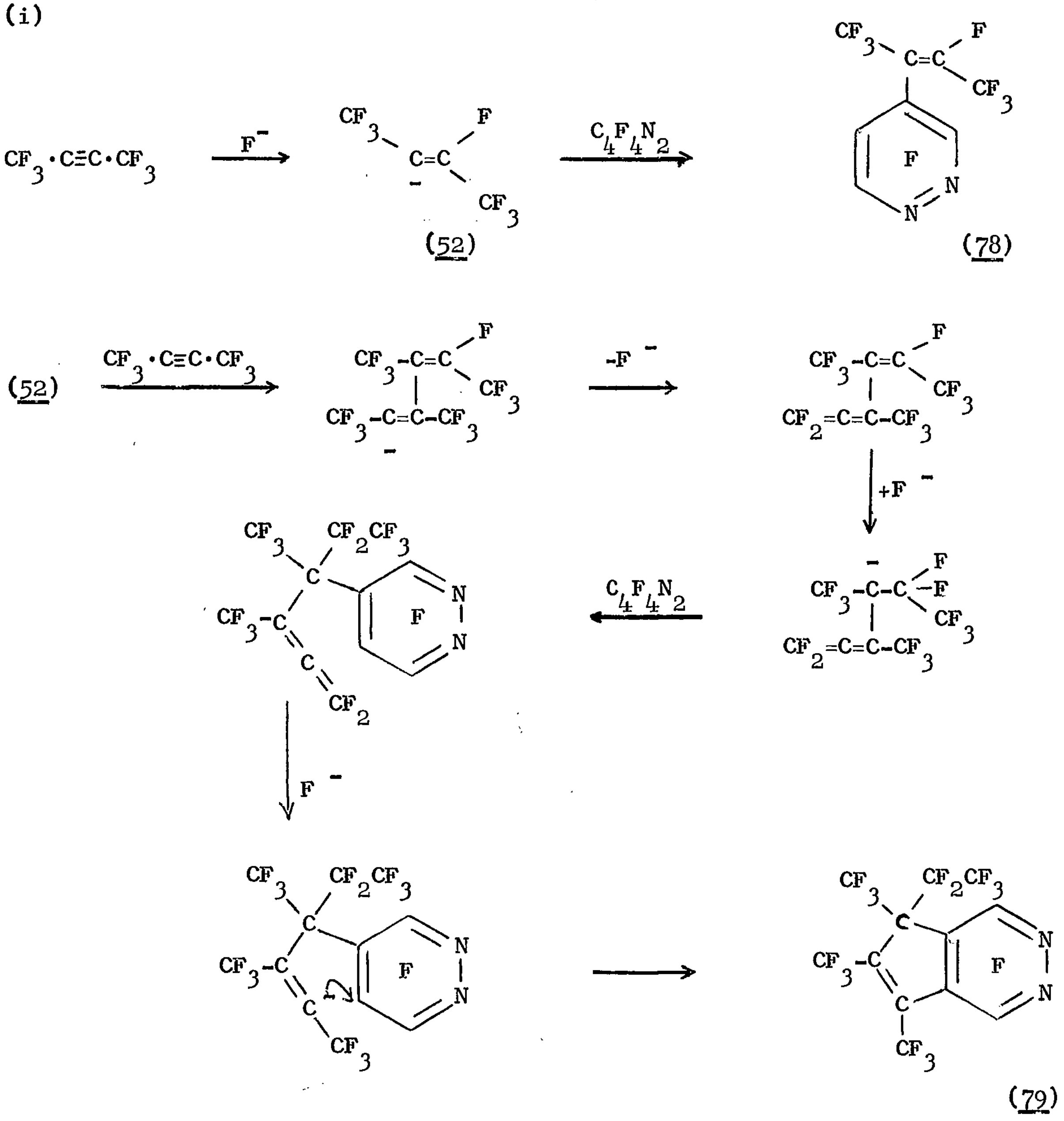


FIGURE 8

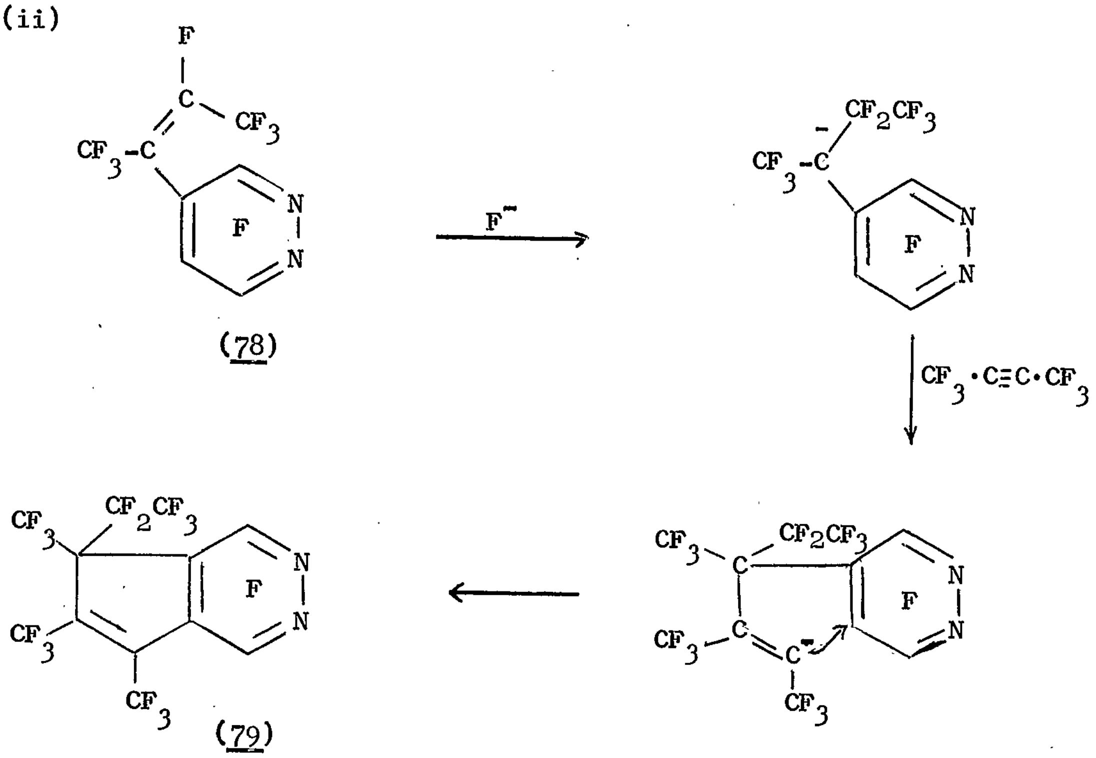
(c) Mechanism

The formation of (78) and (79) can occur via a similar mechanism to that discussed previously for the pentafluoropyridine derivatives (4.2.1). Alternative mechanisms are annexed below.

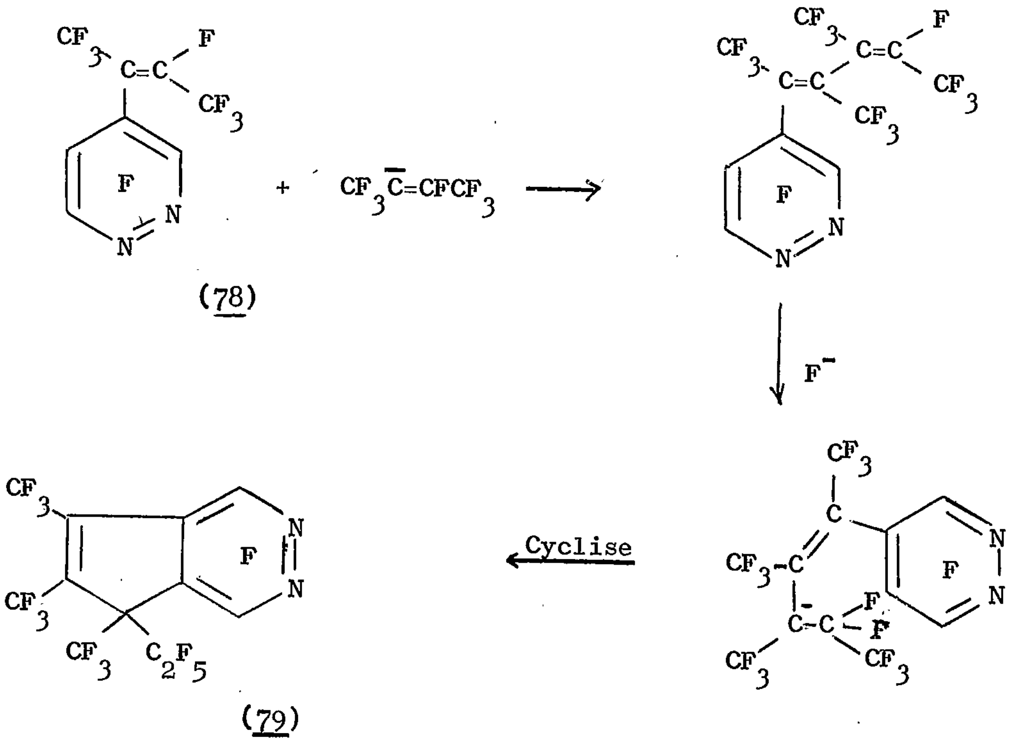
(i)



or (ii)



or (iii)

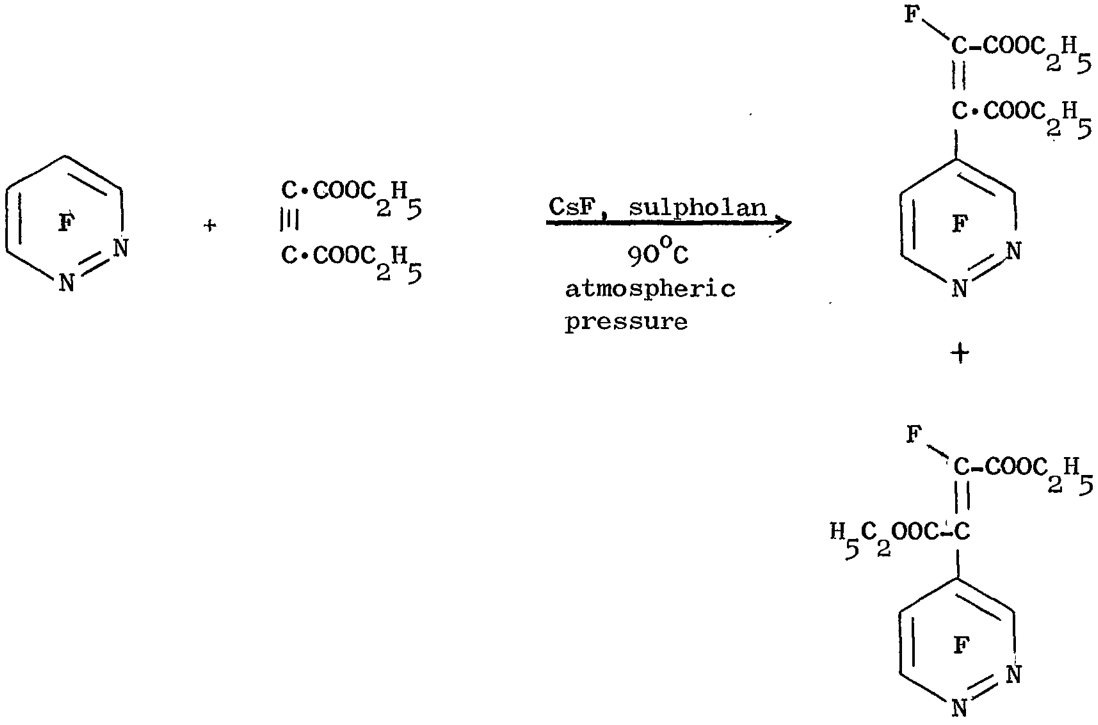


In order to establish whether the formation of (79) involved (78), a reaction was carried out in which hexafluorobut-2-yne was reacted with (78) under fluoride ion conditions, using a static atmospheric pressure system (5.1.1). A reasonable yield (50%) of the cyclic product (79) was obtained, suggesting that mechanisms concerning (78) are involved in the formation of (79). Other evidence, supporting the reactivity of the vinylic fluorine, has been found in nucleophilic substitution reactions involving (78), and previously (4.4.2) with perfluoro-4-(2'-butenyl)pyridine (43). Thus on this basis, the formation of (79) may occur largely through mechanism (iii).

5.1.2 With diethylacetylene dicarboxylate

(a) Reaction conditions and product

Using similar conditions to those reported previously (4.2.3), diethylacetylene dicarboxylate, was added dropwise to a rapidly stirred suspension of tetrafluoropyridazine, caesium fluoride and sulpholan and a cis/trans mixture, 40:60, of the corresponding monosubstituted pyridazines, (90) and (91), isolated.



(90)

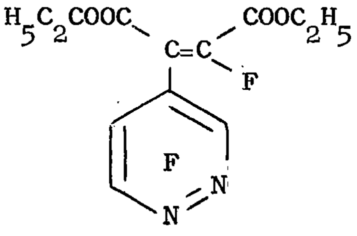
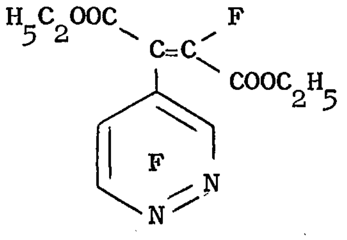
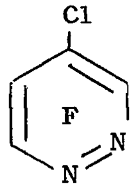
(91)

(b) Structure of the product

The identification of the cis and trans isomers was effected using ^{19}F n.m.r. It was believed that for the trans isomer, the single vinylic fluorine would have little or no effect on the 3,5 ring fluorines and hence resonance patterns similar to those expected in, for example, 4-chloro-3,5,6-trifluoropyridazine (92), should be observed. Thus, resonance patterns at 79·5, 99·0 and 123·0 p.p.m., in the ^{19}F n.m.r. spectrum of the mixture, which were similar to those at 85·5, 100·1 and 129·5 p.p.m. observed for (92).

Conversely, for the cis isomer, the vinylic fluorine can now interact 'through space' with the 3,5 ring fluorines, leading to broad resonances which were observed at 77·5, 98·2 and 121·0 p.p.m. The results are summarise in Table 11.

Table 11

Compound	Chemical Shift (p.p.m.)	Intensity	Assignment
 (90)	77·5	1	3 Ring F
	95·0	1	=C$\underline{F}$
	98·2	1	6 Ring F
	121·0	1	5 Ring F
 (91)	79·5 J_{3-6} 30 Hz	1	3 Ring F
	95·2	1	=C$\underline{F}$
	99·0 J_{6-3} 30 Hz	1	6 Ring F
	123·8 J 24 Hz	1	5 Ring F
 (92)	85·5 J_{3-6} 30 Hz	1	3 Ring F
	100·1 J_{6-3} 30 Hz	1	6 Ring F
	129·5 J 24 Hz	1	5 Ring F

5.2 Reactions involving perfluoro-4-(2'-butenyl)pyridazine

5.2.1 With hexafluorobut-2-yne

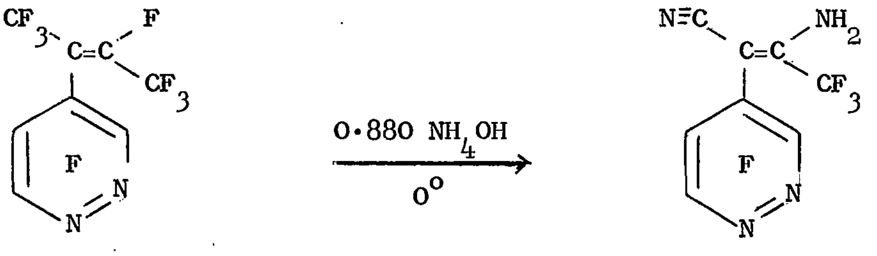
(a) Reaction conditions and product

When perfluoro-4-(2'-butenyl)pyridazine, (78), was reacted with hexafluorobut-2-yne in the presence of caesium fluoride and sulpholan, using a static atmospheric pressure system, a white crystalline product was isolated which had an identical i.r. spectrum with that of perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (79).

5.2.2 Nucleophilic substitution with ammonia

(a) Reaction conditions and product

When perfluoro-4-(2'-butenyl)pyridazine, (78), was added dropwise to rapidly stirred aqueous ammonia (·880) at 0°, a white crystalline solid readily separated.



(78) (93)

(b) Structure

The product (93) which had satisfactory elemental and mass spectral analyses, was too insoluble for a detailed ^{19}F n.m.r. spectrum to be carried out; only a single peak, corresponding to the CF_3 group, 68·9 p.p.m., was observed. However, from i.r. spectroscopy, the presence of the -C≡N and $-NH_2$ groups were confirmed by absorption at 4·5μ and 3·1μ respectively. A similar product has also been isolated with perfluoro-4-(2'-butenyl)pyridine (4.4.3).

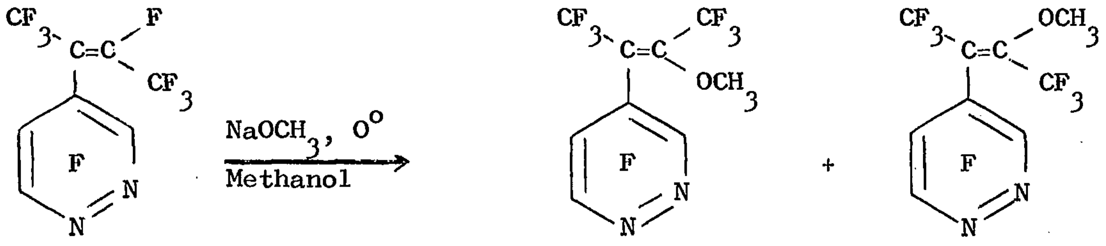
(c) Mechanism

A possible mechanism for the formation of a product similar to (93) has been discussed previously (4.4.3).

5.2.3 Nucleophilic substitution with methoxide ion

(a) Reaction conditions and products

Using similar conditions to those reported previously (4.4.2), sodium methoxide solution was added dropwise to a solution of perfluoro-4-(2'-butenyl)pyridazine in dry methanol at 0°C. A *cis/trans* mixture (66:34) of mono-methoxy products (94) and (95) was obtained



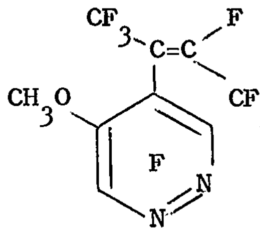
(78) (94) (95)

(b) Structure

Although the products were not separated, mass spectral measurements carried out on the reaction mixture, indicated that a mono-methoxy derivative had been formed. From results obtained previously on the corresponding perfluoropyridine derivative (43), (4.4.3), a *cis/trans* mixture of products was anticipated. However, in perfluoro-monosubstituted pyridazine derivatives, the 5 ring fluorine atom is still extremely susceptible to nucleophilic attack and as such, the possibility of a ring substituted product was also considered.

From ^{19}F n.m.r. measurements carried out on the reaction mixture, peaks at 56·51 and 64·10, both intensity 3, were assigned to two *cis* CF_3 groups, $J_{CF_3-CF_3}$ 12·3 Hz. Peaks at 60·50 and 65·14, intensity 3 and having little or no fine structure were assigned to the *trans* CF_3 groups. Broad absorptions at

60·98, 82·89 and 90·43, all intensity 2, were assigned to the 3,6 and 5 ring fluorines respectively. The ratio of the cis:trans isomers (66:34) was obtained from a comparison of the integration values obtained for the cis and trans CF_3 group absorptions. No evidence observed for the formation of any ring substituted products similar to (96).



(96)

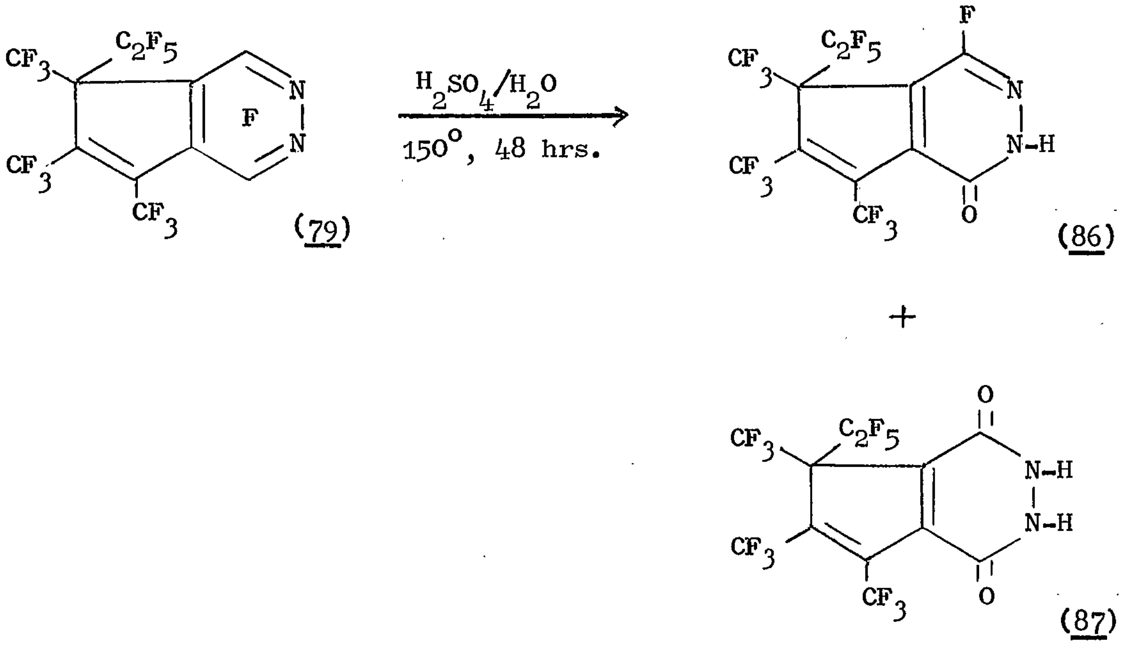
5.3 Reactions involving perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene

5.3.1 With sulphuric acid

(a) Reaction conditions

Under strongly acidic conditions, nucleophilic attack on tetrafluoropyridazine by water leads to substitution of the fluorine atoms at C-3 and C-6[148], in contrast to those at C-4 and C-5, which are more reactive towards nucleophilic reagents under basic conditions.

Thus, when (79) was heated in concentrated sulphuric acid to which a few drops of water had been added, at 150° for 48 hrs., two products were isolated.

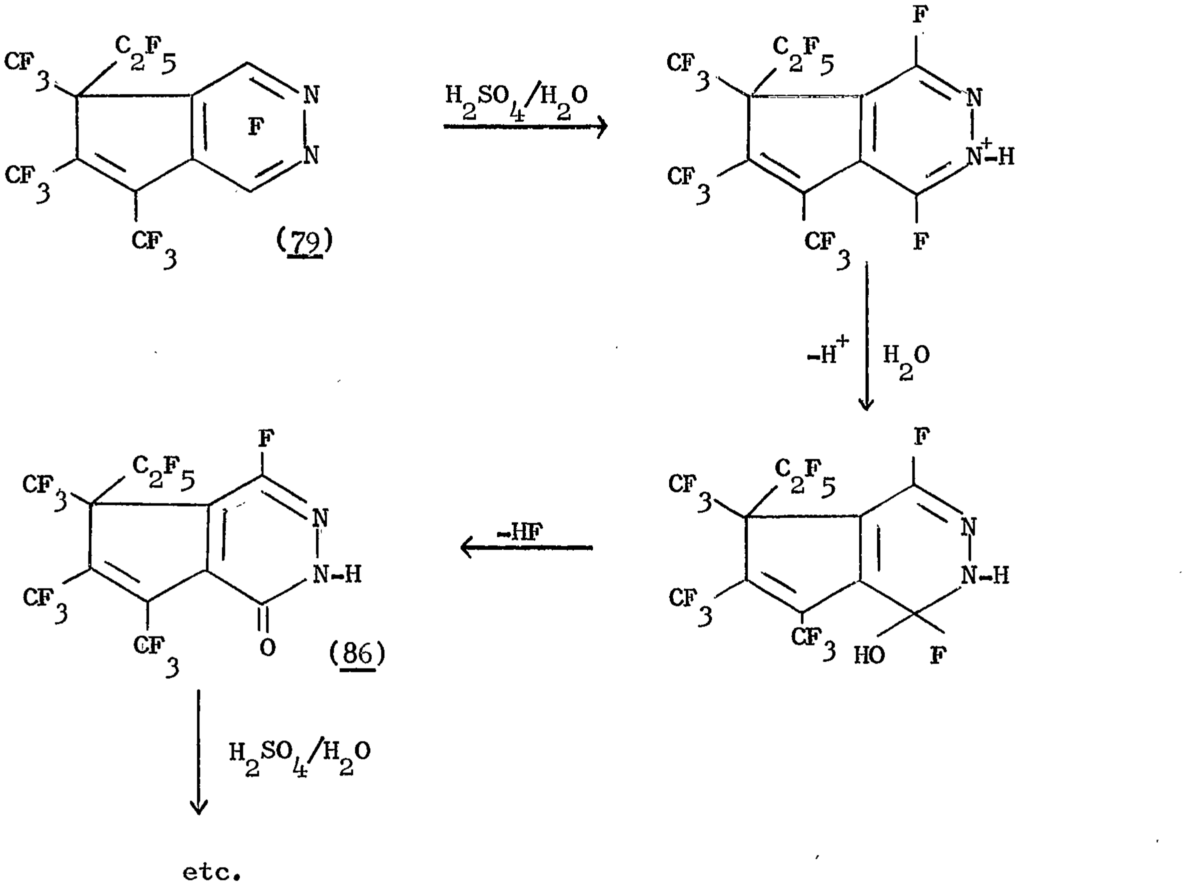


(b) Structure

The structure of the products, (86) and (87), have been discussed previously (5.1.1). Both (86) and (87) had satisfactory mass spectral and elemental analyses.

(c) Mechanism

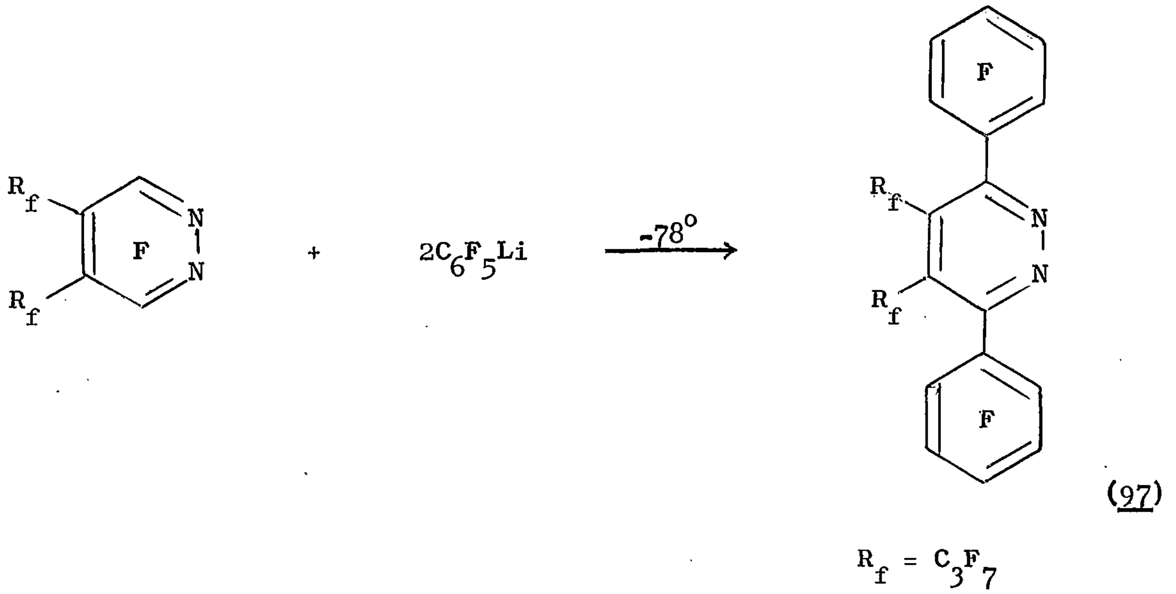
The formation of the two pyridazones (86) and (87) may possibly be formed via the following mechanism:



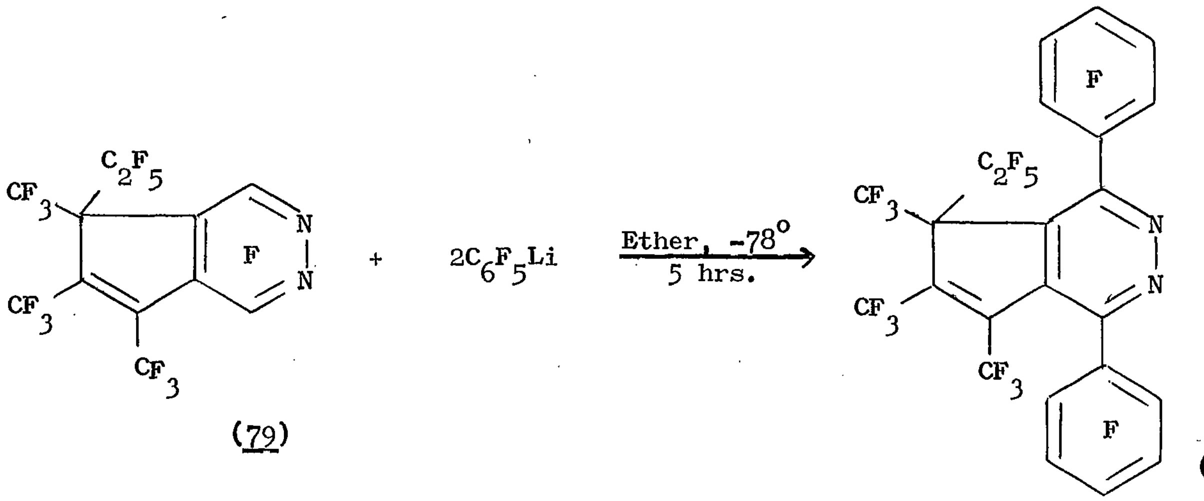
5.3.2 With two equivalents of pentafluorophenyl lithium

(a) Reaction conditions and product

Di-substituted pyridazines are known to react with two molecular proportions of pentafluorophenyl lithium to give the corresponding tetra-substituted derivatives.[149]



Thus, when the cyclic product (79) was treated with two equivalents of pentafluorophenyl lithium, a white crystalline solid, (98), believed to have the structure shown, was isolated.



(98)

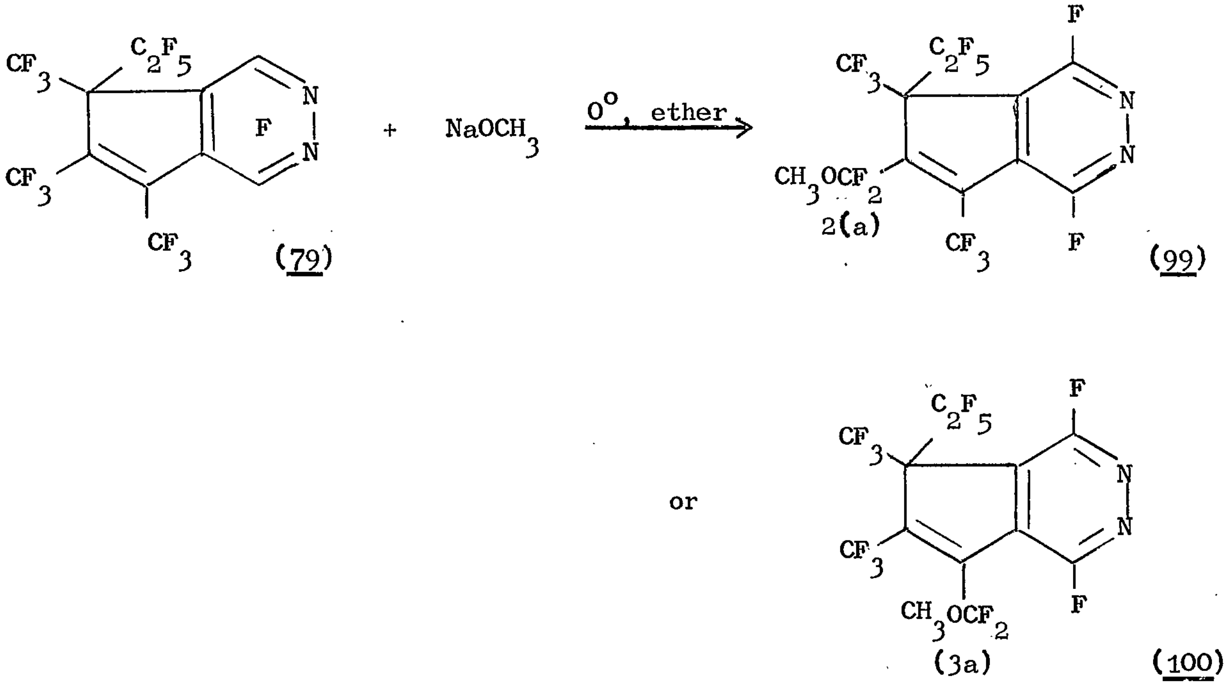
(b) Structure

The product (98), had satisfactory elemental and mass spectral analyses. However, although (98) was found to be almost insoluble in solvents suitable for ^{19}F n.m.r. measurements and only weak resonances were observed, it is believed that (98) has the probable structure shown.

5.3.3 With sodium methoxide

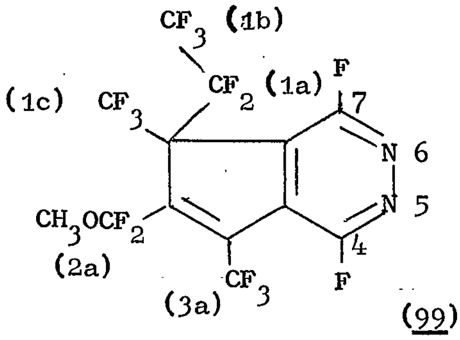
(a) Reaction conditions

When perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene was reacted with sodium methoxide solution at 0°, a white crystalline mono-methoxy derivative was isolated.



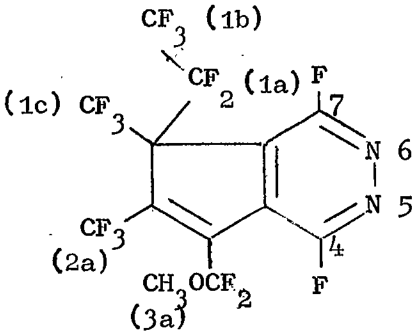
(b) Structure

The mono-methoxy derivative of (79) had satisfactory elemental, and mass spectral analyses. From ^{19}F n.m.r. measurements, resonances at 74·6 and 82·1 p.p.m. were attributed to the 3,6 ring fluorines respectively. Further, the spectrum now contained only three CF_3 group and two CF_2 group resonances, indicating that replacement of a fluorine by a methoxyl residue had occurred at either CF_3 group (2a) or (3a).



(99)

and

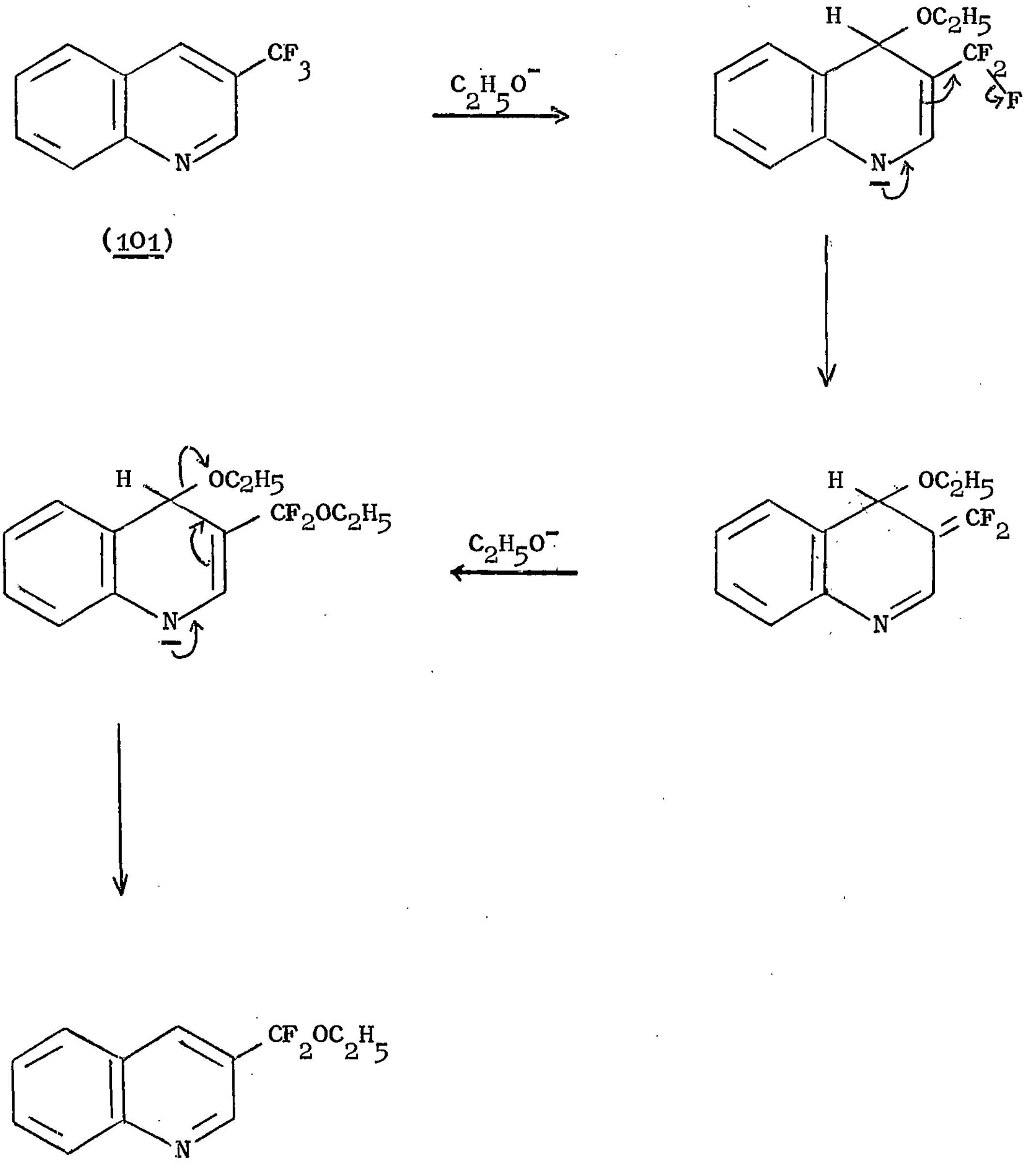


(100)

The remaining CF_3 groups (1c) and (1b) were unaffected. No additional information could be obtained from J values due to the broad resonances observed.

(c) Mechanism

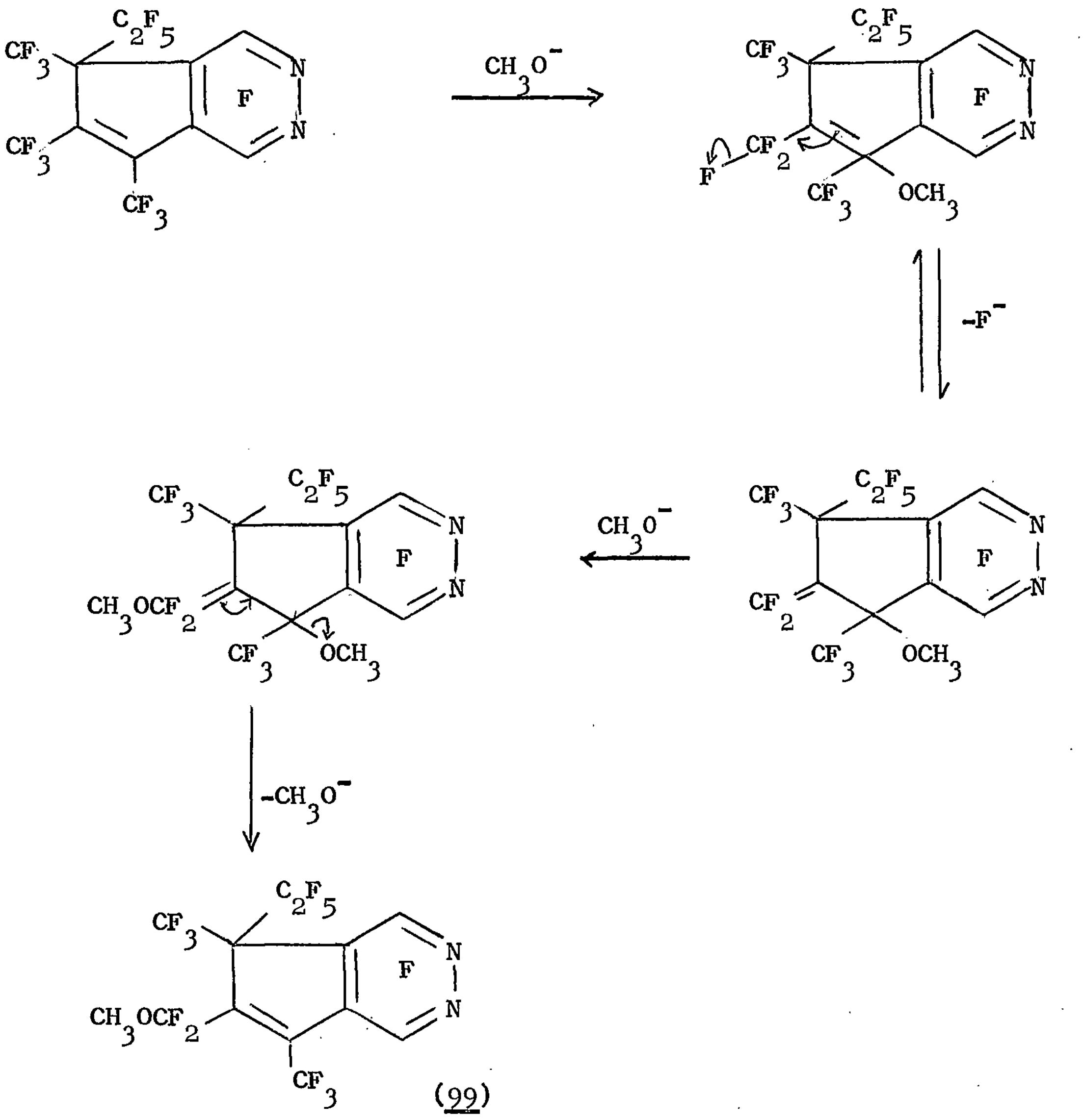
Recently, Kobayashi and co-workers[150] have shown that similar replacements of fluorine in CF_3 groups occur in perfluoroquinoline derivatives.



(101)

(102)

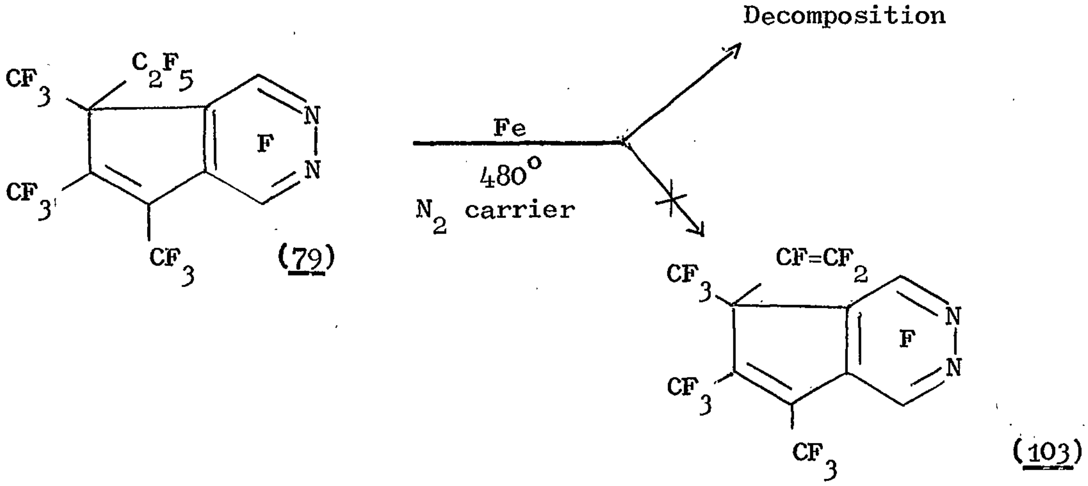
Thus applying a similar mechanism here:



(99)

5.3.4 Defluorination

When perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene (79) was passed over heated iron at a variety of temperatures using dry nitrogen as a carrier in an attempt to form a vinyl compound, complete decomposition of the starting material occurred. Attempts to minimise the decomposition by lowering the temperature and decreasing the contact time, had little effect.



(79)

(103)

5.3.5 Pyrolysis

Similar results to the defluorination reactions described above, were obtained when the cyclic product (79) was passed through a heated silica tube (600°) packed with silica wool, in a vacuum transfer system. However when nitrogen was used as a carrier at 400°, starting material was recovered.

5.3.6 Photolysis reactions

When a photolysis reaction was carried out on (79) in a silica tube, using a medium pressure u.v. lamp for 6 days, complete decomposition of the starting material occurred. Using shorter reaction times i.e. 3 days, some recovery of the starting material was possible although decomposition of (79) still occurred. Attempts to photolyse only the gaseous phase by shielding the solid phase led to higher recoveries of the starting material. No other products were isolated in any of the above reactions.

Other photolysis reactions carried out on (79) using vacuum transfer systems in both pyrex and silica glassware and using u.v. light of specific wavelengths, are still being evaluated.[151]

CHAPTER 6

Other Routes to Perfluoroalkenyl Heterocyclic Compounds

Introduction

It has been demonstrated in the previous chapters, that perfluoroalkenyl pyridines and pyridazines are formed when perfluorobut-2-yne and the heterocycle compound are reacted together under suitable fluoride ion conditions. However, yields are low and, in the case of the perfluoropyridine derivatives, the isolation of the products from the reaction mixture is difficult.

An alternative route leading to unsaturated perfluoroheterocyclic derivatives, has been used recently at the University of Durham, and involves defluorination of perfluoroalkyl heterocyclic compounds using an iron catalyst.

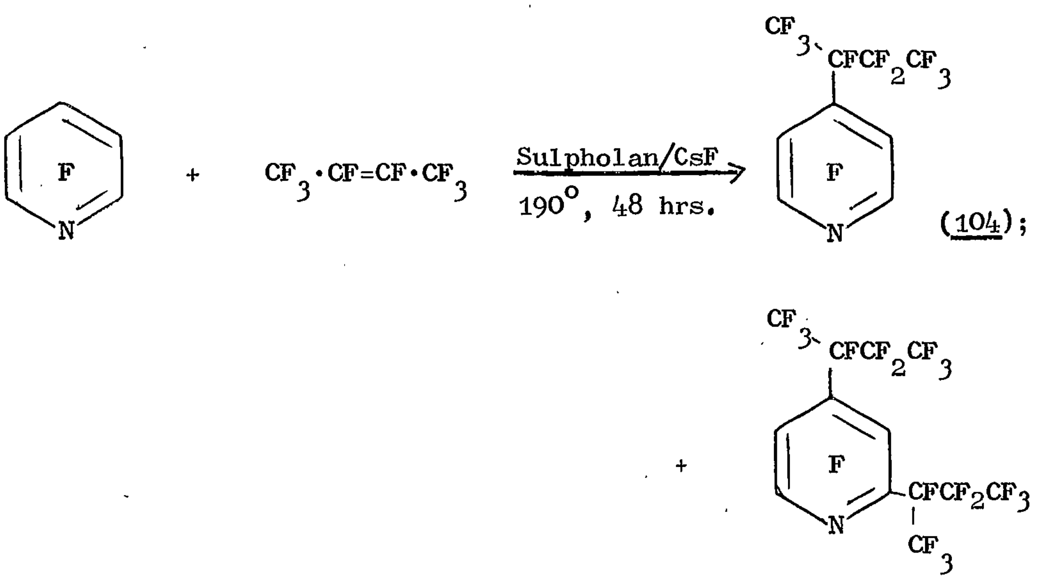
Thus it has now been shown that defluorination of perfluoro-sec-butylpyridine and perfluoro-sec-butylpyridazine compounds, leads to higher yields of perfluoro-4-(2'-butenyl)pyridine and perfluoro-4-(2'-butenyl)pyridazine. The preparation of the corresponding perfluoro-sec-butyl compounds and their subsequent defluorination are described in this chapter. In addition, preliminary attempts to form similar unsaturated compounds, in reactions involving perfluorobutenyl lithium and heterocyclic compounds, are also described.

6.1 Reactions of octafluorobut-2-ene with perfluoroheterocyclic compounds

6.1.1 With pentafluoropyridine

(a) Reaction conditions and products

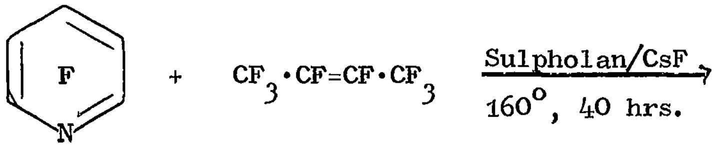
The reaction of pentafluoropyridine and octafluorobut-2-ene in a fluoride ion-process has been previously described[40] using a large excess of the perfluoro-olefin, elevated temperatures and long reaction times.



(104); 50%

(105); 30%

Using lower temperatures, and only a slight excess of the olefin, high yields of (104) were obtained

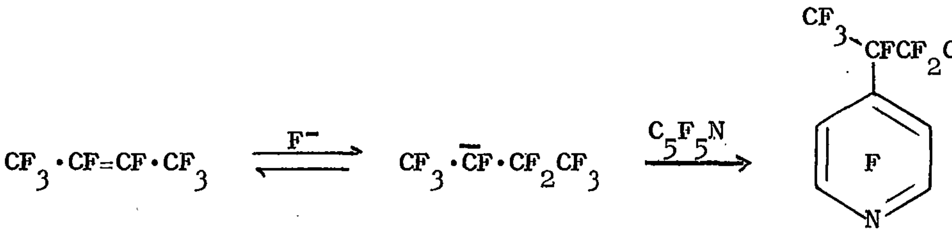


(104); 70%
and (105); 15%

(b) Structure

The two products (104) and (105) had identical i.r. spectra with those reported[40] for perfluoro-4-sec-butylpyridine and perfluoro-2,4-bis-sec-butylpyridine respectively.

(c) Mechanism



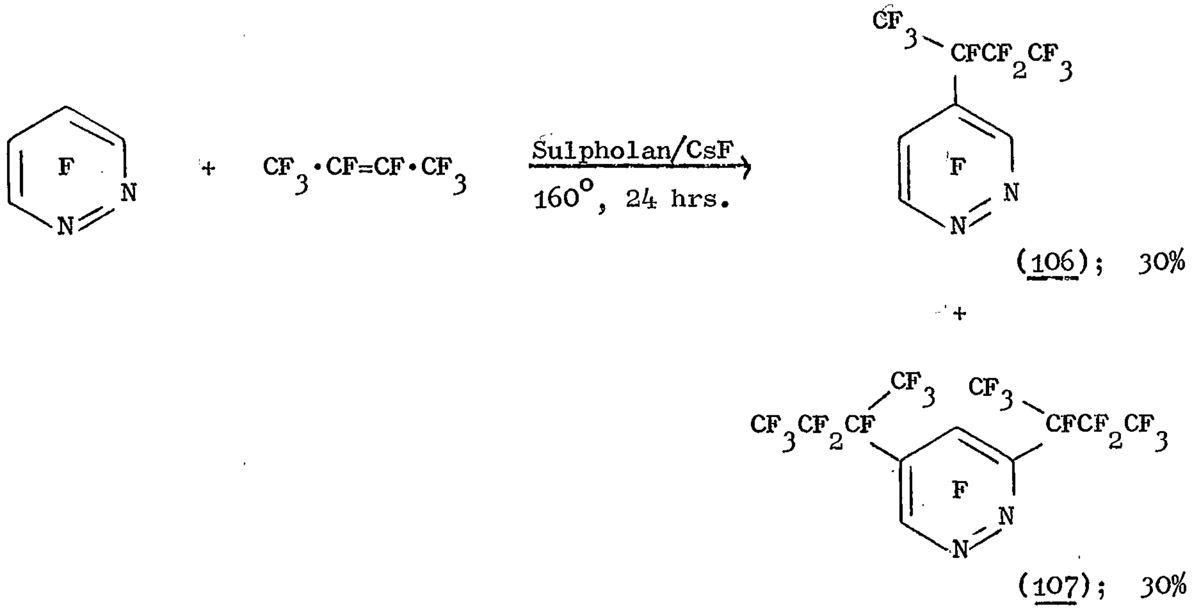
(104)

$$(104) \; + \; CF_3\cdot\bar{C}F\cdot CF_2CF_3 \longrightarrow (105)$$

6.1.2 With tetrafluoropyridazine

(a) Reaction conditions and products

Using similar conditions to those reported previously (6.1.1), tetrafluoropyridazine reacted with octafluorobut-2-ene to form perfluoro-4-sec-butylpyridazine (106) and perfluoro-3,5-bis-sec-butylpyridazine (107).



(b) Structure of products

Both (106) and (107) had satisfactory elemental and mass spectral analyses.

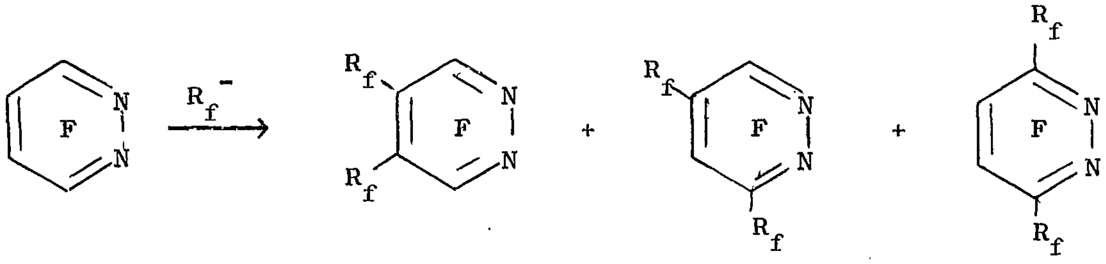
From ^{19}F n.m.r. data, the product (106) was shown to be a 4-substituted perfluoro-sec-butylpyridazine, having resonances at 71•2, 97•8 and 121•3 p.p.m., each intensity 1, assigned to the 3,6 and 5 ring fluorines respectively from coupling constant measurements. Two resonances at 72•7 and 82•2 p.p.m., intensity 3, were attributed to the two CF_3 groups. Other resonances at 121•0 and 182•5 p.p.m. were assigned to the $-CF_2$ and -CF groups respectively.

Similarly, (107) was shown to be a 3,5 di-substituted product. Thus resonances at 69•1 and 102•9 p.p.m. in the ^{19}F n.m.r. spectrum, each intensity 1, were attributed to the 6 and 4 ring fluorines respectively, while resonances at 73·9 and 82·3 p.p.m. were assigned to the four CF_3 groups. A resonance at 121·0 p.p.m. was assigned to the two CF_2 groups and two resonances at 181·5 and 187·0 p.p.m. were attributed to the two CF groups.

(c) Mechanism

The monosubstituted product, (106), may be formed via a mechanism similar to that discussed previously (6.1.1).

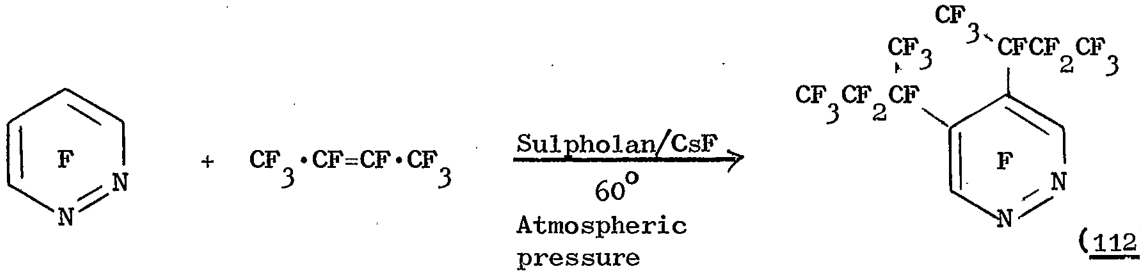
For the disubstituted product, (107), the possibility of forming a kinetic or thermodynamically controlled product can arise. In a recent communication Chambers and co-workers report[152] that a transition can occur from the kinetically controlled product to the thermodynamically controlled product in the following series.



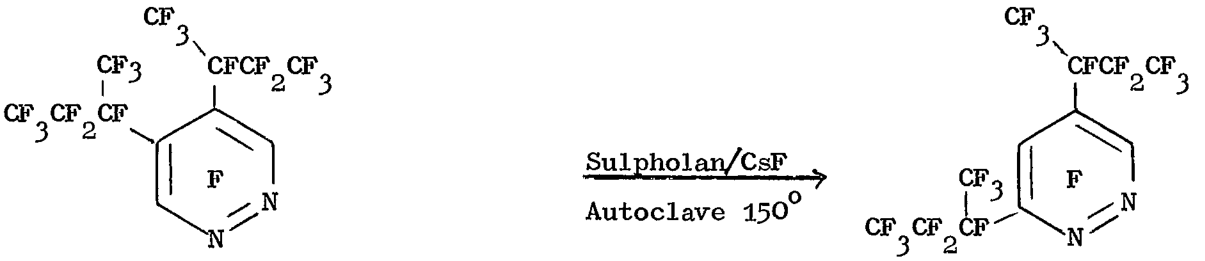
R_f = CF_3CF_2	(108)		
R_f = $(CF_3)_2CF$	(109)	(110)	
R_f = $(CF_3)_3C$			(111)

From $CF_3CF_2^-$, isomer (108) was formed exclusively and was not rearranged by fluoride ion even up to 150°; $(CF_3)_2CF^-$ gave (109) which gave a mixture of (109) and (110) on heating with fluoride ion; while $(CF_3)_3C^-$ gave only (111). They explain the last result in terms of a minimisation of steric interaction when both of the bulky $(CF_3)_2CF$ groups are adjacent to a ring nitrogen rather than flanked by fluorine atoms attached to the ring. Thus the formation of perfluoro-3,5-bis-sec-butylpyridazine can be explained in terms of a minimisation of steric interactions when the groups are in the 3,5 as opposed to the 4,5 position. Under the reaction conditions used, any 4,5 product formed would rearrange to give the 3,5 product (107).

K.C. Srivastava, in this laboratory has shown that perfluoro-4,5-bis-sec-butylpyridazine, (112), is formed when octafluorobut-2-ene reacts with tetrafluoropyridazine in an atmospheric fluoride ion process at 60° and that (112) will rearrange when heated with fluoride ion in sealed tubes at elevated temperatures, to the corresponding 3,5 isomer (107).



(112)

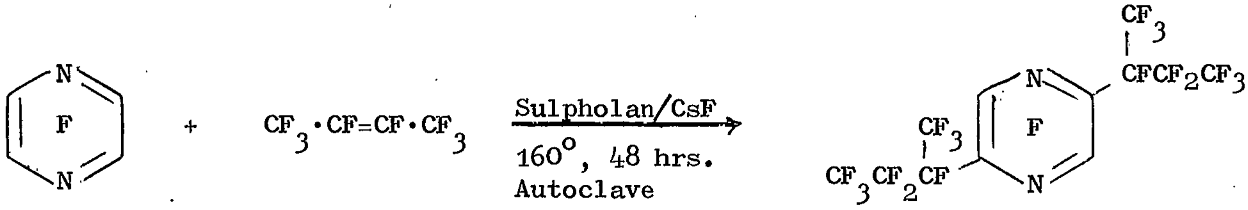


(112) (107)

6.1.3 With tetrafluoropyrazine

(a) Reaction conditions and products

When octafluorobut-2-ene, tetrafluoropyrazine, sulpholan and caesium fluoride, were heated together in a sealed tube, perfluoro-2,5-bis-sec-butylpyrazine (113) was the only product formed.



(113); 80%

(b) Structure

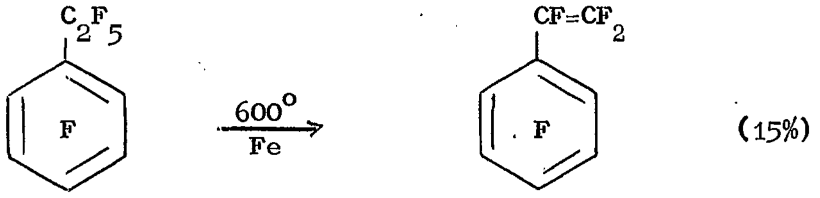
The product, (113), had satisfactory elemental and mass spectral analyses. From ^{19}F n.m.r. spectroscopy, the presence of two perfluoro-sec-butyl groups was confirmed. Further, by comparing the value of a single resonance at 76·6 p.p.m., intensity 2, to that of 76·66 p.p.m., assigned to the 2,5 ring fluorines in perfluoro-2,5-bis-isopropylpyrazine[151], the positions of substitution were ascertained in (113).

(c) Mechanism

The formation of (113) can occur by a similar mechanism to that discussed previously (6.1.1).

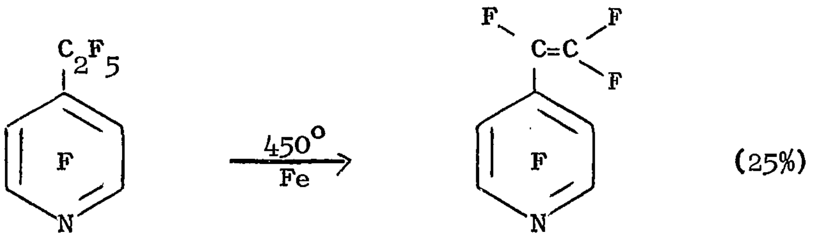
6.2 Defluorination reactions of some perfluoro-sec-butyl heterocyclic compounds

Initially, Tatlow and co-workers, using defluorination techniques, showed that unsaturated perfluoroaromatic compounds could be prepared using defluorination techniques.[153-155]

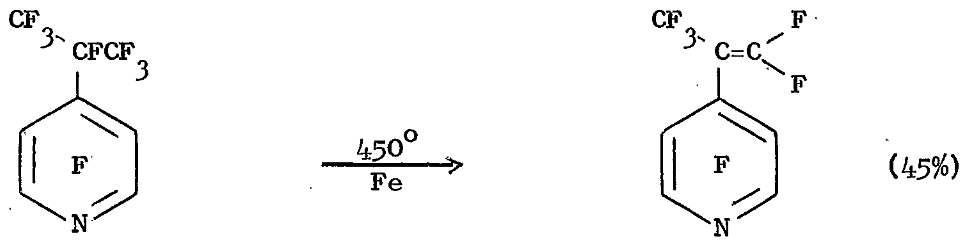


(114) (115)

More recently, it has been shown that defluorination of perfluoroalkyl pyridines leads to the corresponding unsaturated product.[42]



(48) (71)



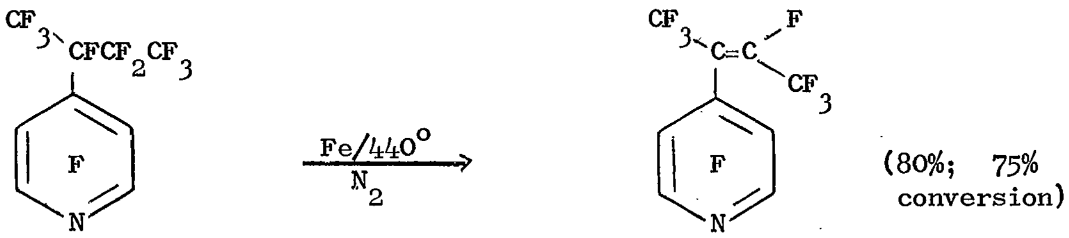
(116) (117)

Using similar conditions, the defluorination of perfluoro-sec-butyl compounds, have now been examined.

6.2.1 Perfluoro-4-sec-butylpyridine

(a) Reaction conditions and products

Several reactions were carried out at various temperatures to determine the best condition for this defluorination. Thus, when perfluoro-4-sec-butylpyridine was passed over heated iron at 440°, perfluoro-4-(2'-butenyl) pyridine (43) was formed in high yield. Recycling the reaction mixtures, failed to give 100% conversion of (104) to (43).



(104) (43)

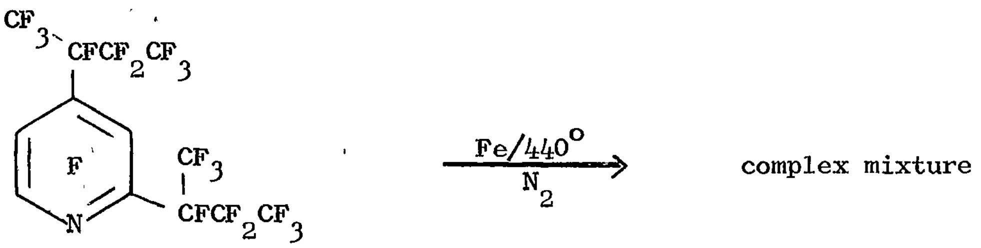
(b) Structure

The product isolated from the reaction had an i.r. spectrum identical with that of an authentic sample of (43).

6.2.2 Perfluoro-2,4-bis-sec-butylpyridine

(a) Reaction conditions and products

It was hoped that defluorination reactions carried out on bis-perfluoro-sec-butyl compounds, would lead to the corresponding bis-perfluoroalkenyl derivatives as these products were not formed in the fluoride ion reactions discussed previously (4.2.1). However when perfluoro-2,4-bis-sec-butylpyridine was passed over heated iron at 440°, a low yield of a complex mixture was obtained.



(105)

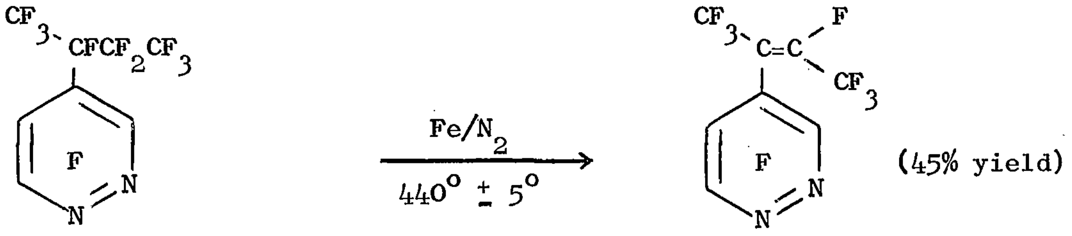
(b) Structure

Mass spectrometry indicated that a mixture of perfluoroalkenyl products had been formed. The presence of a weak absorption in the i.r. at $5{\cdot}8\mu$ indicated a $>C=C<$ residue. Because of the low recovery of the products formed and their complex nature, further investigations were abandoned.

6.2.3 Perfluoro-4-sec-butylpyridazine

(a) Reaction conditions and products

Under similar conditions to those previously (6.2.1) defluorination of perfluoro-4-sec-butylpyridazine, (106), yielded trans-perfluoro-4-(2'-butenyl)-pyridazine, (78).



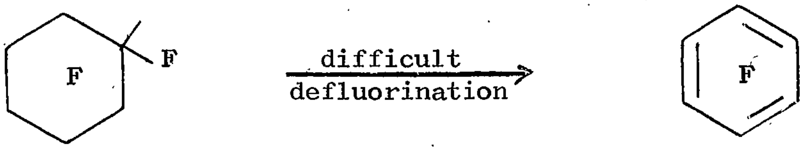
(106) (78)

(b) Structure

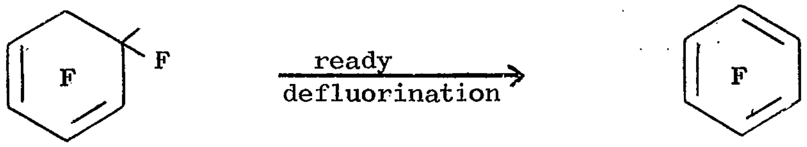
The product had an i.r. spectrum identical with that of an authentic sample of (78).

(c) Mechanism

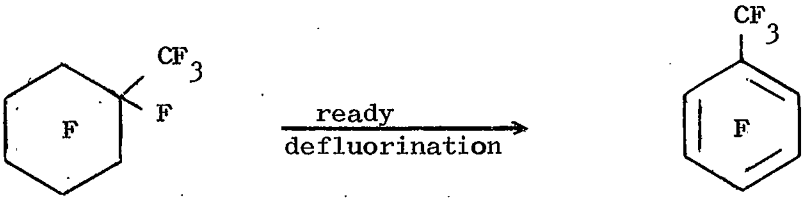
There is some evidence to suggest that the ease of removal of a fluorine atom from a molecule is dependent on conjugation and steric effects, for example:



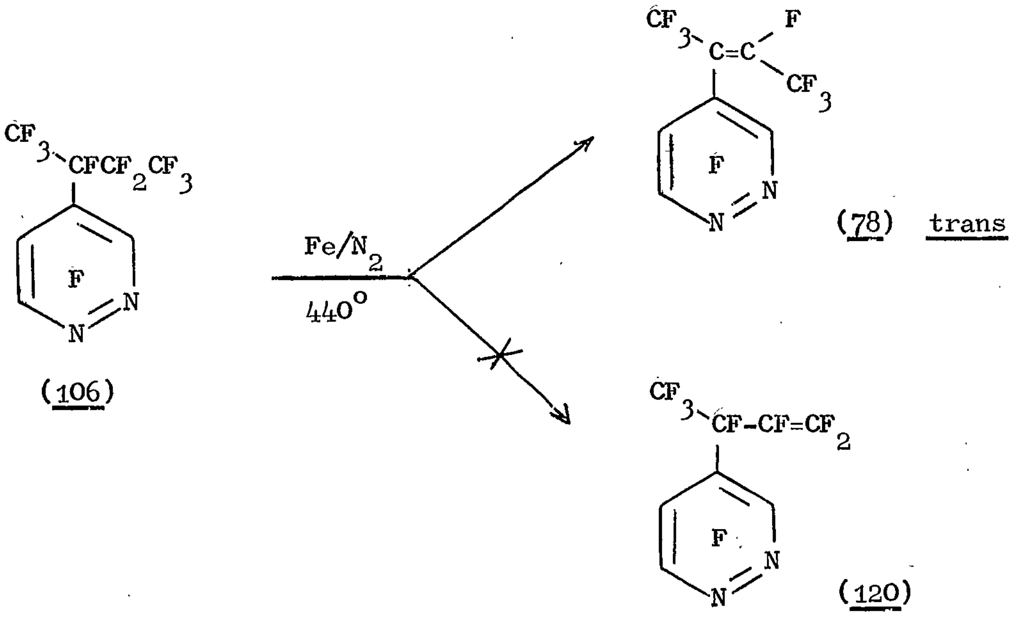
but



and



Thus one would expect that on defluorination of (106), (78) would be formed more easily than (120) and that under the condition used, the most stable, i.e. the trans, isomer would be formed.



(106)

(78) trans

(120)

In addition, as the carbon-fluorine bond strength increases with the number of fluorine atoms attached to a carbon atom, one would not expect to lose fluorine from a CF_3 group if other possibilities, for example, loss of fluorine from $-\overset{|}{\underset{|}{C}}-F$ or $\searrow CF_2$, exist.

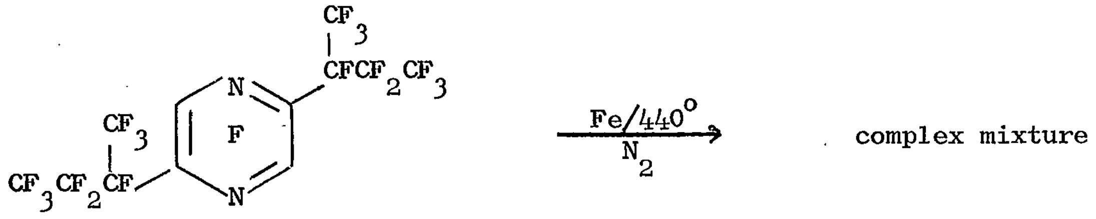
6.2.4 Perfluoro-3,5-bis-sec-butylpyridazine

Defluorination experiments carried out so far on (107) have yielded complex mixtures of products with low recovery of materials. However, a weak absorption at 5·8μ in the i.r. spectrum of the mixture, is indicative of a $>C=C<$ group.

6.2.5 Perfluoro-2,5-bis-sec-butylpyrazine

(a) Reaction conditions and products

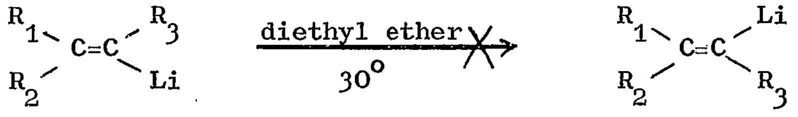
When perfluoro-2,5-bis-sec-butylpyrazine, (113), was passed over heated iron at 440°, a complex mixture of materials was obtained. Mass spectrometry and i.r. measurements indicate the presence of a $>C=C<$ group(s) but attempts to separate the mixture using preparative v.p.c. failed.



(113)

6.3 Reactions involving trans-heptafluorobutenyl lithium

It is known that vinyl lithium compounds can be readily generated and that once formed, using a suitable solvent, for example, diethyl ether, they retain their original stereochemistry without isomerisation for a reasonable period of time.[156,157]



$R_1 = R_3 = C_6H_5$

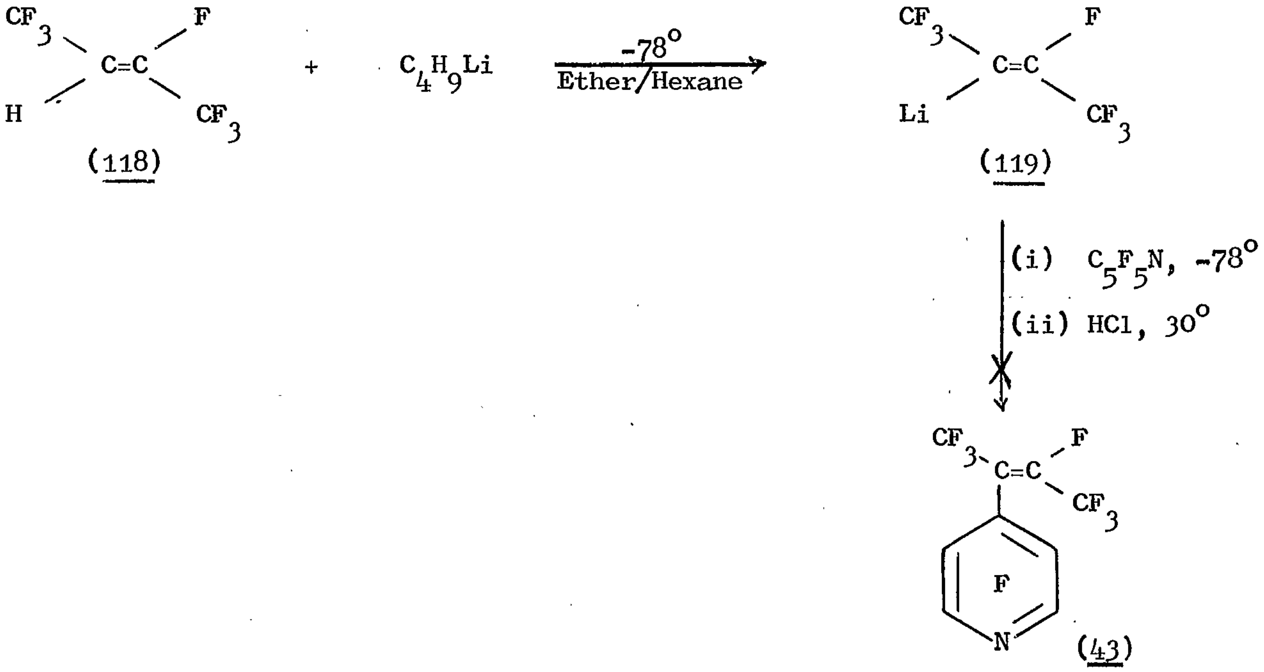
$R_2 = H$

Thus it was anticipated that by using a polyfluorohydro olefin of known configuration, synthesis of perfluoroalkenyl heterocyclic compounds should be possible, via the lithium derivative.

6.3.1 With pentafluoropyridine

(a) Reaction conditions

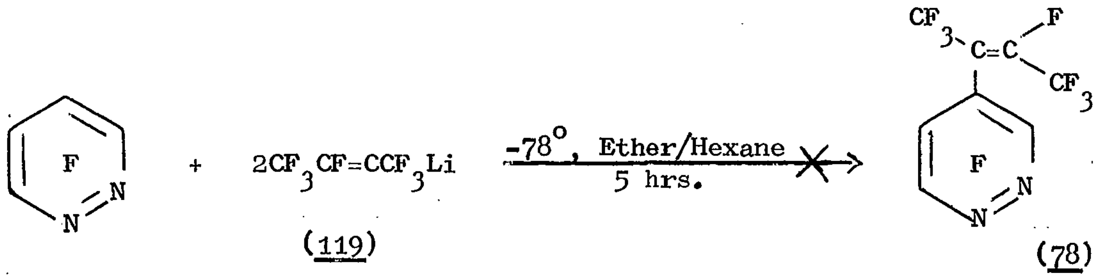
Initially, trans-2H-heptafluorobut-2-ene was reacted with n-butyl lithium at low temperature (-78°) using an ether hexane mixture. Pentafluoropyridine was then added to the resulting lithio derivative at -78°, and the temperature allowed to rise to room temperature. However no evidence for the product corresponding to trans-perfluoro-4-(2'-butenyl)pyridine, (43), was observed.



A further reaction was then carried out using freshly distilled tetrahydrofuran as solvent and determining that complete lithiation of (118) occurred by means of a colour test;[158] no evidence for the formation of (43) was obtained.

6.3.2 With tetrafluoropyridazine

Using similar conditions to those described previously, tetrafluoropyridazine was reacted with an excess of the perfluorobutenyl lithium compound, (119). No formation of the perfluorobutenylpyridazine, (78), occurred.



Although the formation of (119) has been shown to occur smoothly, the reason why it does not then react with pentafluoropyridine, and in particular tetrafluoropyridazine is at present, uncertain. A possible explanation could be that elimination of lithium fluoride occurs in preference to substitution of the heterocyclic ring. Further work involving the reactions of (119) and related intermediates, are at present being carried out in these laboratories.[159]

CHAPTER 7

Miscellaneous Reactions

Introduction

Several reactions, some of which cannot strictly be included under the title 'Fluoride ion-initiated reactions of acetylenes', have been carried out specifically as part of a United State Air Force Research contract. It has, however, been thought worthwhile to include the results of some of these experiments in this chapter.

In the first of these reactions, attempts were made to prepare perfluoro ethers which could be useful as models, potentially leading to the synthesis of high molecular-weight polyethers. Secondly, electron withdrawing groups in the 3,5-positions of pentafluoropyridine should enhance nucleophilic attack in the 2- and 4-position, so producing substrates for polymer formation more active than pentafluoropyridine; their attempted preparation is reported.

7.1 Polyethers

7.1.1 Reactions involving hexafluoroacetone, tetrafluoropyridazine and tetrafluoropyrazine

It has previously been observed that perfluorocarbonyl compounds, in particular hexafluoroacetone, rapidly form addition compounds with the heavier metal fluorides and that they can subsequently react with certain halogenated materials.[48,49,52-56,58,160]

$$(CF_3)_2CO \quad + \quad MF \quad \underset{25^{o}}{\overset{\text{Diglyme}}{\rightleftharpoons}} \quad (CF_3)_2CFOM$$

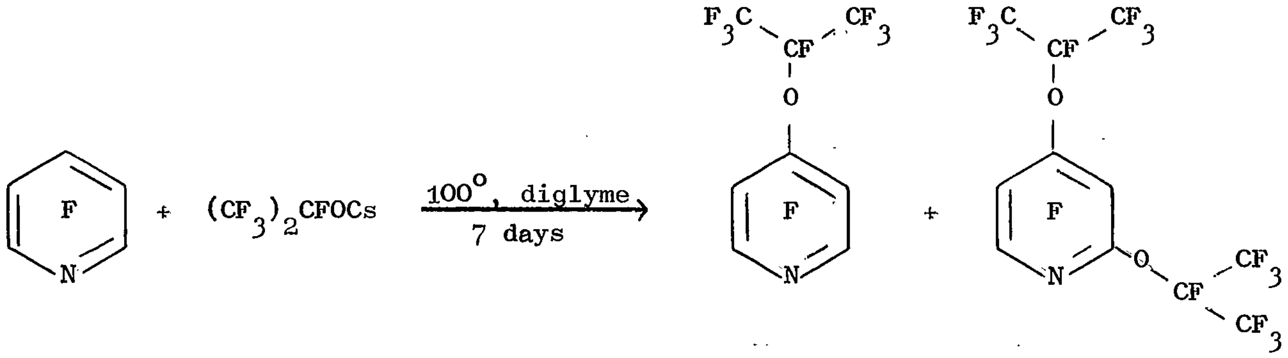
where M = K, Cs or Rb

and $$(CF_3)_2CFOM \quad + \quad BrH_2CCH{=}CH_2 \quad \xrightarrow[55^{o},\ 12\text{ hr. sealed tube}]{\text{Diglyme}} \quad CH_2{=}CHCH_2OCF(CF_3)_2$$

where M = K

All of these solid salts decompose in vacuo to give their constituent parts, although the caesium salts are more thermally stable than the corresponding potassium or rubidium complexes. All are extremely moisture sensitive and as such are prepared and reacted under anhydrous conditions. It should be noted however that the exact structure of the complexes is still uncertain.

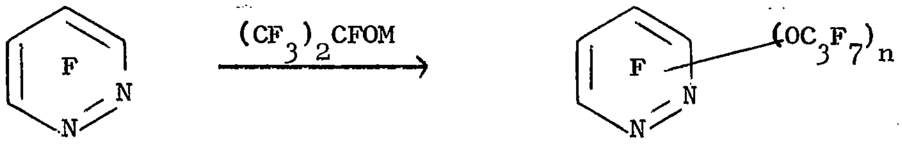
The use of fluorinated alkoxides as synthetic intermediates however is limited by the ease with which they eliminate fluoride ion, although the perfluoroisopropoxide anion, $(CF_3)_2CFO^-$, has been reacted with pentafluoropyridine to give a mixture of perfluoro-4-isopropoxytetrafluoropyridine and perfluoro-2,4-bis(isopropoxy)trifluoropyridine.[161]



(121) (122)

(a) Tetrafluoropyridazine

It was believed that by extending the scope of this reaction to include the use of a more reactive heterocycle, for example, tetrafluoropyridazine, then the possibility of producing highly substituted derivatives could exist. Further, any remaining sites left on the pyridazine nucleus would be sufficiently reactive to be of potential use in cross-linking reactions.

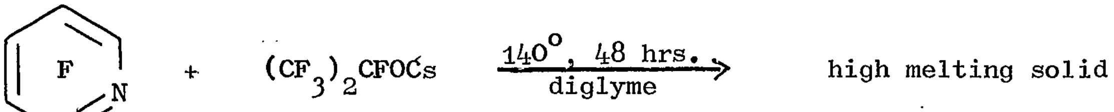


(123)

n = 1-4

M = Cs or K

Initially, experiments were carried out using pre-formed $(CF_3)_2CFOCs$ in diglyme with tetrafluoropyridazine in sealed carius tubes. Products corresponding to (<u>123</u>) were not isolated, although a high melting solid, possibly a hydrolysis product, was obtained.



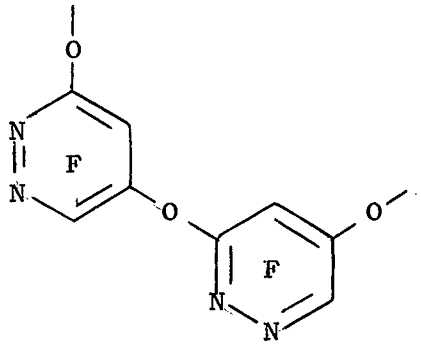
(<u>124</u>)

Varying the solvent, metal fluoride, reaction time and the temperature had little or no effect on the course of the reaction.

At lower temperatures (100° and 70°) and at atmospheric pressure, using both static and flow systems, similar results were obtained. Increasing the reaction time (112 hrs.) and using an excess of metal fluoride in a different solvent, dimethyl formamide, again gave none of the desired reaction products.

In polyfluoroalkylation processes involving diglyme as the solvent, side reactions involving the solvent and intermediates leading to lower recoveries of materials, have been reported.[42,57] All the above reactions gave low recoveries of tetrafluoropyridazine and it was believed that reactions involving $(CF_3)_2CFOCs$, the solvent and possibly the glass apparatus, could be influencing the course of the reaction. A reaction was carried out therefore using sulpholan and nickel apparatus and although higher recoveries of tetrafluoropyridazine were obtained, no substitution products were observed.

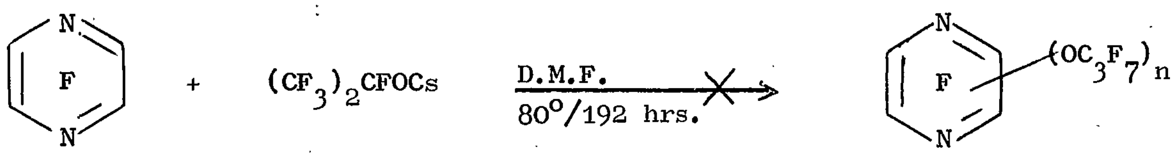
The structure of the high melting solid (<u>124</u>) obtained from the above reactions is unknown, for although the solid is soluble in some common organic solvents, notably acetone, no resonances could be observed in the ^{19}F n.m.r. spectrum. Mass spectrometry proved of little use while i.r. spectroscopy indicated broad diffuse bands over the whole range 2·5-25μ. However if the polymer is formed by hydrolytic side reactions then it may have a structure similar to



(124)

(b) Tetrafluoropyrazine

In reactions involving tetrafluoropyrazine, which is less susceptible to hydrolytic side reactions, only starting material was isolated.



n = 1-4

(125)

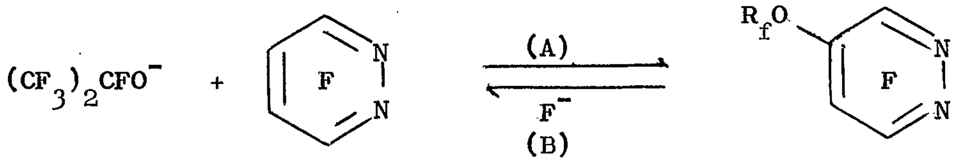
The reason why perfluoroethers were not obtained from reactions involving tetrafluoropyridazine and caesium perfluoroisopropoxide, is still uncertain. However, Shreeve[51] in a recent communication describes the preparation of totally fluorinated esters using $(CF_3)_2CFOM$ and a perfluoroacyl fluoride, only at low temperatures.

$$(CF_3)_2CFOM \quad + \quad R_fCOF \quad \xrightarrow[-105^o]{} \quad R_fCO_2CF(CF_3)_2 \quad + \quad F^-$$

$R_f = F, CF_3, C_2F_5, C_3F_7$

$M = K, Cs$

The esters, which are stable at room temperature and above, have been shown to be decomposed by fluoride ion at temperatures $>-78^o$. Therefore, it may be that reaction does occur between $(CF_3)_2CFOCs$ and tetrafluoropyridazine but at the reaction temperatures employed, the products are immediately decomposed by fluoride ion.



Thus, under the conditions employed reaction (B) is predominating.

Reactions at lower temperatures, which should reduce reaction (B), have been carried out recently[168] using perchloropyridazine and cyanuric chloride respectively, but without success.

7.1.2 Reactions involving hexafluoropropene epoxide

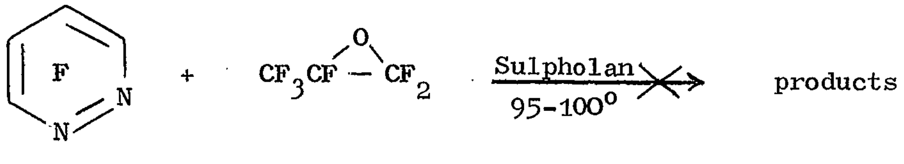
Hexafluoropropene epoxide is known to polymerise[60-66] in the presence of caesium fluoride to form compounds of the type:

$CF_3CF_2CF_2\text{-}O[CF(CF_3)CF_2O]_nR_f$ where n varies from 1-6

and $R_f = CF(CF_3)COF$

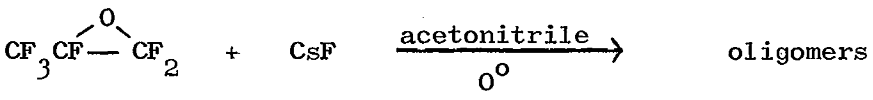
It was anticipated that the extending anion could be trapped by tetrafluoropyridazine to give higher molecular weight materials, which could, in turn, be cross-linked via the remaining reactive positions in the pyridazine nucleus to yield a polymer.

However a fluoride ion-induced reaction between hexafluoropropene epoxide and tetrafluoropyridazine using reported conditions, failed to give any products. Furthermore, homopolymers and oligomers of the perfluoro epoxide were not formed to any appreciable extent in these reactions. Using a static atmospheric pressure reaction conditions at 95-100° for 8 hrs., no identifiable products and only a low recovery of starting materials were obtained.



In an attempt to increase the solubility of the epoxide in the reaction mixture, a flow reaction was carried out, initially at 80° for 5 hrs., and then at 30° for 48 hrs. Again, only the volatile starting materials were isolated from the reaction. Solvent extraction of the reaction mixture failed to reveal the presence of any highly substituted involatile materials. Similar results were obtained using tetraglyme as the solvent.

Attempts to oligomerise hexafluoropropene epoxide alone under reported conditions[64] were, however, successful at low temperatures.



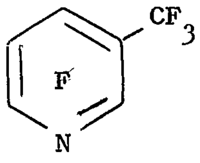
$$CF_3\overset{O}{CF-CF_2} + CsF \xrightarrow[0^{\circ}]{\text{acetonitrile}} \text{oligomers}$$

Using acetonitrile as a solvent a similar flow reaction was then carried out at 0° in the presence of tetrafluoropyridazine. Reaction was extremely rapid and a colourless fluorocarbon layer readily separated. Analytical scale v.p.c. indicated a four component mixture, whilst elemental analysis confirmed the absence of nitrogen in the mixture i.e. the mixture was derived solely from hexafluoropropene; tetrafluoropyridazine was detected in the solvent layer. Use of this fluorocarbon mixture in a separate fluoride ion-initiated reaction with tetrafluoropyridazine was equally unsuccessful.

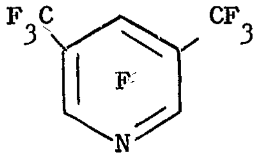
Again, the reason why reactions of this type have been unsuccessful is still uncertain. However in the latter reactions, oligomerisation of the perfluoro epoxide appears to be competing more favourably than the substitution reactions.

7.2 The attempted preparation of perfluoromethylpyridines

During the preparation of pentafluoropyridine from pentachloropyridine and potassium fluoride at 480°,[162] low yields of perfluoromethylpyridines, (126) and (127) have been obtained.

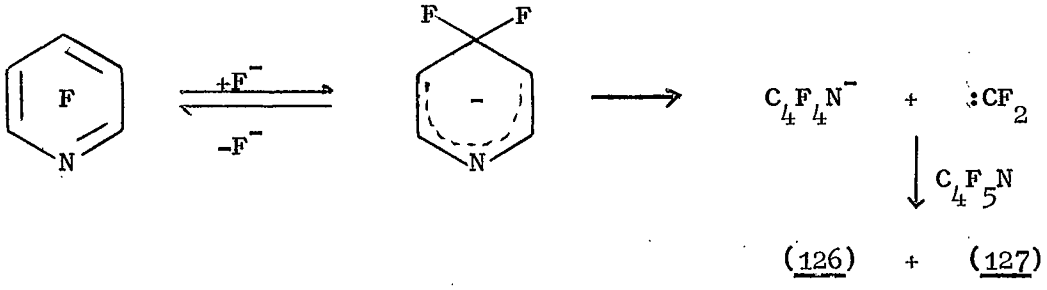


(126)

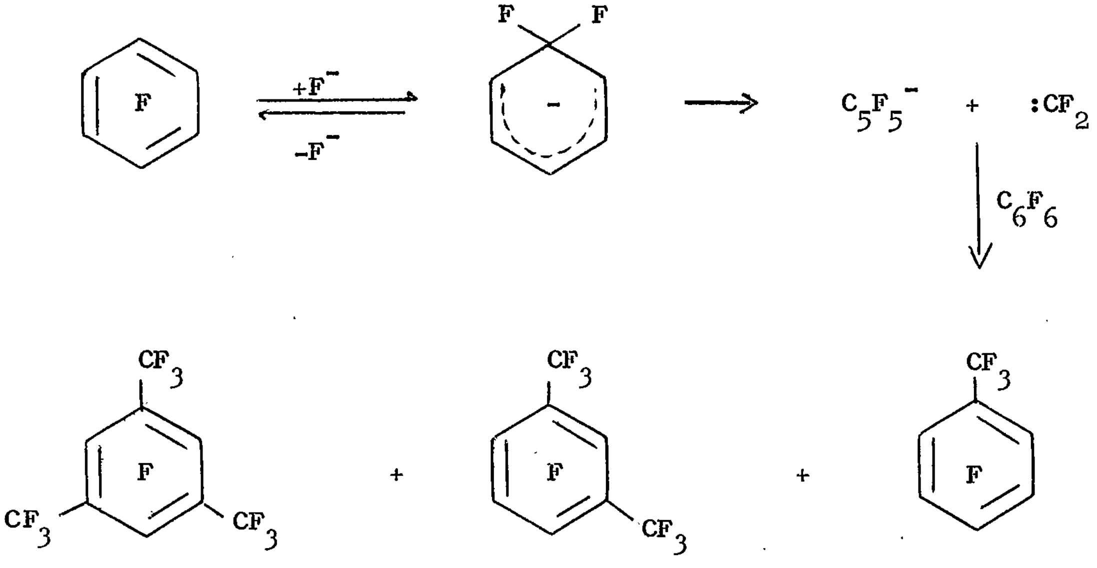


(127)

It is thought that these products arise by attack of difluorocarbene produced by the fluoride ion-catalysed breakdown of pentafluoropyridine, on pentafluoropyridine.



This is analogous to the mechanism postulated by Platonov et al.,[163] to explain the formation of perfluoro-toluene, -*m*-xylene, and -mesitylene on heating hexafluorobenzene with potassium fluoride at 550°



Substitution of pentafluoropyridine by the electron withdrawing perfluoroalkyl groups would be expected to lead to an enhancement of the remaining positions to nucleophilic attack. Thus it was of interest to prepare compounds of this type as potential substrates for polymer formation.

Difluorocarbene can be generated from sodium chlorodifluoroacetate and reactions involving this intermediate fluoride ion and pentafluoropyridine are described below.

7.2.1 Reactions involving sodium chlorodifluoroacetate and pentafluoropyridine

(a) Reaction conditions and products

Chlorodifluoroacetic acid[164,165] and its salts[166] are known to thermally decarboxylate and it is thought that the rate controlling step of the acid decarboxylation is a single concerted process leading directly to difluorocarbene, chloride ion and carbon dioxide. The onset of thermal decomposition

$$ClCF_2CO_2^- \longrightarrow \overset{\delta-}{Cl}{-}{-}{-}{-}\overset{\delta-}{CF_2}{-}{-}{-}{-}\overset{\delta-}{CO_2} \longrightarrow Cl^- + :CF_2 + CO_2$$

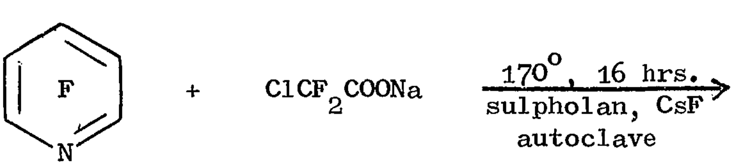
of the salts of chlorodifluoroacetic acid can be lowered by the use of a suitable solvent, for example, diglyme.[166]

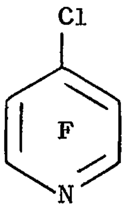
It was anticipated that by thermolysing sodium chlorodifluoroacetate at 130° in the presence of fluoride ion, pentafluoropyridine and diglyme, the difluorocarbene first formed would possibly be trapped by fluoride ion to form a trifluoromethyl anion which could then react with pentafluoropyridine

$$:CF_2 + F^- \longrightarrow {}^-CF_3 \xrightarrow{Ar_f\text{-}F} Ar_f\text{-}CF_3 + F^-$$

$$Ar_f = C_5F_4N$$

Although the initial experiments in diglyme (130°) only led to the recovery of starting materials, at higher temperatures (170°) and using sulpholan as solvent, a single compound, (128), was isolated.





(128); 91%

(b) Structure

In the mass spectrum of (128) a doublet $^m/e$ 185 and 187 ratio 3:1, indicated the presence of a single chlorine atom. The only resonance in the ^{19}F n.m.r. spectrum, which occurred at 91·0 and 143·0 p.p.m. both intensity 2, were attributed to the 2,6 and 3,5 ring fluorines respectively. This suggested that (128) was in fact a 4-substituted polyfluoropyridine. The comparison of the i.r. spectrum of (128) with that of an authentic sample[162] of 4-chloro-2,3,5,6-tetrafluoropyridine proved to be identical.

(c) Mechanism

In this reaction, chloride ion is produced directly in solution and can thus readily react, rather than the difluorocarbene, with pentafluoropyridine. This is in marked contrast to the reactions, involving potassium chloride and pentafluoropyridine[40], previously carried out in this laboratory.

Further reactions have been carried out comparing the effects of solvent temperature and caesium fluoride on the yield of (128); the results are summarised in Table 12.

Comparing reactions 2 and 4 (Table 12) it is apparent that the addition of caesium fluoride is necessary to give high yields of (128). Herkes has shown[164] that the addition of metal fluorides increases the rate of decarboxylation of sodium chlorodifluoroacetate.

Table 12

Reaction	Pentafluoro-pyridine (g.)	$ClCF_2COONa$ (g.)	CsF (g.)	Solvent	Temp. (^oC)	Time (hrs.)	Estimated Yield of C_5F_4ClN (g.)	(%)	Conversion (%)	Recovered Pentafluoro-pyridine (g.)
1	5: (29·6 m.mole)	8; (52·8 m.mole)	4; (26·4 m.mole)	Diglyme	130	16	-	-	-	5
2	5; (29·6 m.mole)	8; (52·8 m.mole)	4; (26·4 m.mole)	Sulpholan	170	16	4·1	85	82	0·9
3(a)	5; (29·6 m.mole)	8; (52·8 m.mole)	4; (26·4 m.mole)	Diglyme	140	16	-	-	-	5
3(b)	5; (29·6 m.mole)	8; (52·8 m.mole)	4; (26·4 m.mole)	Sulpholan	140	16	2·0	85	40	3·0
4	5; (29·6 m.mole)	8; (52·8 m.mole)	-	Sulpholan	170	16	2·2	87	44	2·8

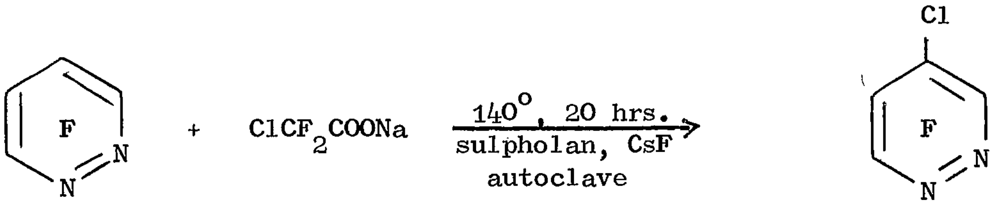
(i) Reactions 3(a) and 3(b) were carried out simultaneously.

(ii) Estimated yields were obtained from Gas Density Balance measurements, and are based on the actual weight of pentafluoropyridine used.

7.2.3 Reaction involving sodium chlorodifluoroacetate and tetrafluoropyridazine

(a) Reaction conditions and products

Using similar conditions to those outlined in 7.2.1, tetrafluoropyridazine was reacted with sodium chlorodifluoroacetate under fluoride ion conditions and a single product isolated.



(129); 50%

(b) Structure

The product (129) had satisfactory mass spectral and elemental analyses for a monochlorotrifluoropyridazine. From ^{19}F n.m.r. measurements, resonances at 85·5, 100·1, and 129·5, all intensity 1, were attributed to the 3,6 and 5 ring fluorines respectively, indicating that (129) was in fact 4-chloro-3,5,6-trifluoropyridazine.

Preliminary reactions involving other halogenoacetates, for example sodium trichloro and tribromo-acetates, and pentafluoropyridine have indicated that the corresponding 4-halogeno derivatives can be prepared conveniently.

The preparation of perfluorotrifluoromethylpyridines have recently been synthesised in these laboratories using difluorocarbene generated by the pyrolysis of P.T.F.E. at elevated temperatures (~550°).

EXPERIMENTAL

Reagents:

The perfluoroheterocyclic compounds, pentafluoropyridine, tetrafluoropyridazine and tetrafluoropyrazine were prepared as described in the literature.[131]

Hexafluorobut-2-yne, hexafluoroacetone and trifluoroethylene were obtained commercially from Peninsular Chem. Research Inc. A sample of diethyl acetylene dicarboxylate was kindly donated by Dr. G.M. Brooke. Hexafluoropropene epoxide[169] and *trans*-2H-heptafluorobut-2-ene[170] were prepared as described in the literature.

The caesium fluoride was reagent grade, dried by heating under high vacuum for 2-3 days, and stored under an atmosphere of dry nitrogen. Potassium fluoride was reagent grade, dried by heating strongly over a bunsen flame for several days, and stored in an oven at 150°.

Sulpholan was purified by high vacuum distillation, collecting only the middle fractions which were solid at room temperature, and dried further by storage over molecular sieves (type 4A) under an atmosphere of dry nitrogen.

Other solvents such as diglyme, dimethyl formamide and acetonitrile were dried in a similar fashion.

Instrumentation:

Infra-red spectra were recorded using a Grubb-Parsons "Spectromaster" spectrometer. Liquid samples were in the form of thin contact films between potassium bromide discs, or, in the case of gases and volatile liquids in a cylindrical glass cell with potassium bromide end windows. The cell could be attached to a vacuum line by means of a ball joint. Solid samples were pressed into thin discs with potassium bromide.

Ultra-violet spectra were recorded using a Unicam S.P. 800 spectrophotometer. Solvents used were cyclohexane and ethanol (Spectrosol grade).

Fluorine (^{19}F) nuclear magnetic resonance spectra were recorded on a Varian A56/60D spectrometer, operating at 56·4 Hz and 60 Hz. A Perkin-Elmer R10 spectrometer was also occasionally used.

Mass spectra were recorded using an A.E.I. M.S.9 spectrometer, and all molecular weights were recorded using this instrument.

E.S.C.A. measurements were carried out using an A.E.I. E.S.100 Electron Spectrometer.

Raman spectra were obtained using a Perkin-Elmer L.R.1 Laser Excited Raman Spectrometer.

Analytical scale vapour phase chromatography (v.p.c.) was carried out using Perkin-Elmer "Fractometer" models 451 and 452, and analysis was performed on columns packed with di-n-decylphthalate on Celite (Column 'A') and silicone elastomer on Celite (Column 'O'). Quantitative chromatographic analysis was carried out on a Griffin and George, D6, Gas Density Balance (G.D.B.), using the same column packings ('A' and 'O'). On this instrument the number of moles of any compound in a mixture is directly proportional to its peak area. Preparative scale chromatography was performed on a Perkin-Elmer, F21, Gas Chromatograph and on a Varian "Aerograph" instrument fitted with columns 'A' or 'O'.

CHAPTER 8

Experimental For Chapter 4

8.1 Fluoride ion-initiated reactions of acetylenes with pentafluoropyridine

8.1.1 With hexafluorobut-2-yne and pentafluoropyridine at atmospheric pressure

The first of several experiments to be carried out in this series simply consisted of allowing the perfluoroacetylene to bubble slowly through the reaction mixture. Although only low yields of products were obtained, this reaction showed that polyfluoroalkenylation reactions carried out at atmospheric pressure, were feasible. All yields, unless stated otherwise, are based on recovered materials.

(a) Hexafluorobut-2-yne (4•1g., 25•3 m.mole) was allowed to bubble slowly through a rapidly stirred suspension of caesium fluoride (1•0g., 6•6 m.mole) in pentafluoropyridine (4•0g., 23•7 m.mole) and sulpholan (60 ml.) at 100° over 1½ hrs. After a further ½ hr., the reaction mixture was cooled to 30°, poured into water and the products extracted with ether (3 x 40 ml.). The extracts were combined, dried ($MgSO_4$), and subsequent removal of the solvent left a pale yellow oil (3•0g.) which was shown by analytical scale v.p.c. (Column 'A', 100°) to be a complex mixture. Separation using preparative scale v.p.c. (Aerograph; Column 'A', 130°) yielded four fractions:

(i) pentafluoropyridine (1•1g.),
(ii) colourless liquid, (0•4g.), M/e 493,
(iii) colourless liquid, (0•1g.), M/e 655,
(iv) colourless liquid, (0•2g.), M/e 655.

Due to the small amounts of materials recovered, no further identification was attempted at this stage.

(b) Caesium fluoride (4•0g., 26•4 m.mole) and sulpholan (40 ml.) were introduced into a 250 ml. conical flask fitted with a side arm and condenser.

The flask was then evacuated at room temperature and when degassing of the solvent had ceased, hexafluorobut-2-yne (8g., 49•6 m.mole) was introduced from a flexible reservoir attached to the top of the condenser. The reaction mixture was then heated to 100° before pentafluoropyridine (5g., 29•6 m.mole) was introduced and the stirring started.

After 5 hrs., volatile material (4•0g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Column 'A', 100°) indicated that only starting materials had been recovered.

Polymeric material (5•7g.) was recovered from the reaction mixture.

Several other reactions using the static system were carried out using different solvents, for example, diglyme and tetraglyme, at different temperatures, for example, 75° to 110°. In all cases, only starting materials and polymer were obtained.

8.1.2 With hexafluorobut-2-yne and pentafluoropyridine at atmospheric pressure using a flow system

In the first of these experiments, hexafluorobut-2-yne was circulated rapidly through the reaction mixture, but under these conditions, polymerisation of the acetylene predominated, and no substitution products derived from pentafluoropyridine were observed. Later, it was found necessary to use hexafluorobut-2-yne which had been heavily diluted with nitrogen, combined with a slow flow rate before any of the desired substitution products were obtained.

(a) Using a high flow rate with potassium fluoride

Hexafluorobut-2-yne (10g., 62•7 m.mole) was circulated, with a high flow rate, through a rapidly stirred suspension of potassium fluoride (10g., 172 m.mole) in pentafluoropyridine (3g., 17•7 m.mole) and sulpholan (140 ml.) at 120°. After $1\frac{1}{2}$ hrs., volatile materials (2•9g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Column 'A', 100°) indicated a three component mixture. Separation of the mixture (Perkin-Elmer F21, Column 'A', 50-55°) yielded two oligomers of hexafluorobut-2-yne,

(i) 0·5g. colourless, volatile liquid, M 344, thought to be C_8HF_{13}

and (ii) 0·4g. colourless, volatile liquid, M 506, thought to be $C_{12}HF_{19}$

and pentafluoropyridine.

(b) Using a high flow rate and caesium fluoride

Using similar reaction procedures and conditions to those employed above, hexafluorobut-2-yne (10g., 62·7 m.mole) was circulated through a suspension of caesium fluoride (3g., 19·8 m.mole) in pentafluoropyridine (3g., 17·7 m.mole) and tetraglyme (140 ml.).

After 4 hrs., pentafluoropyridine (20g.), and polymer (7·0g.) derived from hexafluorobut-2-yne, were the only materials recovered.

(c) Using a low flow rate

Caesium fluoride (3g., 19·8 m.mole) and sulpholan (100 ml.) were introduced into a 250 ml. flask under dry nitrogen. The flask was then evacuated at room temperature. When degassing of the solvent had ceased, hexafluorobut-2-yne (23g., 119·2 m.mole) was introduced into the system from a flexible reservoir. The reaction mixture was then stirred and heated to reaction temperature (110°) and pentafluoropyridine (10g., 59·3 m.mole) was introduced from a syringe through a serum cap. A circulating pump was then started and the perfluorobut-2-yne was bubbled slowly through a sinter into the reaction mixture. Any unreacted perfluorobut-2-yne was re-circulated by the pump (see 4.1.3).

After 2 hrs., at 110° a vacuum began to form and the reaction was quenched by cooling in ice. Distillation of the reaction mixture under high vacuum, at a temperature $\ngtr 60^{\circ}$, yielded 10·0g. of a multi-component mixture (analytical scale v.p.c. Column 'A', 100°). Separation of this mixture using preparative scale v.p.c. (Perkin-Elmer, F21, Column 'A' $\sim 100^{\circ}$) gave:

(i) pentafluoropyridine,

(ii) perfluoro-2-(4'-pyridyl)-3,4-dimethylhexa-2,4-diene (44), b.pt. 169°/760 mm. (Found: C, 31·6; F, 66·1; N, 2·98%; M, 493. $C_{13}F_{17}N$ requires C, 31·6; F, 65·6; N, 2·8%; M, 493). λ_{max} (cyclohexane) = 278, (ε = 2,682), (2·2g., 16%). I.R. spectrum No.2,

(iii) perfluoro-2-(4'-pyridyl)-3,4,5,6-tetramethylocta-2,4,6-triene (45), b.pt. 205°/760mm. (Found: C, 31·4; F, 66·6; N, 2·22%; M, 655. $C_{17}F_{23}N$ requires C, 31·1; F, 66·5; N, 2·14%; M, 655). λ_{max} (cyclohexane) = 251; 314, (ε = 6,265; 3,324), (0·54g., 2%). I.R. spectrum No.3,

(iv) an isomer of (iii), (46), b.pt. 193°/760 mm. (Found: C, 31·4; F, 67·0; N, 2·22%; M, 655. $C_{17}F_{23}N$ requires C, 31·1; F, 66·5; N, 2·14%; M, 655). (1·1g., 6%). I.R. spectrum No.4.

Polymer (47) (8g.), derived from hexafluorobut-2-yne, was also isolated from the reaction mixture.

Yields are based on the initial amount of pentafluoropyridine used; actual yields will thus be higher.

8.1.3 With hexafluorobut-2-yne and pentafluoropyridine at atmospheric pressure using a flow system diluted with nitrogen

(a) Dry nitrogen and hexafluorobut-2-yne (10g., 51·8 m.mole), were pre-mixed in the ratio 50:50 in a flexible reservoir. The mixture was then circulated through a suspension of potassium fluoride (10g., 172 m.mole) in pentafluoropyridine (5g., 29·5 m.mole) and sulpholan (130 ml.) at 120° and atmospheric pressure. Reaction appeared slow and after 5 hrs. volatile material (6·1g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Column 'A', 75°) of the mixture only indicated pentafluoropyridine (3·1g.) and oligomers of hexafluorobut-2-yne (3·0g.).

Hexafluorobut-2-yne (4·0g.) and polymeric material (1·5g.) were recovered from the reservoir and residues respectively. Varying the nitrogen/hexafluorobut-2-yne ratio, for example 60:40, 70:30, had little effect on the course of the reaction.

(b) Caesium fluoride (3g., 19•8 m.mole) and sulpholan (100 ml.) were introduced into a 250 ml. flask under dry nitrogen. The flask was then evacuated at room temperature and when degassing of the solvent had ceased, 600 mm. of dry nitrogen was allowed into the system. The reaction mixture was then heated to reaction temperature (110°) and pentafluoropyridine (10g., 59•3 m.mole) introduced. A circulating pump was then started and the dry nitrogen circulated through the system. Hexafluorobut-2-yne (20g., 102•6 m.mole) was added to the nitrogen in small volumes (5-10 cc.), allowing a partial vacuum to develop after each addition.

After 8 hrs. at 110°, volatile materials (12•5g.) were transferred under vacuum to a cold trap. Analytical scale v.p.c. (Column 'A', 100°) indicated a multi-component mixture. Separation of this mixture using preparative scale v.p.c. (Perkin-Elmer, F21, Column 'A', ~ 100°) gave:

(i) pentafluoropyridine (4•5g.),

(ii) perfluoro-4-(2'-butenyl)pyridine (43), b.pt. 130-1°/760 mm. (Found: C, 32•34; F, 62•8; N, 4•50%; M, 331. $C_9F_{11}N$ requires C, 32•6; F, 63•2; N, 4•24%; M, 331). λ_{max} (cyclohexane) = 278, (ϵ = 4,180), (1•5g., 13%). I.R. spectrum No.1,

(iii) a colourless liquid whose i.r. spectrum was identified with that of perfluoro-2-(4'-pyridyl)-3,4-dimethylhexa-2,4-diene (44), (2•3g., 20%),

(iv) and (v) two colourless liquids whose i.r. spectra were identical with perfluoro-2-(4'-pyridyl)-3,4,5,6-tetramethylocta-2,4,6-triene (45), (•7g., 3%) and its isomer (46) (1•6g., 7%) isolated previously.

Polymeric material (5g.) and untreated hexafluorobut-2-yne (3g.) were also recovered.

(c) Hexafluorobut-2-yne (10g., 51·8 m.mole) was circulated through a rapidly stirred suspension of potassium fluoride (10g., 172 m.mole) in sulpholan (140 ml.) at 120°.

After 2 hrs., a white polymeric solid (9g.) was isolated whose i.r. spectrum was identical with that of the polymer derived from reactions involving hexafluorobut-2-yne and fluoride ion in sealed tube reactions (8.1.4).

8.1.4 With hexafluorobut-2-yne and pentafluoropyridine using an autoclave

(a) Hexafluorobut-2-yne (4·1g., 25·3 m.mole) was condensed into a rocking autoclave (50 ml.) containing a mixture of pentafluoropyridine (4·0g., 23·7 m.mole), caesium fluoride (1·0g., 6·6 m.mole) and sulpholan (25 ml.). The autoclave was then sealed, and rocked and heated to 130°.

After 33 hrs., the autoclave was cooled to room temperature and the contents poured into water (100 ml.); a white polymeric solid (4·0g.) was filtered off. Sublimation of the solid under high vacuum for 24 hrs. at 100° yielded a small quantity of material (0·2g.). Mass spectrometry indicated a molecular weight of $\sim$ 1490 for this sublimate, m.pt $>$ 300°. I.R. spectrum No.5.

(b) An autoclave (50 ml.) containing hexafluorobut-2-yne (4·1g., 25·3 m.mole) and equipped with a pressure gauge and tap was coupled, by means of a stainless steel tube to a similar autoclave (150 ml.) containing pentafluoropyridine (4·0g., 23·7 m.mole), caesium fluoride (1·0g., 6·6 m.mole) and sulpholan (25 ml.). Both autoclaves were inserted into a heater and warmed to 130° and the tap opened. After 1 hr., the system was allowed to cool and the seal broken. The contents of the 150 ml. autoclave were poured into water. A white polymeric solid was collected, filtered, washed well with water and dried. Sublimation of this solid (3g.) gave a small amount of material (0·15g.), whose i.r. spectrum was identical with that of the sample obtained above and which had a molecular weight of ∼ 1500 as determined by mass spectrometry. Pentafluoropyridine (2·5g.) and hexafluorobut-2-yne (1·0g.) were also recovered.

8.1.5 With diethyl acetylene dicarboxylate and pentafluoropyridine

(a) In a nickel tube

A nickel tube containing pentafluoropyridine (4·0g., 23·7 m.mole), diethyl acetylene dicarboxylate (1·5g., 8·8 m.mole), caesium fluoride (1·0g., 6·6 m.mole) and sulpholan (25 ml.) was rotated in an oil bath at 135°C for 5 hrs. After cooling to room temperature, the reaction mixture was poured into water (120 ml.) and the aqueous solution extracted with ether (3 x 40 ml.). High vacuum distillation of the oil, leaving a tarry residue, gave a pale yellow oil (2g.) which was shown by v.p.c. (Column 'O', 180°) to be a three-component mixture. Preparative scale v.p.c. (Aerograph: Column 'O', 180°) enabled the separation of the major component (1·6g.) whose i.r. spectrum was identical with that of a sample obtained previously.[40] This product has now been shown to be a cis/trans mixture of 1-fluoro-1,2-(biscarbethoxy)-2-(2',3',5',6'-tetrafluoropyridyl)ethylene (42), [(0·59g., 20%) estimated], I.R. spectrum No.6.

(b) At atmospheric pressure

Diethylacetylene dicarboxylate (1·5g., 8·8 m.mole) was added dropwise over 3 hrs., to a rapidly stirred suspension of caesium fluoride (1·5g., 9·9 m.mole) in pentafluoropyridine (4·0g., 23·7 m.mole) and sulpholan (25 ml.).

After a further 2 hrs., the reaction mixture was cooled to 50°, diluted with cold water and extracted with ether. The extracts were washed, dried ($MgSO_4$), and removal of the solvent left a yellow brown oil. Preparative scale v.p.c. (Aerograph: Column 'O', 180°) enabled the separation of two components:

(i) a major fraction, whose i.r. spectrum was identical with that of the cis/trans mixture of 1-fluoro-1,2-(biscarbethoxy)-2-(2',3',5',6'-tetrafluoropyridyl)ethylene isolated previously, (1·0g., 35%),

(ii) a minor fraction (0·2g.), thought to be trans-1H-1,2-(biscarbethoxy)-2-fluoroethylene from ^{19}F n.m.r. and mass spectral measurements.

8.2 Fluoride ion-initiated reactions of polyfluoro-olefins with pentafluoropyridine

8.2.1 Reactions involving trifluoroethylene

Caesium fluoride (7g., 46·2 m.mole) and sulpholan (130 ml.) were introduced into a 250 ml. flask under dry nitrogen. The flask was then evacuated at room temperature. When degassing of the solvent had ceased, pentafluoropyridine (5g., 29·6 m.mole) and trifluoroethylene (9·0g., 110 m.mole) were introduced into the system. The rapidly stirred reaction mixture was heated to 140° and the trifluoroethylene circulated through the system.

After 10 hrs., vacuum transfer through a short Vigreux column yielded a volatile liquid (3·3g.) and a white solid (0·3g.) which was recovered from the column.

The liquid fraction had an i.r. spectrum which was identical with that of pentafluoropyridine.

The i.r. spectrum of the solid fraction was found to be identical with that of an authentic sample of 1,1-bis(1',2',5',6'-tetrafluoropyridyl)tetrafluoroethane, (7%), I.R. spectrum No.7.

8.2.2 Reactions involving trans-2H-heptafluorobut-2-ene

(a) At atmospheric pressure using a static system

Caesium fluoride (8g., 52·8 m.mole) and sulpholan (40 ml.) were introduced into a 250 ml. conical flask under dry nitrogen. The flask was then evacuated at room temperature. When degassing of the solvent had ceased, trans-2H-heptafluorobut-2-ene (8·0g., 44·0 m.mole) was introduced from a flexible reservoir. The reaction mixture was then stirred and heated to 130°, and pentafluoropyridine (5g., 29·6 m.mole) was introduced from a syringe through a serum cap.

After 24 hrs., volatile materials (7·5g.) were transferred under vacuum at 70° to a cold trap. Analytical scale v.p.c. (Column 'A', 100°) indicated a two component mixture. Unchanged trans-2H-heptafluorobut-2-ene (5g.) was recovered from the reservoir.

Separation of the liquid fraction, using preparative scale v.p.c. (Perkin-Elmer, F21, at ~ 75°) gave:

(i) a colourless liquid whose i.r. spectrum was identical with that of an authentic sample of perfluoro-4-(2'-butenyl)pyridine; [(5%) estimated],

(ii) unchanged pentafluoropyridine (4g.). Solvent extraction of the material remaining after vacuum transfer gave no higher substitution products.

Similar results were obtained using higher temperatures and sealed nickel tubes.

8.3 Reactions involving trans perfluoro-4-(2'-butenyl)pyridine

8.3.1 With hexafluorobut-2-yne

Caesium fluoride (0·5g., 3·3 m.mole), sulpholan (5 ml.) and trans perfluoro-4-(2'-butenyl)pyridine (1·0g., 3·03 m.mole) were stirred at 90 ± 5°, in a 10 ml. flask under an atmosphere of perfluorobut-2-yne.

After 24 hrs., volatile material (0·6g.) transferred under vacuum to a cold trap. Separation of this mixture (Aerograph: Column 'A', 75°) gave only starting materials (i.r. spectroscopy).

8.3.2 With pentafluoropyridine in a sealed tube

(a) At 150°

Pentafluoropyridine (0·5g., 2·96 m.mole), trans perfluoro-4-(2'-butenyl)-pyridine (1·0g., 3·02 m.mole), caesium fluoride (0·5g., 3·3 m.mole) and sulpholan

(5 ml.) were introduced into a small carius tube. The tube was sealed under vacuum and then rotated in an oil bath at 150°.

After 17 hrs., volatile material (1·0g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Column 'A', 100°) indicated that only starting materials had been recovered.

(b) At 180°

Using a higher temperature (180°) and a longer reaction time (72 hrs.), extensive decomposition of the starting material occurred.

8.3.3 Nucleophilic substitution with methoxide ion

To a stirred solution of trans perfluoro-4-(2'-butenyl)pyridine (0·5g., 1·52 m.mole) in dry methanol (15 ml.) was added 1·5 ml. 0·1M solution of sodium methoxide (1·5 m.mole) in methanol over a period of 30 mins., at room temperature. After 5 hrs., the solvent was removed under vacuum and the residue extracted with chloroform (5 ml.). Removal of the solvent gave a pale yellow oil (b.pt. > 160°/760 mm.). This was shown to be mainly cis 3-methoxy-2-(2',3',5',6'-tetrafluoropyridyl)hexafluorobutene (76), (0·3g., 50%), containing < 5% of the trans-isomer. (Found: C, 34·8; F, 54·7; N, 3·80%; M, 343. $C_{10}H_3F_{10}NO$ requires C, 35·0; F, 55·1; N, 4·1%; M, 343). I.R. spectrum No.8.

8.2.4 Nucleophilic substitution with ammonia

A solution of perfluoro-4-(2'-butenyl)pyridine (0·5g., 1·52 m.mole) in dry ether (~ 5 ml.) was slowly added to ammonia (0·880; 4 ml.), with stirring at 0°. After 1 hr., a pale yellow solid (0·3g.) was filtered, crystallised from methanol and subsequently shown to be the enamine, (77), m.pt. 138-40°. (Found: C, 37·3; H, 1·2; F, 47·4; N, 14·3%; M, 285. $C_9H_2F_7N_3$ requires C, 37·9; H, 0·71; F, 46·7; N, 14·6%; M, 285), (0·3g., 75%). I.R. spectrum No.9.

CHAPTER 9

Experimental For Chapter 5

9.1 Fluoride ion-initiated reactions of acetylenes with tetrafluoropyridazine

9.1.1 With hexafluorobut-2-yne

Initial reactions were carried out employing the atmospheric pressure reaction techniques described previously (4.1.3 and 8.1.2), using hexafluorobut-2-yne heavily diluted with dry nitrogen, and a slow flow rate. Later, reactions are described in which the desired products were obtained using static atmospheric pressure systems.

(a) Hexafluorobut-2-yne (9·0g., 55·5 m.mole), heavily diluted with dry nitrogen, was circulated through a rapidly stirred suspension of caesium fluoride (4·0g., 26·4 m.mole), sulpholan (140 ml.) and tetrafluoropyridazine (4·0g., 26·4 m.mole) at 100°. The reaction was slow and after $6\frac{1}{2}$ hrs. volatile material (4·3g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Column 'A', 100°) showed a two component mixture. Preparative scale v.p.c. (Aerograph; Column 'A', 105°) yielded:

(i) perfluoro-4-(2'-butenyl)pyridazine, (78), b.pt. 136-7° at 760 mm. (Found: C, 30·3; F, 60·7; N, 9·15; M, 314. $C_8F_{10}N_2$ requires C, 30·3; F, 60·5; N, 8·95; M, 314) λ_{max} (cyclohexane) = 259, ϵ = 3526. Yield 1·6g., 30%, based on the weight of tetrafluoropyridazine used. I.R. spectrum No.10,

(ii) tetrafluoropyridazine (1·8g.).

(b) Caesium fluoride (4·0g., 26·4 m.mole) and freshly distilled sulpholan (140 ml.) were introduced into a 250 ml. flask under dry nitrogen. The flask was then evacuated at room temperature. When degassing of the solvent had ceased, dry nitrogen (600 mm.) was allowed into the system and tetrafluoropyridazine (6·3g., 41·5 m.mole) introduced from a syringe through a serum cap. The reaction mixture was then stirred and heated to reaction temperature (100-

105°) and the dry nitrogen circulated through the mixture by means of a pump. Small volumes (~100 mm.) of hexafluorobut-2-yne (8·0g., 49·6 m.mole) were then added to the system.

After 8 hrs., volatile material (7·4g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Column 'A', 100°) indicated a three component mixture. Two liquid components (4·0g.) were separated from the third, a white solid, by careful distillation under vacuum.

Separation of the liquid fraction using preparative scale v.p.c. (Perkin-Elmer F21, Column 'A', ~75°) gave:

(i) perfluoro-4-(2'-butenyl)pyridazine, (78), (0·7g., 15%),

(ii) tetrafluoropyridazine (2·4g.),

The white solid residue, was crystallised from dry ether to give:

(iii) perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (79), m.pt. 59-60° (Found: C, 29·9; F, 63·5; N, 5·6; M, 476. $C_{12}F_{16}N_2$ requires C, 30·2; F, 63·8; N, 5·9; M, 476) λ_{max} (cyclohexane) = 299, ϵ = 5114 (3·6g., 35%). I.R. spectrum No.11.

(c) Using a similar procedure to (b) but at 80° with caesium fluoride (4·0g., 26·4 m.mole), sulpholan (140 ml.) and tetrafluoropyridazine (4·0g., 26·4 m.mole) a higher yield (7·5g., 60%) of perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene (79), was obtained. Perfluoro-4-(2'-butenyl)pyridazine, (78), (0·6g., 13%) was also obtained.

Two reactions were then carried out using a static system at a lower temperature, (30°), and using sulpholan and tetraglyme respectively as solvents.

(d) Sulpholan (140 ml.) and caesium fluoride (4·0g., 26·4 m.mole) were introduced into a 250 ml. Buchner flask under dry nitrogen and the flask evacuated at room temperature. When degassing had ceased, hexafluorobut-2-yne (10g., 62·0 m.mole) was introduced from a flexible reservoir attached to the side arm of the flask. The reaction mixture was stirred at 30° and tetrafluoropyridazine (3g., 19•7 m.mole) introduced through a serum cap.

After 5 hrs., the volatile products (5•5g.) were transferred under vacuum to a cold trap. Analytical scale v.p.c. (Gas Density Balance, Column 'A', 78^{o}) showed these to consist of:

(i) perfluoro-4-(2'-butenyl)pyridazine, (<u>78</u>), (0•8g., 17%),

(ii) perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (<u>79</u>), (3•9g., 60%). Both yields were estimated by v.p.c. measurements on the mixture, (Gas Density Balance, Column 'A', 78^{o}),

(iii) unchanged tetrafluoropyridazine, 0•8g.

(e) Using identical quantities and reaction conditions to (d) but using tetraglyme (140 ml.) as solvent, the reaction proceeded extremely rapidly and after 1½ hrs., volatile material (4•0g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Gas Density Balance, Column 'A', 78^{o}) showed this to consist of:

(i) perfluoro-4-(2'-butenyl)pyridazine, (<u>78</u>), estimated yield (0•5g., 10%),

(ii) perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (<u>79</u>), estimated yield (3•3g., 50%). Both yields were estimated by v.p.c. measurements on the reaction mixture (Gas Density Balance, Column 'A', 78^{o}).

Polymer (5•6g.), which had an i.r. spectrum which was identical with that of an authentic sample of the polymer formed between the reaction of hexafluorobut-2-yne and fluoride ion, was recovered from the residues.

Attempts were then made to increase the yield of perfluoro-4-(2'-butenyl)-pyridazine by carrying out reactions at low temperatures. This necessitated the use of a solvent with a lower freezing point than sulpholan, for example acetonitrile.

(f) <u>At 0^{o}</u>

Caesium fluoride (4•0g., 26•4 m.mole) and acetonitrile (30 ml.) were introduced into a 100 ml. Buchner flask under dry nitrogen and the flask evacuated at room temperature. When degassing of the solvent had ceased, hexafluorobut-2-yne (4•0g., 24•64 m.mole) was allowed into the system until atmospheric pressure had been reached. Tetrafluoropyridazine (5•0g., 33•0 m.mole) was introduced into the flask which was then cooled to 0-5° and the contents rapidly stirred at this temperature. After 3 hrs., the stirring was stopped and, on standing, two layers were observed in the reaction vessel. These were separated and the lower layer (1•1g.) was shown to consist of oligomers of hexafluorobut-2-yne by i.r. spectroscopy. The upper layer was shown by analytical scale v.p.c. (Gas Density Balance, Column 'A', 78°) to consist of acetonitrile and unreacted tetrafluoropyridazine (3•0g.).

(g) At -40°

Acetonitrile (30 ml.), caesium fluoride (3•0g., 19•8 m.mole) and tetrafluoropyridazine (3•0g., 19•8 m.mole) were introduced into a 100 ml. flask equipped with a dry-ice condenser, under dry nitrogen. The flask was cooled to -120°, evacuated, and hexafluorobut-2-yne condensed into the system before allowing the temperature to rise to -40°. After 5 hrs., vacuum transfer of the volatile materials to a cold trap and subsequent analytical v.p.c. analysis (Gas Density Balance, Column 'A', 78°) indicated pyridazine and acetonitrile only. Polymer (4•0g.), derived from hexafluorobut-2-yne was recovered from the residues.

9.1.2 With diethyl acetylene dicarboxylate

Sulpholan (50 ml.), caesium fluoride (4•0g., 26•4 m.mole) and tetrafluoropyridazine (6•0g., 39•6 m.mole) were introduced into a 100 ml. flask under dry nitrogen. The mixture was then stirred at 90-95° and diethyl acetylene dicarboxylate (7•5g., 39•4 m.mole) added dropwise over 30 mins. at this temperature. After a further 1½ hrs., a volatile material (3•0g.) transferred under vacuum to a cold trap and was subsequently shown (i.r. spectroscopy) to be unreacted tetrafluoropyridazine.

The residue was cooled to room temperature, poured into water and ether extracted (3 x 50 ml.). The extracts were combined, washed, dried ($MgSO_4$), and removal of the solvent left an oil (5•9g.). Distillation under high vacuum, collecting the main fraction (2•0g.) boiling at 112-114° at 0•015 mm. gave a cis/trans mixture (40:60) of 1-fluoro-1,2-(biscarbethoxy)-2-(3',5',6'-trifluoropyridazyl)ethylene (91), (Found: C, 44•5; F, 23•5; N, 8•9%; M, 322. $C_{12}H_{10}F_4N_2O_4$ requires C, 44•8; F, 23•6; N, 8•7%; M, 322) (7•8g., 65%). I.R. spectrum No.12.

9.2 Reactions involving perfluoro-4-(2'butenyl)pyridazine (78)

9.2.1 With hexafluorobut-2-yne at atmospheric pressure

Sulpholan (5 ml.) and caesium fluoride (0•5g., 3•3 m.mole) were introduced into a 10 ml. flask under dry nitrogen at 30°. The flask was evacuated and when degassing had ceased, hexafluorobut-2-yne (1•0g., 6•1 m.mole) was allowed into the system until atmospheric pressure had been reached. Perfluoro-4-(2'-butenyl)pyridazine (0•3g., 0•96 m.mole) was then added to the stirred reaction mixture with the immediate formation of an intense yellow colour.

After 6 hrs., vacuum transfer of the volatile material to a cold trap, gave a small quantity of material (0•2g.) which, when crystallised from toluene, had an i.r. spectrum which was identical with that of an authentic sample of perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (79), (0•2g., 50%).

9.2.2 With aqueous ammonia

A solution of perfluoro-4-(2'-butenyl)pyridazine (0•3g., 0•96 m.mole) in carbon tetrachloride (1 ml.) was added slowly to ammonia (4 ml., •880), with stirring, at 0°. An immediate yellow-orange precipitate formed which was filtered after 1 hr. The solid crystallised from water to give the enamine (93), (Found: C, 35•6; F, 42•9; N, 20•2%; M, 268. $C_8H_2F_6N_4$ requires C, 35•8; F, 42•5; N, 20•8%; M, 268), λ_{max} (ethanol) = 262•5, ϵ = 31,930. I.R. spectrum No.13.

9.2.3 With one molecular proportion of sodium methoxide

To a stirred solution of perfluoro-4-(2'-butenyl)pyridazine (0·5g., 1·6 m.mole) in dry methanol (10 ml.) was added 1·6 ml. 0·1M solution of sodium methoxide (1·6 m.mole) in methanol over a period of 30 minutes at room temperature. After 5 hrs., the solvent was removed under vacuum and the residue extracted with chloroform (5 ml.). Removal of the solvent gave a pale yellow oil, which was shown by v.p.c. (Gas Density Balance, Column 'A', 78°) to consist of a two component mixture. Mass spectrometry indicated a molecular weight of 343, which is consistent with a mono-methoxy derivative.

From ^{19}F n.m.r. measurements, the mixture was shown to consist of mainly 3-methoxy-2-(3',5',6'-trifluoropyridazyl)hexafluorobutene [cis/trans mixture (66:34)]. Thus peaks at 56·51 and 64·10 p.p.m., both intensity 3, were assigned to two, cis CF_3 groups, $J_{CF_3-CF_3}$ 12·3 Hz. Peaks at 60·50 and 65·14 p.p.m., both intensity 3 and having little or no fine structure were assigned to trans CF_3 groups. Broad absorptions at 60·98, 82·89 and 90·43 p.p.m., all intensity 2, were assigned to the 3-, 6- and 5-ring fluorines respectively. The ratio of the cis:trans isomers (66:34) was obtained from a comparison of the integration values obtained for the cis and trans CF_3 group absorptions.

9.3 Reactions involving perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene (79)

9.3.1 Hydrolysis with sulphuric acid

Perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene (1·5g., 3·16 m.mole) in concentrated sulphuric acid (10 ml.) to which a few drops of water had been added, was heated to 150° for 48 hrs. The reaction was cooled and the sulphuric acid solution added dropwise to water (50 ml.), with cooling. The resulting precipitate (1·3g.) was filtered, washed and crystallised from aqueous methanol several times. Analytical scale v.p.c. (Gas Density Balance, Column 'O', 200°) showed a two component mixture.

The mixture (∼1g.) was then dissolved in chloroform (5 ml.) to which a few drops of methanol had been added, and the resulting solution eluted down a silica column (1' x ½", 'Silicar CC-7', 100-120 mesh, neutral silica) with chloroform. Two main fractions were collected and on removal of the solvent yielded:

(i) a white solid, identified as <u>1,2,3-tris-(trifluoromethyl)-1-pentafluoroethyl-7-fluoro-4-hydroxy-5,6-diazaindene</u>, (<u>86</u>), m.pt. 163-5° (Found: C, 29·9; H, 0·2; F, 60·2; N, 6·0%; M, 474. $C_{12}HF_{15}N_2O$ requires C, 30·4; H, 0·2; F, 60·0; N, 5·9%; M, 474) λ_{max} (cyclohexane) = 378, ϵ = 4000, (0·2g., 21%). I.R. spectrum No.14,

(ii) a pale yellow solid, identified as <u>1,2,3-tris-(trifluoromethyl)-1-pentafluoroethyl-4,7-dihydroxy-5,6-diazaindene</u>, (<u>87</u>), m.pt. 207-9° (Found: C, 30·7; H, 0·4; F, 56·6; N, 6·1%; M, 472. $C_{12}H_2F_{14}N_2O_2$ requires C, 30·6; H, 0·4; F, 56·5; N, 5·94%; M, 472) λ_{max} (cyclohexane) = 420, ϵ = 9970, (0·3g., 30%). I.R. spectrum No.15.

9.3.2 Nucleophilic substitution with methoxide ion

To a stirred solution of perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (<u>79</u>), (1·0g., 2·1 m.mole) in dry methanol (20 ml.) was added 2·1 ml. 0·1M solution of sodium methoxide (2·1 m.mole) in methanol over a period of 30 minutes, at room temperature. After 5 hrs., the solvent was removed under vacuum and the residue extracted with chloroform (5 ml.). Removal of the solvent gave a white mono-methoxy derivative (<u>99</u>) or (<u>100</u>) (Found: C, 31·7; F, 57·7; N, 5·7%; M, 488. $C_{13}H_3F_{15}N_2O$ requires C, 32·0; F, 58·4; N, 5·7%; M, 488). I.R. spectrum No.16.

9.3.3 Reaction with two molecular equivalents of pentafluorophenyl lithium

Butyl lithium (8·8 ml., 2·5M solution) in dry ether (10 ml.) was added dropwise to a solution of bromopentafluorobenzene (4·9g., 20·0 m.mole) in dry ether (50 ml.) over 30 minutes at -78°. The reaction mixture was stirred at this temperature and after 1 hr., a solution of perfluoro-(1,2,3-trimethyl)-1-

ethyl-5,6-diazaindene (4·76g., 10·0 m.mole) in dry ether (30 ml.) was added over 5 minutes with the formation of an immediate brown colour.

After 2 hrs., the reaction mixture was allowed to warm up to room temperature and after stirring a further 2 hrs., dilute hydrochloric acid (100 ml.) was added. The ether layer was separated, washed and dried ($MgSO_4$). Removal of the solvent left a pale yellow viscous oil (3g.) which readily crystallised from petroleum ether (40-60°) to give a pale yellow solid (2g.), which was shown to be perfluoro-(1,2,3-trimethyl)-1-ethyl-4,7-diphenyl-5,6-diazaindene, (97), m.pt. 162-5° (Found: C, 36·9; F, 57·75; N, 4·3%; M, 772. $C_{24}F_{24}N_2$ requires C, 37·3; F, 59·0; N, 3·63%; M, 772), (2g., 26%). I.R. spectrum No. 17.

9.3.4 Defluorination using an iron catalyst

Several defluorination reactions were carried out in which perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene (0·5g., 1·05 m.mole) was passed through a silica tube containing iron at a variety of temperatures (450-550°) by means of a nitrogen flow. At temperatures $>450°$, complete decomposition of the starting material occurred, whilst at temperatures $\leq 450°$, low recoveries of starting material were obtained.

9.3.5 Pyrolysis reactions

Several reactions were carried out in which perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene (0·5g., 1·05 m.mole) was passed through a silica tube packed with silica wool at a temperature of (400-600°) by means of a nitrogen flow. At 400°, only starting material (0·4g.) was recovered; at higher temperatures, complete decomposition occurred.

Pyrolysis under high vacuum had little or no effect on the course of the reaction.

9.3.6 Photolysis reactions

Perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene (1·0g., 2·1 m.mole) was placed in a silica tube (10" x ½"). The tube was sealed under vacuum and irradiated under a medium pressure u.v. lamp for 144 hrs., after which time the tube was opened. Extensive decomposition had occurred and only a small quantity of starting material (0·2g.) could be recovered.

Other photolysis reactions in which only the vapour phase was irradiated with varying reaction times (1-6 days) had little effect on the reaction.

CHAPTER 10

Experimental For Chapter 6

10.1 Reaction of octafluorobut-2-ene with perfluoroheterocyclic compounds

10.1.1 With pentafluoropyridine

In a typical reaction, pentafluoropyridine (12g., 72•9 m.mole), octafluorobut-2-ene (15•6g., 78•0 m.mole), sulpholan (15 ml.) and caesium fluoride (6g., 39•6 m.mole) were sealed in a nickel tube under dry nitrogen and the tube rotated in an oil bath at 160°.

After 48 hrs., the tube was cooled and vented. Vacuum transfer of the volatile materials to a cold trap, gave a colourless liquid (21•5g.) which was separated, using preparative scale v.p.c. (Aerograph; Column 'O', 110°) into two fractions:

(i) a colourless liquid, (104), whose i.r. spectrum was identical with that of an authentic sample[40] of perfluoro-4-sec.butylpyridine, b.pt. 147°/760 mm., (9•9g., 70%). I.R. spectrum No.18,

(ii) a colourless liquid, (105), whose i.r. spectrum was identical with that of an authentic sample[40] of perfluoro-2,4-di-sec.butylpyridine, b.pt. 194°/760 mm., (2•9g., 15%). I.R. spectrum No.19.

10.1.2 With tetrafluoropyridazine

Tetrafluoropyridazine (8•9g., 58•6 m.mole), caesium fluoride (6•0g., 39•6 m.mole), octafluorobut-2-ene (11•7g., 58•6 m.mole) and sulpholan (15 ml.) were sealed in a nickel tube, and the tube rotated in an oil bath at 160°C.

After 24 hrs., the tube was cooled and vacuum transfer of the volatile material gave a colourless liquid (13•4g.). Analytical scale v.p.c. (Gas Density Balance, Column 'O', 78°) showed a two component mixture which was separated, using preparative scale v.p.c. (Aerograph; Column 'A', 130°) into:

(i) a colourless liquid, which was identified as perfluoro-3,5-di-sec.butylpyridazine, (107), b.pt. 182-4°C/760 mm. (Found: C, 26•56; F, 64•69;

N, 8•7%; M, 352. $C_8F_{12}N_2$ requires C, 26•3; F, 64•8; N, 7•95%; M, 352), (4•0g., 30%). I.R. spectrum No.20.

(ii) a colourless liquid, which was identified as perfluoro-4-sec.butylpyridazine, (106), b.pt. 149-150°C/760 mm. (Found: C, 26•1; F, 65•2; N, 5•75%; M, 552. $C_{12}F_{20}N_2$ requires C, 26•1; F, 68•9; N, 5•1%; M, 552), (4•3g., 30%). I.R. spectrum No.21.

10.1.3 With tetrafluoropyrazine

Tetrafluoropyrazine (5•0g., 33•0 m.mole), caesium fluoride (6•0g., 39•6 m.mole), octafluorobut-2-ene (8•0g., 40•0 m.mole) and sulpholan (15 ml.) were sealed in a nickel tube, and the tube rotated in an oil bath at 160°.

After 48 hrs., careful vacuum transfer of the volatile materials gave:

(i) a white solid (1•2g.). This was identified as tetrafluoropyrazine, having an identical i.r. spectrum with that of an authentic sample,

(ii) a colourless liquid, which was identified as perfluoro-2,5-di-sec.butylpyrazine, (113), b.pt. 165°C/760 mm. (Found: C, 25•94; F, 68•3; N, 6•0%; M, 552. $C_{12}F_{20}N_2$ requires C, 26•1; F, 68•9; N, 5•1%; M, 552), (10g., 80%). I.R. spectrum No.22.

10.2 Defluorination reactions of some perfluoro-sec.butyl heterocyclic compounds

10.2.1 Using perfluoro-4-sec.butylpyridine, (104)

Several reactions were carried out at different temperatures and flow rates to determine optimum conditions for the defluorination of perfluoro-4-sec.butylpyridine. In a typical experiment, a quantity of the perfluoroheterocyclic compound was passed through a silica tube (20" x ½") packed with coarse iron filings using a steady flow of dry nitrogen. Any volatile products were collected in a cold trap attached to the end of the tube. The results of these experiments are shown in Table 13. Attempts to effect complete defluorination of perfluoro-4-sec.butylpyridine by recycling the volatile

Table 13

Experiment Number	Weight of $C_9F_{13}N$ (g.)	Defluorination Tube Temperatures (°C)	Time (hrs.)	Flow Rate (mls./min.)	Total Weight of Recovered Material (g.)	Weight of $C_9F_{11}N$ (g.)	Estimated Yield [b] (%)	Conversion (%)
1	3·0	385 ± 5	9	180	2·3	0·8	59	50
2	2·8	410 ± 5	48	50	2·4	0·9	75	47
3	5·0	420 ± 5	20	120	3·2	2·2	62	80
4	5·0	440 ± 5	25	110	3·9	2·69	80	75
5	3·0	450 ± 5	48	50	1·0	0·7	25	-
6	8·0	420 ± 5	48	110	5·0	3·3	60	78
7	1·0 [a]	440 ± 5	24	50	0·25	-	-	-

[a] The weight of volatile material from experiment 5.

[b] Estimated yields are based on v.p.c. measurements (Gas Density Balance, Column 'A', 78°)

materials from the cold trap were unsuccessful (Table 13, Experiment 7).

The volatile materials obtained from the defluorination reactions were combined (20g.) and separated using preparative scale vapour phase chromatography (Aerograph; Column 'O', 90°) into:

(i) a colourless liquid (7·0g.), which had an identical i.r. spectrum with that of an authentic sample of perfluoro-4-(2'-butenyl)pyridine, (43),

(ii) starting material (4·0g.).

10.2.2 Using perfluoro-2,4-bis(sec.butyl)pyridine, (105)

In a similar experiment, perfluoro-2,4-bis(sec.butyl)pyridine (1·5g., 2·56 m.mole) was passed through a silica tube packed with coarse iron filings at 440 ± 5°C using a flow of dry nitrogen. The colourless liquid (1·0g.) recovered from the cold trap was shown by v.p.c. (Gas Density Balance, Column 'A', 78°) to consist of at least five components and as such further investigations were abandoned. The presence of a weak absorption in the i.r. spectrum of the mixture, at 5·8μ did, however, indicate the presence of a $>C=C<$ grouping(s).

10.2.3 Using perfluoro-4-sec.butylpyridazine, (106)

Perfluoro-4-sec.butylpyridazine (2·9g., 8·2 m.mole) was passed through a silica tube packed with coarse iron filings at 440 ± 5°C using a steady flow of nitrogen. The volatile products (1·3g.) were collected in a cold trap. Analytical scale v.p.c. (Gas Density Balance, Column 'O', 78°) showed a two component mixture, which was separated (Aerograph; Column 'A', 100°) into:

(i) a colourless liquid, 0·6g., whose i.r. spectrum was identical with that of an authentic sample of perfluoro-4-(2'-butenyl)pyridazine. Estimated yield 45%,

(ii) starting material (0·3g.).

10.2.4 Using perfluoro-3,5-di(sec.butyl)pyridazine, (107)

Using a similar procedure to above, perfluoro-3,5-di-(sec.butyl)pyridazine (1·7g., 3·08 m.mole) was defluorinated at 420°. Only a small quantity (0·2g.) of material was recovered indicating that extensive decomposition of the starting material had occurred. An absorption at 5·8μ in the i.r. spectrum indicated the presence of a $>C=C<$ group(s).

10.2.5 Using perfluoro-2,5-bis(sec.butyl)pyrazine, (113)

Perfluoro-2,5-bis(sec.butyl)pyrazine (3g.) was defluorinated at 440°. Only a small quantity of material (0·5g.) was recovered. At a lower temperature, 400°, a higher recovery of a complex mixture was obtained (1·0g.). Mass spectrometry and i.r. spectroscopy indicated the presence of $>C=C<$ group(s).

10.3 Reactions involving *trans*-heptafluorobutenyl lithium

10.3.1 With pentafluoropyridine in ether/hexane

Trans-2H-heptafluorobut-2-ene (4·0g., 22·0 m.mole) was condensed into a flask containing ether (90 ml.) at -78° under dry nitrogen. A solution of n-butyl lithium in hexane (11·5 ml., 22·2 m.mole) was then added dropwise to the cold ether solution over approximately 10 mins. The mixture was stirred at -78° for 2 hrs., before addition of pentafluoropyridine (5·0g., 29·6 m.mole). Stirring was continued and the temperature allowed to rise to room temperature over 18 hrs.

Dilute hydrochloric acid (50ml.) was then added, and after 30 mins., the organic layer was separated, washed and dried ($MgSO_4$). Concentration of the organic layer, by careful removal of the ether by distillation, and subsequent analytical scale v.p.c. (Column 'A', 50°) indicated that substitution of the pyridine nucleus had not occurred.

Varying the ether/hexane ratio had little effect on the course of the reaction.

10.3.2 With pentafluoropyridine in tetrahydrofuran

A similar experiment to above was carried out using identical reactants, but using freshly distilled tetrahydrofuran (100 ml.) as solvent and holding the reaction temperature at -40^{o} for 5 hrs., before warming to room temperature. After hydrolysis and extraction, v.p.c. measurements (Column 'A', 50^{o}) of the organic layer indicated that substitution of the pyridine ring had not occurred.

Several other reactions were carried out in which reaction times and solvents were varied, and testing for complete lithiation of the trans-2H-heptafluorobut-2-ene by means of a colour reaction. In all cases, no evidence was obtained for the formation of the desired substitution products.

10.3.3 Using tetrafluoropyridazine and two molecular proportions of trans-heptafluorobutenyl lithium

Trans-2H-heptafluorobut-2-ene (7g., 38·4 m.mole) was condensed into a flask containing ether (75 ml.) and hexane (10 ml.) at -78^{o} under dry nitrogen. A solution of n-butyl-lithium in hexane (19·2 ml., 38·4 m.mole) was added dropwise to the cold solution over 20 mins. The mixture was stirred at -78^{o} for 2 hrs., before the addition of tetrafluoropyridazine (3g., 19·2 m.mole). Stirring was continued and the temperature allowed to rise to -55^{o}, where it was held for 5 hrs., before reaching room temperature over 18 hrs.

Dilute hydrochloric acid (50 ml.) was then added and after 30 mins., the organic layer was separated, washed, dried ($MgSO_4$) and concentrated by careful distillation. Analytical scale v.p.c. analysis (Column 'A', 50^{o}) indicated that substitution of the pyridazine nucleus had not occurred.

CHAPTER 11

Experimental For Chapter 7

11.1 Polyethers

11.1.1 Reactions involving hexafluoroacetone, tetrafluoropyridazine and tetrafluoropyrazine

(a) At 140° in a sealed tube using tetrafluoropyridazine

Caesium fluoride (2g., 13·2 m.mole), tetrafluoropyridazine (2g., 13·2 m.mole) and diglyme (10 ml.), were introduced into a Carius tube. Hexafluoroacetone (5g., 30 m.mole) was then condensed into the tube. The tube was evacuated, sealed and then shaken at room temperature until a clear solution was obtained, before heating to 140°.

After 48 hrs., volatile material (1g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Column 'A', 75° and Column 'O', 150°) revealed only diglyme and a trace of pyridazine. Treatment of the residue with water (100 ml.) yielded a brown solid (1·9g., m.pt. $>$ 300°). The structure of the solid could not be determined by the usual method.

Varying the reaction time (48-100 hrs.), and solvent, dimethyl formamide, at a lower temperature (100°) had little effect on the course of the reaction.

Other reactions carried out under atmospheric pressure conditions, employing lower temperatures, for example 105° and 80°, and in the presence of excess metal fluoride, were also unsuccessful.

(b) Using tetrafluoropyrazine

Dimethyl formamide (30 ml.) and caesium fluoride (2g., 13·2 m.mole) were introduced into a Carius tube. Hexafluoroacetone (5g., 30·0 m.mole) and tetrafluoropyrazine (4g., 26·4 m.mole) were condensed into the tube which was then evacuated and sealed before heating to 80°.

After 192 hrs., volatile material (4g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Gas Density Balance, Column 'A', 75°

and Column 'O', 150°) revealed only dimethyl formamide and tetrafluoropyrazine (2g.). No further products were obtained on dilution of the residue with water.

11.1.2 Reactions involving hexafluoropropene epoxide

(a) With tetrafluoropyridazine at atmospheric pressure

Caesium fluoride (6g., 39·6 m.mole) and sulpholan (50 ml.) were introduced under dry nitrogen into a 250 ml. flask fitted with a water condenser. The flask was then evacuated at room temperature. When degassing of the solvent had ceased, hexafluoropropene epoxide was allowed into the system until atmospheric pressure was reached and a bladder attached to the top of the condenser was partially inflated. Tetrafluoropyridazine (3·6g., 22·9 m.mole) was introduced into the flask when the reaction temperature had reached 95-100°. The mixture was then heated with stirring at this temperature under an atmosphere of hexafluoropropene epoxide.

After 8 hrs., the volatile materials (6g.) were transferred under vacuum to a cold trap. Analytical scale v.p.c. (Gas Density Balance, Column 'A', 78° and Column 'O', 150°) showed these to consist of tetrafluoropyridazine, unreacted hexafluoropropene epoxide and traces of highly volatile material. Solvent extraction (ether) of the residues gave no further products. Unreacted hexafluoropropene epoxide was also recovered from the reservoir.

Reactions carried out at atmospheric pressure using (i) a static system with tetraglyme as solvent at 100°, and (ii) a flow system with sulpholan, at 80° and 30°, were also unsuccessful.

(b) At atmospheric pressure using a flow system heavily diluted with nitrogen

Acetonitrile (25 ml.) and caesium fluoride (1g., 6·6 m.mole) were introduced under dry nitrogen in a 100 ml. flask fitted with a water condenser. The flask was then evacuated at room temperature. When degassing of the solvent had ceased, dry nitrogen (600 mm.) was allowed into the system.

Tetrafluoropyridazine (3·0g., 19·8 m.mole) was introduced into the flask and the flask cooled to 0-5°. The reaction mixture was then stirred at 0-5° and hexafluoropropene epoxide circulated through the system.

After 5 hrs., the stirring was stopped and the fluorocarbon layer (2·2g.) was readily separated. Analytical scale v.p.c. (Gas Density Balance, Column 'A', 78°) indicated a multi-component mixture containing no pyridazine. Due to the complex nature of the mixture no further work was carried out. Tetrafluoropyridazine (2·8g.) was recovered from the solvent layer.

11.2 Reactions involving sodium chlorodifluoroacetate

11.2.1 With pentafluoropyridine

(a) In diglyme at 130°

Sodium chlorodifluoroacetate (8g., 52·8 m.mole), caesium fluoride (4g., 26·4 m.mole), pentafluoropyridine (5g., 29·6 m.mole) and diglyme (20 ml.) were introduced into a nickel tube under an atmosphere of dry nitrogen. The tube was then sealed and rotated in an oil bath at 130°.

After 16 hrs., the tube was cooled, opened and volatile material (7g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Gas Density Balance, Column 'A', 75°) indicated only pentafluoropyridine (5g.) and diglyme.

(b) In sulpholan at 170°

Using a similar experimental procedure to (a), pentafluoropyridine (5g., 29·6 m.mole), sodium chlorodifluoroacetate (8g., 52·8 m.mole), caesium fluoride (4g., 26·4 m.mole) and sulpholan (30 ml.), were heated in a sealed nickel tube at 170°.

After 16 hrs., volatile materials (6g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Gas Density Balance, Column 'A', 75°) indicated a two component mixture. Separation of the mixture (Aerograph; Column 'O', 110°) gave:

(i) a colourless liquid, (128), whose i.r. spectrum was identical with that of an authentic[42] sample of 4-chloro-2,3,5,6-tetrafluoropyridine, (4·1g., 78% yield),

(ii) pentafluoropyridine (0·9g.).

(c) Several reactions were then carried out using the procedure described above, investigating the effect of solvent, temperature and caesium fluoride on the course of the reaction. The results are summarised in Table 12.

11.2.2 With tetrafluoropyridazine

Tetrafluoropyridazine (4·5g., 29·6 m.mole), sodium chlorodifluoroacetate (8g., 52·8 m.mole), caesium fluoride (4g., 26·4 m.mole) and sulpholan (30 ml.) were introduced into a nickel tube (80 ml.) under dry nitrogen. The tube was sealed, and rotated in an oil bath at 140°.

After 20 hrs., volatile material (3·5g.) transferred under vacuum to a cold trap. Analytical scale v.p.c. (Gas Density Balance, Column 'A', 100°) indicated two components. Separation of the mixture (Aerograph; Column 'O', 150°) gave:

(i) tetrafluoropyridazine (0·8g.),

(ii) 4-chloro-3,5,6-trifluoropyridazine, (129), (Found: C, 28·2; F, 34·0; N, 16·4; Cl, 20·7%; M, 168. $C_4F_3N_2Cl$ requires C, 28·6; F, 33·8; N, 16·6; Cl, 21·0%; M, 168), (2·0g., 50% yield). I.R. spectrum No.23.

Table 12

Reaction	Pentafluoro-pyridine	$ClCF_2COONa$	CsF	Solvent	Temp.	Time	Estimated Yield of C_5F_4ClN		Conversion	Recovered Pentafluoro-pyridine
	(g.)	(g.)	(g.)		(°C)	(hrs.)	(g.)	(%)	(%)	(g.)
1	5: (29·6 m.mole)	8; (52·8 m.mole)	4; (26·4 m.mole)	Diglyme	130	16	-	-	-	5
2	5; (29·6 m.mole)	8; (52·8 m.mole)	4; (26·4 m.mole)	Sulpholan	170	16	4·1	85	82	0·9
3(a)	5; (29·6 m.mole)	8; (52·8 m.mole)	4; (26·4 m.mole)	Diglyme	140	16	-	-	-	5
3(b)	5; (29·6 m.mole)	8; (52·8 m.mole)	4; (26·4 m.mole)	Sulpholan	140	16	2·0	85	40	3·0
4	5; (29·6 m.mole)	8; (52·8 m.mole)	-	Sulpholan	170	16	2·2	87	44	2·8

(i) Reactions 3(a) and 3(b) were carried out simultaneously.

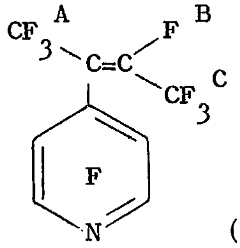
(ii) Estimated yields were obtained from Gas Density Balance measurements, and are based on the actual weight of pentafluoropyridine used.

APPENDIX I

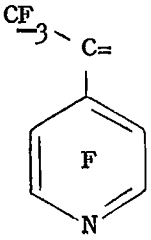
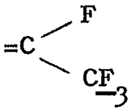
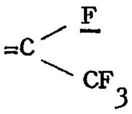
^{19}F N.m.r. Data

All chemical shifts were measured upfield from an external $CFCl_3$ reference.

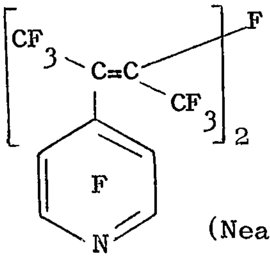
1. Trans-perfluoro-4-(butenyl)pyridine, (43)



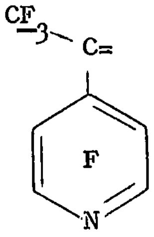
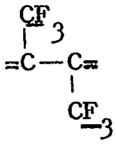
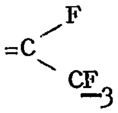
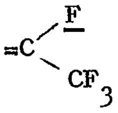
(Neat)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
61·3	Doublet of doublets J_{AB} 21, J_{AC} 1	3	
69·0	Doublet of doublets J_{BC} 7·5, J_{AC} 1	3	
88·0	Broad multiplet	2	2,6 Ring F's
103·9	Multiplet, J_{AB} 21, J_{BC} 7·5	1	
140·0	Broad multiplet	2	3,5 Ring F's

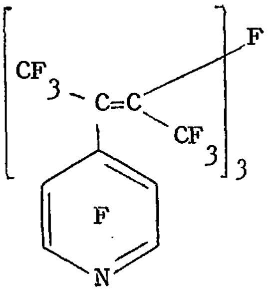
2. Perfluoro-2-(4-pyridyl)-3,4-dimethylhexa-2,4-diene, (44)



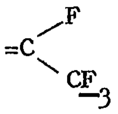
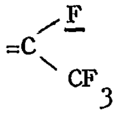
(Neat)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
60•4	Doublet, J 16	3	
62•0	Singlet	6	
69•75	Broad singlet	3	
88•25	Multiplet, J_{FF} 13	2	2,6 Ring F's
102•5	Multiplet, J 7	1	
139•5	Broad multiplet	2	3,5 Ring F's

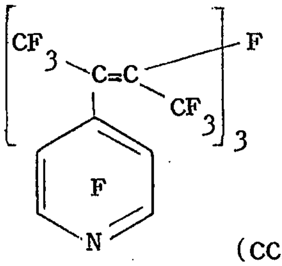
3. Perfluoro-2-(4'-pyridyl)-3,4,5,6-tetramethylocta-2,4,6-triene, (45)



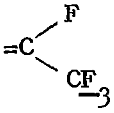
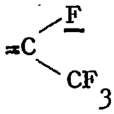
(CCl_4)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
57·0	Broad singlet	3	Side chain CF_3's
61·7	Doublet, J 20	6	
63·0	Singlet	3	
64·2	Singlet	3	
70·4	Multiplet	3	
88·5	Broad multiplet J 13	2	2,6 Ring F's
100·1	Broad multiplet	1	
140·5	Broad multiplet	2	3,5 Ring F's

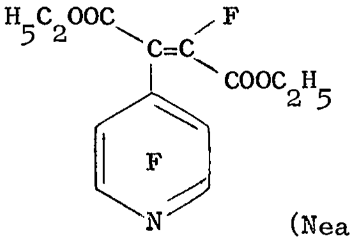
4. Isomer of perfluoro-2-(4'pyridyl)-3,4,5,6-tetramethylocta-2,4,6-triene, (46)



(CCl_4)

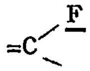
Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
59·75	Broad singlet	9	Side chain CF_3's
61·5	Singlet	3	
63·0	Singlet	3	
70·25	Singlet	3	
87·0	Broad multiplet J 13	2	2,6 Ring F's
102·3	Broad multiplet	1	
138·3	Broad multiplet	2	3,5 Ring F's

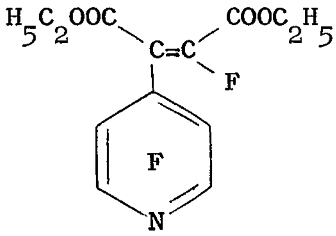
5. Cis- and trans-1-fluoro-1,2-(biscarbethoxy)-2-(2',3',5',6'-tetrafluoropyridyl)ethylene, (42)



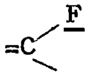
(Neat)

Trans isomer

Chemical Shift (p.p.m.)	Relative Intensity	Assignment
83·5	2	2,6 Ring F's
92·2	1	
140·6	2	3,5 Ring F's



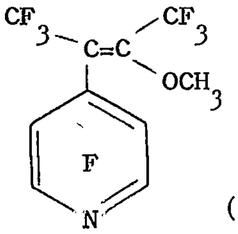
Cis isomer

Chemical Shift (p.p.m.)	Relative Intensity	Assignment
84·4	2	2,6 Ring F's
92·2	1	
142·0	2	3,5 Ring F's

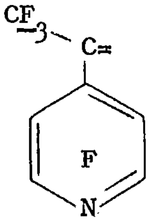
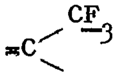
^{19}F n.m.r. measurements were carried out on a mixture of the two isomers.

Ratio of isomers, cis:trans = 50:50

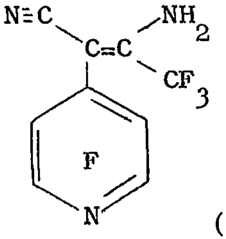
6. Cis-perfluoro-2-(2',3',5',6'-tetrafluoropyridyl)-3-methoxybutene, (76)



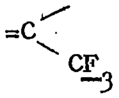
(Neat)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
57·9	Doublet, $J_{CF_3CF_3}$ 12	3	
65·7	Doublet, $J_{CF_3CF_3}$ 12	3	
92·1	Multiplet	2	2,6 Ring F's
142·0	Multiplet	2	3,5 Ring F's

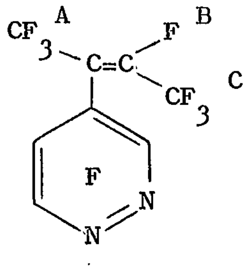
7. Enamine derivative of perfluoro-4-(2'-butenyl)pyridine



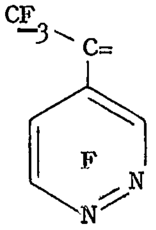
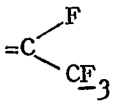
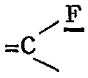
(Acetone)

Chemical Shift (p.p.m.)	Fine Structure	Relative Intensity	Assignment
83·4	Singlet	3	
95·3	Broad multiplet	2	2,6 Ring F's
143·0	Broad multiplet	2	3,5 Ring F's

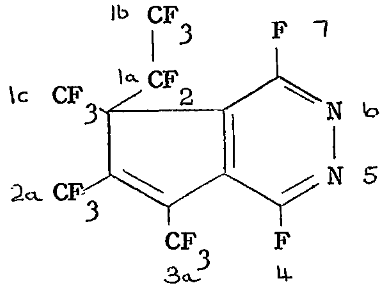
8. Trans-perfluoro-4-(2'-butenyl)pyridazine, (78)



(CCl_4)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
61·5	Doublet of doublets, J_{AB} 21, J_{AC} 1	3	
70·5	Doublet of doublets, J_{BC} 7, J_{AC} 1	3	
78·4	Multiplet, J, 32	1	3 Ring F's
97·0	Doublet of doublets, J, 32	1	6 Ring F's
103·2	Multiplet, J_{AB} 21, J_{BC} 7	1	
121·5	Multiplet	1	5 Ring F's

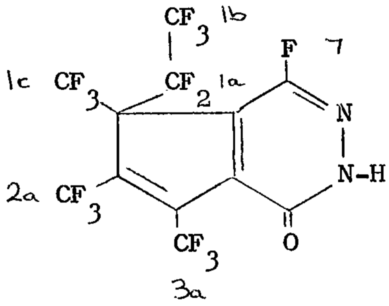
9. Perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (79)



(Acetone)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
54·9	Broad multiplet, $J_{2a,1c}$ 10, $J_{2a,3a}$ 14	3	2a
58·7	Hextet, $J_{3a,2a}$ 14, $J_{3a,4}$ 28	3	3a
60·8	Octet, $J_{1c,2a}$ 10, $J_{1c,1a}$ 10, $J_{1c,7}$ 20	3	1c
78·2	Multiplet, $J_{4,3a}$ 28, $J_{7,1c}$ 20	2	4,7 Ring F's
80·0	Singlet	3	1b
106·8	$J_{1a,1c}$ 10	2	1a

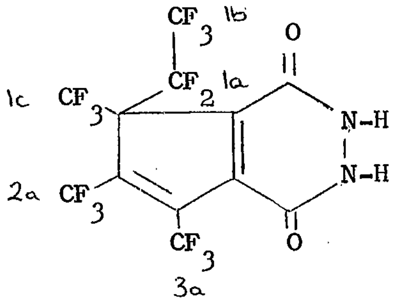
10. 1,2,3-Tris-(trifluoromethyl)-1-pentafluoroethyl-7-fluoro-4-hydroxy-5,6-diazaindene, (86)



(Acetone)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
55·9	Broad multiplet $J_{2a,3a}$ 14, $J_{2a,1c}$ 11	3	2a
60·1	Octet, $J_{1c,2a}$ 11 $J_{1c,7}$ 22, $J_{1c,1a}$ 11	3	1c
61·5	Quartet, $J_{3a,2a}$ 14	3	3a
82·0	Singlet	3	1b
94·3	Broad unresolved multiplet, $J_{7,1c}$ 22	1	7 Ring F's
100·8	Broad multiplet, $J_{1a,1c}$ 11	2	1a

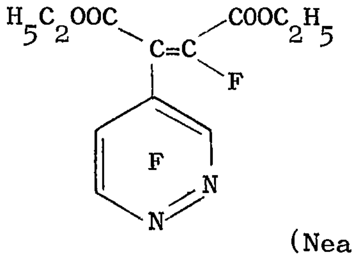
11. 1,2,3-Tris-(trifluoromethyl)-1-pentafluoroethyl-4,7-dihydroxy-5,6-diazaindene, (87)



(Acetone)

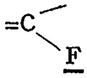
Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
56·7	Broad multiplet $J_{2a,3a}$ 13·5, $J_{2a,1c}$ 10	3	2a
57·2	Hextet, $J_{1c,1a}$ 10, $J_{1c,2a}$ 10	3	1c
59·6	Quartet, $J_{2a,3a}$ 13·5	3	3a
80·5	Singlet	3	1b
104·3	Multiplet, $J_{1a,1c}$ 10	2	1a

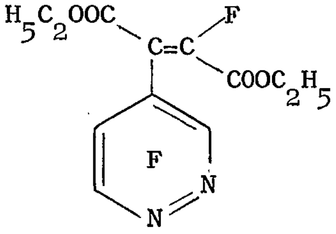
12. Cis- and trans-1-fluoro-1,2-(biscarbethoxy)-2-(3',5',6'-trifluoropyridazyl) ethylene



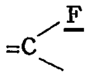
(Neat)

(90)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
77•5	Multiplet	1	3 Ring F's
95•0	Multiplet	1	
98•2	Multiplet	1	6 Ring F's
121•0	Multiplet	1	5 Ring F's



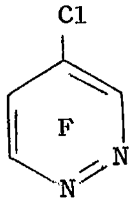
(91)

79•5	Multiplet, $J_{3,6}$ 30	1	3 Ring F's
95•2	Multiplet	1	
99•0	Multiplet, $J_{6,3}$ 30	1	6 Ring F's
123•8	Multiplet, J, 24	1	5 Ring F's

^{19}F measurements were carried out on a mixture of the two isomers

Ratio of isomers, Cis:Trans = 40:60

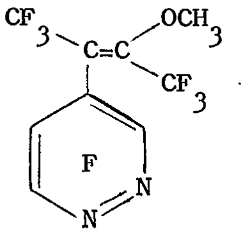
13. 4-Chlorotrifluoropyridazine, (92)



(Neat)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)		Relative Intensity	Assignment
85·5	$J_{3,6}$	30	1	3 Ring F's
100·1	$J_{6,3}$	30	1	6 Ring F's
129·5	$J_{3,5}$	24	1	5 Ring F's

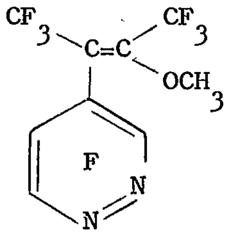
14. <u>Cis</u>- and <u>trans</u>-perfluoro-2-(3',5',6'-trifluoropyridazyl)-3-methoxybutene



(Neat)

(<u>94</u>)

Chemical Shift (p.p.m.)	Coupling Constant (Hz.)	Relative Intensity	Assignment
60·50	Multiplet	3	$\underline{CF_3}\diagdown C=$
65·14	Multiplet	3	$=C\diagdown \underline{CF_3}$
60·98	Multiplet	1	3 Ring F's
82·89	Multiplet	1	6 Ring F's
90·43	Multiplet	1	5 Ring F's



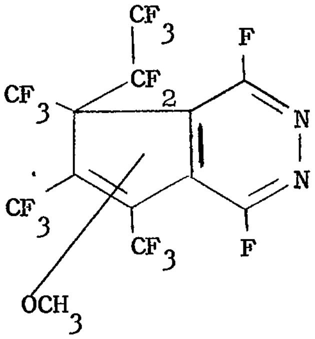
(<u>95</u>)

56·51	Multiplet $J_{CF_3-CF_3}$ 12·3	3	$\underline{CF_3}\diagdown C=$
64·10	Multiplet $J_{CF_3-CF_3}$ 12·3	3	$=C{\diagup \underline{CF_3} \atop \diagdown OCH_3}$
60·98	Multiplet	1	3 Ring F's
82·89	Multiplet	1	6 Ring F's
90·43	Multiplet	1	5 Ring F's

^{19}F measurements were carried out on a mixture of the two isomers.

Ratio of isomers, <u>Cis</u>:<u>Trans</u> = 66:34

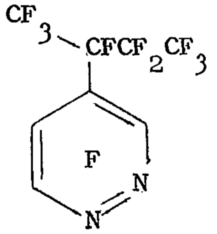
15. Methoxy derivative of perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene



$CHCl_3/CCl_4$

Chemical Shift (p.p.m.)	Fine Structure	Relative Intensity	Assignment
59·1	Multiplet	3	CF_3
61·2	Multiplet	2	CF_2
63·2	Multiplet	3	CF_3
74·6	Multiplet	1	4 Ring F's
81·0	Singlet	3	$CF_2\underline{CF_3}$
82·1	Multiplet	1	7 Ring F's
109·0	Multiplet	2	$-\underline{CF_2}CF_3$

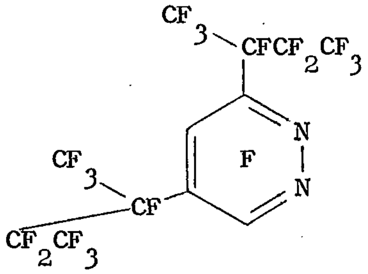
16. Perfluoro-4-sec-butylpyridazine, (106)



(Neat)

Chemical Shift (p.p.m.)	Fine Structure	Relative Intensity	Assignment
71·2	Broad multiplet	1	3 Ring F'S
72·7	Broad singlet	3	$\underline{CF_3}$-CF
82·2	Multiplet	3	$\diagdown\underset{\mid}{C}FCF_2\underline{CF_3}$
97·8	Multiplet	1	6 Ring F's
121·15	Multiplet	2	$\diagdown\underset{\mid}{C}F\underline{CF_2}CF_3$
182·5	Broad multiplet	1	$\diagdown\underset{\mid}{C}\underline{F}$-

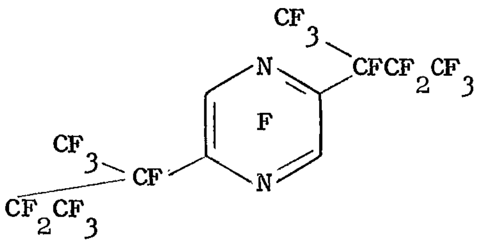
17. Perfluoro-3,5-bis-sec-butylpyridazine, (107)



(Acetone)

Chemical Shift (p.p.m.)	Fine Structure	Relative Intensity	Assignment
69·1	Broad multiplet	1	6 Ring F's
73·9	Broad singlet	6	$\underline{CF_3}\diagdown\underset{\mid}{C}F$-
82·3	Singlet	6	$\diagdown\underset{\mid}{C}FCF_2\underline{CF_3}$
102·9	Broad singlet	1	4 Ring F's
121·0	Broad multiplet	4	$\diagdown\underset{\mid}{C}F\underline{CF_2}-CF_3$
181·5	Multiplet	1	$\left.\right\}$ $CF_3C\underline{F}CF_2$-
187·0	Multiplet	1	

18. Perfluoro-2,5-bis-sec.butylpyrazine, (113)



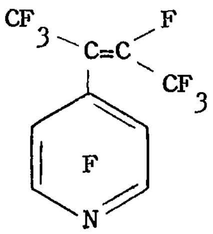
Chemical Shift (p.p.m.)	Relative Intensity	Assignment
74·6	6	$\underline{\mathrm{CF}_3}\diagdown\underset{\vert}{\mathrm{CF}}-$
76·7	2	3,6 Ring F's
82·5	6	$\diagdown\underset{\vert}{\mathrm{CF}}\mathrm{CF}_2\underline{\mathrm{CF}_3}$
122·0	4	$\diagdown\underset{\vert}{\mathrm{CF}}\underline{\mathrm{CF}_2}\mathrm{CF}_3$
188·0	2	$\mathrm{CF}_3\diagdown\underline{\mathrm{CF}}\mathrm{CF}_2-$

APPENDIX II

Mass Spectral Data

The mass to charge ($^m/e$) values are given with the relative abundance (% of base peak) in parentheses. All peaks of > 5% of the base peak (arbitrarily 100%) and certain others of diagnostic value < 5%, are recorded.

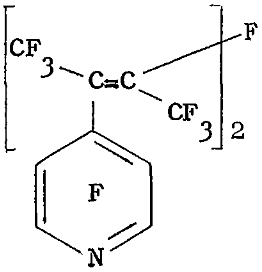
1.



(43)

332(8), 331(68), 312(26), 263(9), 262(100), 224(9), 212(28), 193(15), 162(8), 148(8), 131(8), 125(13), 118(15), 93(13), 69(91).

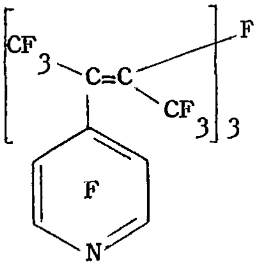
2.



(44)

494(18), 493(93), 475(10), 474(50), 424(20), 373(13), 353(13), 335(15), 304(13), 285(25), 211(13), 199(8), 117(5), 91(8), 69(100).

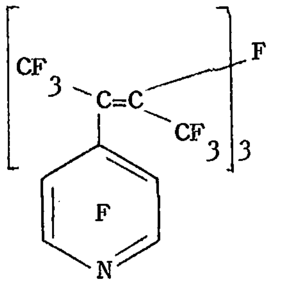
3.



(45)

656(21), 655(100), 637(6), 636(34), 446(6), 292(6), 69(37).

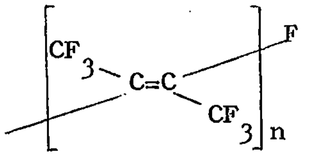
4.



(46)

656(29), 655(97), 637(10), 636(45), 496(8), 445(11), 439(7), 398(7), 380(7), 373(13), 369(9), 309(8), 292(16), 223(7), 199(12), 119(19), 114(7), 93(7), 69(100).

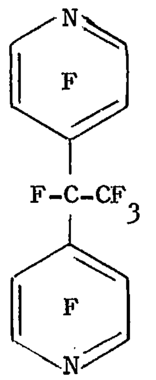
5.



(47)

1496(9), 1426(9), 1333(14), 1264(9), 1171(26), 1152(9), 1102(11), 1009(57), 990(23), 940(20), 847(14), 200(10), 181(9), 149(9), 131(9), 119(11), 117(7), 100(6), 69(100), 57(11), 56(9), 55(9), 44(9), 43(11), 41(14).

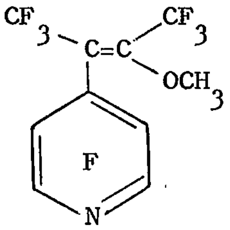
6.



(69)

401(14), 400(88), 381(17), 332(15), 331(100), 290(14), 285(17), 280(48), 262(19), 236(6), 231(10), 224(6), 217(6), 200(23), 186(8), 141(6), 131(6), 117(12), 100(12), 93(12), 86(6), 69(7), 31(17).

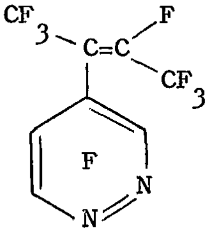
7.



(76)

344(8), 343(61), 324(33), 286(33), 274(44), 259(25), 240(68), 231(22), 224(11), 212(33), 200(11), 181(14), 162(31), 143(14), 131(11), 124(11), 117(20), 93(11), 81(25), 69(100), 59(100), 33(11), 31(14).

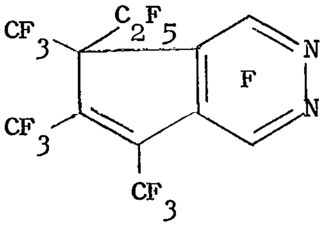
8.



(78)

315(11), 314(100), 295(18), 245(35), 217(29), 200(6), 186(8), 167(27), 148(8), 117(22), 98(6), 93(13), 69(41), 44(7), 31(14).

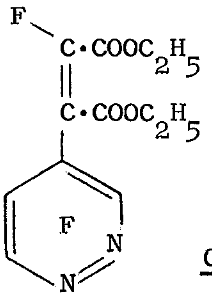
9.



(79)

477(5), 476(33), 457(26), 357(9), 338(14), 319(7), 279(5), 269(11), 260(6), 241(13), 210(6), 191(8), 172(5), 141(13), 119(87), 117(10), 100(5), 93(7), 85(5), 69(100), 31(11).

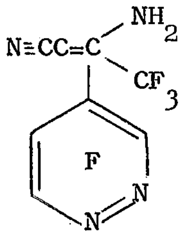
10.



Cis and *Trans* (90 and 91)

322(33), 295(7), 294(8), 278(13), 277(55), 276(8), 266(19), 265(33), 250(27), 249(100), 238(28), 237(60), 229(7), 222(21), 221(80), 217(16), 209(11), 205(13), 201(12), 198(15), 194(7), 190(8), 189(45), 185(8), 178(34), 177(49), 176(25), 174(10), 172(14), 162(9), 161(37), 159(9), 146(11), 144(13), 143(11), 133(9), 118(8), 117(33), 110(9), 99(13), 98(21), 93(7), 86(9), 79(8), 71(13), 69(9), 64(9), 55(10), 45(41), 44(69), 43(21), 41(10), 31(18).

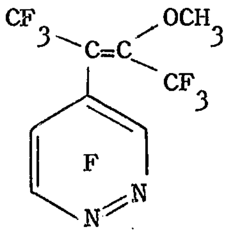
11.



(93)

269(11), 268(64), 197(14), 196(100), 180(11), 170(8), 169(19), 149(14), 129(22), 124(8), 123(8), 122(11), 121(6), 114(6), 113(8), 104(22), 96(14), 94(8), 79(8), 78(19), 77(39), 70(14), 69(28), 52(14), 51(11), 48(11), 46(11), 31(17).

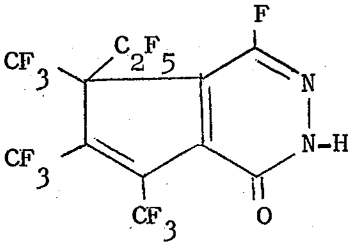
12.



Cis and *Trans* (94 and 95)

326(4), 117(7), 105(10), 103(67), 101(100), 69(23), 68(5), 66(15), 47(13), 32(65), 31(99).

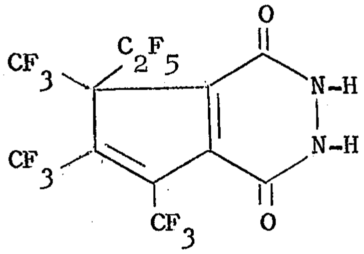
13.



(86)

475(16), 474(100), 456(7), 455(49), 355(37), 336(10), 335(32), 327(10), 317(32), 307(16), 299(10), 287(25), 280(15), 267(10), 249(12), 229(16), 141(10), 119(25), 117(7), 69(50).

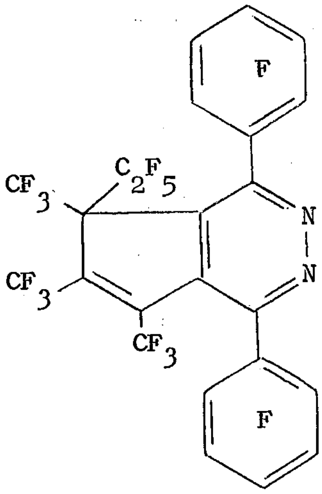
14.



(87)

473(21), 472(100), 454(7), 453(41), 423(14), 373(17), 345(7), 333(7), 324(10), 323(86), 305(10), 304(28), 295(16), 285(7), 277(21), 276(17), 267(7), 249(10), 229(10), 208(10), 199(10), 198(7), 179(10), 119(10), 117(7), 69(16).

15.



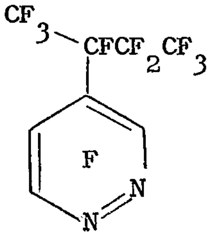
(98)

761(24), 760(76), 742(6), 741(18), 692(14), 691(46), 642(24), 641(71), 584(21), 575(10), 565(12), 556(12), 551(16), 488(10), 478(86), 438(8), 274(8), 272(16), 270(12), 240(38), 238(100), 236(100), 204(86), 203(15), 202(14), 201(18), 168(8), 166(19), 119(13), 117(8), 93(6), 69(57).

16. Methoxy derivative of (98) i.e. (99)

488(15), 469(9), 457(11), 420(15), 419(100), 338(9), 319(9), 300(33), 285(13), 281(7), 241(7), 141(7), 119(22), 81(7), 69(41), 31(6).

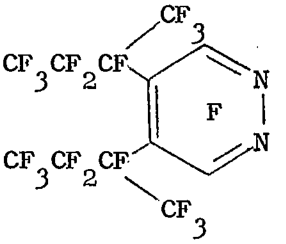
17.



(106)

352(24), 233(16), 205(6), 184(6), 183(61), 155(15), 119(24), 117(17), 105(8), 100(8), 93(11), 74(8), 69(100), 31(18).

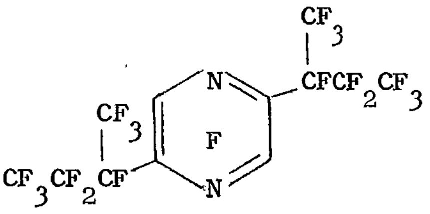
18.



(107)

553(11), 552(66), 534(6), 533(33), 483(9), 432(28), 382(12), 355(13), 317(6), 305(8), 286(8), 267(15), 255(8), 236(8), 217(9), 131(6), 119(31), 117(8), 100(6), 93(8), 69(100), 31(6).

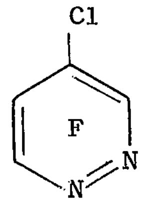
19.



(113)

552(21), 534(6), 533(44), 469(12), 421(9), 420(27), 381(9), 380(56), 347(12), 300(18), 268(15), 249(53), 218(7), 184(6), 143(6), 124(6), 119(38), 100(16), 93(15), 69(100).

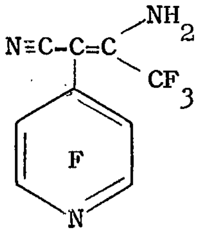
20.



(129)

170(33), 169(6), 168(100), 140(11), 111(11), 109(30), 105(18), 92(11), 90(27), 88(6), 74(11), 69(9), 54(14), 37(2), 35(3).

21.



(77)

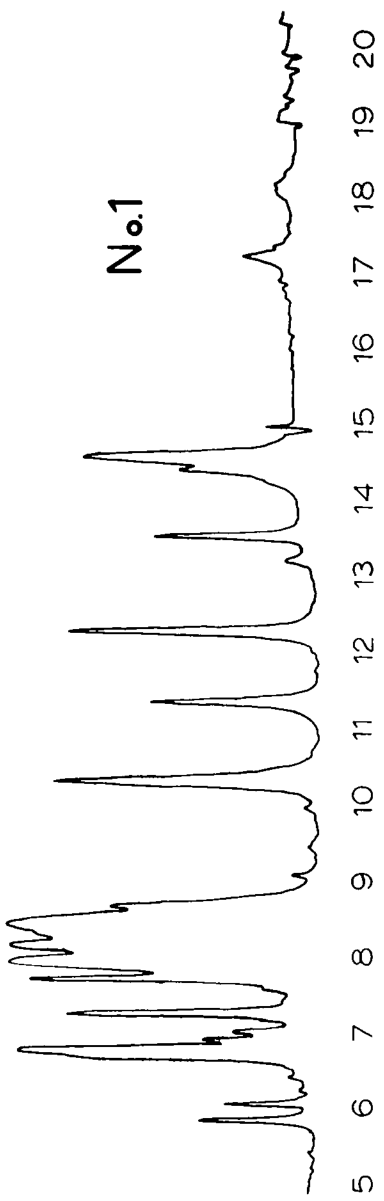
286(11), 285(93), 267(11), 266(100), 265(11), 246(20), 245(21), 216(27), 215(20), 196(10), 189(27), 169(18), 162(15), 124(8), 69(16), 38(7), 36(20), 31(8).

APPENDIX III

Infra-red Spectra

Spectrum No.	Compound	State
1.	Perfluoro-4-(2'-butenyl)pyridine, (43)	l.
2.	Perfluoro-2-(4'-pyridyl)-3,4-dimethylhexa-2,4-diene, (44)	l.
3.	Perfluoro-2-(4'-pyridyl)-3,4,5,6-tetramethylocta-2,4,6-triene, (45)	l.
4.	Isomer of (45) perfluoro-2-(4'-pyridyl)-3,4,5,6-tetramethylocta-2,4,6-triene, (46)	l.
5.	Polymer of hexafluorobut-2-yne, (47)	s.
6.	1-Fluoro-1,2-(biscarbethoxy)-2-(2',3',5',6'-tetrafluoropyridyl)ethylene (cis/trans mixture 50:50), (42)	l.
7.	1,1-Bis(1',2',5',6'-tetrafluoropyridyl)tetrafluoroethane, (69)	s.
8.	Cis 3-methoxy-2-(2',3',5',6'-tetrafluoropyridyl)-hexafluorobutene, (76)	l.
9.	Enamine of perfluoro-4-(2'-butenyl)pyridine, (77)	s.
10.	Perfluoro-4-(2'-butenyl)pyridazine, (78)	l.
11.	Perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (79)	s.
12.	1-Fluoro-1,2-(biscarbethoxy)-2-(3',5',6'-trifluoropyridyl)ethylene (cis/trans mixture 40:60), (91)	l.
13.	Enamine of perfluoro-4-(2'-butenyl)pyridazine, (93)	s.
14.	1,2,3-Tris-(trifluoromethyl)-1-pentafluoroethyl)-7-fluoro-4-hydroxy-5,6-diazaindene, (86)	s.
15.	1,2,3-Tris-(trifluoromethyl)-1-pentafluoroethyl-4,7-dihydroxy-5,6-diazaindene, (87)	s.
16.	Mono-methoxy derivative of perfluoro-(1,2,3-trimethyl)-1-ethyl-5,6-diazaindene, (99) or (100)	s.
17.	Perfluoro-(1,2,3-trimethyl)-1-ethyl-4,7-diphenyl-5,6-diazaindene, (97)	s.
18.	Perfluoro-4-sec.butylpyridine, (104)	l.
19.	Perfluoro-2,4-di-sec.butylpyridine, (105)	l.

20.	Perfluoro-3,5-di-sec.butylpyridazine, (107)	1.
21.	Perfluoro-4-sec.butylpyridazine, (106)	1.
22.	Perfluoro-2,5-di-sec.butylpyrazine, (113)	1.
23.	4-Chloro-3,5,6-trifluoropyridazine, (129)	1.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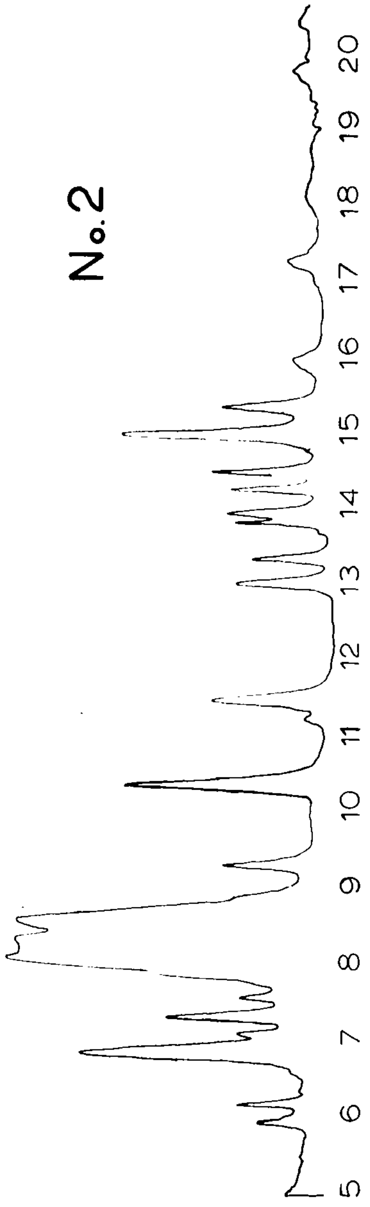
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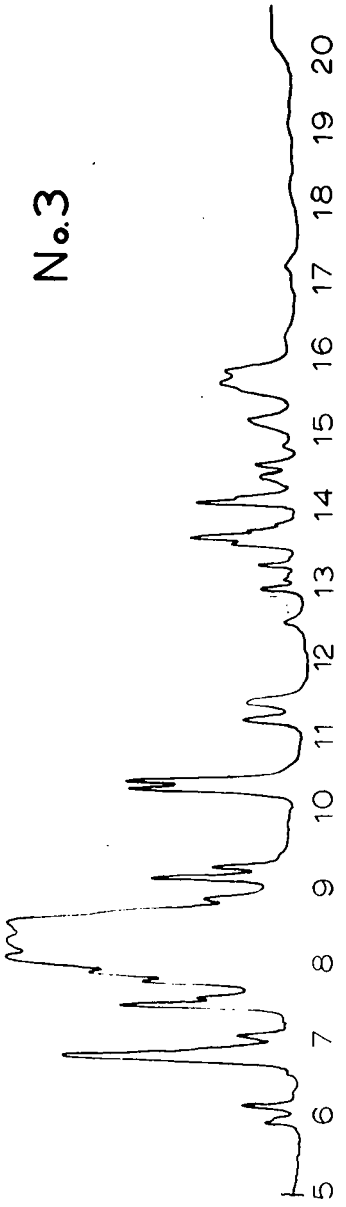
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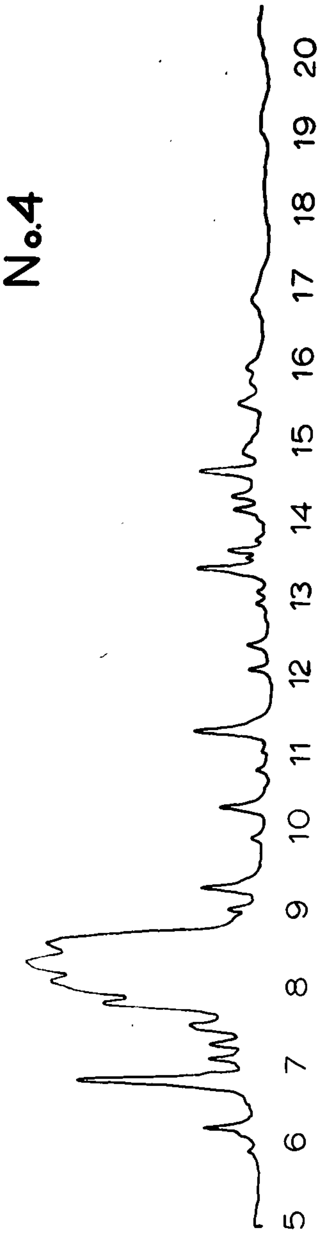

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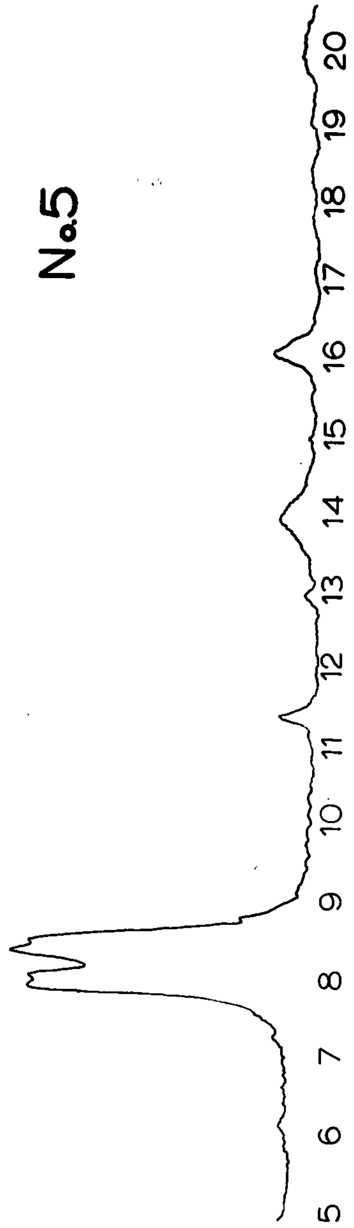

No.5

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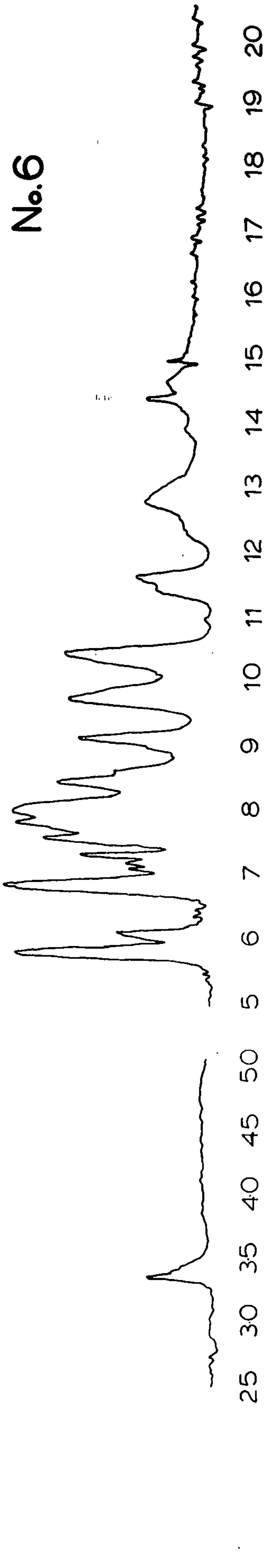

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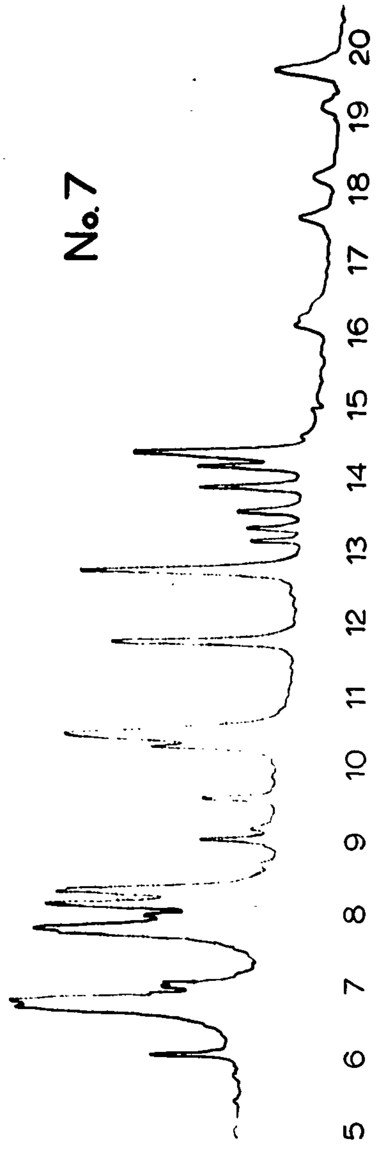
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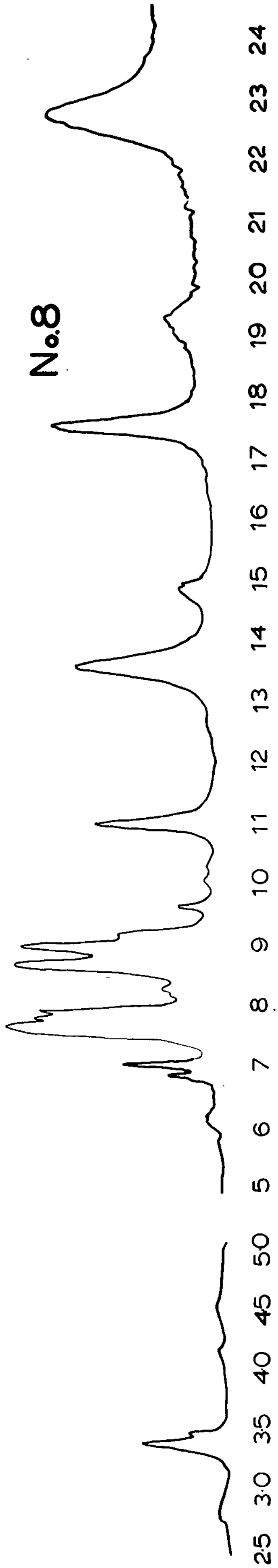
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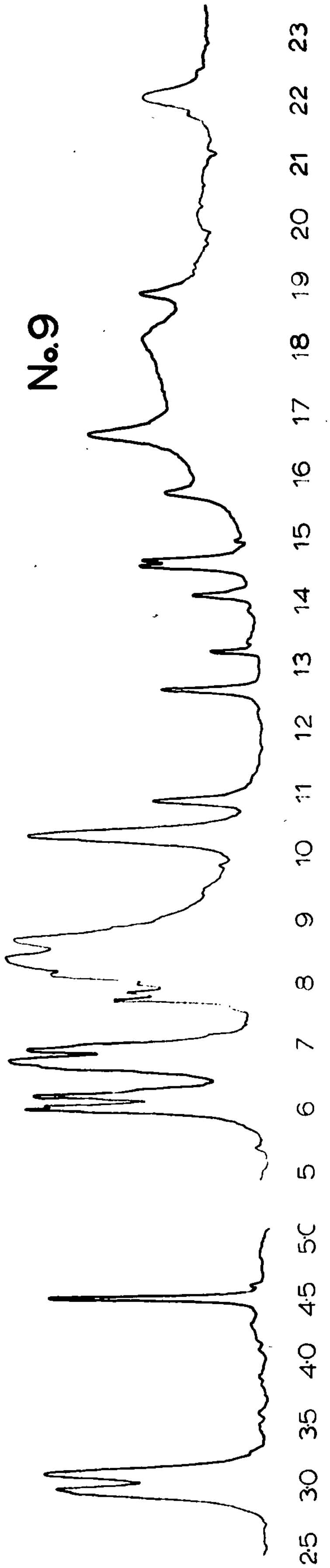
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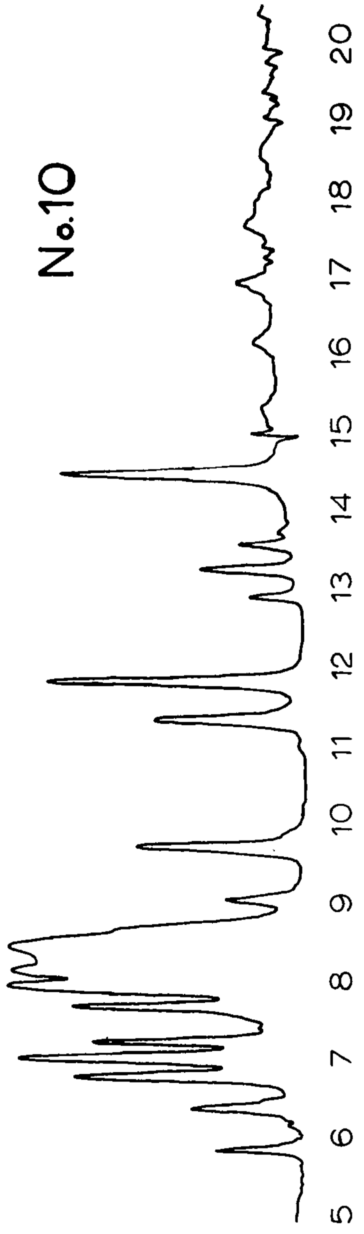
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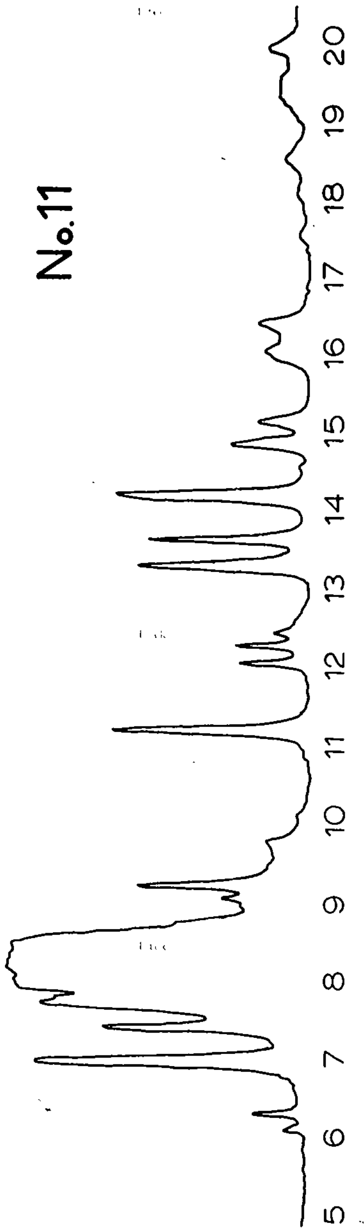
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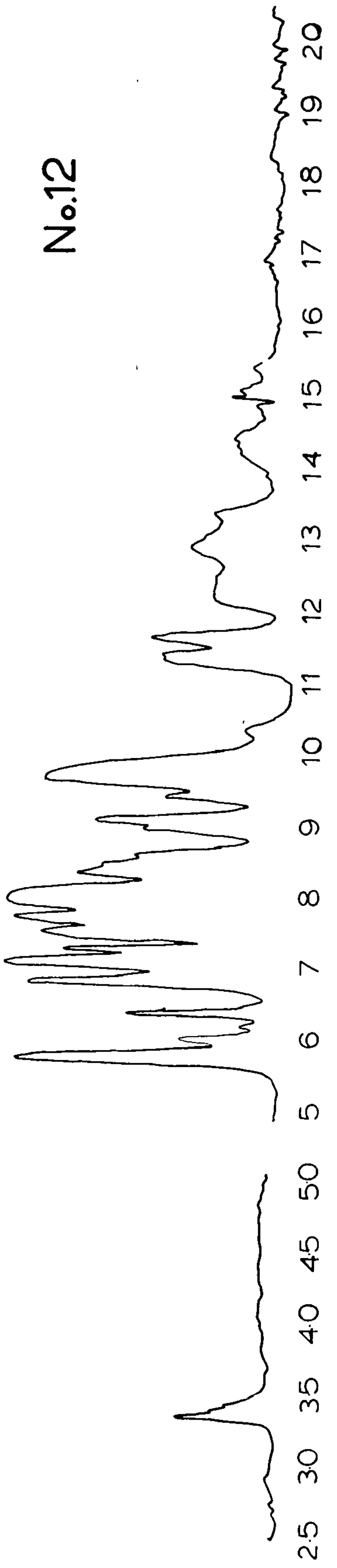
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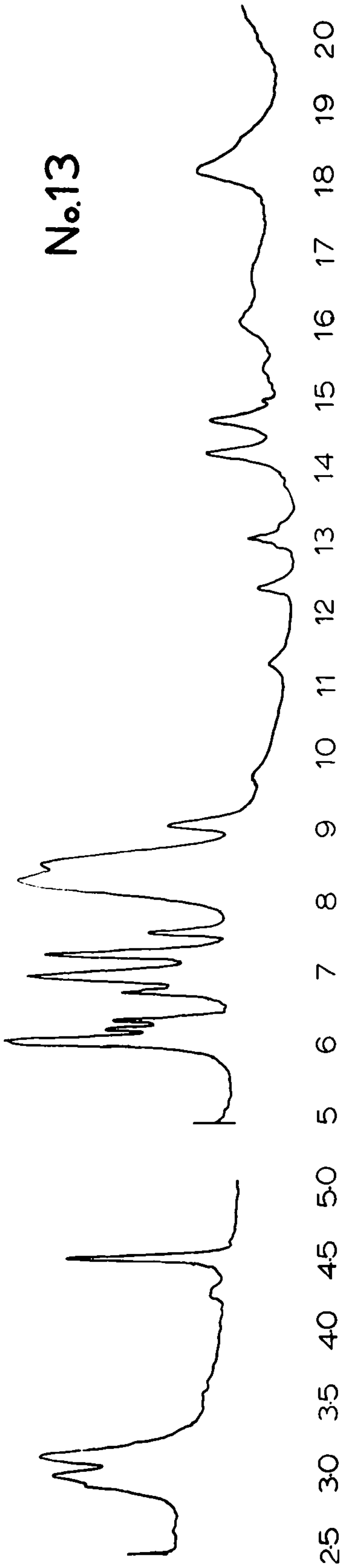

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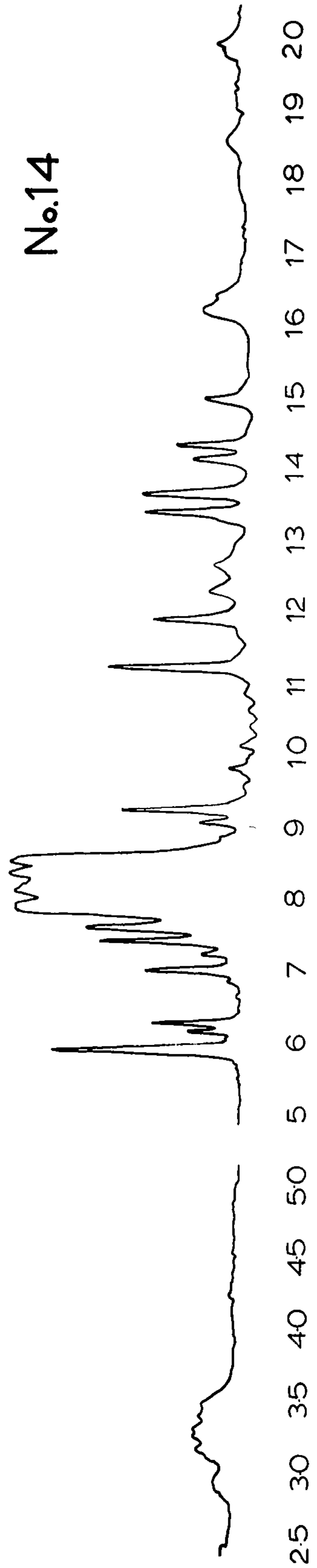

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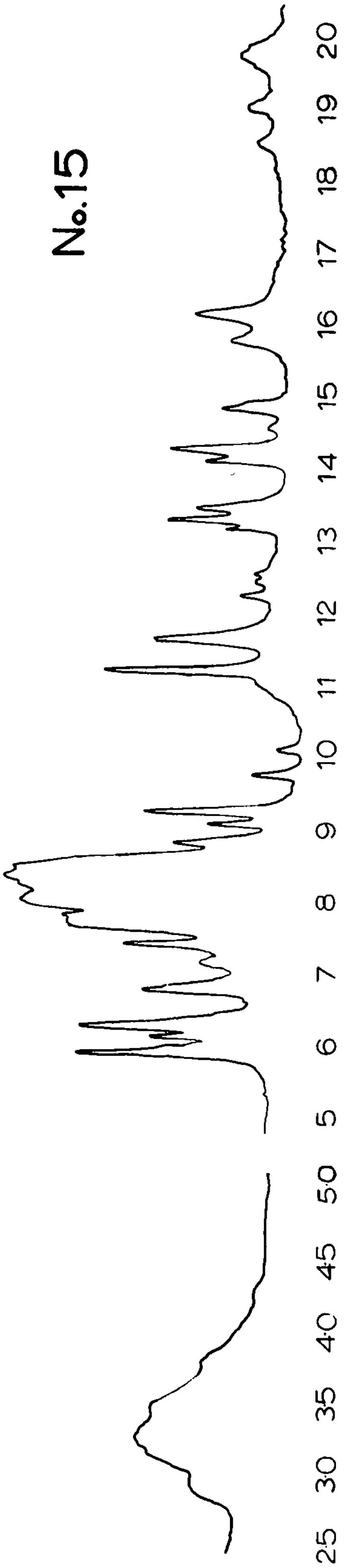

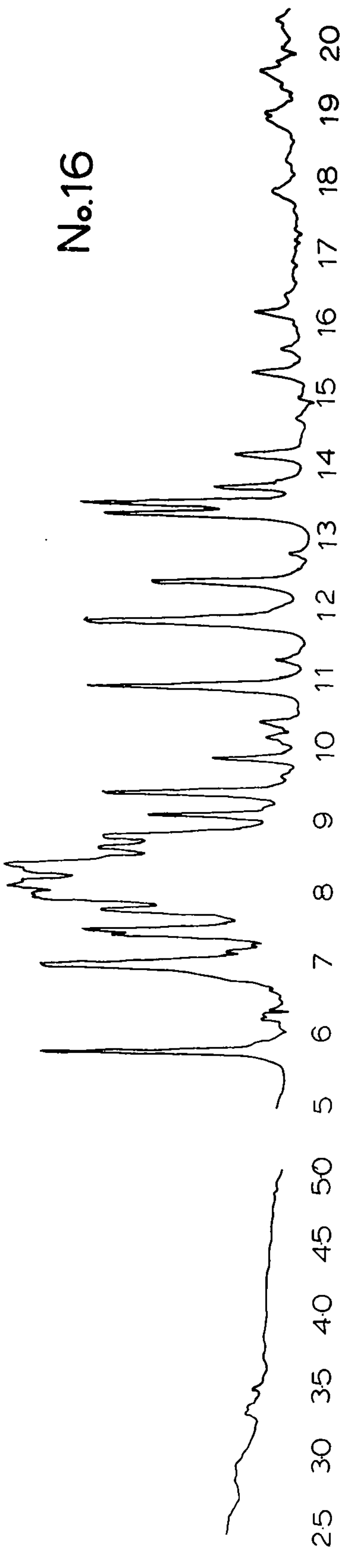

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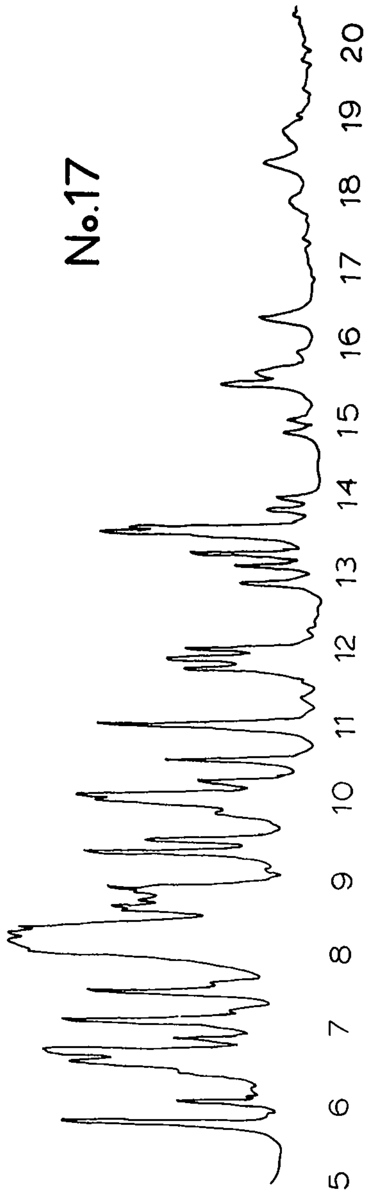

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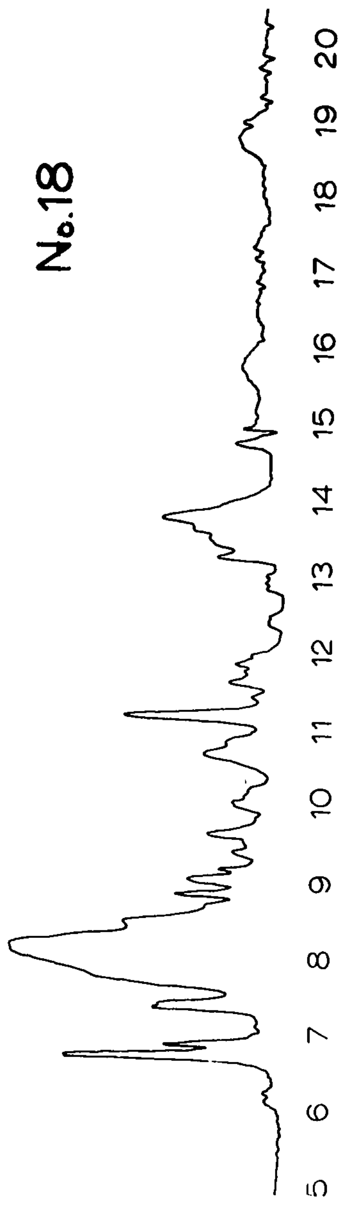

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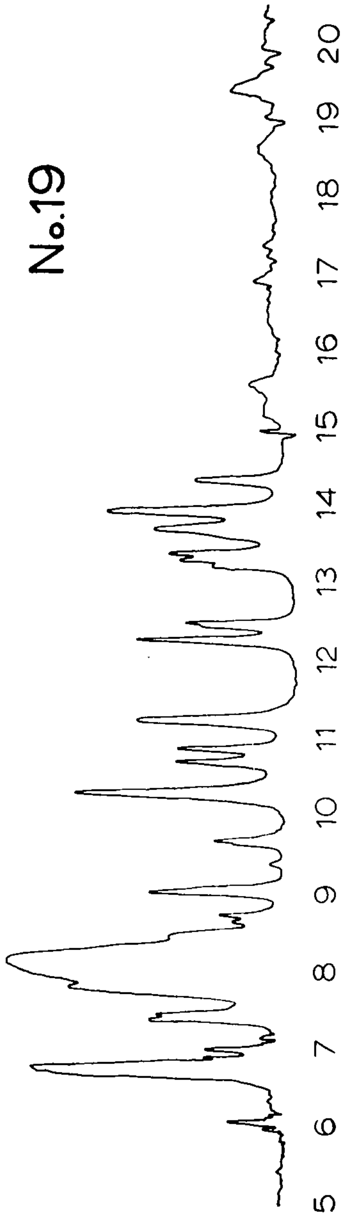

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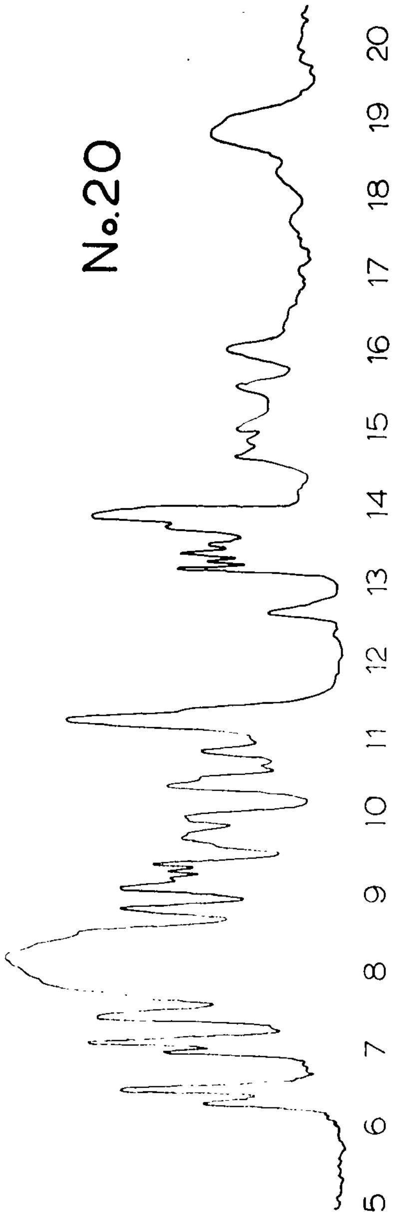

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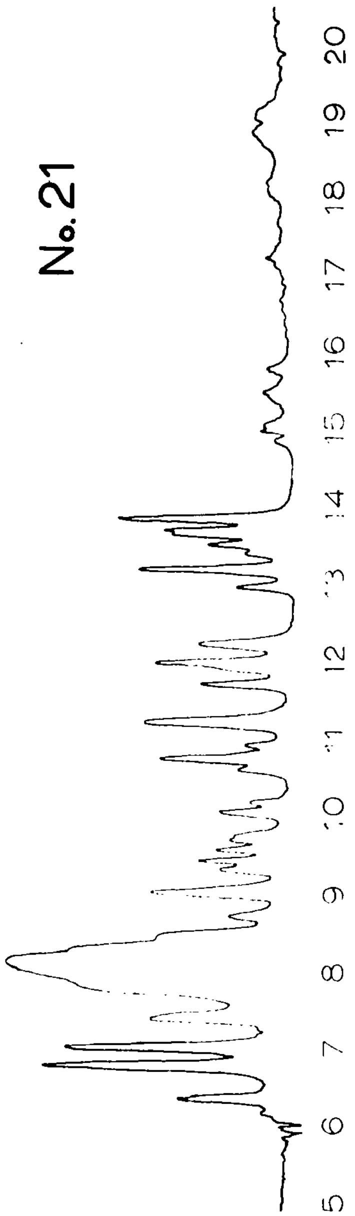

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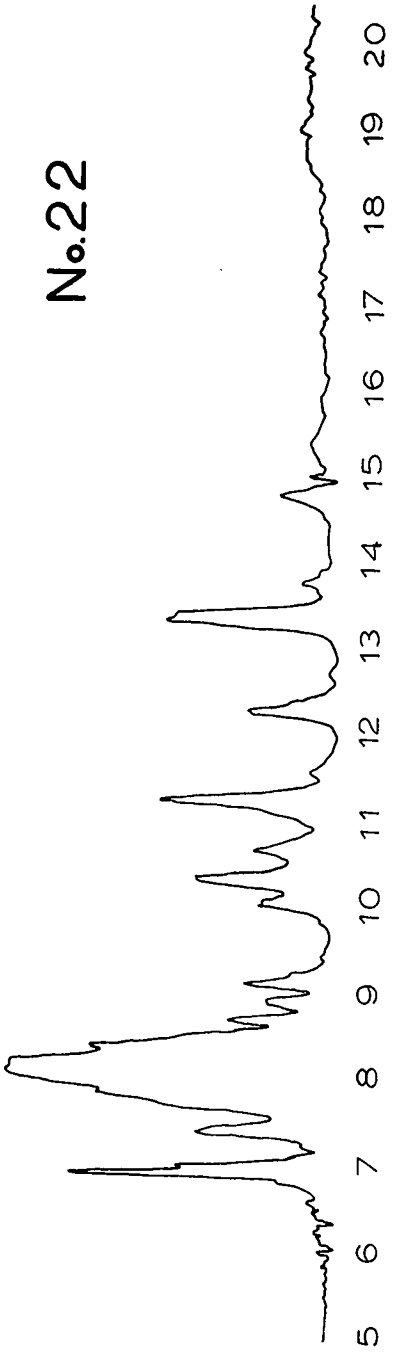
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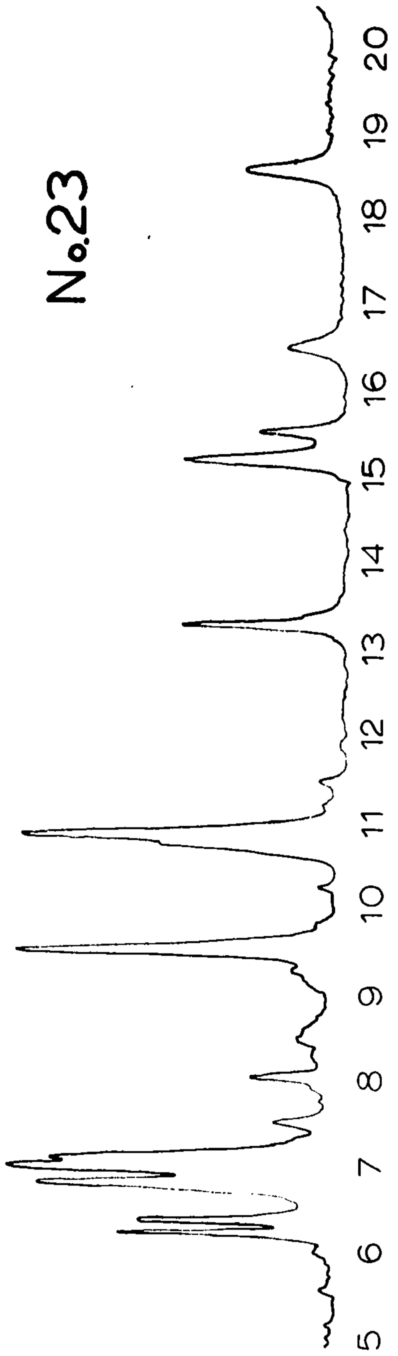
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