Fluoride ion-initiated reactions of perfluorocycloalkenes

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UNIVERSITY OF DURHAM

A THESIS

entitled

FLUORIDE ION-INITIATED REACTIONS OF PERFLUOROCYCLOALKENES

submitted by

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(Graduate Society)

A Candidate for the degree of Doctor of Philosophy

1971

'noli desperare quale sit, quam latum nota'

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TO

CHRISTINE

MEMORANDUM

The work described in this thesis was carried out in the University of Durham between January 1968 and December 1970. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

SUMMARY

Fluoride Ion-initiated Reactions of Perfluorocycloalkenes

This work is concerned mainly with the fluoride ion-initiated reactions of perfluorocycloalkenes with perfluoroheterocyclic systems. Perfluoro-(4-cycloalkylpyridines) were formed by the reaction of pentafluoropyridine with perfluorocyclo-hexene, -hexadienes, -pentene and -butene, in the presence of caesium fluoride and sulpholan. Using more vigorous reaction conditions, the 2,4-di- and 2,4,6-tri-substituted products were obtained in the case of perfluorocyclohexene. Self-condensation of the perfluorocycloalkene, initiated by fluoride ion, was an important side reaction in the perfluorocycloalkylation of pentafluoropyridine, and perfluorocyclopentene and perfluorocyclobutene readily formed a dimer and a trimer respectively, whereas the dimer of perfluorocyclohexene was formed only under vigorous conditions. The reaction of perfluorocyclohexa-1,4-diene was also investigated and, although the results were not fully understood, it was thought that a complex fluorocarbanion may exist in solution.

Treatment of the perfluoro-(4-cycloalkylpyridines) with sodium methoxide in methanol gave the corresponding 2-methoxy derivatives, but methoxide ion was found to substitute in the cycloalkenyl ring of perfluoro-(4-cyclohexenylpyridine), the latter being so reactive that nucleophilic substitution by methoxide ion occurred with methanol alone.

The relative rates of reactivity of a series of perfluoro-(4-alkylpyridines) was found to be in the order perfluorocyclobutyl- > perfluorocyclohexyl- > perfluorocyclopentyl- > perfluoroisopropyl- > perfluoroethyl-.

Defluorination of perfluoro-(4-cyclohexylpyridine) by passage over iron at 500° gave perfluoro-(4-phenylpyridine), whereas perfluoro-(4-cyclopentyl-

pyridine) and perfluoro-(4-cyclobutylpyridine) were converted to perfluoro-(4-cyclopentenylpyridine) and perfluoro-(4-cyclobutenylpyridine), respectively, under the same conditions.

The normal pattern of orientation of substitution was followed when the 2-cyclohexyl- and 2,4-dicyclohexyl- derivatives of perfluoro-(4-isopropylpyridine) were prepared by the fluoride ion-initiated reaction of the latter with perfluorocyclohexene.

The polyfluoroalkylation reaction was investigated using tetrafluoropyridazine and perfluoro-(4-cyclohexylpyridazine) was isolated in good yield from the reaction of tetrafluoropyridazine and perfluorocyclohexene with caesium fluoride and sulpholan at moderate temperatures. Substitution of perfluoro-(4-cyclohexylpyridazine) with ammonia occurred readily at 0° to give the 5-amino derivative, and treatment of the former with concentrated sulphuric acid gave a pyridazone. Photolysis of perfluoro-(4-cyclohexylpyridazine) gave perfluoro-(6-cyclohexylpyrazine) whereas partial defluorination of the cyclohexyl ring occurred on pyrolysis.

Oxidation of perfluorocyclopentene dimer with potassium permanganate gave a dihydroxy derivative by addition to the exocyclic double bond, and defluorination of the dimer afforded perfluorobicyclopentenyl which was stable to further defluorination. Perfluorobicyclopentenyl readily formed a dimethoxy derivative by reaction with sodium methoxide, and gave a perfluorodiisopropyl derivative by a fluoride ion-initiated reaction with hexafluoropropene. The oligomers of the perfluorocycloalkenes were all unchanged on photolysis.

Mass spectrometric studies have been carried out on a series of perfluorocycloalkenes and perfluoroalkylpyridines.

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GENERAL INTRODUCTION

The study of fluorocarbon systems is becoming of increasing importance. Fluorine is unique since extensive and complete replacement of hydrogen, in a hydrocarbon system, by fluorine is possible, and this is achieved without gross distortion of the geometry of the system. The differences in properties between fluorocarbons and hydrocarbons are thus not dominated by stereochemical differences, although steric effects cannot be ignored. It is easy to see, therefore, a completely new field of synthetic organic chemistry, based on carbon and fluorine, rather than on carbon and hydrogen.

There are several methods available for the introduction of fluorine into organic compounds by the selective replacement of hydrogen or halogens by fluorine, although polyfluorinated organic compounds are best prepared by the following methods.

1. Replacement of Hydrogen by Fluorine

Three methods are available for the conversion of hydrocarbons or their derivatives into saturated fluorocarbons: direct vapour-phase fluorination, indirect fluorination with certain high-valency metal fluorides, and electrolysis in anhydrous hydrogen fluoride.

(a) Direct vapour-phase fluorination of hydrocarbons [1]

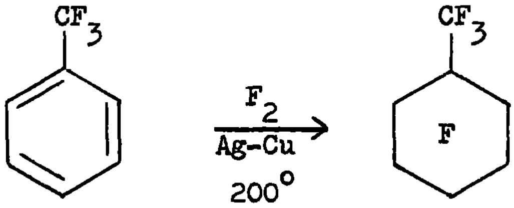
The reaction of a hydrocarbon with fluorine proceeds via a free-radical chain mechanism, and a perfluoro-alkane or -cycloalkane is formed by the progressive replacement of hydrogen and saturation of any multiple bonds or aromatic systems by fluorine. The bond dissociation energy of fluorine is relatively small, and at high temperatures fluorine atoms, for initiation of chain reactions, will be produced by thermal dissociation.

$$F_2 \rightleftharpoons 2F\cdot$$

$$RH \xrightarrow{F\cdot} HF + R\cdot \xrightarrow{F_2} RF + F\cdot \longrightarrow \text{etc.} \longrightarrow CF_4$$

These reactions are highly exothermic and are normally carried out in the presence of a gold or silver/copper catalyst. The controlled replacement of hydrogen by fluorine is difficult but perfluorinated derivatives are obtained in relatively high yields e.g.[2]

$$n\text{-}C_7H_{16} \xrightarrow[\text{Ag-Cu}\ 135^\circ]{F_2} n\text{-}C_7F_{16} \qquad (62\%)$$

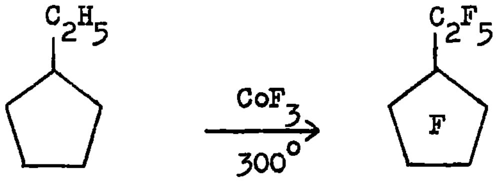


(85%)

(b) Fluorination with cobalt fluoride

The cobalt fluoride method of fluorination[3,4] is more convenient and gives better yields of saturated fluorocarbons than the catalytic method mentioned previously. Fluorination is achieved by passing the hydrocarbon vapour over a heated bed of cobalt trifluoride, and at high temperatures, complete replacement of hydrogen by fluorine can be obtained, and addition of fluorine to unsaturated or aromatic compounds can also be effected.

e.g.



(59%) [3]

The cobalt trifluoride is reduced to cobalt difluoride, but the former can be conveniently regenerated by passage of fluorine through the system.

$$-CH_2- \ + \ 4CoF_3 \longrightarrow -CF_2- \ + \ 4CoF_2 \ + \ 2HF$$

$$2CoF_2 \ + \ F_2 \longrightarrow 2CoF_3$$

Fluorinations with cobalt trifluoride are less exothermic, and hence more easily controlled, than those using elemental fluorine.

(c) Electrochemical fluorination

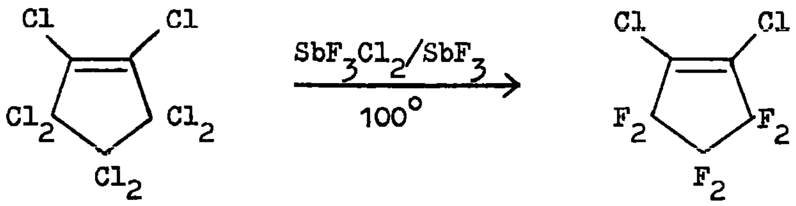
Many organic compounds, particularly those containing polar groups, dissolve in anhydrous hydrogen fluoride, and electrolysis of such solutions results in virtually complete replacement of hydrogen by fluorine.[5] The fluorination occurs by some anodic process and hydrogen is liberated at the cathode. A distinct feature of this method is the formation of products possessing the original functional groups in addition to the fully fluorinated products, e.g.[6]

$$CH_3 \cdot SO_2F \longrightarrow CF_3 \cdot SO_2F \qquad (96\%)$$

2. Replacement of Halogens by Fluorine

Fluorination by halogen exchange is by far the most widely used method of synthesising organic fluorine compounds,[7] and a comprehensive review of the applications of this method was made by Barbour.[7] Although several inorganic fluorides have been used to effect halogen exchange, those of hydrogen, antimony and potassium are perhaps the most frequently used. The preparation of fluorinated compounds using antimony fluorides was originated by Swarts and this method has found extensive application in the preparation of polyfluoroalkanes, more efficient fluorination being achieved by the presence of pentavalent antimony.

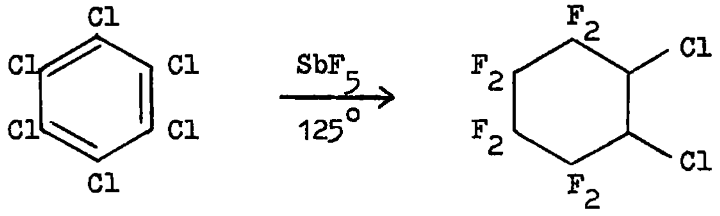
e.g.



[8]

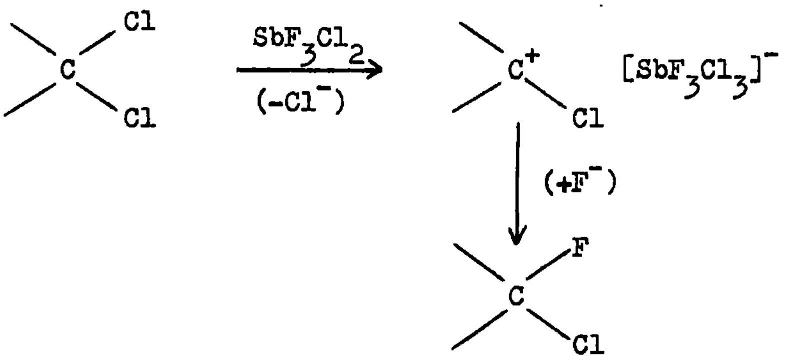
Saturation of double bonds occurs with antimony pentafluoride.

e.g.

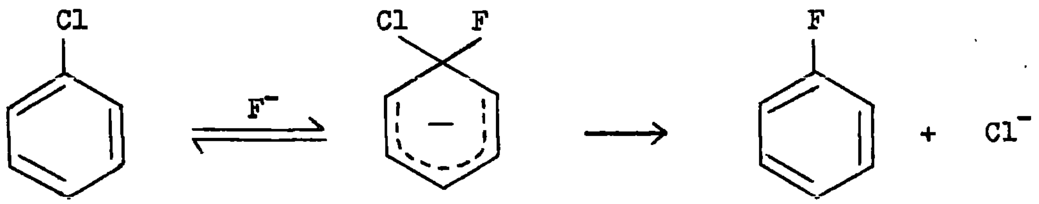


[9]

The mechanism proposed[10] for the Swarts reaction was the co-ordination of two halogens by the antimony, with an increase in covalency, although a mechanism involving an intermediate carbonium ion is possible, i.e.



Potassium fluoride is a useful reagent for the replacement of isolated halogen atoms by fluorine, and has found increasing use in the preparation of fluorinated aromatic compounds. This type of reaction may be carried out by heating the reactants together or in a suitable solvent. A probable mechanism[11] for the reaction between an aryl halide and potassium fluoride involves the rate-determining addition of fluoride ion to the substrate.



The versatility of potassium fluoride as a fluorinating agent is exemplified by its current application in the preparation of fluorinated heterocyclic compounds. Perfluoro-N-heteroaromatic compounds are prepared by halogen exchange between the corresponding perchloro-N-heteroaromatic compounds and potassium fluoride in the absence of solvent.

Fluorocarbons are of considerable interest for two reasons. Firstly, the replacement of hydrogen in a molecule by fluorine results in the functional groups being in different electronic environments, due to the difference in electronegativity between hydrogen and fluorine. This leads to a new series of compounds whose chemistry is different to that of the corresponding hydrocarbon compounds. Secondly, unsaturated fluorocarbon compounds exhibit a chemistry that is complimentary to that of the corresponding hydrocarbon compounds, since reactions in hydrocarbon chemistry frequently involve electrophilic attack with intermediate carbonium ions whereas unsaturated fluorocarbons undergo nucleophilic attack leading to carbanion intermediates.

The work described in this thesis is a study of the nucleophilic attack of perfluorinated heterocyclic substrates by carbanions derived from perfluorinated cyclic olefins and fluoride ion, and is an extension of the polyfluoroalkylation process. A study was also made of the orientation and rate of nucleophilic substitution in the resulting perfluoroalkylated compounds.

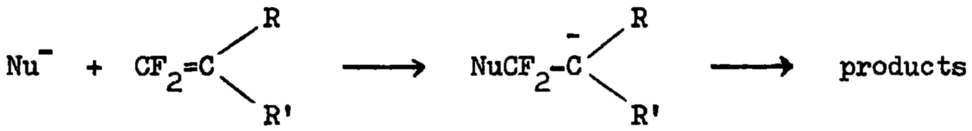
INTRODUCTION

CHAPTER 1

NUCLEOPHILIC REACTIONS OF FLUORO-OLEFINS

Introduction

The replacement of hydrogen by fluorine in an olefinic system results in a removal of electron density from the π-system, and this might be expected considering the electronegativity of fluorine. Thus, in contrast to the readiness of hydrocarbon olefins to undergo electrophilic attack, perfluoroolefins are more susceptible to nucleophilic attack.



Before discussing the nucleophilic reactions of fluoro-olefins it is important to consider the substituent effects on fluorocarbanions, since the relative stability of the carbanion will determine the direction of initial nucleophilic attack.

1.1 Stabilisation of Carbanions by Substituents

The effects of substituents on fluorocarbanions have been determined mainly from studies of the rates of base-catalysed hydrogen/deuterium exchange reactions, and these effects are considered to apply to the intermediate carbanion as well as the transition state (see Fig. 1).

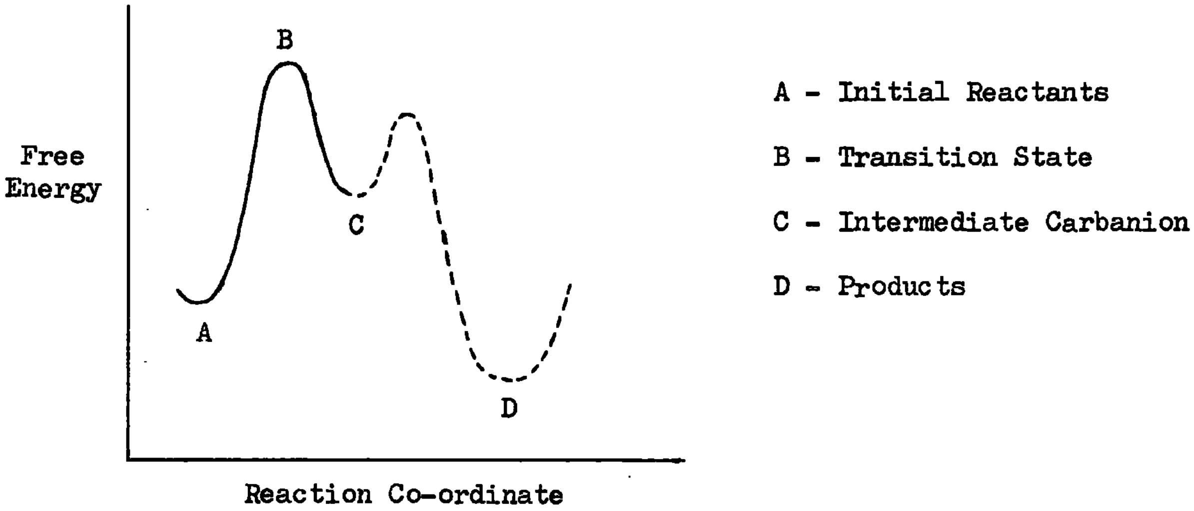
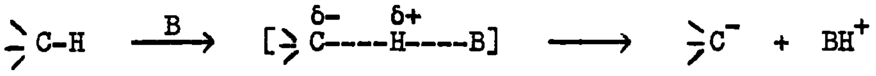


Fig. 1.

1.1.1 α-Halogen substituents

From a study of the kinetic acidity (rate of base-catalysed hydrogen/deuterium exchange) of a series of haloforms i.e. CHF_3, $CHCl_3$, $CHBr_3$ and CHI_3, Hine[12] found that the ability of the halogens to stabilise an adjacent (i.e. α) carbanion was in the order F < Cl < Br < I. In facilitating carbanion formation the α-halogen substituents lower the free energy of the carbanionic transition state,

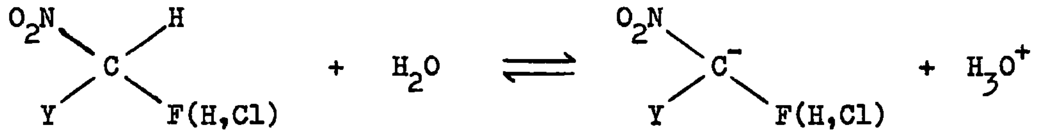


$$>C{-}H \xrightarrow{B} [> \overset{\delta-}{C}{-}{-}{-}{-}\overset{\delta+}{H}{-}{-}{-}{-}B] \longrightarrow >C^- + BH^+$$

and hence the corresponding carbanion.

Adolph and Kamlet[13] measured the ionisation constants for a series of fluoronitromethanes,

e.g.



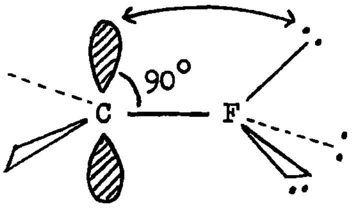
(Y = Cl, COOEt, $CONH_2$, NO_2)

and found that the pKa values were in the order F > H > Cl for a given Y group (except for Y = NO_2, where Cl ≈ H).

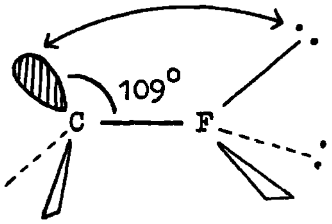
The conformation of the carbanion and the electronic configuration of the carbanionic carbon atom were shown by Hine[14] to be important factors in determining the effects of fluorine on carbanion stability. Carbanions with α-substituents which exert strong mesomeric effects (e.g. NO_2) tend towards a planar geometry (i.e. sp^2 hybridised), the degree of planarity depending on the strength of the mesomeric effect. Fluorine has a strong stabilising effect if the carbanion is sp^3 in electronic configuration, but this effect decreases as the carbanion approaches planarity (sp^2), and in fact, fluorine is destabilising relative to hydrogen in a planar carbanion.

To explain this, Hine[14] has suggested that the halogen bond to sp^2 carbon is weaker than to sp^3 carbon, since the former is more electronegative, and that this effect, which depends on the square of the electronegativity difference between the atoms involved, is larger for fluorine than for chlorine. Thus the formation of a planar carbanion (sp^2) from a tetrahedral (sp^3) initial state would require more energy when the substituent was fluorine than when it was chlorine or hydrogen. As the carbanion becomes less planar, the magnitude of this effect will decrease.

An alternative explanation[13] was based on the Iπ effect. In a planar carbanion it is possible to get a coulombic repulsion[15] between the electron pair in a p orbital on the carbon atom and the electrons in a filled p orbital on the fluorine. This effect (Iπ interaction) will be at a maximum for an sp^2 hybridised carbanion.



sp^2 carbanion



sp^3 carbanion

The order of Iπ repulsion effects for the halogens has been shown to be F > Cl > Br > I,[15] and these effects would be less important in the case of chlorine due to reduced overlap between the p orbitals on the halogen and those of the π system.

The order of carbanion stabilising ability has also been explained in terms of electrostatic polarisation of the halogen by the carbanionic charge, since the polarisabilities of the halogens increase with increasing atomic size.

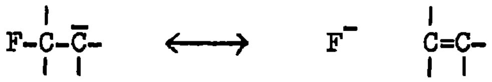
It can thus be seen that a variety of factors need to be considered in order to rationalise the substituent effects of the halogens on adjacent carbanions, and these include two opposing inductive effects (Iσ and Iπ), hybridisation effects, mesomeric effects and involvement of d-orbitals.

1.1.2 β-Halogen substituents

Andreades[16] measured the rate of hydrogen/deuterium exchange for a series of monohydroperfluoroalkanes, the results of which (see below) showed that fluorine and fluorocarbon groups greatly facilitated carbanion formation at the adjacent position.

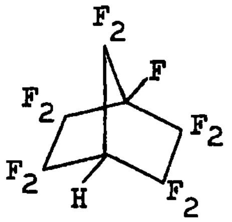
Compound	CF_3H	$CF_3(CF_2)_5CF_2H$	$(CF_3)_2CFH$	$(CF_3)_3CH$
Relative reactivities	1	6	2×10^5	10^9
pKa	31	30	20	11

The stabilisation of a carbanion by a β-fluorine atom was attributed by Andreades[16] to a 'negative hyperconjugation' effect, i.e.



$$F-\overset{|}{\underset{|}{C}}-\underset{|}{\bar{C}}- \longleftrightarrow F^- \quad \overset{|}{\underset{|}{C}}=\underset{|}{C}-$$

but Streitweiser[17] explained the stabilisation in terms of an inductive effect, from the results of the base-catalysed hydrogen/tritium exchange in 1-H-undecafluorobicyclo[2.2.1]heptane

		$(CF_3)_3CH$
Relative rates	5	1

The intermediate carbanion produced from this bridgehead compound will have an enforced pyramidal structure, and will be incapable of stabilisation by negative hyperconjugation.

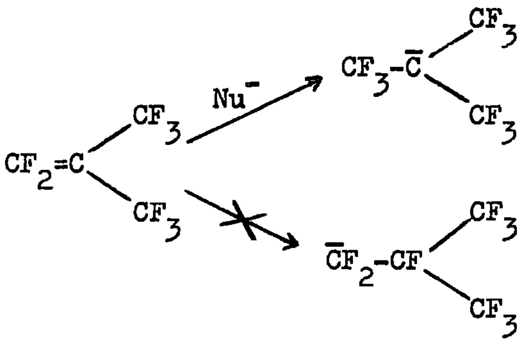
It was concluded that a β-fluorine atom stabilises a carbanion primarily by its inductive effect, and Andreades[16] found that the order of ability to stabilise a carbanion was β-fluorine > α-fluorine > hydrogen.

1.2 Nucleophilic Reactions of Acyclic Fluoro-olefins

From a consideration of the effects discussed above it can be seen that nucleophilic attack in a fluoro-olefin would be favoured at a position that would give rise to a tertiary carbanion. This is in agreement with an increase in reactivity towards nucleophilic attack along the series:

$$CF_2{=}CF_2 < CF_2{=}CF{-}CF_3 < CF_2{=}C(CF_3)_2$$

Also, an olefin containing a terminal difluoromethylene group is the most reactive to nucleophiles, and the terminal difluoromethylene group is the most reactive position in a terminal olefin towards nucleophilic attack, for example, perfluoroisobutene invariably undergoes nucleophilic addition at the $=CF_2$ group.



nine β fluorine atoms

no α fluorine atoms

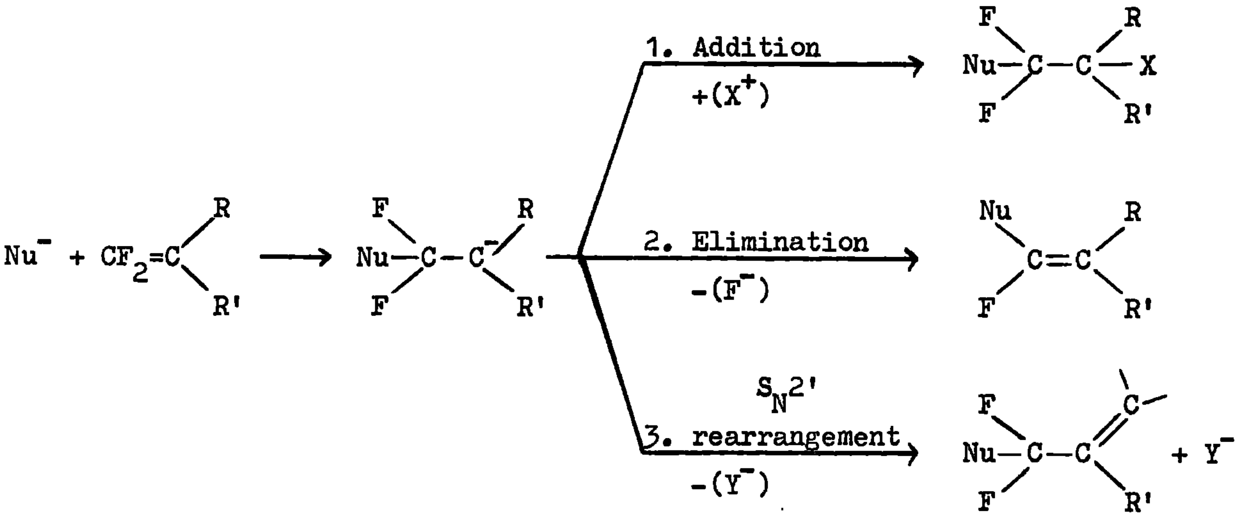
one β fluorine atom

two α fluorine atoms

It is difficult to compare the relative reactivity of a series of fluoro-olefins towards a nucleophile because of considerable variation in solubility of the olefins in the medium employed.

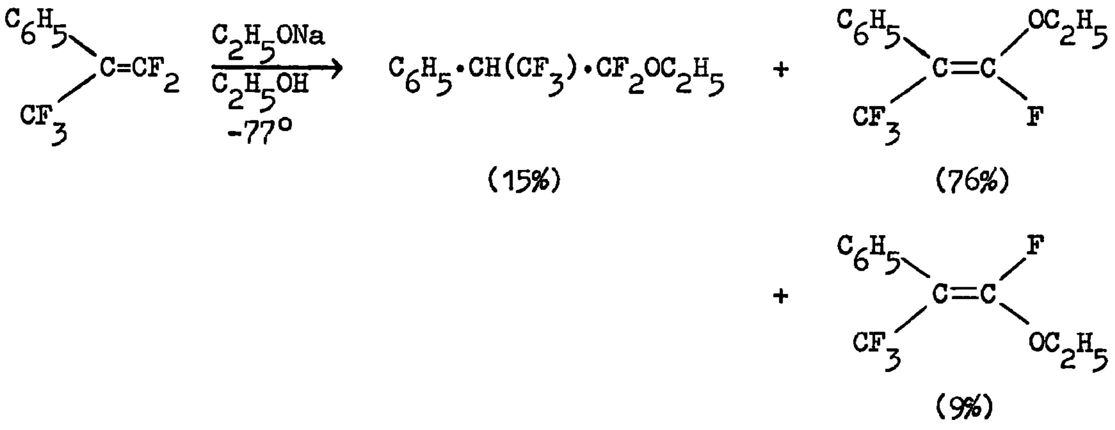
1.2.1 Mechanistic considerations

The generally accepted mechanistic interpretation of nucleophilic substitution reactions of fluoro-olefins involves a bimolecular, rate-determining carbanion formation, a concept first advanced by Miller and co-workers[18] in rationalising the base-catalysed addition of alcohols to chlorotrifluoroethylene. The general scheme for nucleophilic attack on a fluoro-olefin can be summarised as follows:



[Y = F, Cl, Br, I, H, OR]

Recent evidence for the formation of a carbanion intermediate in vinyl and allyl displacement reactions[19] has been produced from the results of reactions involving ethoxide ion attack on a series of fluoro-olefins of general formula $C_6H_5 \cdot C(R)=CF_2$. In three cases, where R = F, CF_3 and CF_2Cl, unsaturated ethers were obtained, e.g.



Kinetic data was obtained, and the similarity of the rates of reaction for the three olefins (where R = F, CF_3 and CF_2Cl) strongly suggests that the rate-determining step in all three cases is the initial attack of ethoxide on $CF_2=$ to form an intermediate carbanion which then reacts to form the various observed products.

Reagents used for nucleophilic attack on fluoro-olefins[20] include alcohols, phenols, thiols, thiophenols, alkoxides, fluoride ion, amines, Grignard reagents and organometallic compounds.

The reactions of fluoro-olefins with nucleophiles are discussed in terms of the three reaction sequences following the initial formation of a carbanion. Nucleophilic reactions of cyclic polyfluoro-olefins are discussed separately at the end of this chapter.

1.2.2 Addition reactions

The carbanion is stabilised by abstraction of a proton from the solvent, and the resulting product is a 1:1 adduct formed by nucleophilic addition across the double bond. This is common for fluoroethylenes, for example, tetrafluoroethylene combines readily with alcohols, phenols, thiols, thiophenols and ketoximes in the presence of their sodium salts to yield 1:1 adducts.[21]

Unsymmetrical olefins tend to be more reactive, and specific addition occurs in almost every case to give products in which the nucleophile becomes attached to the difluoromethylene group.

The addition of alcohols to hexafluoropropene is base-catalysed, giving mainly saturated ethers, e.g.

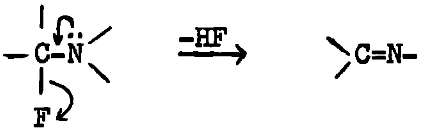
$$CF_2{=}CF{-}CF_3 \; + \; CH_3OH \; \xrightarrow[60^\circ]{KOH} \; \underset{(83\%)}{CH_3O{\cdot}CF_2{-}CHF{-}CF_3} \; + \; CH_3O{\cdot}CF{=}CF{-}CF_3 \qquad ^{22}$$

The great majority of addition reactions of lower fluoro-olefins with alcohols are base-catalysed. Perfluoroisobutene, however, reacts with alcohols in neutral media[23] at room temperature to give mainly saturated ethers of the form $RO{\cdot}CF_2{-}CH(CF_3)_2$, e.g.

$$(CF_3)_2C{=}CF_2 \; + \; C_2H_5OH \; \longrightarrow \; (CF_3)_2CH{-}CF_2{-}O{-}C_2H_5 \qquad (59\%)$$

Unsaturated ethers were also formed with higher alcohols, and these additions in neutral media have been rationalised on the basis of the formation of an intermediate carbanion of the type $RO \cdot CF_2-\bar{C}(CF_3)_2$.

Addition reactions of fluoro-olefins in which nitrogen acts as the nucleophile include the use of ammonia, primary and secondary amines, N-substituted amides, and diamines. These reactions are usually followed by elimination of HF, which is possibly due to mesomeric electron release by nitrogen as shown below,



1.2.3 Elimination reactions

The saturated compound, once formed, may undergo elimination via proton abstraction by the base. The main products of base-catalysed additions of hydroxy compounds to fluoroethylenes are usually saturated ethers, but by increasing the concentration of the base, or by using alkali metal salts, appreciable amounts of the unsaturated ethers (elimination products) can be formed.

e.g. $$CF_2{=}CFCl \xrightarrow[XSKOH/90^{\circ}]{C_2H_5OH} C_2H_5O \cdot CF{=}CFCl \qquad 24$$

$$CF_2{=}CFCl \xrightarrow[ether]{C_2H_5SNa} C_2H_5S \cdot CF{=}CFCl \qquad 25$$

Also there is an increase in the tendency for an elimination reaction to occur with higher fluoro-olefins, and this is well illustrated by the relative reactions of tetrafluoroethylene, hexafluoropropene, and octafluoroisobutene with dimethylamine (see Table 1).[26]

Table 1

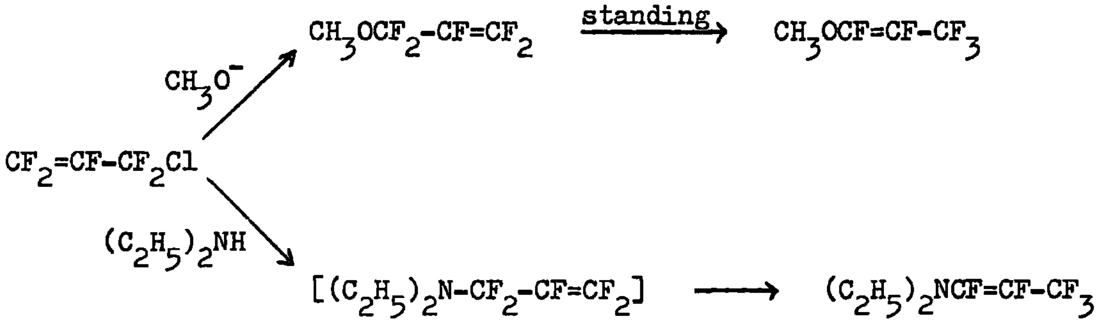
Fluorinated olefin	Product(s)
$CF_2{=}CF_2$	$CF_2H{-}CF_2{\cdot}N(C_2H_5)_2$ (100%)
$CF_3{\cdot}CF{=}CF_2$	$CF_3CFH{-}CF_2{\cdot}N(C_2H_5)_2$ (70%) + $CF_3CF{=}CF{\cdot}N(C_2H_5)_2$ (30%)
$(CF_3)_2C{=}CF_2$	$(CF_3)_2C{=}CF{\cdot}N(C_2H_5)_2$ (100%)

Hence, as with alcohols, the ratio between the primary addition product and the final unsaturated amine (enamine) depends largely on the structure of the olefin.

1.2.4 Allylic rearrangement

Olefins of the type $CF_2{=}\overset{|}{C}{-}CX_3$ in which at least one X is a halogen other than fluorine undergo preferential substitution of such allylic halogen easily. Reactions of this type are considered to take place via a S_N2' rearrangement.

Allylic displacement of chlorine in 3-chloro-pentafluoropropene was observed with methoxide ion and diethylamine.[27]



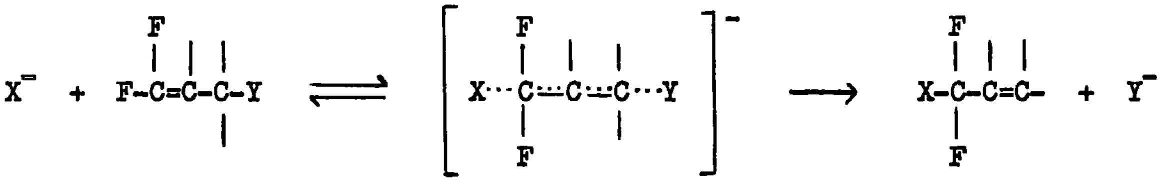
Miller[28,29] carried out a series of reactions in which halide ions were used as the nucleophile, e.g.[29]

$$CF_2{=}CF{-}CF_2Cl \xrightarrow[\text{acetone}]{\text{NaI}} CF_2{=}CF{-}CF_2I$$

and the use of fluoride ion as the nucleophile in S_N2' allylic displacement reactions has opened up a new field of fluoro-olefin chemistry, e.g.[30]

$$CF_2=CF-CF_2Cl \xrightarrow{F^-} CF_2-CF=CF_2$$

The relative nucleophilic reactivity of halide ions towards fluoro-olefins in S_N2' reactions was shown to be in the order $F^- \gg Cl^- > Br^-, I^-$.[28] Miller[28] and Park[31] established the order of leaving groups to be I > Br > Cl > F > OR > H, and Miller[28] proposed a low energy S_N2' transition state.



$$X^- + F-\overset{F}{C}=C-C-Y \rightleftharpoons \left[X\cdots\underset{F}{\overset{F}{C}}\cdots C\cdots C\cdots Y \right]^- \longrightarrow X-\underset{F}{\overset{F}{C}}-C=C- + Y^-$$

A concerted mechanism is favoured, however, since attempts to trap a fluorocarbanion using water[32] or carbon dioxide[33] have been unsuccessful.

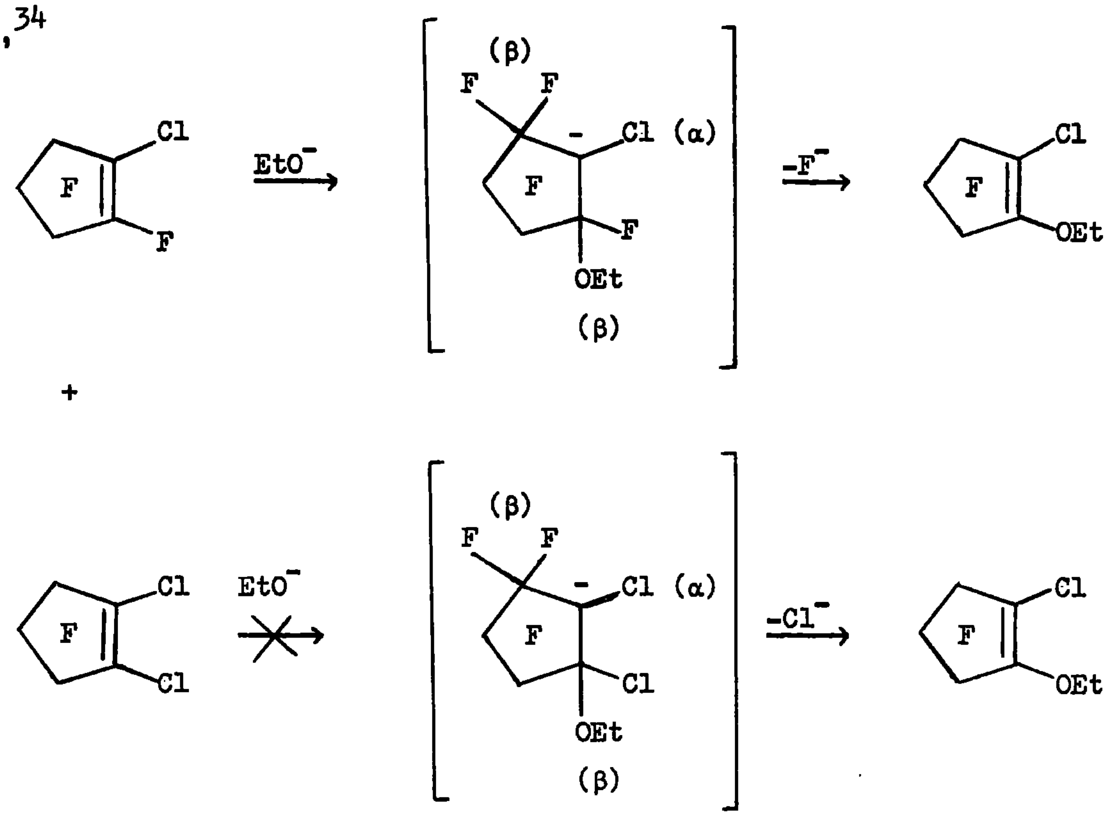
Reactions involving fluoride ion and fluoride ion catalysed rearrangements are discussed in Chapter 2.

1.3 Nucleophilic Reactions of Cyclic Polyfluoro-olefins

1.3.1 General mechanistic considerations

Cyclic fluoro-olefins exclusively form unsaturated products by reaction with nucleophiles, and the mechanism proposed for these reactions is a compromise between a concerted displacement of vinylic halide and an addition-elimination of hydrogen halide. It is not possible to differentiate between the two courses from available information.

Comparison of the relative stability of carbanions arising from nucleophilic attack on an asymmetrically substituted olefin indicates that products are generally derived from the more stable intermediate, and this assumes that the transition state closely resembles the carbanionic intermediate. However, when a mixture of chloroheptafluorocyclopentene and 1,2-dichlorohexafluorocyclopentene was allowed to compete for a deficiency of ethoxide ion, the former was found to react to the near exclusion of the latter,[34]

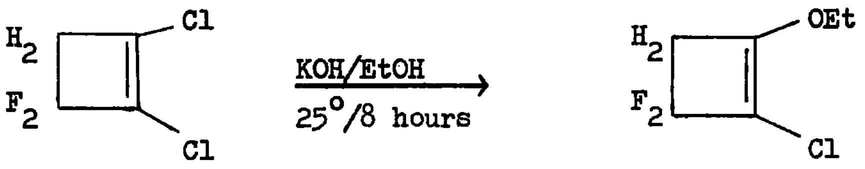


The stabilisation by α-substituents is identical for both carbanions, and it can be seen that the relative stabilisation by substituents β to the negative charge actually favours the carbanion not involved, since a β-chlorine is superior to a β-fluorine in the stabilisation of a carbanion. These results support the concept of ground-state activation, and the speed and exothermic nature of these reactions indicated that the transition state resembled the cyclic olefin more closely than the products or intermediates. This was in agreement with the postulate of Hammond[35] which stated that in highly exothermic steps the transition states resembles the reactants closely and in endothermic steps the products will provide the best models for the transition state. Thus the first stage of the reaction is independent of the relative stability of the carbanion formed.

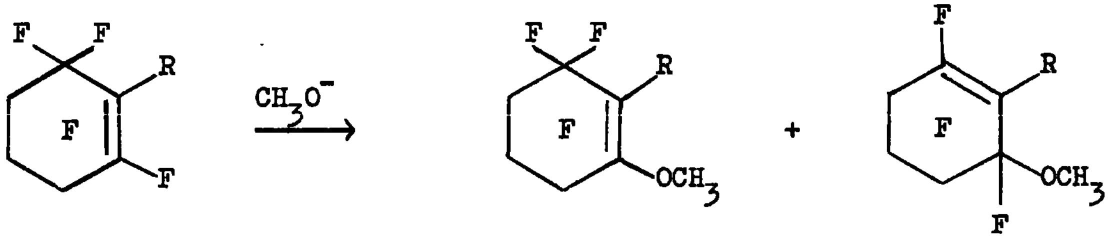
These two electronic directive effects are not necessarily conflicting since many examples falling between the two extremes may exist where both factors contribute to the observed result.

Only limited evidence is available concerning the effects of steric factors, but it has been suggested[36] that stereochemical factors may influence the reaction, particularly when electronic effects are of the same magnitude.

Park and co-workers[31] have proposed, on the basis of what is known about carbanion stabilities, that nucleophilic displacement reactions of olefins highly substituted with electron-withdrawing substituents may best be considered as proceeding through a carbanionic intermediate. Also,[37] a nucleophile will attack the carbon atom leading to the carbanion best stabilised by α-substituents. When the α-substituents are the same, then nucleophilic attack will occur at that end of the double bond that will give the carbanion best stabilised by β-substituents, e.g.[37]



Tatlow and co-workers[38] have found that additional factors need to be considered with polyfluorocyclohexenes. Methoxide ion attack on a series of nonafluorocyclohexenes gave two isomers in each case, with the product ratios as shown below,



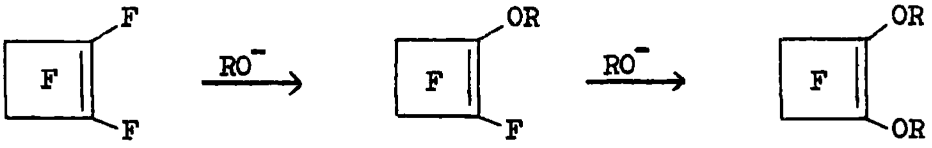
R	%	%
-H	48·5	51·5
$-CH_3$	54	46
$-OCH_3$	38	62

and this was best explained by assuming a trans addition of the nucleophile with retention of configuration of the carbanion during its short lifetime. The stereochemistry of a carbanion formed from decafluorocyclohexene would favour an outward (displacement with rearrangement) elimination, i.e. loss of F from $>CF_2$, but this is electronically unfavourable since $>CF_2$ is the more stable group. An inward (vinylic displacement) elimination involving loss of F from $>C(F)OR$ would be more electronically favourable. The product distribution results from the competition between these two elimination mechanisms.

1.3.2 Reactions with nucleophiles

A comprehensive account of the reactions of halogenated cyclic olefins with nucleophiles has recently been compiled by Park, McMurtry and Adams.[36] The review is chiefly concerned with the reactions involving alkoxide as the nucleophile although other nucleophilic species are included.

Both vinylic fluorines in perfluorocyclobutene and perfluorocyclopentene are displaced stepwise by alkoxide ion,



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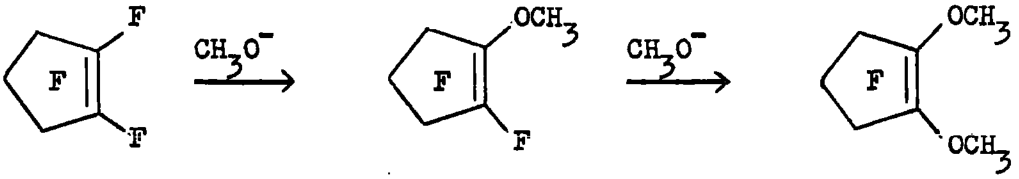
(R = $-CH_3$, $-C_2H_5$, $-nC_3H_7$, and $-nC_4H_9$)



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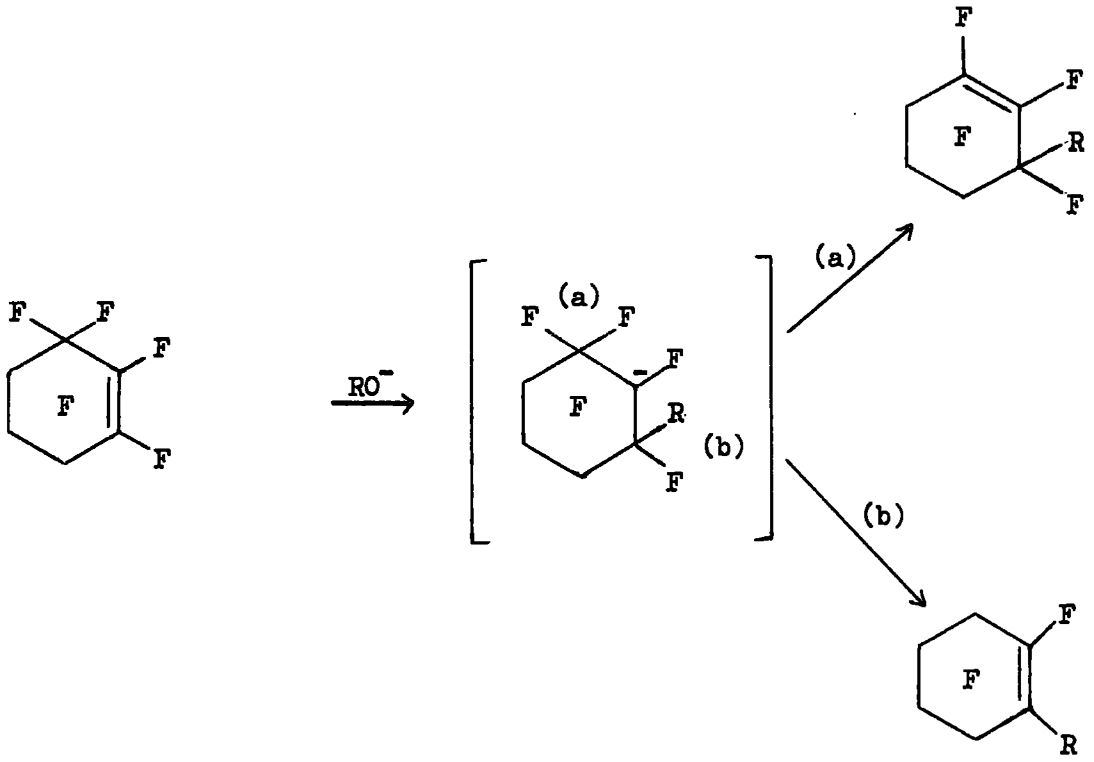
but the reaction of perfluorocyclohexene with alkoxide ion gave two main products (isomers),[38]



(R = $-CH_3$, $-C_2H_5$, $-CH_2CF_3$, $-CH(CH_3)_2$, $-CH_2{\cdot}CF_2{\cdot}CHF_2$)

The ratio of isomers was found to be dependent on the electronic character of R, i.e. the more the inductive electron-attracting power of R, the higher the proportion of the 3-substituted product arising from pathway (a).

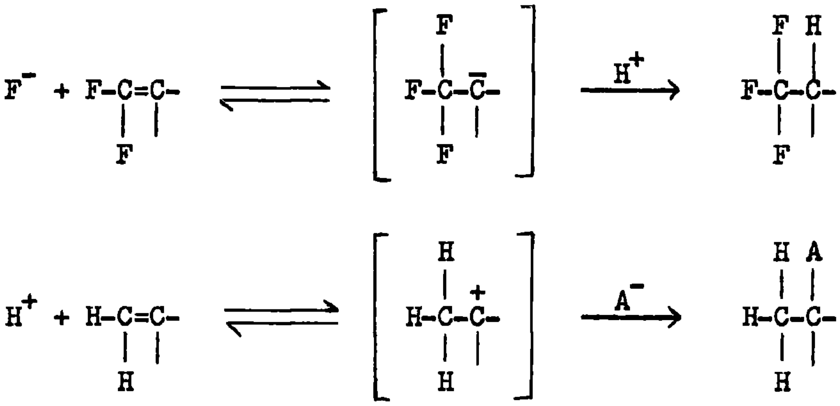
Tatlow[38] has also detected the formation of a 3-isomer in analogous reactions of perfluorocyclopentene and perfluorocyclobutene with alkoxide ion.

CHAPTER 2

REACTIONS INVOLVING FLUORIDE ION

Introduction

The basis for this type of work was provided by Miller who systematically studied the reactions of fluoride and other halide ions with fluoro-olefins, and underlined the analogous role of fluoride ion in fluorocarbon chemistry to that of the proton in hydrocarbon chemistry.



The experimental conditions necessary for reactions involving fluoride ion, that is, the choice of solvent and source of fluoride ion, is important and warrants discussion. This will be followed by the more important reactions in which fluoride ion is involved.

2.1 Experimental Conditions

The choice of reaction conditions suitable for studying the behaviour of fluoro-olefins with fluoride ion is not easily made. In the formation of a fluorocarbanion by addition of fluoride ion, unconsumed fluoride ion remains in the system and an equilibrium exists between the polyfluoro-olefin, fluoride ion, and the carbanion.

$$R_FCF{=}CF_2 + F^- \rightleftharpoons R_F\bar{C}FCF_3$$

This equilibrium could be displaced to the right, favouring formation of the carbanion, by increasing the concentration of fluoride ion, but this is restricted by solubility limitations of alkali metal fluorides. Also, side reactions, such as proton abstraction by the carbanion, must be minimised by the solvent in order to maintain the equilibrium. Dipolar aprotic solvents have been found to be particularly useful in this respect, solvation by the solvent and the lattice energy of the metal fluoride being the most important factors.

2.1.1 Dipolar aprotic solvents

Dipolar aprotic solvents are classed[41] as those with dielectric constants greater than 15, which, although they may contain hydrogen, cannot donate suitably labile hydrogen atoms to form strong hydrogen bonds with an appropriate species. Examples of such solvents include nitrobenzene, acetonitrile, acetone, dimethylformamide (D.M.F.), N-methyl-2-pyrrolidone, dimethylsulphoxide (D.M.SO.), dimethylsulphone (D.M.SO_2) and tetramethylene-sulphone (sulpholan).

In dipolar aprotic solvents, anions are poorly solvated, and much less so than cations,[42] solvation increasing with increasing size of the anion.[43]

Solvation was found to increase along the series

$$I^- > SCN^- > Br^- > N_3^-, Cl^- \gg F^-$$

The low solvation appears to be due to a steric resistance to solvation of small anions by the bulky dipoles present in the solvents, with the result that the positive end of the dipole cannot fit closely round the small anion. There is no significant contribution to solvation by hydrogen bonding in these solvents, though if it occurred it would be more important for the smaller anions. Conversely, in protic solvents (e.g. H_2O, CH_3OH, $HCONH_2$) where solvation is by the small unshielded proton, steric resistance is negligible, so that small anions are highly solvated by the close fitting dipoles of the protic solvent. Also, hydrogen bonding is important in protic solvents, and these bonds are stronger the smaller the anion. Thus, small anions are more solvated than large anions in protic solvents, and solvation decreases in the reverse order to that in dipolar aprotic solvents.

It can be seen from the above that fluoride ion is much less solvated in dipolar aprotic solvents, and is consequently a powerful nucleophile.

In contrast to the low solvation of anions in dipolar aprotic solvents, cations are highly solvated by these solvents, and this is the major reason for the solubility of electrolytes in these solvents. The ability to solvate cations is due to them having a region of high electron density, localised on a bare oxygen atom, allowing strong interaction with the cation. The type of dipole present is also important. Cations, however, may be poorly solvated if the negative portion of the dipole is dispersed, even in solvents of high dielectric constant (e.g. nitrobenzene).

2.1.2 Sources of fluoride ion

Alkali metal fluorides, in particular those of potassium and caesium, are the most widely used sources of fluoride ion. The observed order of reactivity of the alkali metal fluorides i.e.

$$LiF < NaF < KF < RbF < CsF$$

closely resembles their relative crystal lattice energies.

Compound	Lattice Energy (k.cals./g. formula wt.) [44]
LiF	240
NaF	213·4
KF	189·7
RbF	181·6
CsF	173·6

A similar order of reactivity, i.e. CsF > RbF > KF, NaF, LiF, was found[45] when a series of exchange reactions was carried out between hexafluoropropene and the alkali metal fluorides, e.g.

$$CF_3CF{=}CF_2 + RbF^{18} \rightleftharpoons C_3F_6{}^{18} + RbF$$

in order to determine the relative reactivity of the alkali metal fluorides as catalysts for reactions involving fluorocarbons.

From a consideration of the lattice energies, solubility will increase with increasing size of the cation (i.e. from Li ⟶ Cs). Also the degree of dissociation of the metal fluoride will increase with a larger cation, so that the concentration of fluoride ion in solution increases from Li to Cs, and this could account for the observed order of reactivity. If the ion-pair of the alkali fluoride is the reactive species, then the observed order of reactivity may be accounted for by the increasing degree of polarisation of the ion-pair with increasing size of the cation, together with the increasing solubility of the metal fluoride from Li to Cs.

Potassium fluorosulphite (KSO_2F)[46] and alkali metal bifluorides such as KHF_2 [47] have also been used as sources of fluoride ion although the latter compounds are of limited applicability because of low solubility in aprotic solvents.

2.1.3 Solvent-initiator systems

The use of two fluoride ion-solvent systems was reported by Miller,[30] but both of these systems have serious limitations. Although formamide will dissolve relatively large amounts of potassium fluoride,[28] it is a poor solvent for fluoro-olefins. It readily yields a proton to a fluorocarbanion, and also fluoro-olefins sometimes show appreciable reactivity towards the solvent at high temperatures. Tetraethylammonium fluoride is a more soluble fluoride and has been used successfully in halogenated solvents,[30,48] but it has disadvantages since it is very hygroscopic, thermally unstable, and difficult to obtain pure.

Solvents which have been used successfully with inorganic fluorides for reactions involving fluoride ion are glycols,[49,50] dimethylsulphone,[51] acetonitrile,[52] and N-methyl-2-pyrrolidone together with several other solvents.[51]

More recently the use of sulpholan as a solvent medium for reactions involving fluoride ion has increased, and Fuller[53] found this to be very effective for reactions involving the displacement of chlorine and bromine in an aromatic nucleus. The successful use of sulpholan in these reactions is due to its high thermal stability, the low susceptibility towards proton abstraction by a carbanion, and the low solvation of anions.

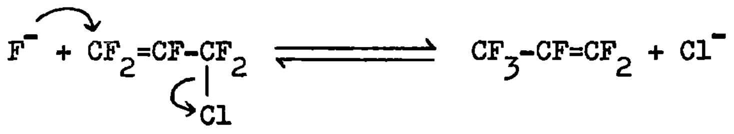
Graham and co-workers[33,54,55] demonstrated the suitability of the glymes (di-, tri-, and tetra-) as solvents for reactions involving carbanions, derived from fluoro-olefins by the addition of fluoride ion from caesium fluoride, with carbon dioxide and other carbonyl compounds. Various combinations of potassium and caesium fluorides with sulpholan and tetraglyme were later shown by workers at the University of Durham to be effective solvent-initiator systems for the polyfluoroalkylation of aromatic and heterocyclic substrates (see Section 2.5).

2.2 Reactions of Fluoro-olefins with Fluoride Ion and Related Reactions

Reactions of fluoride ion with fluoro-olefins are a means of generating carbanions and therefore are very important in synthesis. The reactions are important in a more theoretical sense because of the complimentary nature of the respective roles of the proton in hydrocarbon chemistry and fluoride ion in fluorocarbon chemistry.

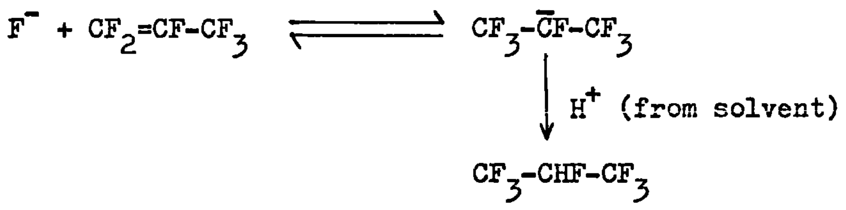
Miller and co-workers established two different reaction pathways for the reaction of halide ions with fluoro-olefins.

(i) Substitution with rearrangement (S_N2'), e.g.



$$F^- + CF_2{=}CF{-}CF_2Cl \rightleftharpoons CF_3{-}CF{=}CF_2 + Cl^-$$

(ii) Addition, e.g.



$$F^- + CF_2{=}CF{-}CF_3 \rightleftharpoons CF_3{-}\bar{C}F{-}CF_3 \xrightarrow{H^+ \text{ (from solvent)}} CF_3{-}CHF{-}CF_3$$

2.2.1 Substitution with rearrangement (S_N2')

It has been established in a series of publications[28,29,30] that the reactions of fluoroallyl halides are governed by the S_N2' process, and it was deduced that attack by fluoride ion on the terminal difluoromethylene group was followed by allylic shift of the double bond and elimination of halide ion. From a study of the reactions of $CF_2=CF-CF_2Cl$ and $CF_2=CCl-CF_2Cl$ with iodide ion it was shown that the α-carbon was not attacked, since under equivalent reaction conditions $C_6H_5-CF_2Cl$, $CFCl=CF-CF_2Cl$, and $CCl_2=CCl-CF_2Cl$ were all unreactive.[29]

The relative order of reactivity of halide ions in the S_N2' process is

$$F^- > Cl^- \gg I^- \quad ^{29}$$

$$\text{e.g.} \quad X^- + CF_2=CH-CFCl_2 \longrightarrow X-CF_2-CH=CFCl + Cl^-$$

(X = F, Cl, or I)

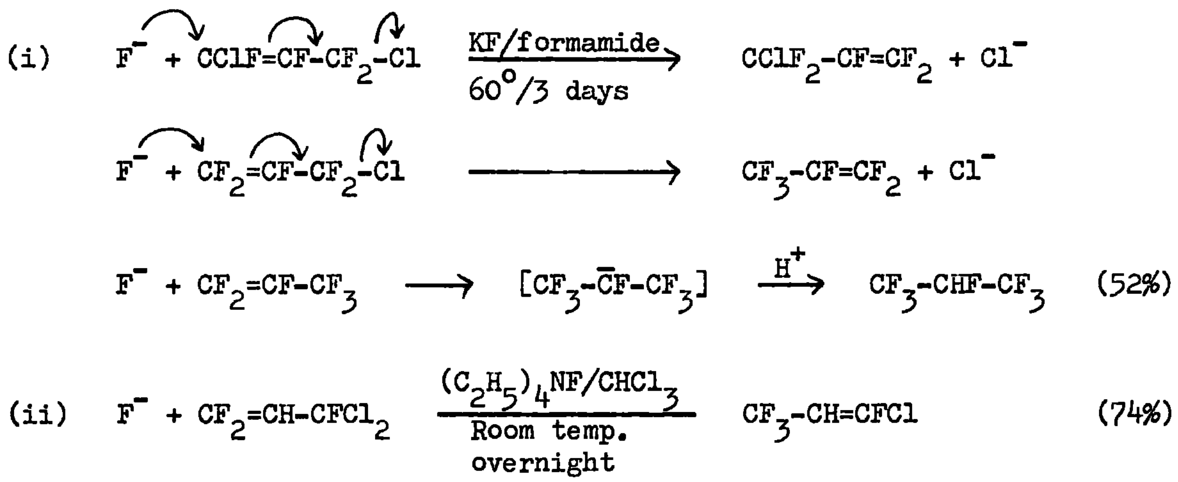
In S_N2' reactions, however, the relative nucleophilicities of halide ions in bond formation to carbon are in the order,

$$I^- > Cl^- > F^-$$

an explanation for which is that the polarisability of large halide ions is offset by steric hindrance in the reaction of fluoro-olefins with halide ions, the strength of the new bond being the most important factor.[56] The replacement of allylic chlorine by iodine in $CF_2=CX-CF_2Cl$ (X = F or Cl) yielding $CF_2=CX-CF_2I$[29] is an exception, and occurs as a result of the low solubility of sodium chloride in anhydrous acetone.

$$NaI + CF_2=CF-CF_2Cl \xrightarrow[\text{Room temp. 10 days}]{\text{Acetone}} \underset{(60\%)}{CF_2=CF-CF_2I} + NaCl$$

Substitution of allylic or vinylic halogen by fluorine occurs in preference to the addition of hydrogen fluoride by a carbanion intermediate, and also a terminal difluoromethylene group ($CF_2=$) is more susceptible to attack by fluoride ion than a terminal chlorofluoromethylene group ($CFCl=$). These facts are well illustrated by a comparison of the reactions of $CFCl=CF-CF_2Cl$ and $CF_2=CH-CFCl_2$ with fluoride ion,[30] the former requiring relatively vigorous conditions whereas the latter reacted quickly at room temperature. The reaction of $CFCl=CF-CF_2Cl$ with fluoride ion was interpreted as proceeding by two S_N2' replacements of chlorine by fluoride ion, followed by addition of hydrogen fluoride to give $CF_3-CHF-CF_3$.



(i) $F^- + CClF=CF-CF_2-Cl \xrightarrow[60^\circ/3\ days]{KF/formamide} CClF_2-CF=CF_2 + Cl^-$

$F^- + CF_2=CF-CF_2-Cl \longrightarrow CF_3-CF=CF_2 + Cl^-$

$F^- + CF_2=CF-CF_3 \longrightarrow [CF_3-\bar{C}F-CF_3] \xrightarrow{H^+} CF_3-CHF-CF_3$ (52%)

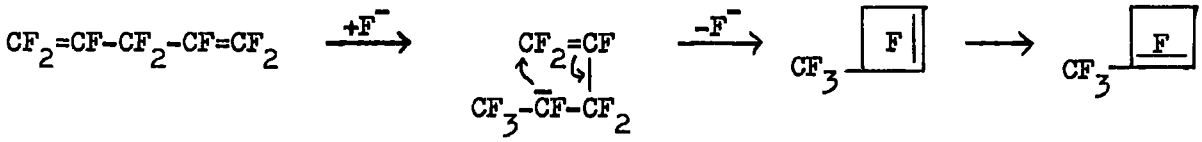
(ii) $F^- + CF_2=CH-CFCl_2 \xrightarrow[\text{Room temp. overnight}]{(C_2H_5)_4NF/CHCl_3} CF_3-CH=CFCl$ (74%)

2.2.2 Rearrangements catalysed by fluoride ion

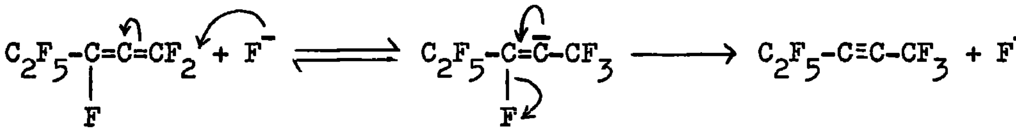
Fluoride ion catalysed rearrangements involve S_N2' displacement of fluorine by fluoride ion and, since a terminal olefin is more susceptible to nucleophilic attack than an internal olefin, there is a tendency for a terminal olefin to rearrange to an internal olefin by an S_N2' mechanism. Under vigorous conditions, however, attack at internal unsaturation can occur and subsequent double bond migration will give the most thermodynamically stable product i.e. the most highly substituted olefinic structure. This is illustrated by the rearrangement of perfluoro-1-heptene to perfluoro-2-heptene, in which an increase in the conversion of internal olefin was observed on increasing the reaction time and the concentration of fluoride ion.[30]

$$n\text{-}C_5F_{11}CF{=}CF_2 \xrightleftharpoons{F^-} n\text{-}C_4F_9CF{=}CF\text{-}CF_3 \xrightleftharpoons{F^-} n\text{-}C_3F_7CF{=}CF\text{-}C_2F_5$$

Fluoride ion-catalysed rearrangements of perfluorodienes and perfluoroallenes have been reported. When perfluoro-1,4-pentadiene was passed over caesium fluoride at 440°, perfluoro-1-methylcyclobutene-1 was obtained.[56] This was probably formed by fluoride ion addition to one terminal carbon atom and cyclisation by internal attack of this carbanion on the other terminal carbon atom, followed by rearrangement and elimination of fluoride ion to give the most highly substituted olefin.[56]



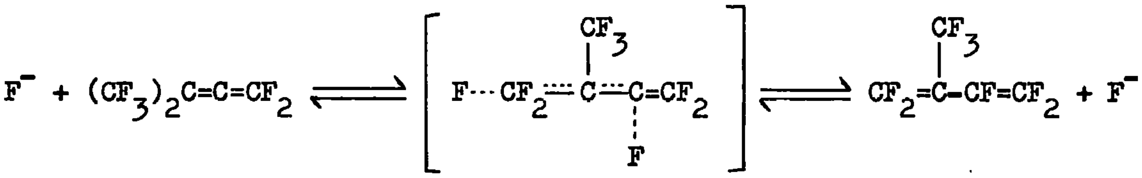
Recently Haszeldine and co-workers[57a-c] reported the fluoride ion-catalysed isomerisations of polyfluoroallenes. Perfluoropenta-1,2-diene undergoes a fluoride ion-initiated rearrangement to perfluoropent-2-yne in the presence of anhydrous caesium fluoride,[57a]



$$C_2F_5\text{-}CF{=}C{=}CF_2 + F^- \rightleftharpoons C_2F_5\text{-}CF{=}\bar{C}\text{-}CF_3 \longrightarrow C_2F_5\text{-}C{\equiv}C\text{-}CF_3 + F^-$$

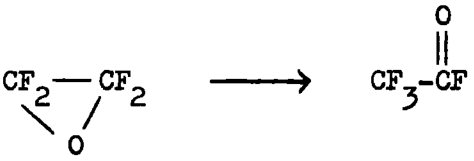
whereas passage of perfluoro-(3-methylbuta-1,2-diene) vapour over anhydrous caesium fluoride causes isomerisation to perfluoroisoprene.[57b] The latter rearrangement can be visualised as proceeding through a carbanion

$(CF_3)_2\bar{C}-CF=CF_2$ or by an S_N2' process:

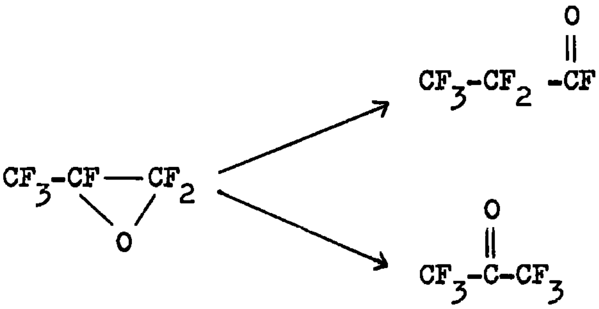


$$F^- + (CF_3)_2C=C=CF_2 \rightleftharpoons \left[F\cdots CF_2 \overset{CF_3}{\overset{|}{\cdots C \cdots}} \underset{\underset{F}{\vdots}}{C}=CF_2 \right] \rightleftharpoons CF_2=\overset{CF_3}{\overset{|}{C}}-CF=CF_2 + F^-$$

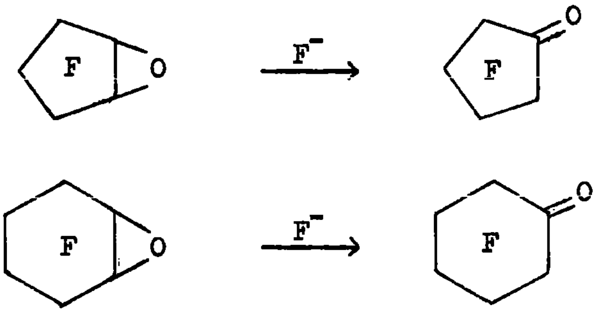
The rearrangement of perfluoro-epoxides is catalysed by the heavier alkali metal fluorides.[58] Tetrafluoroethylene epoxide can only rearrange to the corresponding perfluoroacetyl fluoride,



whereas unsymmetrically substituted epoxides such as hexafluoropropylene epoxide can rearrange to give either an acid fluoride or the isomeric ketone,



although the acid fluoride is usually formed from hexafluoropropylene oxide and alkali fluorides. Symmetrically substituted fluoro-epoxides rearrange to give the corresponding ketones, e.g.



The fluoride ion-catalysed rearrangements of perfluoroalkylated systems are discussed in detail in Chapter 4.

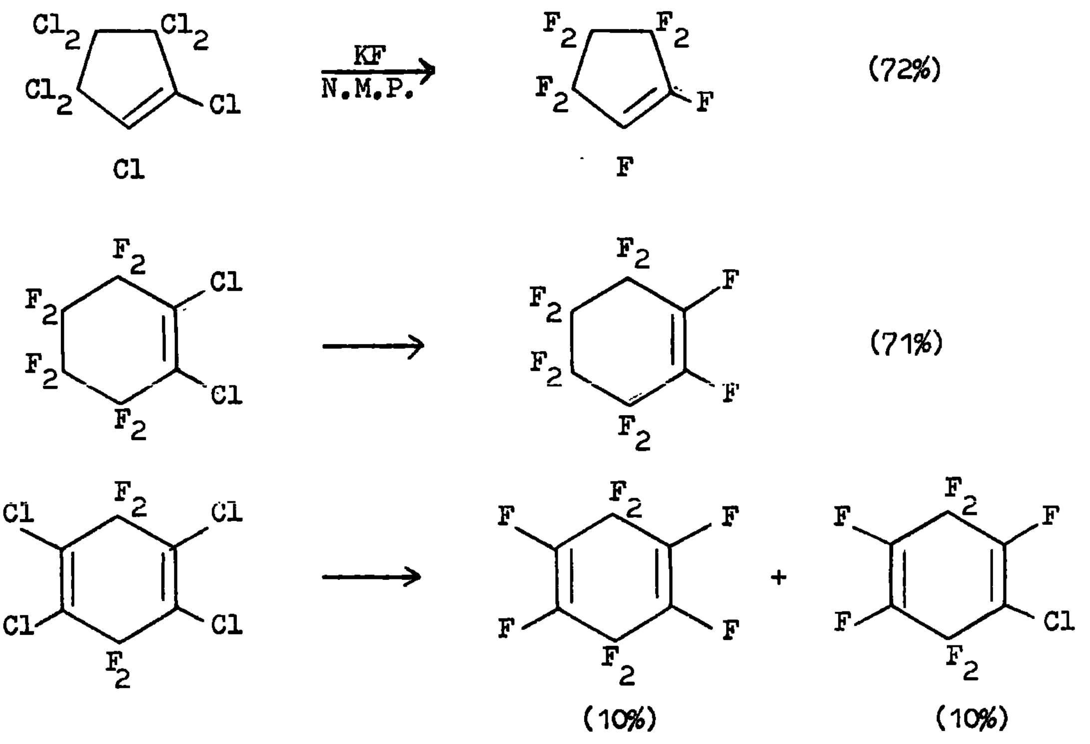
2.2.3 Direct vinyl substitution

Substitution of vinylic chlorine in $CClF{=}CF{-}CF_2Cl$ by fluoride ion was mentioned earlier, and is thought to proceed through two S_N2' sequences. Also, direct single step substitution of vinylic chlorine is proposed as the mechanism for the first step in the reaction of $CClF{=}CCl{-}CF_3$ with fluoride ion,[8] yielding $CF_3{-}CHCl{-}CF_3$

$$F^- + CClF{=}CCl{-}CF_3 \xrightarrow[60^\circ]{KF/formamide} CF_2{=}CCl{-}CF_3$$

$$F^- + CF_2{=}CCl{-}CF_3 \longrightarrow [CF_3{-}\bar{C}Cl{-}CF_3] \xrightarrow[(solvent)]{H^+} CF_3{-}CHCl{-}CF_3 \qquad (55\%)$$

Maynard[51] later found that polychlorofluoro-olefins, including cyclic olefins, were converted to their perfluorinated analogues by potassium fluoride in N-methyl-2-pyrrolidone at temperatures >190°. Good yields of products were obtained, and these reactions probably involve direct substitution of vinylic chlorine by fluoride ion.



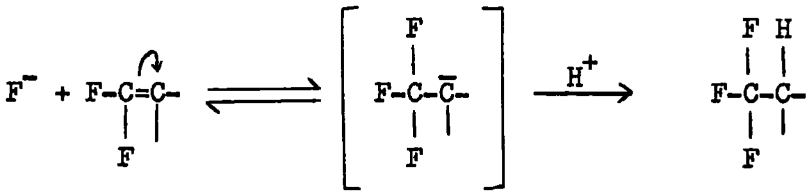
2.2.4 Addition reactions

(a) Addition of hydrogen fluoride

It was shown in the previous reactions that, when substitution of allylic or vinylic halogen by fluoride ion could occur, it did so in preference to an addition process. However, when addition of fluoride ion does take place, then the resultant carbanion can abstract a proton from the solvent.

e.g. $CF_2{=}CFCl + F^- \xrightarrow[55^\circ]{KF/formamide} [CF_3{-}\bar{C}ClF] \xrightarrow[(solvent)]{H^+} CF_3{-}CHClF$ (72%)

Miller et al[30] carried out several hydrogen fluoride addition reactions with a series of fluoro-olefins, and the only consistent mechanism involves the initial addition of fluoride ion,

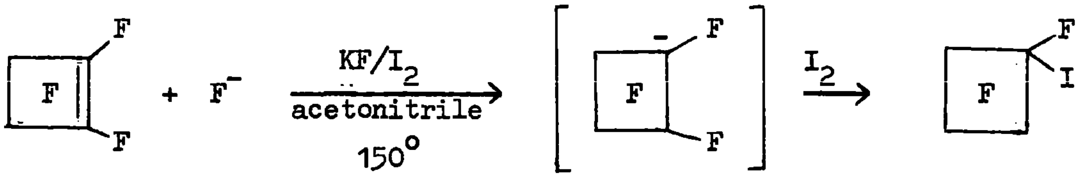


since all these reactions occurred in mildly basic media with a high concentration of fluoride ion present.

(b) Addition of iodine fluoride

The synthesis of fluoroalkyl iodides reported by Krespan[52] is a good example of the way in which a perfluorocarbanion can act as a nucleophile. The carbanion formed by the addition of fluoride ion to the olefin then reacts with iodine in solution.

e.g.



(27%)

(c) Addition of metal fluorides

Perfluoroalkyl mercurials were obtained by the addition of mercuric fluoride to fluoro-olefins in AsF_3 or anhydrous HF solutions, and Miller[59] concluded that addition of mercury fluoride occurred by electrophilic attack on the fluoro-olefin by a metal cation. Knunyants and co-workers,[60] however, recently showed that the mercuration of fluoro-olefins can be easily carried out via perfluoroalkyl carbanions, by the interaction of fluoro-olefins and mercury salts in the presence of alkali metal fluorides in aprotic solvents.

$$CF_3\text{-}CR{=}CF_2 \xrightarrow{F^-} (CF_3)_2\bar{C}R \xrightarrow{HgX_2} (CF_3)_2CR\text{-}Hg\text{-}CR(CF_3)_2$$

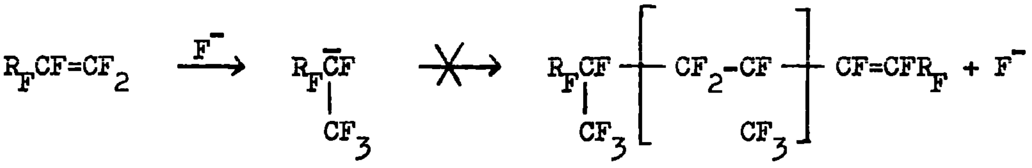
$$(R = F,\ CF_3)$$

Thus the mercuration of fluoro-olefins can be realised both by electrophilic and nucleophilic addition, depending on the conditions, since reactions in the absence of solvent and catalyst cannot be regarded as favouring carbanion formation.

2.3 Oligomerisation and Polymerisation of Fluoro-olefins

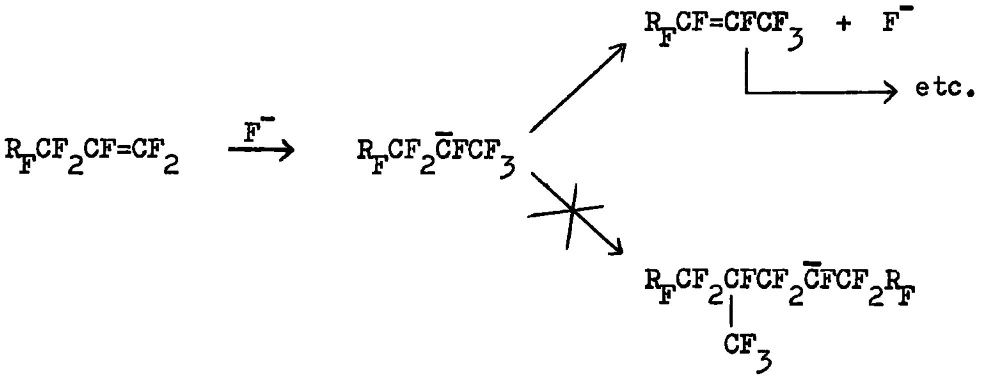
2.3.1 Acyclic olefins

The extensive anionic polymerisation of fluoro-olefins, according to the following scheme, is prevented by several factors.[61]



$$R_FCF{=}CF_2 \xrightarrow{F^-} R_F\underset{\large CF_3}{\underset{|}{\bar{C}F}} \not\longrightarrow R_F\underset{\large CF_3}{\underset{|}{CF}}\left[CF_2\text{-}\underset{CF_3}{CF}\right]CF{=}CFR_F + F^-$$

An olefin containing more than three linear carbon atoms will undergo double-bond migration rather than self-condensation, the initial carbanion eliminating fluoride ion and not attacking another molecule of the olefin, e.g.



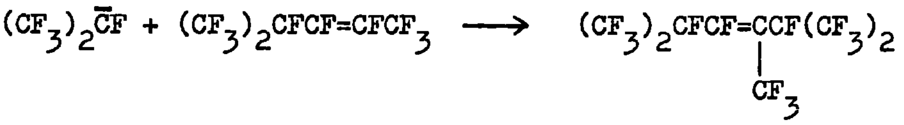
When structural factors prevent the elimination of fluoride ion, and hence rearrangement, then these olefins tend to form highly branched, internally unsaturated polymers of low molecular weight. Perfluoroisobutene and perfluoropropene cannot rearrange to internal olefins by double-bond migration but, although they are prone to nucleophilic attack, they do not polymerise. Hexafluoropropene, however, has been condensed to dimers and trimers under a variety of conditions, the nature of the products and their ratio depending on the reaction conditions.[54,56,62,63,64] The mechanism of self-condensation is probably as follows:

$$CF_3CF=CF_2 \xrightarrow{F^-} (CF_3)_2\bar{C}F$$

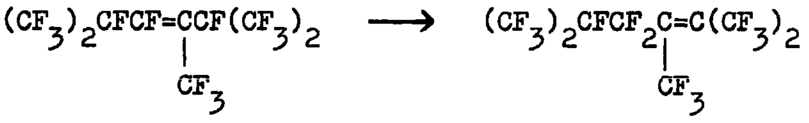
$$(CF_3)_2\bar{C}F + CF_3CF=CF_2 \longrightarrow (CF_3)_2CFCF_2\bar{C}FCF_3$$

$$(CF_3)_2CFCF_2\bar{C}FCF_3 \longrightarrow (CF_3)_2CFCF=CFCF_3 + F^- \qquad \text{(a)}$$

$$(CF_3)_2CFCF=CFCF_3 \xrightarrow{F^-} (CF_3)_2C=CFCF_2CF_3 \qquad \text{(b)}$$



$$(CF_3)_2\bar{C}F + (CF_3)_2CFCF=CFCF_3 \longrightarrow (CF_3)_2CFCF=C(CF_3)CF(CF_3)_2 \qquad \text{(c)}$$

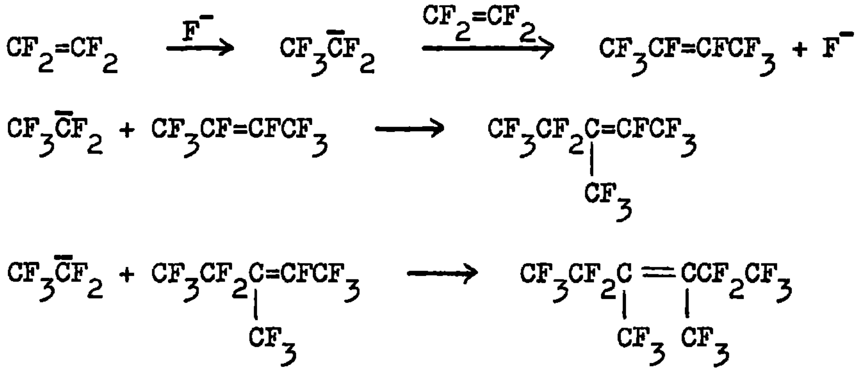


$$(CF_3)_2CFCF=C(CF_3)CF(CF_3)_2 \longrightarrow (CF_3)_2CFCF_2C(CF_3)=C(CF_3)_2 \qquad \text{(d)}$$

A mixture of (a), (b), (c), and (d) has been obtained by passing hexafluoropropene through a mixture of potassium bifluoride and dimethylformamide,[64] and also by heating the olefin with caesium fluoride in an autoclave in the absence of solvent at 100-200°.[56]

Perfluoroisobutene does not condense in the absence of solvent,[61] and only dimerised when a solvent was employed.[54]

Tetrafluoroethylene undergoes self-condensation with caesium fluoride in diglyme[54] and a mixture of C_8, C_{10}, C_{12}, and C_{14} fractions were obtained. The formation and subsequent reaction of internal rather than terminal olefins accounts for the extensive branching in these structures, probably by the following mechanism,



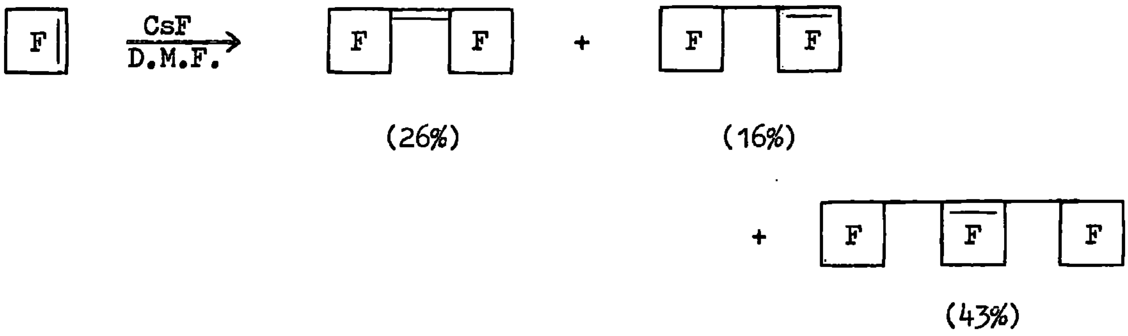
$$\mathrm{CF_2{=}CF_2 \xrightarrow{F^-} CF_3\bar{C}F_2 \xrightarrow{CF_2=CF_2} CF_3CF{=}CFCF_3 + F^-}$$

$$\mathrm{CF_3\bar{C}F_2 + CF_3CF{=}CFCF_3 \longrightarrow CF_3CF_2\underset{\displaystyle CF_3}{\underset{|}{C}}{=}CFCF_3}$$

$$\mathrm{CF_3\bar{C}F_2 + CF_3CF_2\underset{\displaystyle CF_3}{\underset{|}{C}}{=}CFCF_3 \longrightarrow CF_3CF_2\underset{\displaystyle CF_3}{\underset{|}{C}}{=}\underset{\displaystyle CF_3}{\underset{|}{C}}CF_2CF_3}$$

2.3.2 Cyclic olefins

In the reactions of perfluorocyclobutene with pyridine Pruett and co-workers[65] isolated the trimer of perfluorocyclobutene as the major product in most cases. In some of their reactions a mixture of the dimers of perfluorocyclobutene was also obtained. More recently, the dimerisation of perfluorocyclobutene by a fluoride ion-initiated reaction has been investigated by Fraticelli.[63] Both an exo- and an endo- dimer were obtained, in a ratio approximately 3:2, while the trimer was predominantly a single isomer.



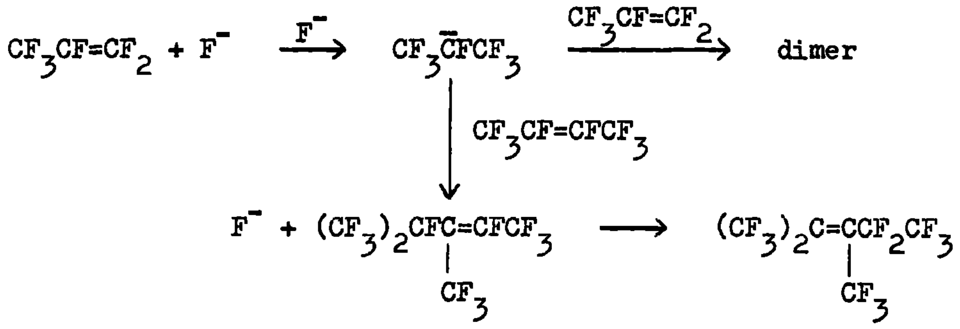
The same trimer of perfluorocyclobutene was formed as a major product in a series of polyfluoroalkylation reactions, carried out by the author, in which perfluorocyclobutene and a perfluorinated heterocycle were heated in the presence of fluoride ion and sulpholan. The formation of this and other oligomers of perfluorocycloalkenes are discussed in Chapter 4.

2.4 Co-dimerisation of Fluoro-olefins

Alternative modes of reaction are possible when a mixture of two fluoro-olefins is heated with an alkali metal fluoride. One or both of the olefins may dimerise or the carbanion formed from one olefin may react with the other olefin to give a co-dimer. The products formed depend on the reactivity of each olefin towards fluoride ion, and also on the reactivity of each olefin towards its own carbanion and that of the other olefin.

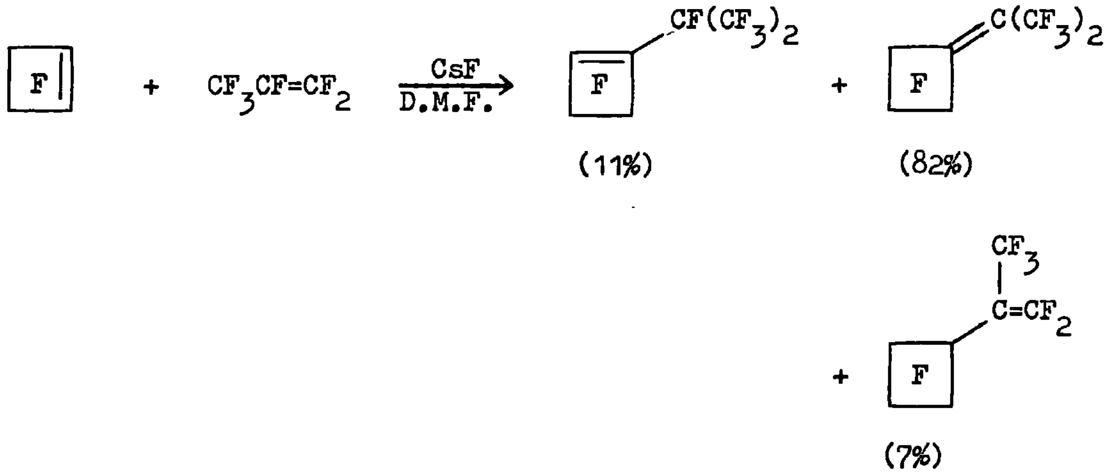
In the absence of solvent the major process for several pairs of olefins was found to be the independent reaction of one or both olefins with fluoride ion,[61] but co-dimers were obtained with pairs of olefins which were individually reactive toward caesium fluoride.

The fluoride ion catalysed co-dimerisation of several fluoro-olefins in solution has been investigated by Fraticelli.[63] Perfluoropropene and perfluorobutene-2 reacted to form a heptene and the dimer of perfluoropropene, the former being obtained preferentially in dimethylformamide, but dimerisation was the major process in tetrahydrofuran.

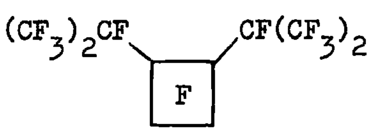


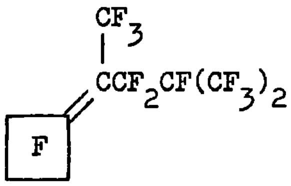
The olefin $CF_3CF{=}C(CF_3)CF_2CF_3$ was obtained from the reaction of perfluorobutene-2 and 1,1-dichlorodifluoroethylene, and accounted for by the replacement of chlorine by fluorine in the intermediate $CF_3CCl_2C(CF_3){=}CFCF_3$.

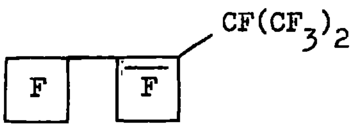
Relatively little work seems to have been done involving cyclic fluoro-olefins in co-dimerisation reactions. Fraticelli,[63] however, obtained a mixture of co-dimers and -trimers from the reaction of perfluorocyclobutene and perfluoropropene in the presence of caesium fluoride and dimethylformamide.



The products obtained and their relative ratios varied with the solvent employed and the concentration of fluoride ion in solution. The mixed trimers were also isolated and shown to have the following structures:



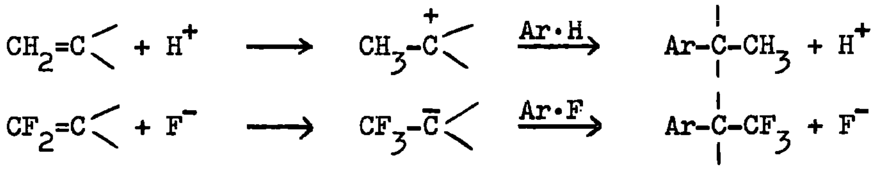




It can be seen from these results that there is a strong tendency for the double bond to lie exo- to the cyclobutane ring. Also the reactions carried out in the presence of solvent were less specific (i.e. more products formed) than the reactions involving no solvent.

2.5 Perfluoroalkylation of Aromatic Compounds

The predominant feature of polyfluoro-olefins[20,66] and polyfluoroaromatic compounds[67,68,69] is their susceptibility to nucleophilic attack. It was mentioned earlier that carbanions can be generated by reaction of polyfluoro-olefins with fluoride ion, and subsequent reactions of these carbanions have substantiated the analogy between the fluoride ion in fluorocarbon chemistry and the proton in hydrocarbon chemistry. On this basis, workers at Durham investigated the reactions of polyfluorocarbanions, generated from fluoro-olefins, with polyfluoroaromatic compounds, and were the first to report the formation of the corresponding polyfluoroalkyl derivatives,[70] in a process which is the nucleophilic equivalent of the Friedel-Crafts reaction in hydrocarbon chemistry.



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

$$CF_2=C\langle + F^- \longrightarrow CF_3-\overset{-}{C}\langle \xrightarrow{Ar\cdot F} Ar-\overset{|}{\underset{|}{C}}-CF_3 + F^-$$

Pentafluoropyridine was chosen as the substrate since it is considerably more susceptible to attack by nucleophiles than hexafluorobenzene,[68,69] and a series of reactions was carried out with hexafluoropropene as the olefin.[62,70,71,72] When pentafluoropyridine and hexafluoropropene were heated with potassium fluoride and sulpholan in a sealed tube at 120°, a high yield of perfluoro-(4-isopropylpyridine) was obtained together with a trace of the di-substituted compound.[72]

$$C_5F_5N + CF_3CF{=}CF_2 \xrightarrow[130^\circ/12\text{ hours}]{\text{KF/sulpholan}} 4\text{-}[(CF_3)_2CF]C_5F_4N \quad (94\%)$$

$$+ \; 2,4\text{-}[(CF_3)_2CF]_2C_5F_3N \quad (\text{trace})$$

Storey[71] varied the conditions for the reaction between pentafluoropyridine and hexafluoropropene in order to establish the relative effectiveness of sulpholan, diglyme, triglyme and dimethylformamide as solvents, and potassium fluoride and caesium fluoride as initiators. His results[72] indicate that sulpholan is the most suitable solvent for this system, although this may not be the case when other fluoro-olefins are involved. In fact, Jackson[62] showed that tetraglyme was a better solvent than sulpholan for the polyfluoroalkylation of octafluorotoluene with hexafluoropropene. Caesium fluoride is the more effective initiator, possibly due to its greater solubility in dipolar aprotic solvents, although this agrees with the results obtained in fluorination reactions with alkali metal fluorides,[73] in which the effectiveness of the fluoride decreases with increase in the lattice energy.[74,75]

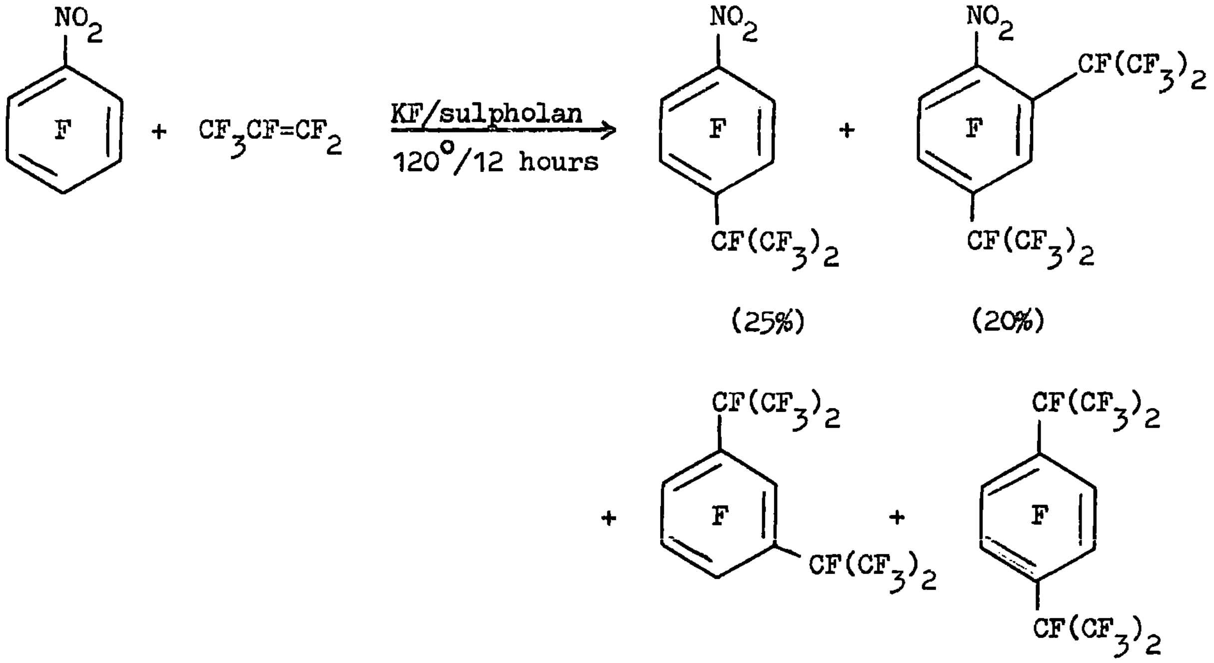
Further substitution in pentafluoropyridine was not achieved by increasing the concentration of olefin, since the latter was consumed by self-condensation to dimers and trimers. However, 4-, 2,4-bis-, and a mixture of the 2,4,5- and 2,4,6-tris-(heptafluoroisopropyl) derivatives were obtained when the reaction was carried out at an elevated temperature and a higher pressure (ca. 30 atm.).[62,72,76] These conditions undoubtedly increased the concentration of olefin at the reaction site, i.e. the surface of the catalyst.

e.g. $C_3F_6 + C_5F_5N \xrightarrow[\text{Autoclave/130°}]{\text{KF/sulpholan}} C_5F_4N(C_3F_7) + C_5F_3N(C_3F_7)_2$ [76]

$+ C_5F_2N(C_3F_7)_3$ + olefin dimers and trimers

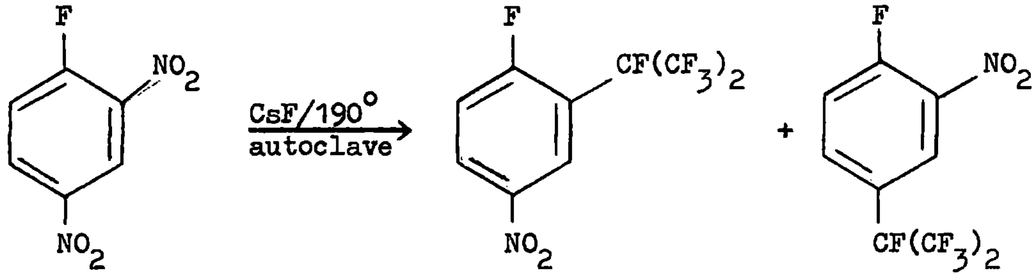
(2 isomers)

This reaction was extended to the use of other substrates, and a range of polyfluorobenzenes with various substituents was investigated. The expected 4-substituted products were obtained from both octafluorotoluene and methylpentafluorobenzoate with hexafluoropropene. Pentafluoronitrobenzene, which is of similar reactivity to nucleophiles as pentafluoropyridine,[77] was polyfluoroalkylated under the conditions used with pentafluoropyridine, and using hexafluoropropene. Displacement of the nitro-group occurred in addition to the formation of the 4-isopropyl- and 2,4-diisopropyl-derivatives.



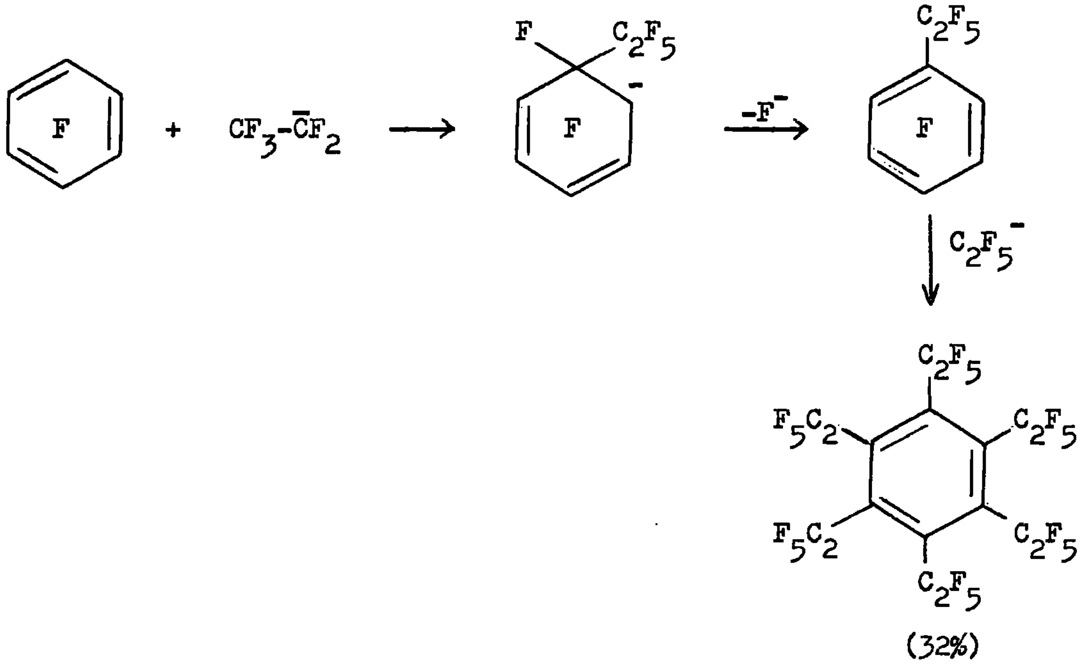
Under these conditions, hexafluorobenzene, bromopentafluorobenzene, and 1,3,5-trichlorotrifluorobenzene were unreactive towards hexafluoropropene. The 4-heptafluoroisopropyl derivative of pentafluorobenzonitrile, however, was easily obtained at 20°, reaction at higher temperatures being uncontrollable.

The fluoride ion-initiated reaction of 2,4-dinitrofluorobenzene with hexafluoropropene resulted in the replacement of a nitro-group.



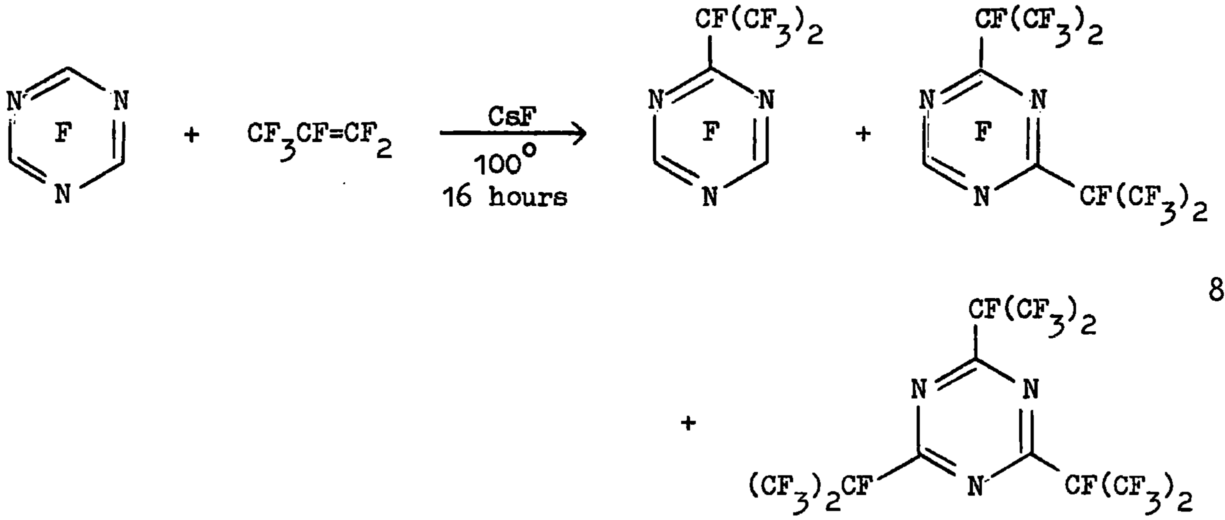
A mixture of mono- to pentakis-pentafluoroethyl derivatives was obtained from the reaction of pentafluoropyridine with tetrafluoroethylene,[72] and this illustrates the greater reactivity of the pentafluoroethyl (primary) anion, $CF_3\bar{C}F_2$-, over the heptafluoroisopropyl (secondary) anion, $(CF_3)_2\bar{C}F$-. This is in accordance with the results of Andreades[16] who demonstrated the greater stability of a secondary polyfluorocarbanion than that of a primary ion, the latter being a better nucleophile. A mixture of perfluoro-(mono-, di-, tri-, tetra-, penta-, and hexa-ethylbenzenes) was obtained from the reaction of hexafluorobenzene and tetrafluoroethylene at 135° using potassium fluoride as the initiator.[78] More recently, Haszeldine[79] reported the formation of hexakis-(pentafluoroethyl)benzene in reasonable yield by heating hexafluorobenzene and tetrafluoroethylene in the presence of fluoride ion at 135°.

$$CF_2{=}CF_2 \xrightarrow[\text{diglyme}]{\text{CsF}} CF_3\text{-}\bar{C}F_2$$



The relative ease of polysubstitution was accounted for by the greater susceptibility of perfluoroethylbenzene over hexafluorobenzene to nucleophilic attack.

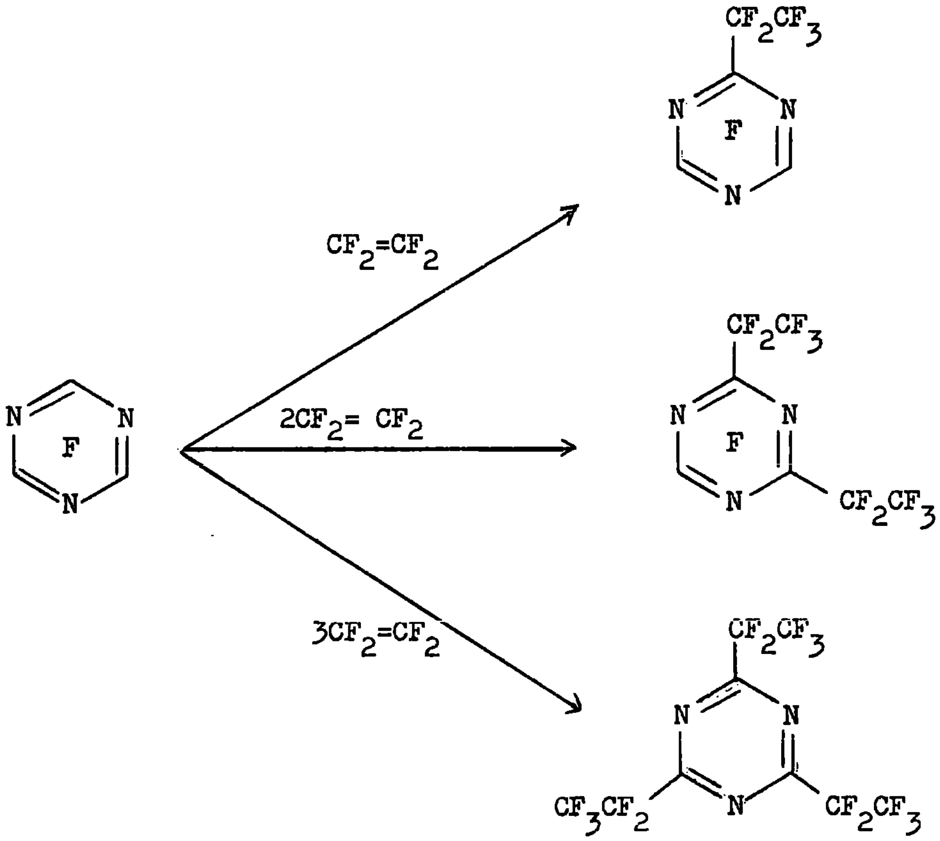
Fluorotriazines readily undergo fluoride ion-catalysed reactions with polyfluoro-compounds containing carbon-carbon or carbon-nitrogen double bonds. Cyanuric fluoride, 2,4,6-trifluoro-1,3,5-triazine, in which the fluorine is very easily displaced by nucleophiles, gave a mixture of the mono-, di-, and tri-substituted perfluoroisopropyl compounds (>90%) when heated with hexafluoropropene and caesium fluoride, in the absence of solvent, at 100°.



80

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

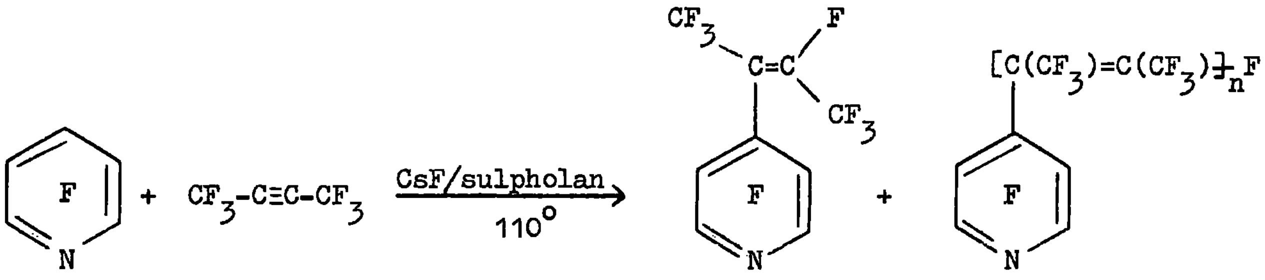
More recently, Deem[81] reported the perfluoro-alkylation of fluorotriazines using tetrafluoroethylene and perfluorobutenes in addition to perfluoropropene, e.g.



Favourable reaction conditions included caesium fluoride and acetonitrile at 80°-100° and 30-40 atmospheres pressure.

The scope of the polyfluoroalkylation reaction has been considerably extended in recent years at the University of Durham, and mono- and bis-heptafluoroisopropyl derivatives of tetrafluoropyridazine and tetrafluoropyrazine have been prepared by the fluoride ion-initiated reactions of these diazines with hexafluoropropene.[82]

Reactions involving fluoride ion attack on a perfluoro-acetylene to generate a perfluorovinyl carbanion, which then reacts with perfluoro-aromatic and -heterocyclic substrates to give perfluoro-alkenyl and -alkadienyl derivatives, have been reported. Chambers and co-workers[83] found that the fluoride ion-initiated reaction of pentafluoropyridine and hexafluorobut-2-yne at atmospheric pressure gave three substitution products,

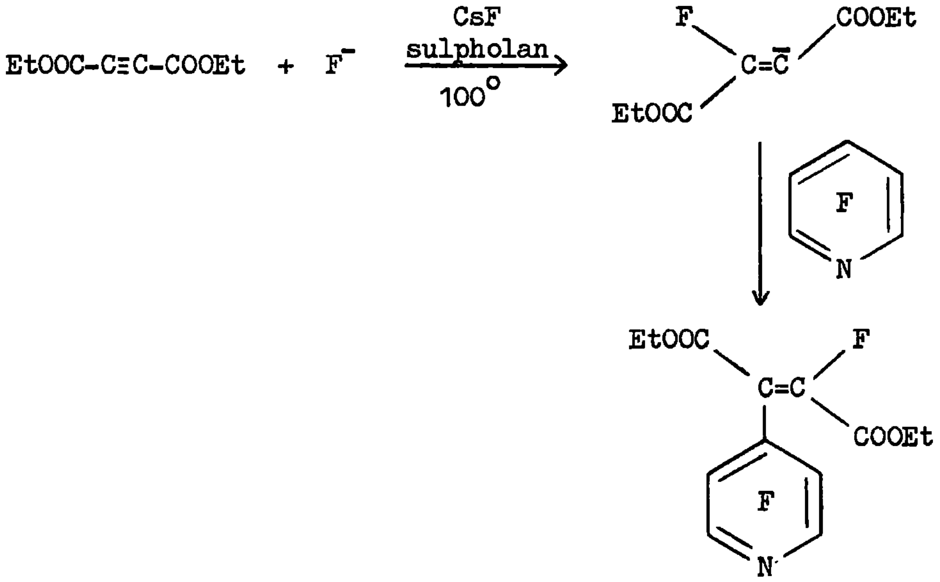


(n = 2, n = 3)

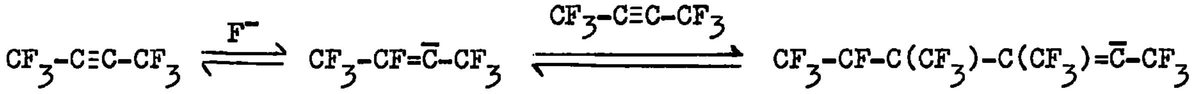
and it was suggested that the alkadienyl and alkatrienyl derivatives are formed by reactions of the anions $FC(CF_3)=C(CF_3)-C(CF_3)=\bar{C}(CF_3)$ and $F[C(CF_3)=C(CF_3)]_2C(CF_3)=\bar{C}(CF_3)$ with pentafluoropyridine, and not, for example, by displacement of the vinyl fluorine in the alkenyl compound by the alkenyl carbanion. Similar results were obtained with tetrafluoropyridazine.

The same workers[83] also generated a vinyl anion from acetylenedicarboxylic ester and found that this could be trapped with perfluoroheterocyclic compounds,

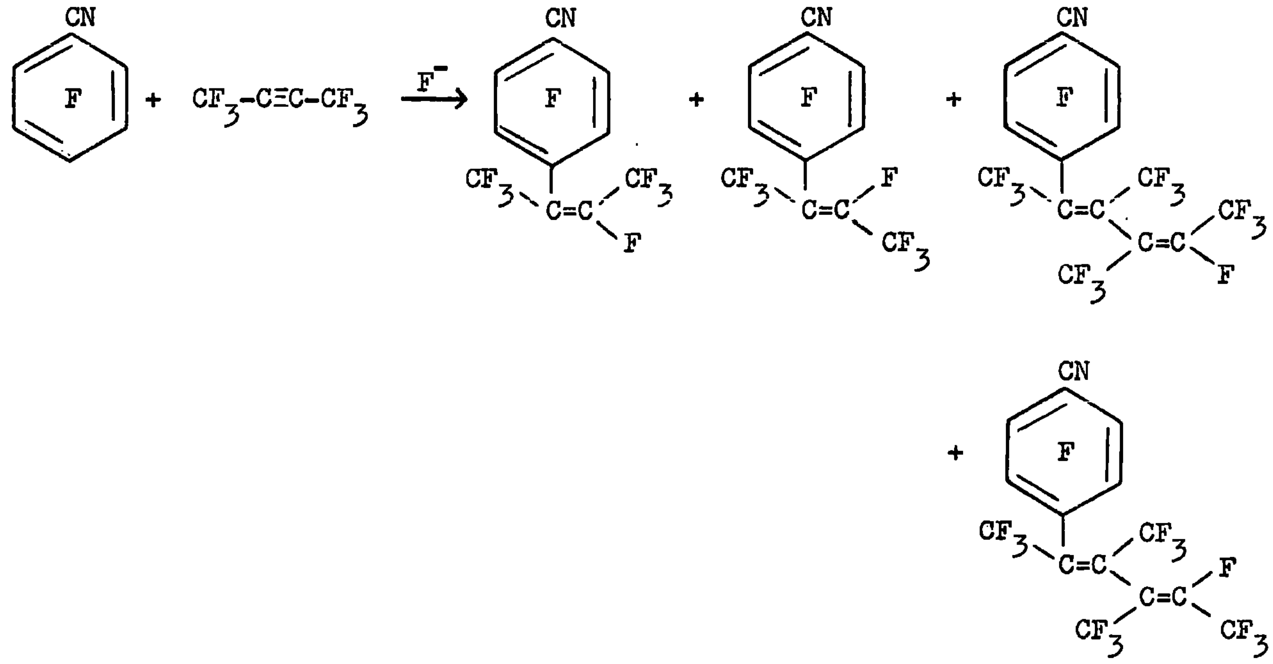
e.g.



Haszeldine and co-workers[84] obtained a mixture of the perfluoro-alkenyl and -alkadienyl derivatives from the fluoride ion-initiated reaction of pentafluorobenzonitrile and hexafluorobut-2-yne. They suggested that an equilibrium existed between the acetylene and the alkenyl and alkadienyl carbanions, and showed that the products were formed by attack of the corresponding carbanion on the pentafluorobenzonitrile.



$$CF_3\text{-}C{\equiv}C\text{-}CF_3 \overset{F^-}{\rightleftharpoons} CF_3\text{-}CF{=}\bar{C}\text{-}CF_3 \overset{CF_3\text{-}C{\equiv}C\text{-}CF_3}{\rightleftharpoons} CF_3\text{-}CF\text{-}C(CF_3)\text{-}C(CF_3){=}\bar{C}\text{-}CF_3$$



2.6 Fluoro-anions other than Carbanions

2.6.1 Perfluoro-oxyanions

Although primary and secondary perfluorinated alcohols are assumed to be incapable of existence because of the ease with which compounds having a fluorine atom in a position α to a hydroxyl group would eliminate hydrogen fluoride, the preparation of perfluorinated alkoxides of the heavier alkali metals has been reported.[85] Treatment of potassium, rubidium, and caesium fluorides with carbonyl fluoride have the corresponding trifluoromethoxides which are stable, crystalline, ionic salts. The scope of this reaction has been extended to the preparation of the analogous ethoxides, n-propoxides, iso-propoxides, and n-butoxides from the appropriate acyl fluorides.

1. $MF + COF_2 \rightleftharpoons MOCF_3$

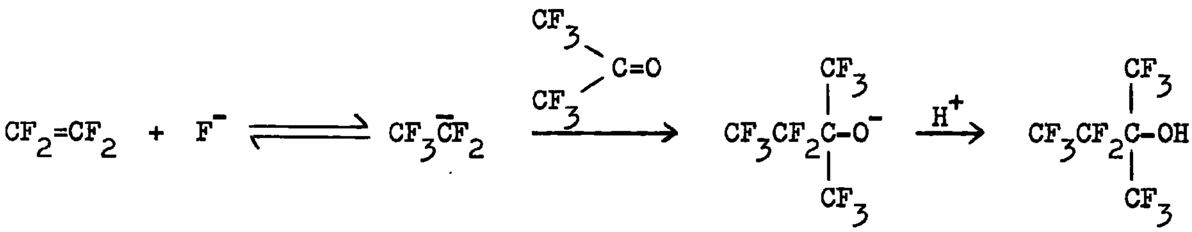
2. $MF + R_FCOF \rightleftharpoons MOCF_2R_F$

3. $MF + (CF_3)_2CO \rightleftharpoons MOCF(CF_3)_2$

(M = Rb or Cs. $R_F = CF_3, C_2F_5$ or C_3F_7)

Adducts of hexafluoroacetone have been prepared from different metal fluorides in acetonitrile and other polar organic solvents.[75,85,86] It was shown[75] that certain alicyclic chlorofluoroketones and the cyclic perfluoro ketones, perfluorocyclohexanone and perfluorocyclopentanone, formed similar adducts. The probability of adduct formation (indicated by a rise in temperature) and the relative stability of the adducts were related to the lattice energies of the salts involved, the stability decreasing with increasing lattice energy of the metal fluoride. Perfluorocyclohexanone and perfluorocyclopentanone are less reactive than hexafluoroacetone, and cyclic ketones form adducts which are less stable than those of straight-chain ketones, probably owing to steric interaction.

The heptafluoroisopropoxide ion has been used successfully in nucleophilic displacement reactions.[86] This ion is a relatively weak nucleophile and this was illustrated by the isolation of an alcohol, and not the ether $(CF_3)_2CFOCF_2CF_2H$, from the reaction of tetrafluoroethylene with hexafluoroacetone and caesium fluoride in diglyme.[55]



$$CF_2{=}CF_2 + F^- \rightleftharpoons CF_3\bar{C}F_2 \xrightarrow{(CF_3)_2C{=}O} CF_3CF_2C(CF_3)_2O^- \xrightarrow{H^+} CF_3CF_2C(CF_3)_2OH$$

The free alcohol is obtained on acidification.

Also, the loss of fluoride ion from perfluoroalkoxides can lead to halogen exchange and regeneration of the carbonyl compound,[87]

e.g. $(CF_3)_2CFO^- + (CH_3)_3SiCl \longrightarrow (CF_3)_2C{=}O + (CH_3)_3SiF + Cl^-$

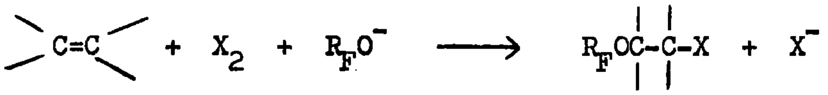
$(CF_3)_2CFO^- + R_FCOCl \longrightarrow (CF_3)_2C{=}O + R_FCOF + Cl^-$

The suggested mechanism involved intramolecular fluorine transfer rather than attack by free fluoride ion,

$$\equiv SiCl + F^- \longrightarrow \equiv SiF + Cl^-$$

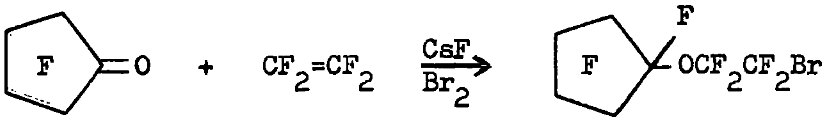
$$\equiv SiOCF(CF_3)_2 + F^- \longrightarrow \equiv SiF + (CF_3)_2CFO^-$$

It was later found[75b] that, if an adduct of a perhalogenated carbonyl compound and a metal fluoride reacted with a fluoro-olefin in the presence of a halogen, the corresponding fluorinated ether is formed.

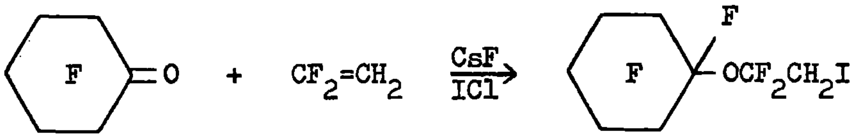


$$>C{=}C< + X_2 + R_FO^- \longrightarrow R_FOC\text{-}C\text{-}X + X^-$$

e.g.



(40%)



(75%)

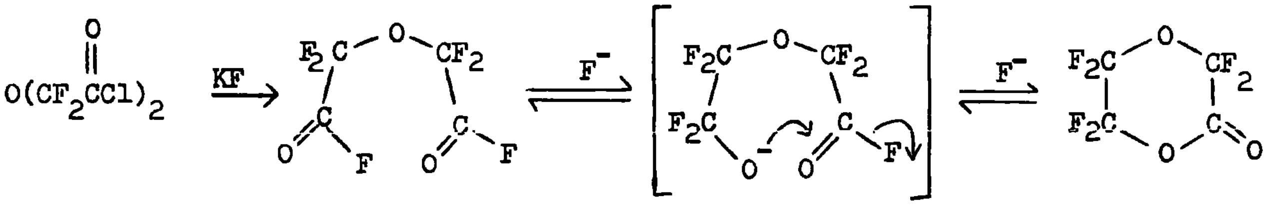
Cyclic ketone-caesium fluoride adducts were as reactive as the hexafluoroacetone-potassium fluoride adduct, but olefins such as hexafluorocyclobutene were unreactive due mainly to steric hindrance.

A useful synthesis of perfluoro-carboxylic acids involves the direct addition of a metal fluoride complex of a perfluoro-olefin, in a suitable solvent, to carbon dioxide.[33] The product is isolated by acidification and distillation.

$$R\text{-}CF{=}CF_2 \xrightarrow[CsF/diglyme]{CO_2} CF_3\underset{\displaystyle R}{\underset{|}{C}}FCOO^-Cs^+ \xrightarrow{H^+} CF_3\underset{\displaystyle R}{\underset{|}{C}}FCOOH$$

(R = F, Cl or CF_3)

The fluoride ion-catalysed reaction of perfluoro-oxydiacetyl chloride yielded two isomeric perfluorinated products, one of which was a lactone, and this was rationalised by postulating the formation of a perfluoroalkoxide intermediate followed by cyclisation.[88]

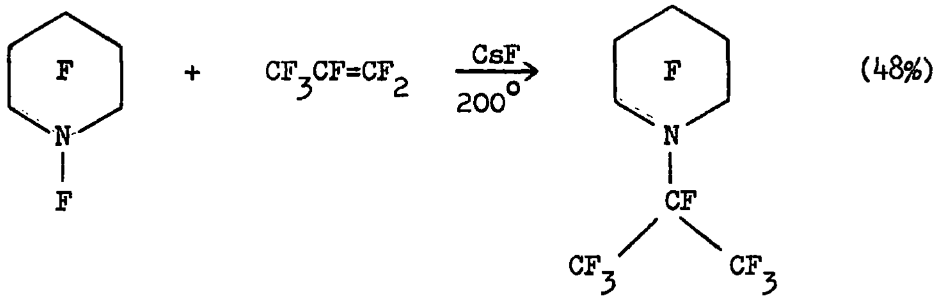


(lactone)

2.6.2 Perfluoroanions containing nitrogen or sulphur

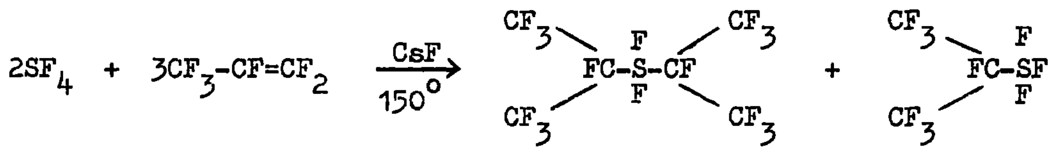
The generation of fluorocarbanions and fluoro-oxyanions, catalysed by fluoride ion, has been discussed in the previous sections. Displacement reactions on fluoro-sulphur and -nitrogen compounds have also been reported.

A reaction involving an N-F bond is that of perfluoropropene with perfluoropiperidine.[56] In the absence of alkali metal fluorides no reaction occurred below 300° but, with caesium fluoride in the absence of solvent, an adduct was obtained at 200°.



Perfluoroalkyl sulphur derivatives were obtained by the fluoride ion-catalysed addition of SF_4 to fluoro-olefins,[89]

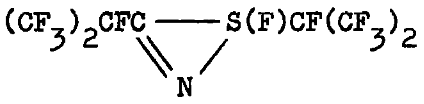
e.g.



the mechanism involving a perfluorocarbanion and subsequent nucleophilic attack of SF_4. The fluoride ion-catalysed heterogeneous reactions involving fluoro-olefins and sulphur fluorides were then extended to the use of the iminosulphur difluorides.[90] When a mixture of hexafluoropropene and iminosulphur difluoride was treated with powdered caesium fluoride at 80°-90°, the perfluoroisopropyl carbanion generated complexed with the sulphur atom, and fluoride ion was eliminated.

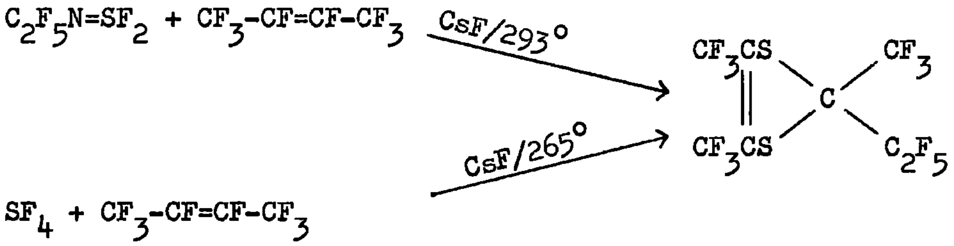
$$CF_3-CF=CF_2 + CF_3N=SF_2 \xrightarrow[83^\circ/5\text{ hrs.}]{CsF} CF_3N=SF-CF(CF_3)_2$$

Another product isolated from this reaction was thought to have the following structure,

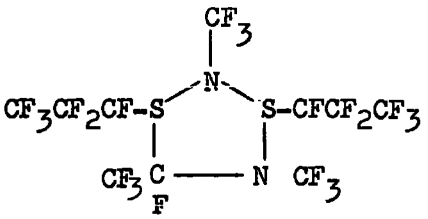


and formed via fluoride ion elimination from α-carbon atoms after fluoride ion addition to the sulphur atoms in an intermediate species.[91]

Higher temperatures were required to obtain similar reactions between perfluorobut-2-ene and $C_2F_5N{=}SF_2$ over caesium fluoride.[91] In fact, above the temperature at which $C_2F_5N{=}SF_2$ is stable, the main product isolated other than CF_3CN, a decomposition product of the iminosulphur difluoride, was the same as that isolated from the reaction of SF_4 with perfluorobut-2-ene or perfluorobut-2-yne, i.e.



The reactions between perfluorobut-2-yne and $C_2F_5N{=}SF_2$ and $C_3F_7N{=}SF_2$ over caesium fluoride[91] were uncomplicated giving $C_2F_5N{=}S(F)C(CF_3){=}CFCF_3$ and $C_3F_7N{=}S(F)C(CF_3){=}CFCF_3$. However, in the reaction involving $CF_3N{=}SF_2$, the main product was thought to have the following structure,



demonstrating the labile nature of fluorine atoms on carbon adjacent to the N=S unsaturation. The corresponding monomer $CF_3N{=}S(F)C(CF_3){=}CF(CF_3)$ was isolated but the rate of dimer formation was much more rapid than that of monomer formation.

It must be noted that, although the above reactions are thought to be catalysed by fluoride ion, the mechanism by which some of these novel cyclic compounds are formed are somewhat obscure.

CHAPTER 3

NUCLEOPHILIC SUBSTITUTION IN POLYFLUOROAROMATIC COMPOUNDS

Introduction

Nucleophilic displacement of fluorine as fluoride ion is a characteristic reaction of polyfluoroaromatic compounds, and this is analogous to the electrophilic replacement of hydrogen as a proton in hydrocarbon chemistry. The nucleophilic substitution of hexafluorobenzene and pentafluorophenyl derivatives has been studied extensively and some of the factors controlling the substitution process successfully elucidated. Substitution in polyfluorohomocyclic compounds is now well established but an increasing amount of knowledge is currently being acquired on the nucleophilic substitution of polyfluoroheterocyclic compounds. Investigations carried out initially on pentafluoropyridine have been extended to other polyfluorinated heterocycles, including quinolines and diazines. In addition, the orientation of nucleophilic attack has been reported for polyfluoroheterocyclic oxygen and sulphur compounds.

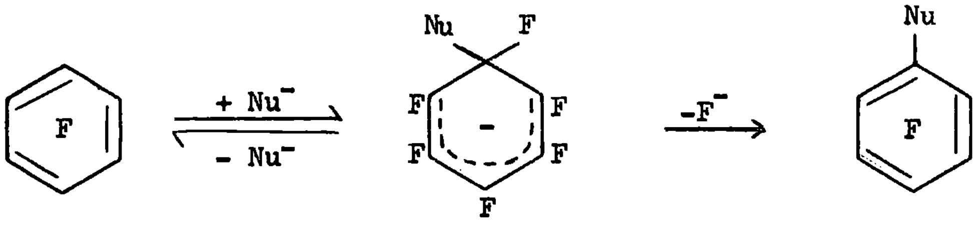
It will be convenient to discuss briefly nucleophilic substitution in polyfluorohomocyclic compounds followed by a more detailed discussion of the substitution in polyfluoro-N-heteroaromatic compounds.

3.1 Nucleophilic Substitution in Polyfluorohomocyclic Compounds

Hexafluorobenzene will react, under moderate conditions, with many nucleophilic species such as $^{-}OCH_3$,[92] ^{-}OH,[93] ^{-}SH,[94] NH_3,[95] $N_2H_4 \cdot H_2O$,[95] CH_3NH_2,[95] $^{-}CH_3$,[96] and $^{-}C_6H_5$[97] to give good yields of the corresponding pentafluorophenyl derivatives. Nucleophilic substitution in pentafluorophenyl compounds of general formula C_6F_5X is of greater interest because of the occurrence of positional isomerism. A large number of nucleophilic replacement reactions of C_6F_5X compounds are now known,[67,98] and the orientation of nucleophilic substitution in these compounds has been studied using a variety of nucleophiles. In general, nucleophilic attack occurs predominantly at the para position[67] when X = H, CH_3, SCH_3, CF_3, $N(CH_3)_2$, SO_2CH_3, C_6F_5, and halogen. However, when X = O^{-} or NH_2, meta substitution predominates,[99] and if X = OCH_3 or $NHCH_3$, then comparable amounts of meta and para replacement occur.[100] In certain cases, when X = NO_2, NO, COO^{-}, the orientation of substitution is influenced by solvent effects[101,102] or specific interaction between the nucleophile and the substituent group on the substrate.[98,103]

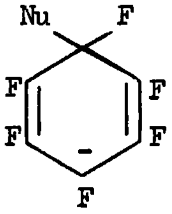
3.1.1 Rationalisation of the orientation of nucleophilic substitution

Burdon[104] has rationalised the observed orientation and reactivity in nucleophilic replacement reactions of aromatic polyhalo-compounds by considering the relative stabilities of the Wheland-type intermediates for all possible positions of attack by the nucleophile, since these intermediates usually provide good guides to transition states. For the reaction of hexafluorobenzene with a nucleophile Nu^{-}, the Wheland-type intermediate (I) was used as an approximation to the transition state.

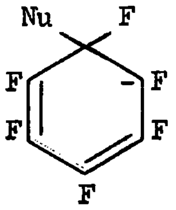


(I)

Also, it was assumed that the para-quinonoid resonance hybrid (II) made a greater contribution to the intermediate (I) than the ortho-quinonoid structure (III),



(II)



(III)

i.e. in the transition state the electron density was localised largely at the position para to the site of attack and to a much lesser extent at the ortho position. This assumption is supported by molecular orbital calculations.[105]

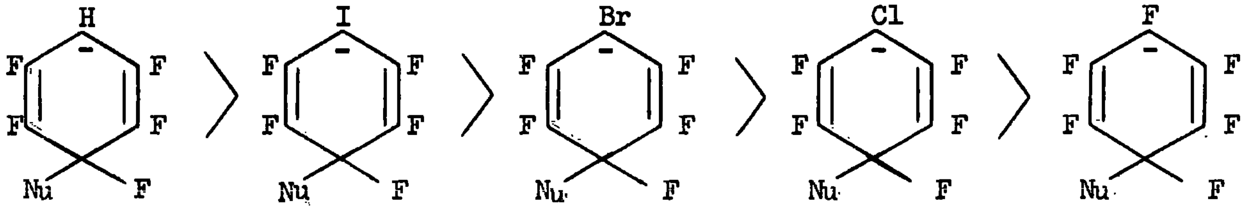
In considering substitution in C_6F_5X compounds, the problem resolves itself into a consideration of the influence of the substituent X on the localisation of charge at the carbon atom to which X is attached. If the substituent X is capable of stabilising the carbanion more effectively than fluorine, then nucleophilic attack will take place at the carbon atom para to X, and to a lesser extent, at the ortho position, whereas attack at the carbon atom meta to X will result if the substituent X is less effective than fluorine in stabilising the carbanion. In the event that the substituent X has exactly the same influence as fluorine on the stability of the negative charge, then a statistical ratio of ortho:meta:para replacement (i.e. 2:2:1) would result.

The halogens were assumed to stabilise on adjacent carbanion in the order $F < Cl < Br < I < H$,[104] and this was attributed to the Iπ effect (see section 1.1). It should be noted, however, that carbanions which are part of an aromatic system have an enforced planar geometry, and this will maximise the Iπ effect. The magnitude of the Iπ repulsion effects for nitrogen and oxygen were unobtainable, but were assumed to be in the order $N > O > F$.

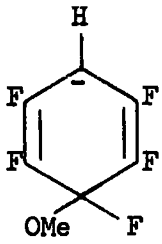
One can now understand the results of the nucleophilic attack of a series of C_6F_5X compounds (X = H, I, Br, Cl) with methoxide ion,[106] in which an increasing amount of ortho substitution occurred in the series

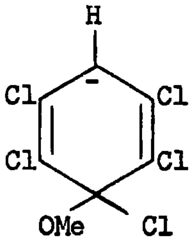
Compound	C_6F_5H	C_6F_5I	C_6F_5Br	C_6F_5Cl
% ortho	3	5	12	17

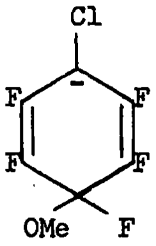
since this is the order of stability of the para-quinonoid hybrids of type (II), i.e.



The nucleophilic substitution of pentafluorobenzene, pentachlorobenzene, and chloropentafluorobenzene was rationalised using this theory. Substitution in pentafluorobenzene and pentachlorobenzene occurs para to the hydrogen, and in chloropentafluorobenzene, para to the chlorine. Considering the intermediates of type (II),

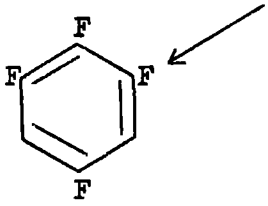


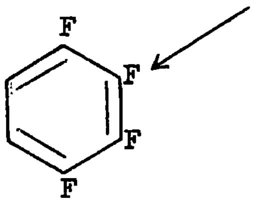


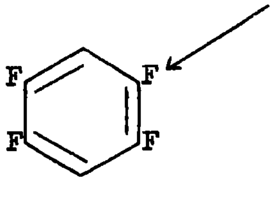


the orientation is explained, since the relative stabilities of the negative charges on a carbon bearing hydrogen, chlorine, and fluorine are in the order H > Cl > F.

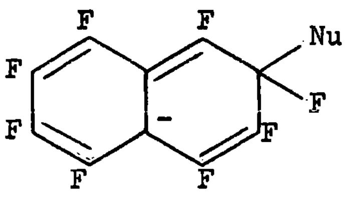
The orientation of nucleophilic substitution in the three isomeric tetrafluorobenzenes[107] can be understood in terms of the ability of fluorine to stabilise an adjacent carbanion less effectively than hydrogen, in systems of this type. The position of attack in each case is shown by an arrow.



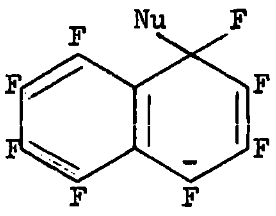




The orientation in octafluoronaphthalene can be rationalised in terms of the Iπ destabilising effect of fluorine, substitution occurring at the 2-position, i.e.



is more stable than



In certain cases, steric factors must be considered. The orientation of nucleophilic substitution in certain C_6F_5X compounds, where X = $N(CH_3)_2$,[99] $NHCH_3$,[99] and OCH_3,[100] has been explained in terms of steric repulsion between the substituent X and the two ortho ring fluorine atoms. On the basis of Iπ repulsions (N > O > F), meta substitution would be expected to predominate; steric repulsion, however, forces the plane of the p-orbitals of the substituent hetero-atom out of the plane of the ring, and thus reducing the Iπ repulsions between the p-electrons of the hetero-atom and the ring π-electrons. This would account for the observed para attack.

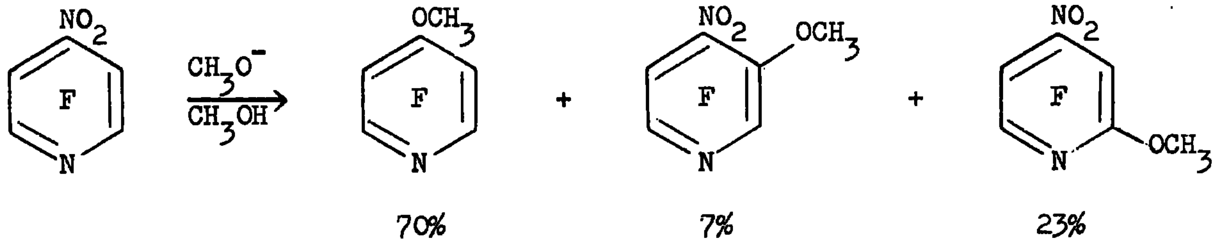
3.2 Nucleophilic Substitution in Polyfluoroheterocyclic Compounds

Due to the fact that polyfluoroheterocyclic compounds have only recently become available, less is known about nucleophilic substitution in these systems compared with polyfluorohomocyclic compounds. Investigations have been carried out chiefly with heterocyclic nitrogen compounds, although systems containing other hetero-atoms such as oxygen and sulphur have been studied.

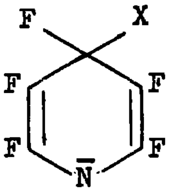
3.2.1 Polyfluoroheterocyclic nitrogen compounds

Nucleophilic substitution in pentafluoropyridine has been studied extensively, and a wide variety of nucleophiles will react with this compound to give 4-substituted tetrafluoropyridines.[68,69] It was noticeable that pentafluoropyridine was more reactive to nucleophilic attack than hexafluorobenzene. Nucleophilic substitution reactions have been carried out with these 4-substituted tetrafluoropyridines, and treatment of the 4-methoxy-[69] and 4-bromo-[108]tetrafluoropyridines with nucleophilic reagents afforded replacement of the 2-fluorine, excess methoxide giving the corresponding

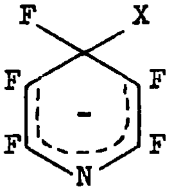
2,6-dimethoxy derivative. However, the reaction of 2,3,5,6-tetrafluoro-4-nitropyridine with methoxide ion[77] gave products resulting from the replacement of the 2- and 3-fluorines by methoxide, but the major product was formed by the replacement of the nitro-group.



Since the nitro-group was not displaced by nucleophilic reagents from 2,3,5,6-tetrafluoronitrobenzene, the above results were rationalised[77] by assuming that the ring nitrogen is the greatest single factor governing the orientation of substitution, the $I\pi$ effect being of minor importance. This is due to the nitrogen atom being able to stabilise a negative charge when localised on this atom, the hybrid (A) being the main contributor to the transition state (B).

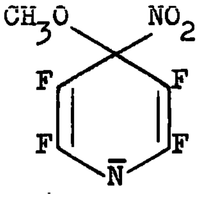


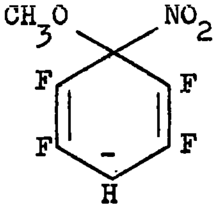
(A)



(B)

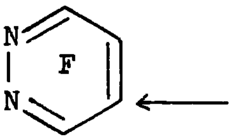
On the basis of the $I\pi$ effect alone the orientation of nucleophilic substitution in 4-nitro-tetrafluoropyridine should be analogous to that in 2,3,5,6-tetrafluoronitrobenzene, since in both cases the negative charge can be localised on a ring atom which does not carry a fluorine atom.

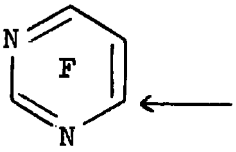


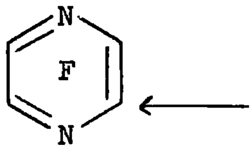


The tetrafluoronitrobenzene, however, undergoes substitution ortho to the nitro group, and this emphasises the considerable ability of the ring nitrogen to influence the orientation of substitution. Because a high electron density occurs on the nitrogen atom in the transition state the electron density on the ring carbon atoms will be correspondingly reduced relative to substitution in a polyfluorobenzene, and this explains the decreased importance of the Iπ effect.[109]

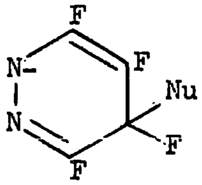
The replacement reactions of the three isomeric tetrafluorodiazines also provide evidence for the influence of the ring nitrogen atom on the orientation of nucleophilic substitution. All three compounds were found to be more reactive than pentafluoropyridine, displacement of fluorine occurring at the indicated positions.

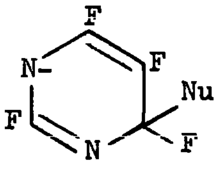


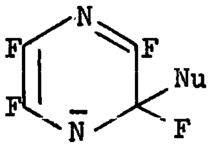




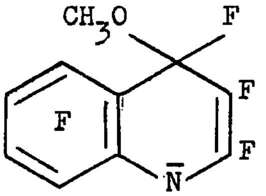
Tetrafluoropyridazine[109] and tetrafluoropyrimidine[110] were found to be more reactive than tetrafluoropyrazine[111] towards nucleophiles, and this can be explained from a consideration of the intermediate transition states. It can be seen that transition states of type II for tetrafluoropyridazine and tetrafluoropyrimidine result in the negative charge being localised on a nitrogen atom, whereas in the tetrafluoropyrazine only a type III canonical is possible, i.e.

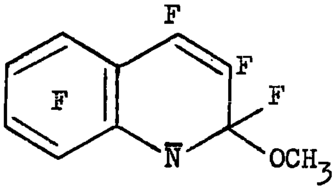






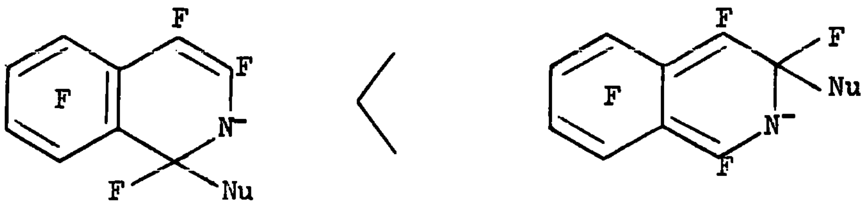
Additional evidence for the importance of a ring nitrogen in the transition state is provided by the nucleophilic substitution in perfluoroquinoline and -isoquinoline.[112] It was found that heptafluoroquinoline reacted with methoxide ion in methanol[112] to give a mixture of 2-methoxy and 4-methoxyhexafluoroquinoline in the ratio 3·4:1, whereas heptafluoroisoquinoline gave only 1-methoxyhexafluoroisoquinoline.[112] The orientations of substitution in the heptafluoroquinoline can be rationalised in terms of localisation of the negative charge on to the nitrogen atom.





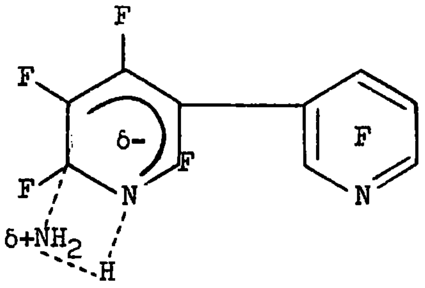
That 2-substitution predominates indicates that the ring nitrogen is allowing a considerable contribution from the type III canonical in the transition state.

From a consideration of the orientation of substitution in heptafluoroquinoline and octafluoronaphthalene, nucleophilic attack would be predicted to occur at the 3-position in heptafluoroisoquinoline. The observed 1-substition, however, has been rationalised in terms of charge localisation on the nitrogen atom, the localisation energy of the transition state for 1-substitution being less than that for 2-substitution, possibly because the former maintains the aromaticity of the carbocyclic ring.



localisation energy

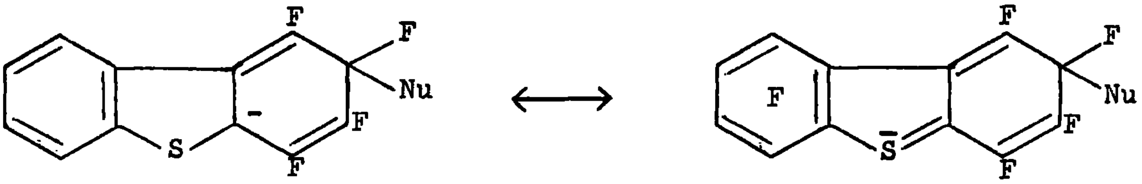
The influence of the heterocyclic ring nitrogen on the orientation of substitution has also been observed in the nucleophilic reactions of octafluoro-2,2'-bipyridyl.[113] Replacement of the fluorine atoms para to the ring nitrogen atoms occurred, and this is analogous to the replacement of the 4-fluorine atom in pentafluoropyridine by nucleophiles. The orientation in octafluoro-3,3'-bipyridyl,[114] however, was shown to be dependent on steric and solvent factors. With methoxide ion in methanol an equimolar mixture of the 4,4'- and 4,6'-dimethoxy derivatives was obtained, and this and other results with larger alkoxide groups (e.g. EtO^- and $iPrO^-$) indicated that the dominant factor affecting the orientation of substitution by alkoxides is the steric requirement of the nucleophile. The reactions of octafluoro-3,3'-bipyridyl with ammonia in ether and methyl lithium in ether gave exclusive substitution in the 6-position, and this was explained by invoking a charged transition state in which the attacking nucleophile is held in the 6-position by fractional charges.

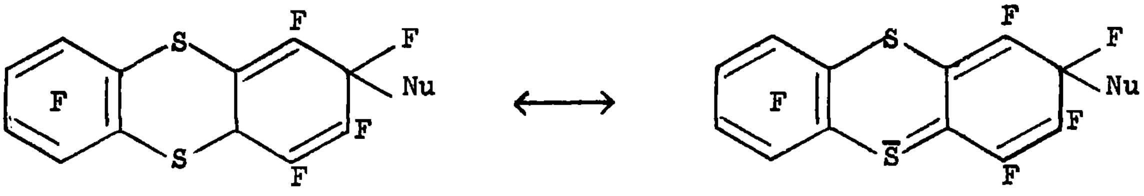


The most probable influence on orientation in the reaction with ammonia is the polarity of the solvent, and evidence for the influence of solvent polarity on the alkoxide reactions was obtained from the results of a series of reactions in which the ratio of 4- and 6-substituted products in solvent mixtures of differing dielectric constants was determined.

3.2.2 Polyfluoroheterocyclic sulphur compounds

A sulphur atom can stabilise an adjacent carbanionic centre by delocalisation of the charge into the 3d orbitals of the sulphur atom. This explanation has been used to rationalise the orientation of nucleophilic substitution in octafluorodibenzothiophen and octafluorothianthren,[115] both of these compounds undergoing nucleophilic displacement by methoxide ion at the 2-position, further substitution giving the corresponding 2,8-dimethoxy derivatives. The results are thus explained in terms of d-orbital stabilisation of the type II canonicals in the transition state.





It can thus be seen, in conclusion, that the orientation of nucleophilic substitution in polyfluorohomocyclic compounds can be rationalised, to a great extent, in terms of the Iπ effect. In rationalising the orientation of substitution in polyfluoroheterocyclic compounds, however, one must consider the different electronegativities of the ring atoms since this may lead to localisation of the charge, in the transition state, on the heteroatom, and this in some cases gives rise to orientations which are not in accord with those predicted by the Iπ effect.

DISCUSSION OF EXPERIMENTAL

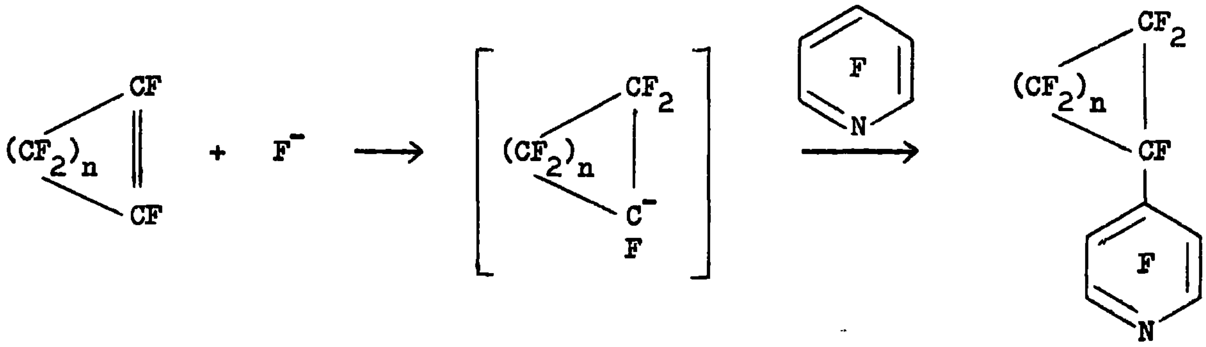
CHAPTER 4

PREPARATION AND REACTIONS OF PERFLUOROCYCLOALKYLPYRIDINES

Introduction

It was mentioned earlier that polyfluoroalkyl anions, generated by the reaction of fluoride ion with fluoro-olefins, react with activated polyfluoroaromatic compounds, in what can be regarded as the nucleophilic equivalent of Friedel-Craft reactions. Polyfluoroalkylation of heterocyclic polyfluoro-compounds has been achieved with several acyclic fluoro-olefins including tetrafluoroethylene, hexafluoropropene and octafluorobutene, and also with fluoroacetylenes such as hexafluorobut-2-yne. The aim of this work was to extend the polyfluoroalkylation process to the use of cyclic olefins, and synthesise perfluorocycloalkyl derivatives of perfluoro-N-heterocyclic compounds by nucleophilic attack of the anion, produced by addition of fluoride ion to a perfluorocycloalkene, on the heterocyclic substrate.

e.g.

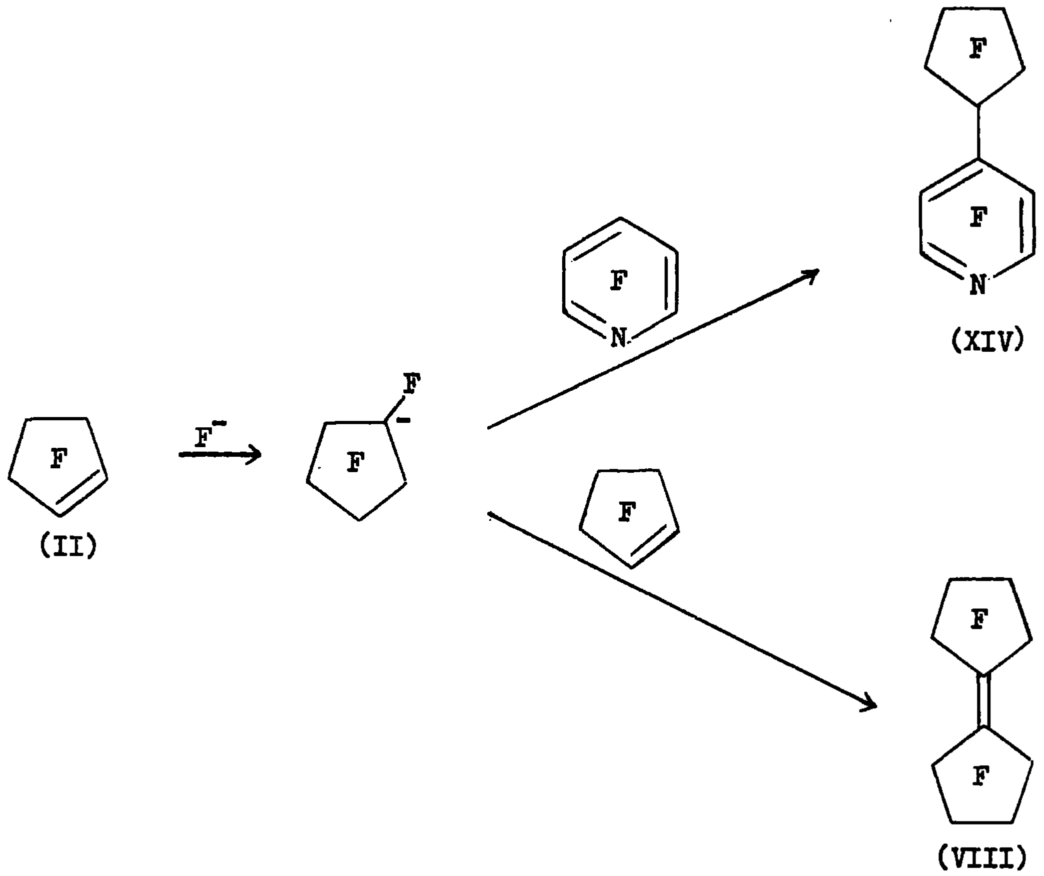


A discussion of the reactions of perfluorocycloalkenes with fluoride ion is included in this chapter since, as with acyclic fluoro-olefins, oligomerisation occurs by the fluoride ion-initiated self-condensation of perfluorocycloalkenes.

Nucleophilic substitution of the perfluorocycloalkylpyridines with methoxide ion was used to determine the relative reactivity of these compounds to nucleophilic attack, and novel perfluorocycloalkenylpyridines were obtained by defluorination.

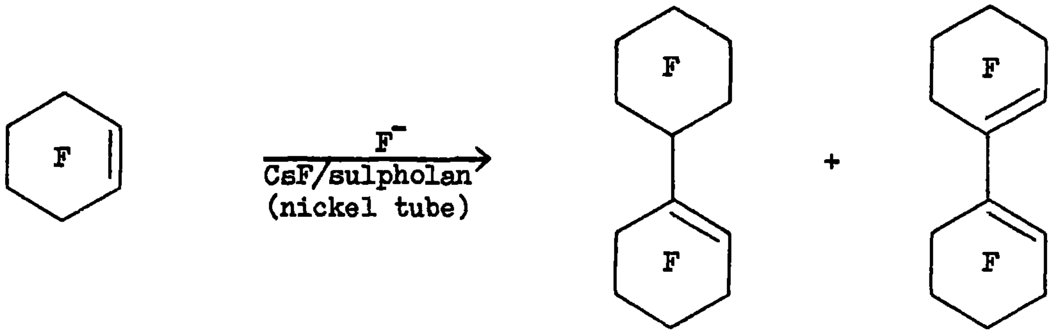
4.1 Reactions of Perfluorocycloalkenes with Fluoride Ion

In the fluoride ion-initiated reactions of pentafluoropyridine with various perfluorocycloalkenes (see section 4.2), products arising from the self-condensation reaction of a particular olefin were often obtained in addition to the perfluorocycloalkylated pyridine derivatives. For example, as shown in the annexed reaction scheme,



dimerisation of the perfluorocyclopentene occurred to give (VIII) in addition to the formation of perfluoro-(4-cyclopentylpyridine) (XIV). In order to study this oligomerisation process, reactions were carried out involving the olefin alone with fluoride ion under similar conditions to those used for the preparation of the substituted pyridine derivatives.

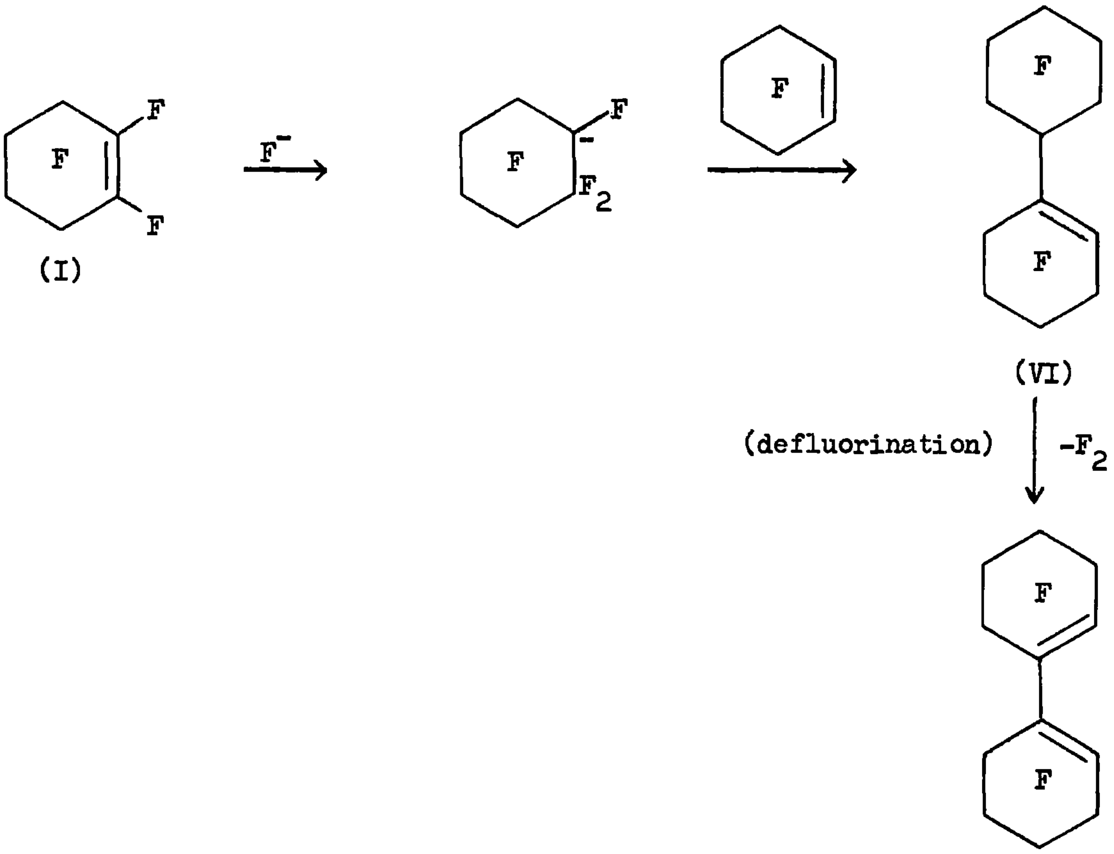
When perfluorocyclohexene was heated under vigorous conditions with caesium fluoride and sulpholan (65 hours at 170°), the two main products obtained, in addition to some unchanged perfluorocyclohexene, were perfluoro-(1-cyclohexylcyclohexene) (the dimer of perfluorocyclohexene) (VI) and perfluorobicyclohexenyl (VII).



(I) (VI) (57%) (VII) (19%)

The dimer of perfluorocyclohexene (VI) was shown to have the structure given above by ^{19}F n.m.r. spectroscopy. It was interesting to note that the i.r. spectrum of (VI) displayed two bands in the $>C=C<$ region at 1689 cm.$^{-1}$ (5·92μ) and 1672 cm.$^{-1}$ (5·98μ), the higher frequency band being the stronger. The two double-bond stretching bands may be thought to arise from the equatorial and axial isomers of this compound. The preparation of perfluoro-(1-cyclohexylcyclohexene) (VI) was claimed in a recent communication as unpublished results by Camaggi and Gozzo,[116] and Serboli[117] confirmed, by variable temperature i.r. spectroscopy on this compound, that the two double-bond stretching bands, also found by Camaggi and Gozzo during the characterisation of (VI), are due to the equatorial and axial isomers of this compound. He showed that the 1686 and 1672 cm.$^{-1}$ bands arise from the more stable, equatorial isomer and from the less stable, axial isomer, respectively.

Perfluorobicyclohexenyl (VII) is most probably formed by partial defluorination of the dimer (VI) at the surface of the nickel, since the defluorination of perfluoroalicyclic systems by metals,[118-120] including nickel,[121] is well known. The probable mechanism for the reaction of perfluorocyclohexene (I) with fluoride ion is as follows:



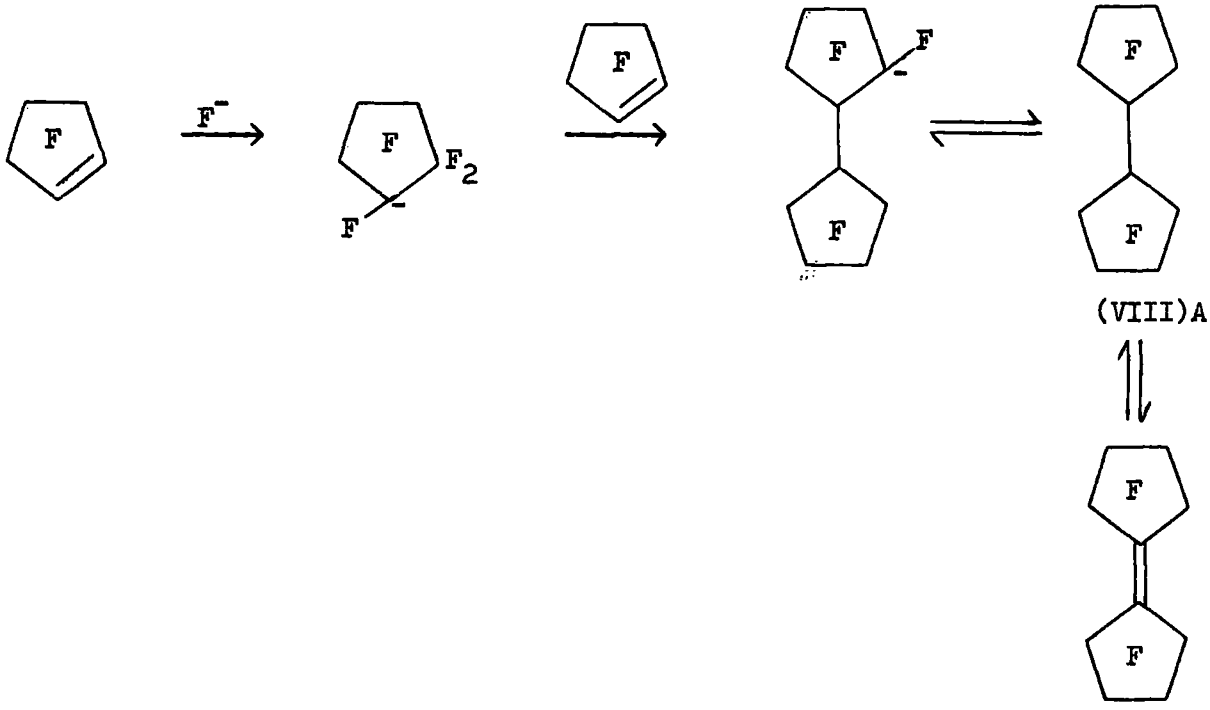
(I)

(VI)

(VII)

Only the structure for (VII) given above is consistent with the ^{19}F n.m.r. spectrum of this compound.

When perfluorocyclopentene (II) was heated for 40 hours at 125° with caesium fluoride and sulpholan, one product was obtained. This was shown to be the dimer of perfluorocyclopentene (VIII) and, unlike perfluoro-(1-cyclohexylcyclohexene) (VI), the ^{19}F n.m.r. spectrum of (VIII) contained only two broad singlets of equal height. Hence the dimer of perfluorocyclopentene has the structure shown for (VIII), and must be formed via the following mechanism involving bond migration, producing the thermodynamically most stable isomer.

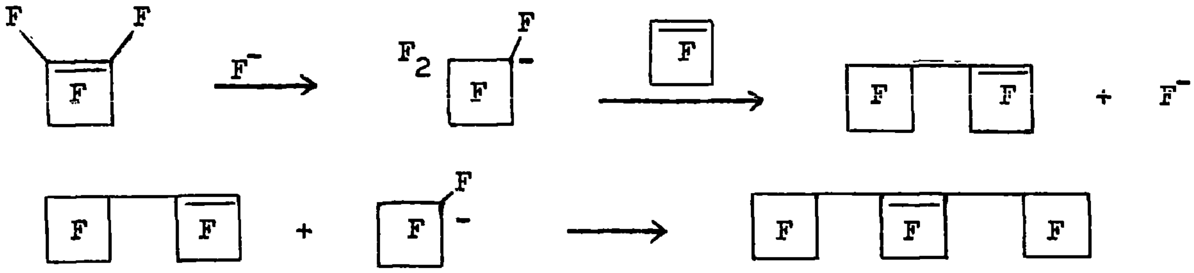


(VIII)A

(VIII)

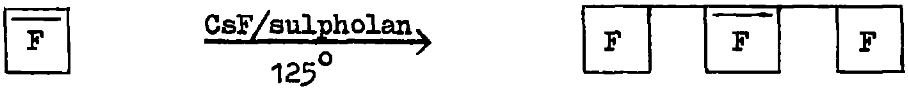
A structure of the form (VIII)A is incompatible with the observed n.m.r. data. It is interesting to note that, under more vigorous conditions, a small amount of the defluorinated derivative of (VIII) was also formed (see section 6.1), but a compound of the structure (VIII)A was never isolated.

The reaction of perfluorocyclobutene (III) with fluoride ion, under similar conditions as for perfluorocyclopentene, resulted in the exclusive formation of perfluorocyclobutene trimer (X). Only one isomer was obtained under these conditions, and the most likely structure for (X), from i.r. and ^{19}F n.m.r. data, is as shown below, and possibly formed by the following S_N2' mechanism.



(X)

No dimers of perfluorocyclobutene were isolated under these conditions



(X)

Fraticelli[63] obtained the same trimer using an alkali fluoride in dimethylformamide under less vigorous conditions, and under these conditions he also isolated dimers of perfluorocyclobutene. Reactions carried out at higher temperatures by the author, however, gave trace amounts of other components, but always insufficient for isolation.

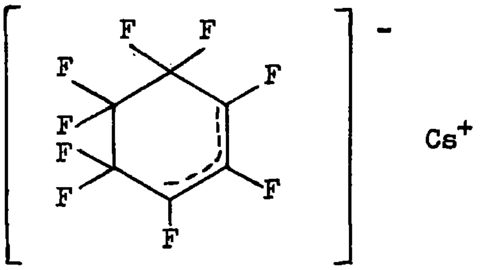
The results obtained from the reactions of the individual perfluorocycloalkenes with fluoride ion are consistent with the observations that, in fluoride ion-initiated reactions with pentafluoropyridine, perfluorocyclopentene (II) and perfluorocyclobutene (III) readily form a dimer and trimer respectively. Perfluorocyclohexene (I), however, showed little tendency to form oligomers, except under vigorous conditions, and reaction with pentafluoropyridine was therefore favoured.

Reactions involving perfluorocyclohexa-1,4-diene (IV) with heterocyclic substrates in the presence of fluoride ion, however, invariably gave low yields of substituted products, but no oligomers of the diene, produced by self-condensation initiated by fluoride ion, were ever isolated. To investigate the reaction of (IV) with fluoride ion several reactions were carried out in the absence of a heterocycle, and it was difficult to account for several observations in these reactions.

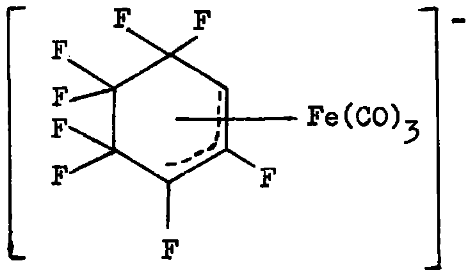
Firstly, intense colours were always produced and unreacted diene was never recovered from reactions carried out at high temperatures. Initially the diene (IV), caesium fluoride and sulpholan (small amount) were contained in a sealed Carius tube which was allowed to stand overnight at room temperature, after which time the 'sulpholan layer' was deep red in colour. After shaking the tube at room temperature for a further 24 hours, unchanged perfluorocyclohexa-1,4-diene (IV) was recovered quantitatively by distillation under vacuum. When the above reaction was repeated by rotating a Carius tube containing the same three reactants at 80° for 24 hours, the recovery of unchanged diene (IV) was only 10%. At higher temperatures than this, no diene was recovered.

Secondly, it was shown that intense colours were obtained only when all three reactants were present together since identical tubes containing (a) diene and caesium fluoride and (b) diene and sulpholan showed no change even after standing in an oil bath at 80° for 30 hours. At this stage the tube containing the diene, caesium fluoride and sulpholan exhibited an intense red colour and the diene layer was reduced to about two-thirds of its original volume. Furthermore, it was shown that the presence of a minimal amount of sulpholan was sufficient to initiate a reaction between the diene and fluoride ion, since only a 45% recovery of unchanged diene was achieved after perfluorocyclohexa-1,4-diene (2·0g.), caesium fluoride (1·0g.) and sulpholan (a few drops) had been heated in a Carius tube at 80° for 18 hours.

No polymeric material was precipitated during solvent extraction of the involatile products from the above reactions, although intractable gums remained after solvent extraction. Also, since no oligomers of perfluorocyclohexa-1,4-diene (IV) were formed in these reactions, the formation of intense colours may possibly be due to complex formation and the existence of a complex fluorocarbon anion as shown below.



The formation of a stable π-allyl complex involving the cyclic fluorocarbanion shown below has been reported,[122] and was obtained from the reaction of perfluorocyclohexa-1,3-diene and caesium fluoride in tetrahydrofuran.



To further investigate this possibility, perfluorocyclohexa-1,4-diene, caesium fluoride and sulpholan were heated at 130° for 24 hours. No unchanged diene was recovered, but the remaining materials were filtered under nitrogen and the residual solid shown to be caesium fluoride, mainly by the absence of carbon from elemental analysis, although the i.r. spectrum contained absorptions (broad) at 6•9, 13•5, and 20•7μ, which are not due to sulpholan. The filtrate was poured into water and carefully extracted with ether, but a careful distillation of the extract gave only ether as the distillate. Any complex dissolved in the sulpholan would be hydrolysed on adding to water giving the original diene which would have been extracted by ether. An i.r. spectrum of the filtrate (mainly sulpholan), however, did contain absorptions in the region 6•0 - 10•5μ which are not characteristic of sulpholan.

The formation of a π-bonded complex by the reaction of perfluorocyclohexadiene with fluoride ion in sulpholan would seem to be a feasible explanation for the low reactivity of this di-olefin towards polyfluoroheterocyclic substrates in fluoride ion-initiated reactions. It may be that the complex, if it is formed, is adsorbed on to the surface of the caesium fluoride. It is perhaps a little surprising, however, that a π-allyl complex is formed from the 1,4-diene, the unavailability of the 1,3-isomer being the main reason for this not being employed in these reactions.

4.2 Fluoride Ion-initiated Reactions of Perfluorocycloalkenes with Pentafluoropyridine

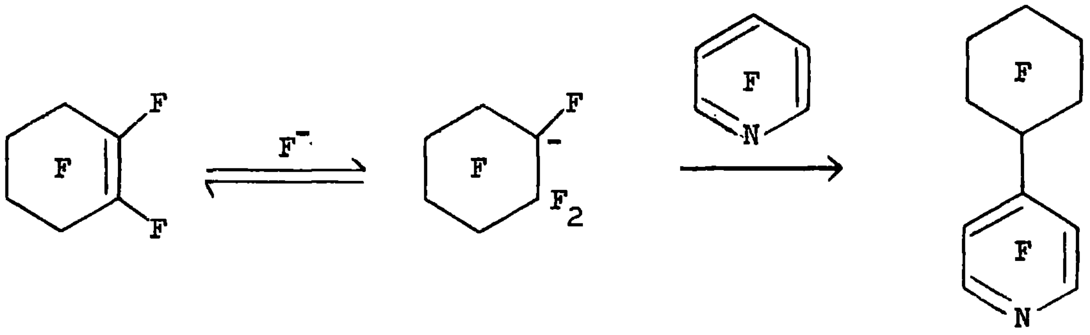
Pentafluoropyridine was chosen as a suitable substrate for these reactions since it has been shown to be considerably activated to attack by nucleophiles,[68] and also because it has already been used successfully for polyfluoroalkylation with acyclic fluoro-olefins.[72] The perfluorocycloalkenes used to generate carbanions in these reactions were perfluorocyclohexene (I), -pentene (II), -butene (III), and the perfluorocyclohexa-1,4- (IV) and -1,3- (V) dienes. Anhydrous caesium fluoride in dry sulpholan was employed as the solvent-initiator system in most reactions. It will be convenient to discuss the reactions according to the perfluorocycloalkene used.

4.2.1 Reactions involving perfluorocyclohexene

Several preliminary reactions were carried out with pentafluoropyridine and perfluorocyclohexene (I) in mixtures with caesium fluoride and sulpholan in order to optimise reaction conditions for the formation of the required products.

When equimolecular proportions of pentafluoropyridine and perfluorocyclohexene (I) were shaken vigorously with caesium fluoride and sulpholan in a sealed glass tube at room temperature, starting materials were recovered almost quantitatively. When the same reaction was carried out by heating the reactants at 130° for 64 hours, perfluoro-(4-cyclohexylpyridine) (XI) was obtained in approximately 20% yield, and the yield of product was increased to 45% when the reaction was repeated at 180° for 24 hours. Subsequent reactions of equimolecular proportions of pentafluoropyridine and perfluorocyclohexene with caesium fluoride in sulpholan gave a 65% yield of (XI) when carried out in a stainless-steel autoclave at 175° for 24 hours, and a 83% yield of (XI) when carried out in a nickel tube under the same conditions.

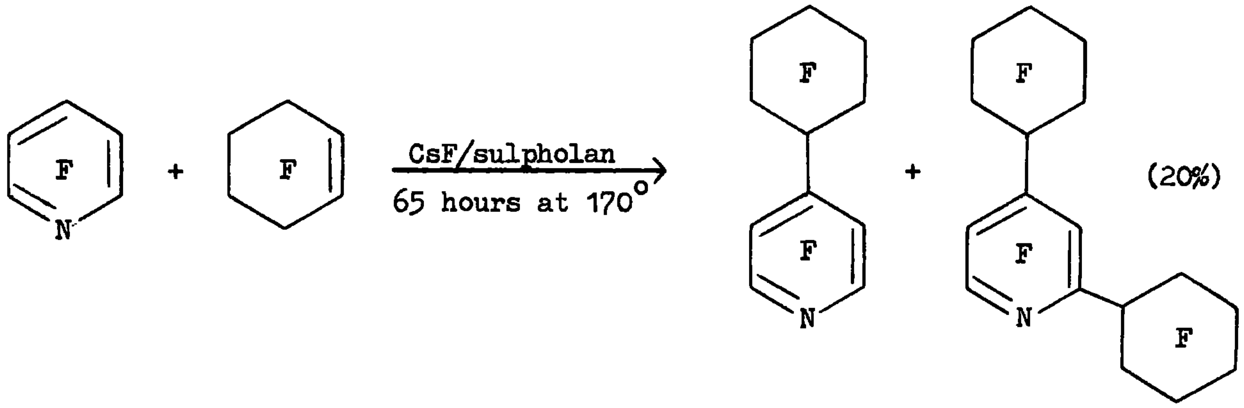
Perfluoro-(4-cyclohexylpyridine) (XI) is probably formed by the following mechanism:



(I) (XI)

It was found that the reaction of pentafluoropyridine with (I) could also be effected at atmospheric pressure but a low yield (ca. 7%) of (XI) resulted.

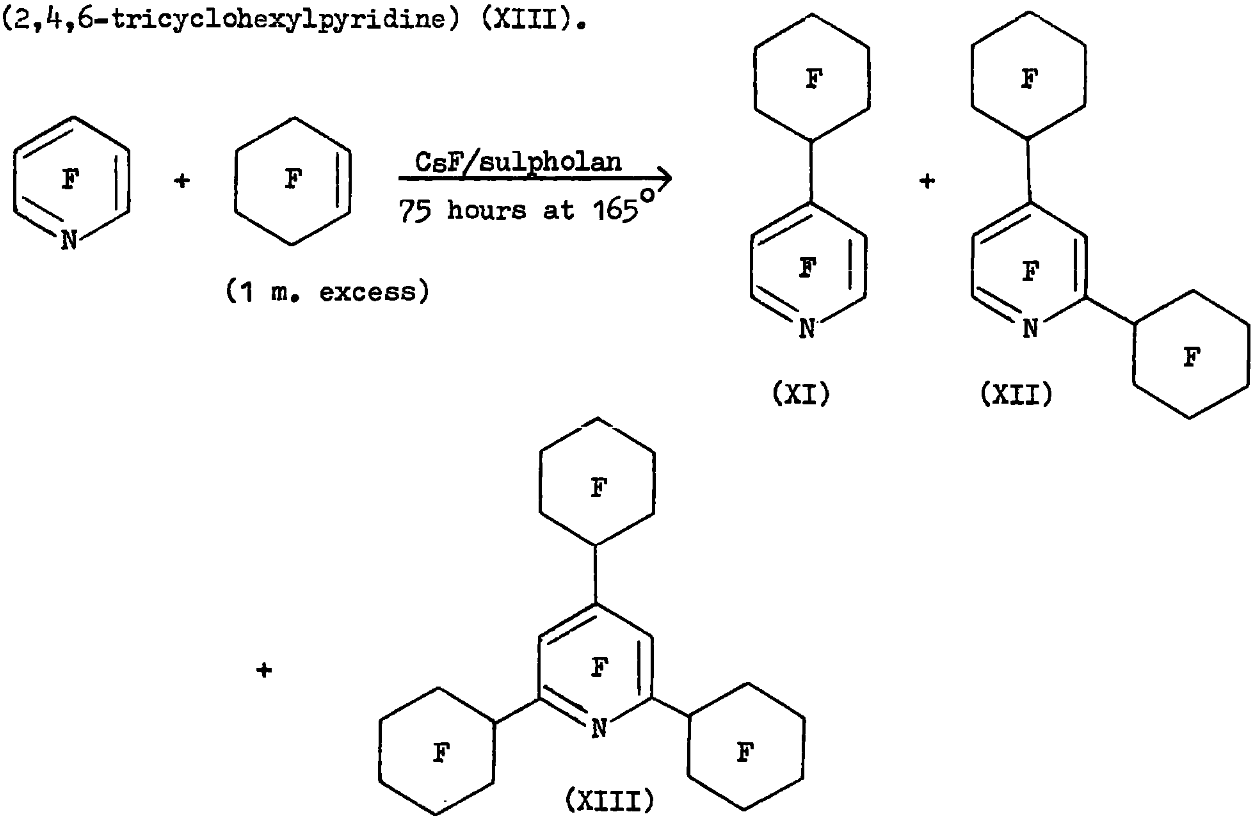
When pentafluoropyridine was heated with a one-molar excess of perfluorocyclohexene (I) for 65 hours at 170° in the presence of caesium fluoride and sulpholan, perfluoro-(2,4-dicyclohexylpyridine) (XII) was isolated in approximately 20% yield, together with the dimer of the olefin (VI) and the monosubstituted pyridine (XI).



(I) (XI) (XII)

The ^{19}F n.m.r. spectrum of (XII) was complex (see later) but, from a consideration of the substitution of a methoxy-group in perfluoro-(4-cyclohexylpyridine) (XI), it was concluded that the second perfluorocyclohexyl group was substituted into the 2-position of the pyridine ring giving the structure as shown for (XII).

When the above reaction was repeated, under identical conditions except for an increased amount of caesium fluoride and somewhat longer reaction time, a white insoluble solid was isolated in addition to the mono- and di-substituted products, (XI) and (XII). This was shown to be perfluoro-(2,4,6-tricyclohexylpyridine) (XIII).



(XI) (XII) (XIII)

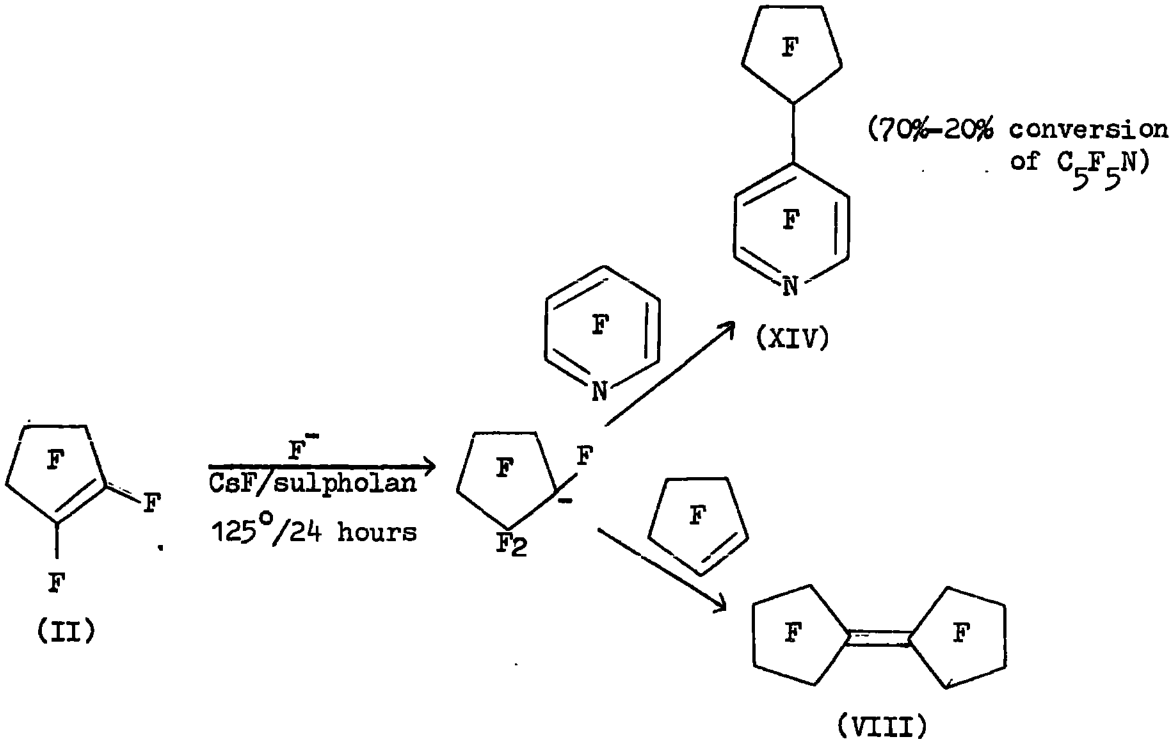
There was no chromatographic evidence for the existence of more than one isomer of (XIII) and the tri-substituted compound was shown to be the 2,4,6-isomer by ^{19}F n.m.r. spectroscopy. The formation of a 2,4,6-trisubstituted pyridine together with the absence of any of the 2,4,5-isomer is contrary to the previous results obtained in the polyfluoroalkylation of pentafluoropyridine. Using hexafluoropropene[123] and tetrafluoroethylene[124] to generate the polyfluoroalkylanions, the corresponding 2,4,5-trisubstituted pyridine was formed initially in both cases, and treatment of the 2,4,5-isomer with fluoride ion afforded the corresponding 2,4,6-isomer by migration of a polyfluoroalkyl substituent. It must be remembered, however, that perfluoro-(2,4,6-tricyclohexylpyridine) (XIII) was isolated from the reaction of pentafluoropyridine and perfluorocyclohexene under very vigorous conditions, and this is in accord with the results of the polyfluoroalkylation of pentafluoropyridine with hexafluoropropene under vigorous conditions[123] in which the 2,4,6-tri-isopropylpyridine is formed as the predominant isomer. The absence of a 2,4,5-trisubstituted compound using perfluorocyclohexene would suggest an equilibrium system for this reaction, and not an initial formation of the kinetically favoured 2,4,5-isomer followed by an intermolecular fluoride ion-catalysed rearrangement to the thermodynamically favoured 2,4,6-isomer.

In order to see if perfluoro-(2,4,6-tricyclohexylpyridine) (XIII), a highly substituted compound, would undergo a molecular rearrangement photochemically, the compound (insoluble in most organic solvents) was dissolved in pentafluoropyridine (as solvent) and irradiated with u.v. light for 4 days. The solid product recovered, after removal of the pentafluoropyridine (itself shown to be unchanged by i.r. spectroscopy), was shown to be pure by v.p.c. and confirmed as unchanged starting material by i.r. spectroscopy.

4.2.2 Reactions involving perfluorocyclopentene

The first reaction involving perfluorocyclopentene (II) was carried out in a stainless-steel autoclave using equimolecular proportions of the reactants and under the same conditions as for perfluorocyclohexene, i.e. shaken at 175° for 21 hours. This produced, in addition to a high recovery of pentafluoropyridine, a number of minor components whose mass spectra were difficult to interpret. Identification by further analysis was hindered by the small quantities of these products.

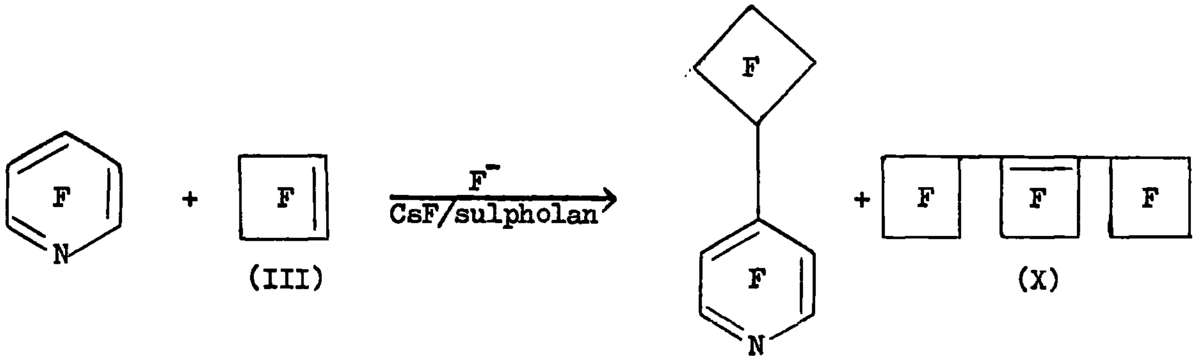
Since the recovery of material was low in this reaction and also some decomposition had occurred, the reaction was repeated at a lower temperature, and the reactants heated in a nickel tube at 125° for 24 hours. Perfluoro-(4-cyclopentylpyridine) (XIV) was isolated in 70% yield under these conditions but, although these conditions were optimum for the preparation of (XIV), perfluorocyclopentene dimer (VIII) was always formed as a major product in these reactions.



Attempts to prepare higher substituted products with perfluorocyclopentene, by using an excess of (II) and increased reaction temperatures, were unsuccessful, the excess olefin being consumed by self-condensation to the dimer (VIII).

4.2.3 Reactions involving perfluorocyclobutene

When pentafluoropyridine was shaken with perfluorocyclobutene (III) in the presence of fluoride ion and sulpholan in a Carius tube at room temperature, the major product was perfluorocyclobutene trimer (X). However, perfluoro-(4-cyclobutylpyridine) (XVI) was obtained in very low yield (ca. 5% of the product mixture) when the same reactants were heated in a nickel tube (a) at 150° with a 2-molar excess of (III) and (b) at 180° with a 4-molar excess of (III).



(III)

(XVI)

(X)

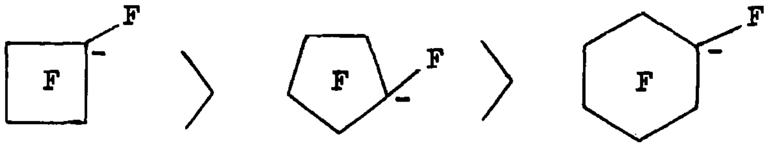
In order to induce more favourable competition between the polyfluorocyclobutyl anion and pentafluoropyridine and simultaneously suppress the tendency for the olefin to form a trimer, it was decided to utilize a system which involves injecting the olefin into the reaction mixture at the reaction temperature. This technique has recently proved successful for reactions involving hexafluoropropene,[123] tetrafluoroethylene[124] and hexafluorobut-2-yne.[83] A series of reactions was carried out in which the olefin (III) was bubbled through a stirred mixture of pentafluoropyridine and caesium fluoride in sulpholan, over a temperature range of 120°-140°

and at atmospheric pressure, by means of a circulating pump. The olefin was circulated for approximately 5-7 hours and in each case the reaction was stopped when it was apparent that no further olefin was being used up in the reaction. The compositions of the product mixtures were analysed quantitatively by v.p.c. on a gas density balance, and the results are shown in Table 8 (section 7.2.8). A temperature of 140° is the highest working temperature for this system, but the results show that the percentage conversion of pentafluoropyridine is not increased by an increase in temperature, although this technique was successful in suppressing self-condensation of the olefin. In reactions (ii) and (iii) the olefin was circulated with nitrogen as diluent, and it can be seen from the results that by using this technique at 140° the perfluorocyclobutene was consumed only by reaction with pentafluoropyridine to give perfluoro-(4-cyclobutylpyridine) (XVI) and not by self-condensation to give the trimer (X).

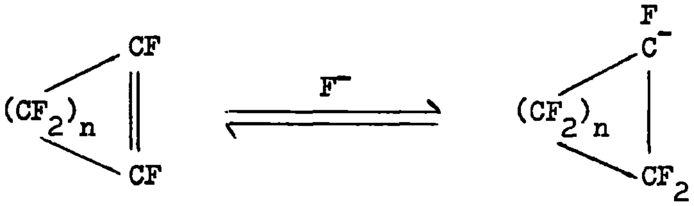
A product ratio similar to that in reaction (ii) (Table 8) was obtained when this reaction was carried out at atmospheric pressure in a static system instead of continuous circulation of the olefin through the reaction mixture.

It can be seen from the results of the fluoride ion-initiated reactions of pentafluoropyridine with perfluorocycloalkenes that, although relatively high yields of the perfluorocyclohexyl compound (XI) were obtained, the perfluorocyclo-pentyl (XIV) and -butyl (XVI) derivatives were only isolated in low yields. However, in the case of perfluorocyclopentene (II) and perfluorocyclobutene (III) there was competition between oligomerisation of the olefin and polyfluoroalkylation of the heterocyclic substrate, the final products depending on the fate of the intermediate perfluorocycloalkyl anion.

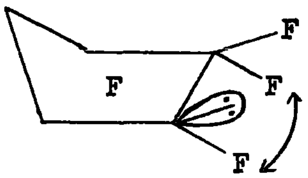
The observed order of reactivity of the perfluorocycloalkyl anions was found to be as follows,

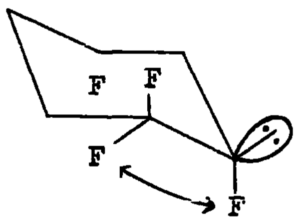


It is difficult to account for these results since the course of the reaction is dependent on two factors, the reactivity of the olefin with fluoride ion and the stability of the anion, once formed, in each case, according to the following equilibrium.



Considering the perfluorocycloalkyl anions, strain is relieved most for the perfluorocyclobutyl anion, and the equilibrium is possibly to the right. Thus the anion may be so reactive that, once formed, it will react immediately. However, self-condensation with perfluorocyclobutene may occur in preference to reaction with the heterocycle. In addition, the stereochemistry of the perfluorocyclohexyl anion is very different from that of the perfluorocyclopentyl anion. Adjacent bonds in the cyclopentyl anion are eclipsed,

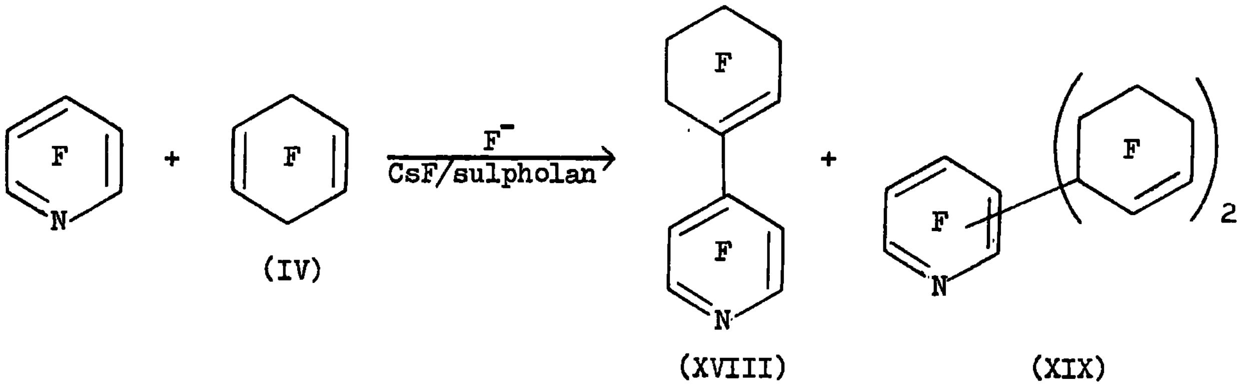




whereas corresponding bonds in the cyclohexyl anion are staggered. Thus the cyclohexyl anion would be more stable, and hence less reactive, so that the equilibrium between perfluorocyclohexene and its anion may lie to the left, elimination of fluoride ion being the preferred mode of reaction.

4.2.4 Reactions involving perfluorocyclohexadienes

The reactions of pentafluoropyridine and perfluorocyclohexa-1,4-diene in the presence of caesium fluoride and sulpholan almost invariably gave two products corresponding to mono- and di-substitution i.e.



The structures of (XVIII) and (XIX) are discussed later. The results obtained from a series of fluoride ion-initiated reactions of (IV) with pentafluoropyridine are summarised in Table 2.

When equimolecular amounts of pentafluoropyridine and perfluorocyclohexa-1,3-diene were heated for 26 hours at 150° in the presence of caesium fluoride and sulpholan, perfluoro-(4-cyclohexenylpyridine) (XVIII) was formed in 30% yield, together with a trace of $C_{17}F_{21}N$ (XIX). The mono-substituted pyridine (XVIII) was identical with the product obtained from the reaction of pentafluoropyridine with the 1,4-diene (IV).

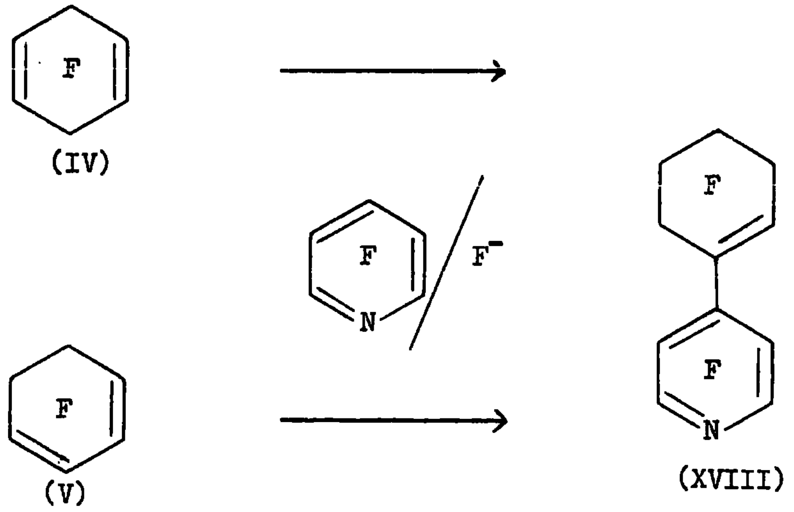
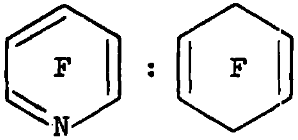
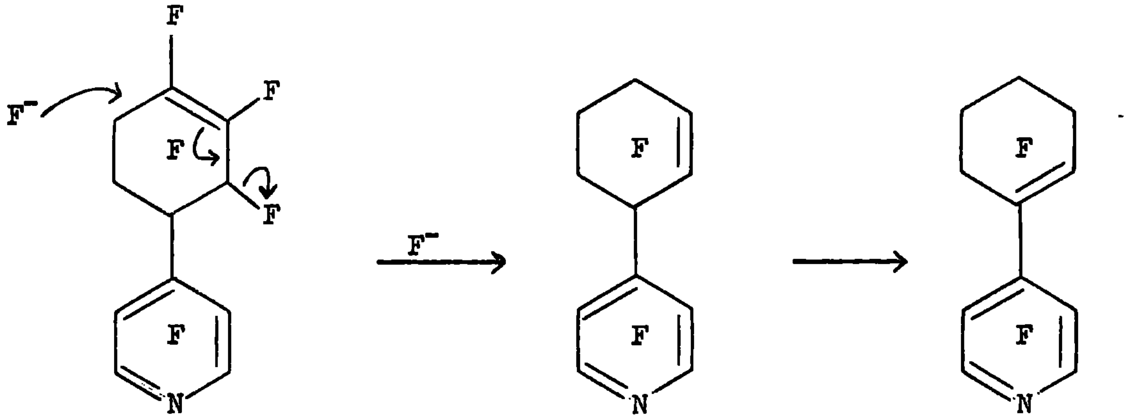


Table 2

Ratio of reactants	Reaction vessel	Reaction conditions	Yields of Products		% conversion of
			$C_{11}F_{13}N$	$C_{17}F_{21}N$	C_5F_5N
2 : 1	Stainless-steel autoclave	24 hours at 175°	23%	-	45
2 : 1	Stainless-steel autoclave	24 hours at 120°	28%	7%	50
1 : 1	Stainless-steel autoclave	24 hours at 160°	16%	-	60
1 : 1	Nickel tube	24 hours at 125°	50%	14%	20
1 : 1	Nickel tube	50 hours at 50°	90% recovery of C_5F_5N but high yields of $C_{11}F_{13}N$ and $C_{17}F_{21}N$ based on C_5F_5N consumed.		
1 : 3	Nickel tube	24 hours at 125°	Very low recovery of products but the product mixture consisted of $C_{11}F_{13}N$ (25%) + $C_{17}F_{21}N$ (20%) + C_5F_5N (52%)		

It is to be expected that the product (XVIII) is the most thermodynamically stable isomer, obtained by fluoride ion-induced rearrangements, e.g.



In order to compare the relative reactivity and the products formed from the fluoride ion-initiated reaction of pentafluoropyridine and perfluorocyclohexa-1,3- and 1,4-diene, two reactions were carried out using identical reaction conditions (24 hours at 120°). In addition to unchanged pentafluoropyridine, the two products formed were (XVIII) and (XIX), and the product ratio was the same for both reactions (see Table 11 section 7.2.11).

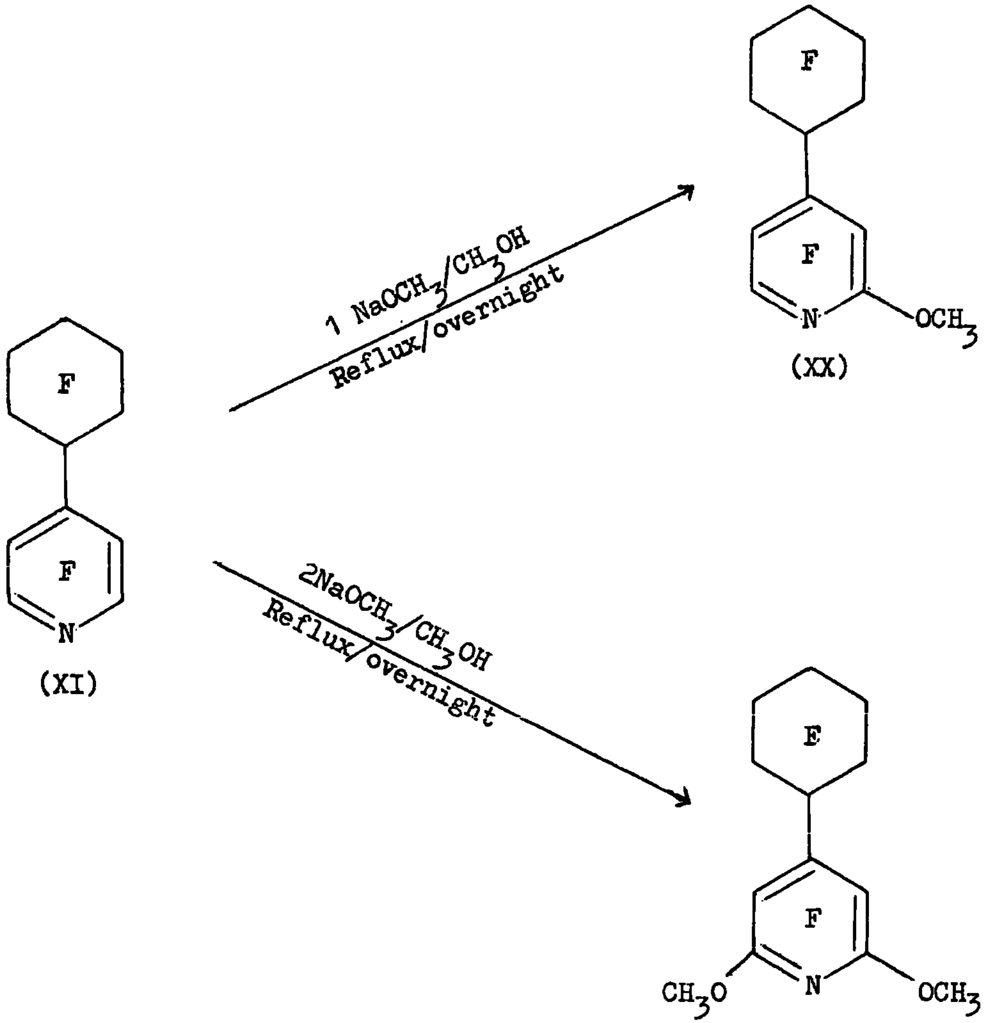
An important aspect of all the reactions involving perfluorocyclohexadienes was the low recovery of materials and low yields of products, and although unreacted pentafluoropyridine was easily recovered, it was difficult to account for the consumed diene since no oligomers were ever isolated. The possible explanations for these observations were discussed in section 4.1.

4.3 Reactions of Perfluorocycloalkylpyridines

Two principal reactions of the perfluorocycloalkylpyridines were investigated. Firstly, nucleophilic substitution of the perfluorocycloalkylpyridines with methoxide ion enabled the preparation of derivatives, a study of which assisted in the determination of the orientation of substitution of additional cycloalkyl groups in the heterocyclic ring and the directional effects of perfluorocycloalkyl groups. A measure of the relative reactivity of the various perfluorocycloalkylpyridines towards nucleophilic substitution was attempted by carrying out competition reactions, using a deficiency of methoxide ion. Secondly, the compounds were passed over iron at high temperatures to ascertain the ease with which the perfluorocycloalkyl substituent could be defluorinated, and subsequently acquire further confirmation of the structure of these compounds.

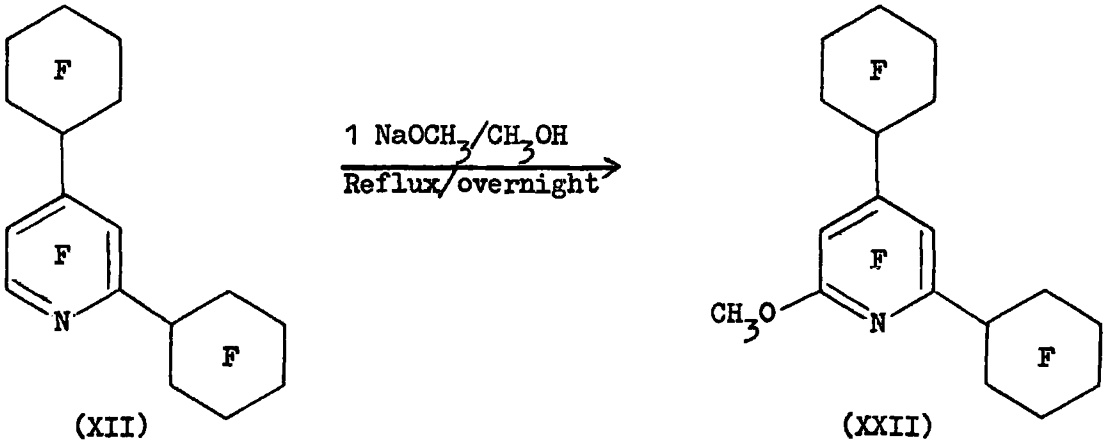
4.3.1 Nucleophilic substitution with methoxide ion

Mono- and di-methoxy derivatives of perfluoro-(4-cyclohexylpyridine) (XI) were prepared by refluxing (XI) with one and two molecular proportions, respectively, of sodium methoxide in methanol.



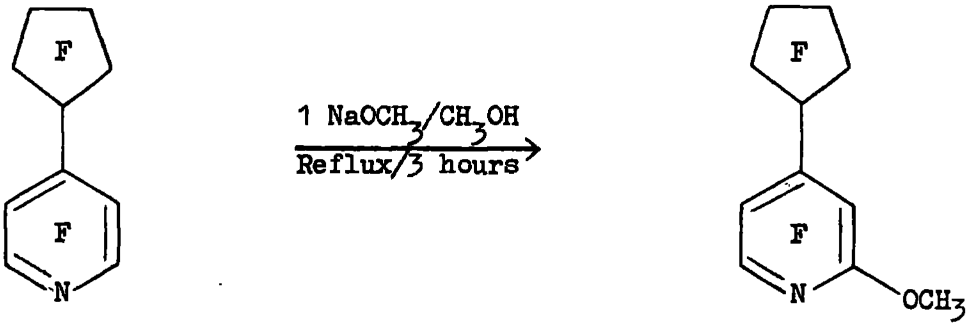
The orientation of substitution of the methoxyl group(s) was shown by ^{19}F and ^{1}H n.m.r. spectroscopy to be 2-(mono-) and 2,6-(di-) (see later) giving 4-perfluorocyclohexyl-2-methoxy-3,5,6-trifluoropyridine (XX) and 4-perfluorocyclohexyl-2,6-dimethoxy-3,5-difluoropyridine (XXI). In the preparation of (XXI) there was no indication of accompanying isomers from chromatographic analysis and n.m.r. data, and thus the normal pattern of nucleophilic substitution in pentafluoropyridine was followed, the perfluorocyclohexyl group having no unusual directive effects on the second methoxyl substituent.

The treatment of perfluoro-(2,4-dicyclohexylpyridine) (XII) with one molecular proportion of sodium methoxide afforded the corresponding monomethoxy derivative (XXII), and substitution by the methoxyl group was shown by n.m.r. to occur at the 6-position of the pyridine ring giving 2,4-perfluorodicyclohexyl-6-methoxy-3,5-difluoropyridine (XXII).

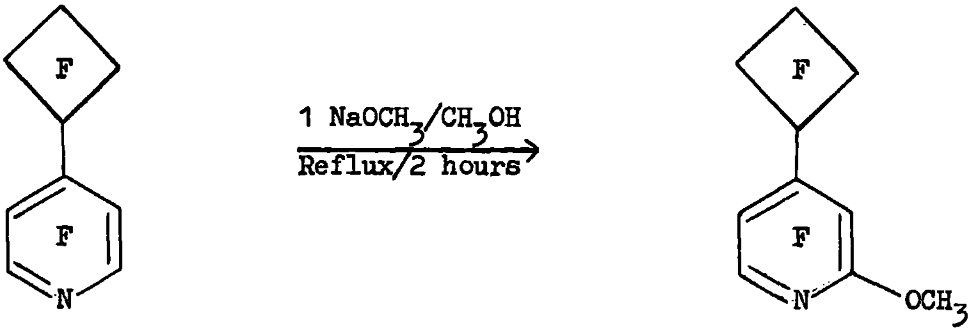


(XII) (XXII)

The monomethoxy derivatives of perfluoro-(4-cyclopentylpyridine) (XIV) and perfluoro-(4-cyclobutylpyridine) (XVI) were similarly prepared by refluxing with equimolar quantities of sodium methoxide in methanol, and that substitution occurred at the 2-position, as with perfluoro-(4-cyclohexylpyridine), was clearly shown by the good agreement between the



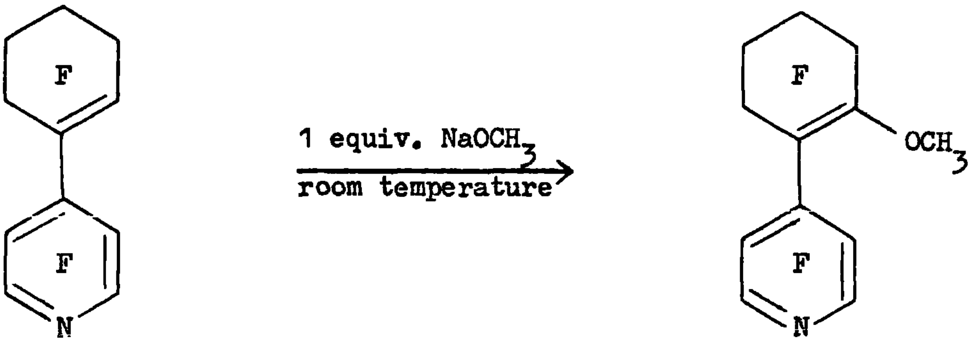
(XIV) (XXIII)



(XVI) (XXIV)

observed and calculated substituent chemical shifts for the introduction of a methoxy group in the 2-position of the pyridine ring (see Chapter 10).

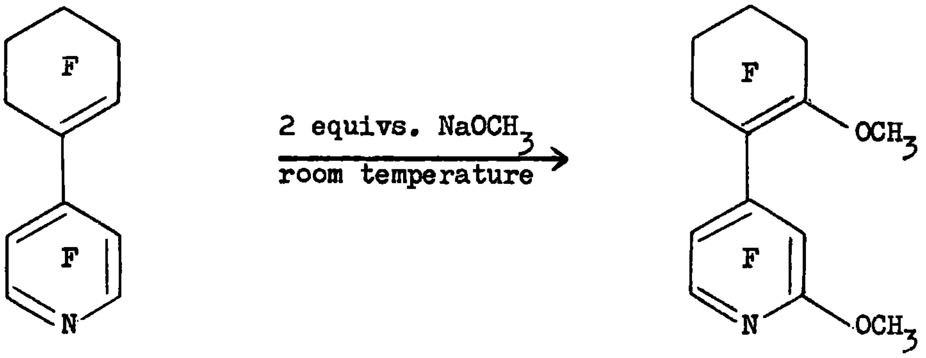
The reaction of perfluoro-(4-cyclohexenylpyridine) (XVIII) with methoxide ion under the conditions used above was unsuccessful for the isolation of pure derivatives. In fact, (XVIII) appeared to be so reactive towards nucleophilic attack by CH_3O^- that the monomethoxy derivative was obtained pure only when the reaction was carried out at room temperature for a few minutes. At higher temperatures a mixture of mono- and di-methoxy derivatives



(XVIII) (XXV)

was always produced. Substitution of the methoxyl group in the alicyclic ring was indicated by n.m.r. studies, in particular the ^{1}H n.m.r. spectrum.

The dimethoxy derivative of (XVIII) was obtained by using two equivalents of sodium methoxide in methanol at room temperature, and the



(XVIII) (XXVI)

^{1}H n.m.r. spectrum of (XXVI) showed the presence of two methoxyl groups in different environments.

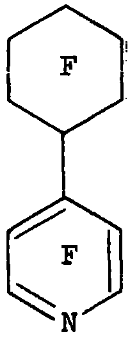
When a series of competition reactions was carried out (see section 4.3.2) involving perfluorocycloalkylpyridines and including perfluoro-(4-cyclohexenylpyridine) (XVIII), it was observed that unusually large proportions of (XXV) were being produced in reactions involving (XVIII). As a result of this, (XVIII) was refluxed with methanol alone, and it was found that the monomethoxy derivative (XXV) of perfluoro-(4-cyclohexenylpyridine) (XVIII) was formed in appreciable yield and identified by its chromatographic retention time. This result is very interesting since it seems that the methanol itself is acting as a nucleophile, which then attacks the very reactive cyclohexenyl derivative.

$C_{17}F_{21}N$ (XIX) was found to be as reactive as perfluoro-(4-cyclohexenylpyridine) (XVIII) towards methoxide ion, and several reactions were carried out in an attempt to isolate pure methoxy derivatives. A mono-methoxy derivative was characterised but the complex nature of the n.m.r. spectrum restricted the determination of the orientation of substitution.

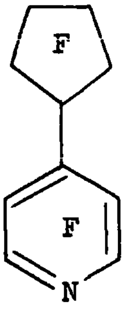
It can thus be seen that nucleophilic substitution of perfluorocycloalkylpyridines with methoxide ion results in substitution at the 2-position. With perfluorocycloalkenylpyridines such as (XVIII) and (XIX), however, the methoxy group can substitute in the heterocyclic ring or in the cycloalkenyl ring, the latter being more reactive towards nucleophilic attack by methoxide ion in perfluoro-(4-cyclohexenylpyridine) (XVIII).

4.3.2 Relative rates of nucleophilic substitution in perfluoroalkylpyridines

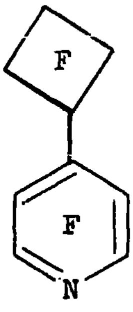
It has been found that perfluoroalkyl- and perfluorocycloalkyl-pyridines are susceptible to nucleophilic substitution, and the 2-methoxy derivatives of perfluoro-(4-cyclohexylpyridine) (XI), -(4-cyclopentylpyridine) (XIV), -(4-cyclobutylpyridine) (XVI) (see previous section), -(4-isopropylpyridine)[62] and -(4-ethylpyridine)[125] have been prepared. In order to study the relative rates of nucleophilic substitution in these compounds by methoxide ion, competition reactions were carried out with (XI), (XIV) and (XVI). The two perfluoroalkylpyridines, (4-isopropyl- and 4-ethyl-) were included to compare the effects of perfluoroalkyl- and perfluorocycloalkyl- groups on nucleophilic substitution at the 2-position, and to determine the position of these compounds in the series.



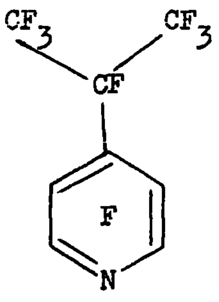
(XI)



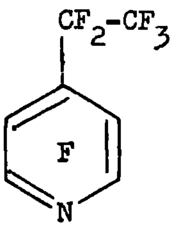
(XIV)



(XVI)



4-isopropyl



4-ethyl

Ten reactions were carried out in which any two of the above compounds in turn were reacted with a deficiency of methoxide ion. The resulting mixture was then analysed quantitatively by v.p.c. on a gas density balance, and the relative rates of reactivity could be calculated from the relative amounts of each methoxy derivative formed in the reaction. The results of these reactions and the relative rate values are given in Table 3. No values were obtained for $\frac{k_B}{k_E}$ and $\frac{k_D}{k_E}$ from chromatographic analysis since the products and/or reactants possessed identical retention times giving overlapping peaks.

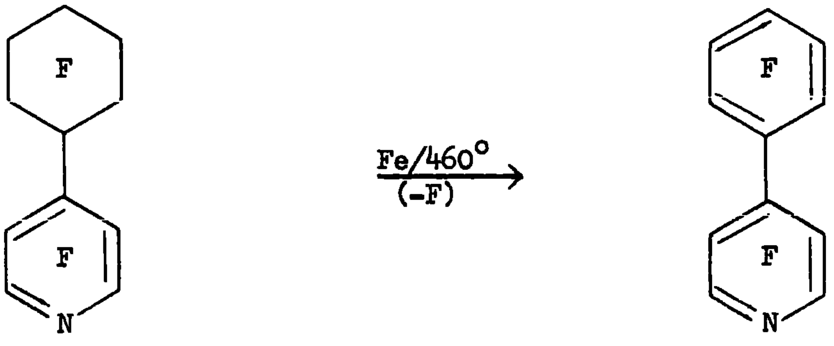
The results in Table 3 can be expressed in the following series:

$$\underset{(A)}{C_9F_{11}N} > \underset{(B)}{C_{11}F_{15}N} > \underset{(C)}{C_{10}F_{13}N} > \underset{(D)}{C_8F_{11}N} > \underset{(E)}{C_7F_9N}$$

and although there are no significantly large values for adjacent compounds in the series, there is, nevertheless, a consistent trend in reactivity with the cyclobutyl derivative being the most reactive member of the series towards nucleophilic attack by methoxide ion. Although these results cannot be related to the rate of nucleophilic attack by methoxide in pentafluoropyridine itself, it can be seen that the presence of a perfluorocycloalkyl group enhances the reactivity to methoxide ion relative to the perfluoroalkyl groups.

4.3.3 Defluorination reactions

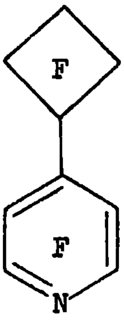
Perfluoro-(4-cyclohexylpyridine) (XI) was converted to perfluoro-(4-phenylpyridine) (XI)A when passed over iron at 460°.

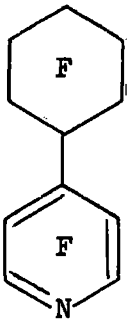


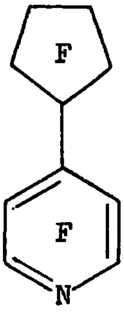
(XI) (XI)A

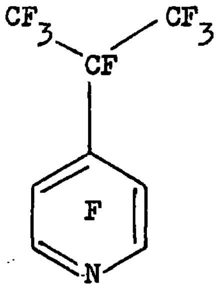
Table 3

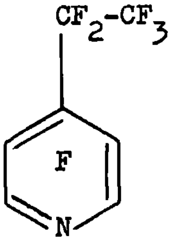
Competition Reactions - Relative Rates


(A)


(B)


(C)


(D)


(E)

$$\frac{k_A}{k_B} \approx 1{\cdot}02$$

$$\frac{k_A}{k_C} \approx 1{\cdot}20$$

$$\frac{k_A}{k_D} \approx 1{\cdot}57$$

$$\frac{k_A}{k_E} \approx 1{\cdot}87$$

$$\frac{k_B}{k_C} \approx 1{\cdot}13$$

$$\frac{k_B}{k_D} \approx 1{\cdot}52$$

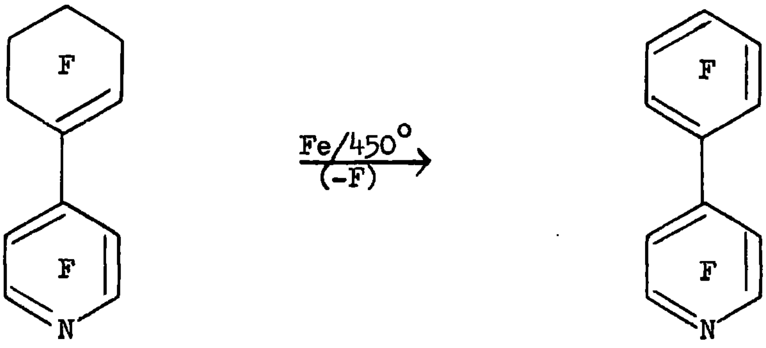
No Value

$$\frac{k_C}{k_D} \approx 1{\cdot}35$$

$$\frac{k_C}{k_E} \approx 1{\cdot}61$$

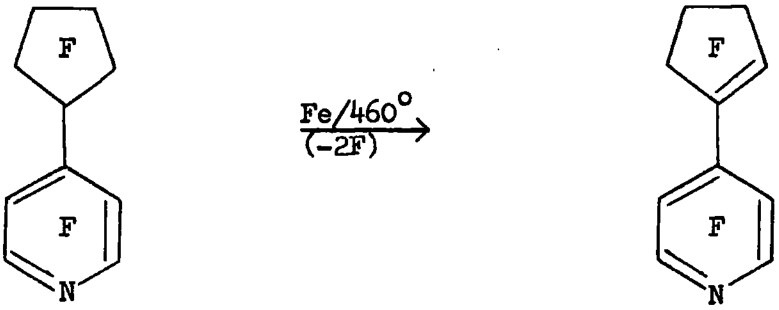
No Value

(XI)A was obtained in 70% yield and identified by i.r.[68] and mass spectrometry. Perfluoro-(4-phenylpyridine) was also isolated in small quantity when perfluoro-(4-cyclohexenylpyridine) (XVIII) was passed over iron at 450°.



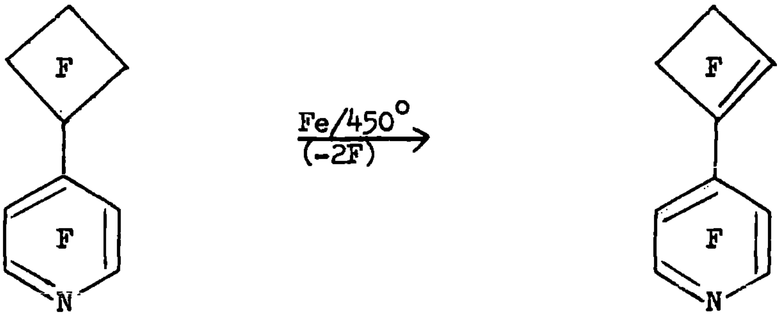
(XVIII) (XI)A

However, partial defluorination occurred with perfluoro-(4-cyclopentylpyridine) (XIV) and perfluoro-(4-cyclobutylpyridine) (XVI), under similar conditions, and the corresponding perfluorocycloalkenylpyridines, (XV) and (XVII) were produced.



(45% yield)

(XIV) (XV)

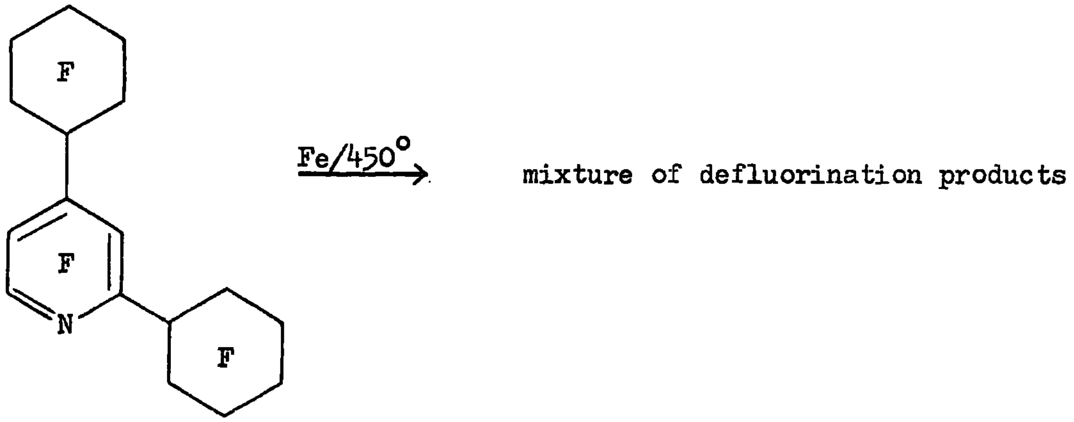


(small quantity)

(XVI) (XVII)

The structure of (XV) is in accord with the ^{19}F n.m.r. spectrum of this compound (see later). Perfluoro-(4-cyclobutenylpyridine) (XVII), however, could only be isolated in very small quantities and, although the compound was fully characterised, confirmation of the structure by n.m.r. was not possible.

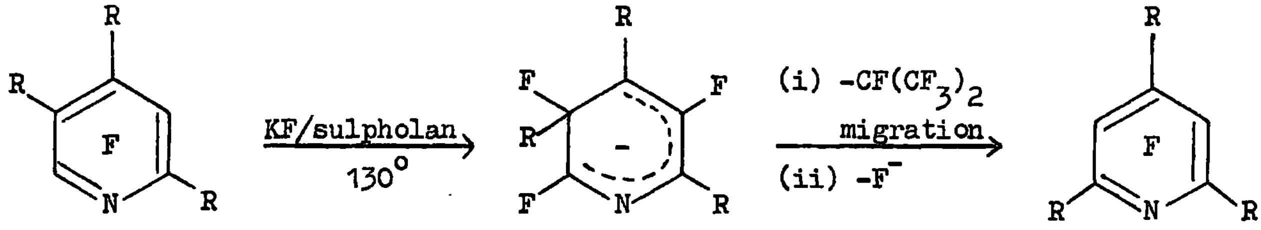
Attempts to defluorinate disubstituted cycloalkylpyridines resulted in the formation of a mixture of products. Defluorination of perfluoro-(2,4-dicyclohexylpyridine) (XII) gave a product which was shown by gas chromatography to contain only two major components, although mass spectrometry indicated that other defluorination products were present.



On standing for an appreciable time, a solid crystallised out from the liquid product mixture and this was shown to correspond to perfluoro-(diphenylpyridine) by mass spectrometry.

4.4 Fluoride Ion-initiated Reactions of Perfluorocycloalkenes with Perfluoro-(4-isopropylpyridine)

Polyfluoroalkylation of perfluoro-(4-isopropylpyridine)[126] was investigated to establish whether the perfluoroisopropyl group would sufficiently activate the normally much less reactive 2,6-positions in the pyridine ring and allow further substitution by perfluorocycloalkyl anions. Also tri-substituted products are of considerable interest because a novel fluoride ion-induced rearrangement of perfluoro-(2,4,5-tri-isopropylpyridine) has been observed.[76] This was first noticed following the isolation of a mixture of two isomeric tri-substituted derivatives from the fluoride ion-initiated reaction of pentafluoropyridine and hexafluoropropene,[76] which were shown by ^{19}F n.m.r. to be the 2,4,5- and 2,4,6-isomers.[127] It was found that, under the conditions of the polyfluoroalkylation, the 2,4,5-isomer rearranges to the 2,4,6-derivative.

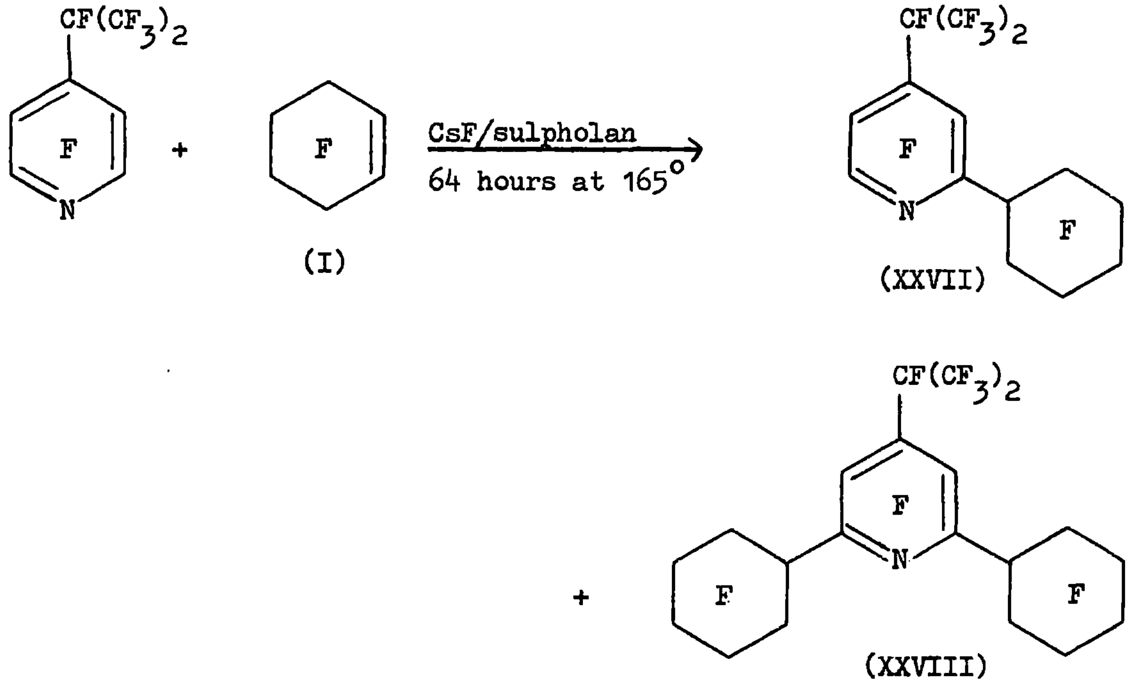


(R = $-CF(CF_3)_2$)

That the 2,4,6-isomer is the more thermodynamically stable is quite consistent with the unusually large steric requirements of the perfluoroisopropyl group, indicated by variable temperature n.m.r. studies.[127] The rearrangement was shown to be an intermolecular process from the observation of cross-over products with perfluoroquinoline, a substrate which is easily polyfluoroalkylated.[62]

4.4.1 Preparation of perfluorocyclohexyl derivatives of perfluoro-(4-isopropylpyridine)

The reaction of perfluoro-(4-isopropylpyridine) with a 1·5 molar excess of perfluorocyclohexene (I) in the presence of caesium fluoride and sulpholan, and under vigorous conditions (64 hours at 165°) gave a mixture of products from which was isolated the corresponding mono- and di-perfluorocyclohexyl derivatives, (XXVII) and (XXVIII), of perfluoro-(4-isopropylpyridine).



In common with all other nucleophilic substitutions in pentafluoropyridine, attack by the first cyclohexyl anion occurs at the 2-position, and this was confirmed by ^{19}F n.m.r. spectroscopy. Only one tri-substituted product was indicated by gas chromatography and n.m.r. data, and the structure given for (XXVIII) above (2,4,6-isomer) is in accord with the n.m.r. spectrum (see later). It must be noted, however, that (XXVIII) was produced under vigorous reaction conditions, similar to the preparation of perfluoro-(2,4,6-tricyclohexylpyridine) (XIII) (see section 4.2.1), and again this may explain the absence of a 2,4,5-isomer of (XXVIII). This is contrary to the ortho-directing effect of a heptafluoroisopropyl group on another such group in the polyfluoroalkylation of pentafluoropyridine. The only other products isolated in the above reaction were perfluoro-(1-cyclohexylcyclohexene) (VI) and perfluorobicyclohexenyl (VII), the self-condensation products of perfluorocyclohexene (I) in the presence of fluoride ion.

4.4.2 Reactions with other perfluorocycloalkenes

When perfluoro-(4-isopropylpyridine) was heated with perfluorocyclopentene (II), in the presence of caesium fluoride and sulpholan, at 150° overnight, the heterocycle was recovered almost quantitatively and the olefin was consumed by dimerisation. This is comparable with the inability to obtain a dicyclopentylpyridine (see section 4.2.2), and shows that the activity of the 2-position to attack by a perfluorocyclopentyl anion is not sufficient to overcome the reaction of this anion with another molecule of the olefin to give the dimer (VIII).

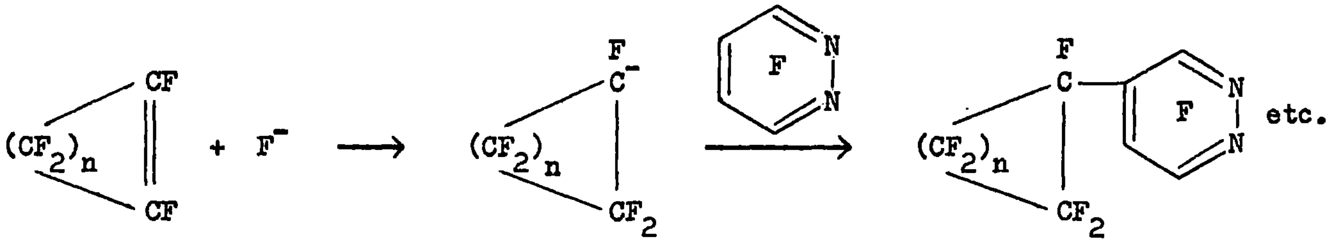
Perfluoro-(4-isopropylpyridine) was recovered quantitatively from the fluoride ion-initiated reaction of this compound with perfluorocyclohexa-1,4-diene at 130°.

CHAPTER 5

PREPARATION AND REACTIONS OF PERFLUOROCYCLOALKYLPYRIDAZINES

Introduction

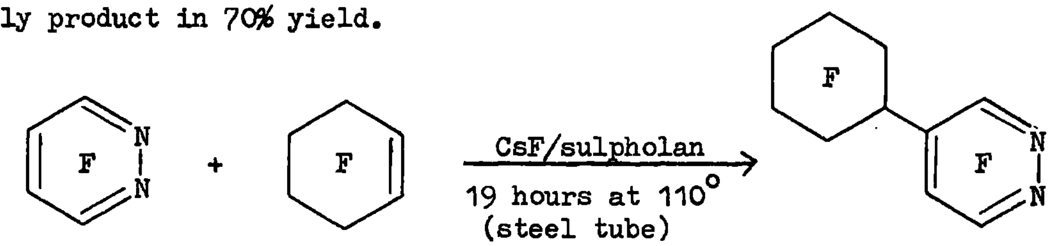
The preparation of perfluorocycloalkylated pyridines by fluoride ion-induced reactions of pentafluoropyridine with a series of perfluorocycloalkenes was discussed in Chapter 4. With the exception of perfluorocyclohexene, monosubstitution was achieved in each case. One approach to increasing molecular weight in these perfluoroalkyl systems lies in using more reactive heterocycles so that either (a) polysubstitution occurs directly or (b) reactive sites remain which can be exploited by reaction with other nucleophiles to increase molecular weight. Tetrafluoropyridazine is known to be the most reactive of the fluorinated nitrogen heterocycles, being particularly susceptible to nucleophilic attack, and a preliminary survey of the reactions of perfluorocycloalkenes with tetrafluoropyridazine is discussed. Perfluoroalkylpyridazines are important since thermal and



photochemical nuclear rearrangements of the pyridazine to the pyrimidine and pyrazine ring systems have already been achieved, in addition to the intermolecular rearrangement of substituents in the pyridazine ring, as in the pyridine system.

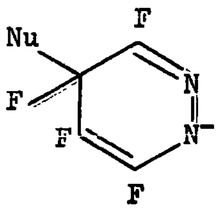
5.1 Fluoride Ion-initiated Reactions of Perfluorocycloalkenes with Tetrafluoropyridazine

Initial reactions were carried out using perfluorocyclohexene (I) to generate the fluorocarbanion. When equimolar proportions of tetrafluoropyridazine and perfluorocyclohexene (I) were heated in a stainless-steel tube with caesium fluoride and sulpholan for 19 hours at 80°, some unchanged starting materials were recovered in addition to the formation of the monosubstituted pyridazine (XXIX). When the reaction was repeated by heating the reactants for 19 hours at 110°, no unchanged starting materials were recovered and perfluoro-(4-cyclohexylpyridazine) (XXIX) was obtained as the only product in 70% yield.

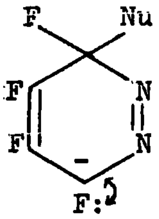


(I) (XXIX)

It has been shown[109] that nucleophilic substitution in tetrafluoropyridazine occurs initially at the 4- and 5-positions. Attack at these positions is preferred since in the transition state charge density is probably greatest at the position para to the point of entry of the nucleophile,[104] and while it is energetically favourable to generate charge on nitrogen, as in (A), charge on a carbon atom bearing fluorine, as in (B), is unfavourable due to repulsion by electron pairs on fluorine.



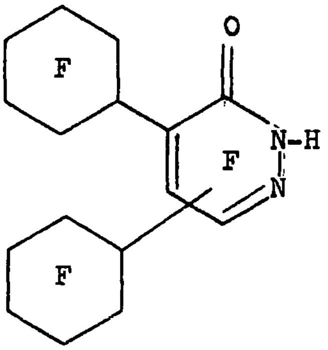
(A)



(B)

The ^{19}F n.m.r. spectrum of (XXIX) showed that the cyclohexyl group was substituted at the 4-position giving the expected orientation of substitution.

The reaction of tetrafluoropyridazine with two molecular proportions of perfluorocyclohexene (I) gave, in addition to the monosubstituted pyridazine (XXIX) (45% yield), a high melting-point solid which was obtained by solvent extraction of the involatile products from an aqueous solution. Although no information on the composition of this solid could be obtained from chromatography, it was obvious from mass spectrometry that it contained products corresponding to the hydrolysis of the substituted pyridazine. Recrystallisation of the crude solid from hot benzene afforded a small quantity of a yellow crystalline solid which was shown to correspond to the dicyclohexyl-substituted pyridazone (XXX) below,

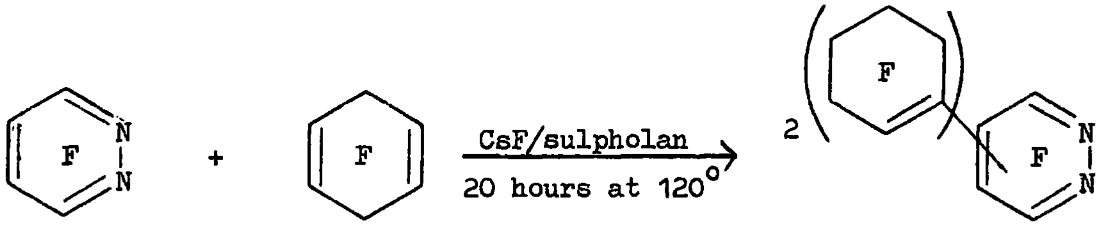


(XXX)

by elemental analysis and i.r. and mass spectrometry. Absorptions due to the $>$C=O and $>$N-H were present in the i.r. spectrum of (XXX), but the small amount of product prevented the confirmation of the structure by n.m.r. spectroscopy.

Hence, although optimum conditions were found for the preparation of perfluoro-(4-cyclohexylpyridazine) (XXIX) in relatively high yield, the isolation of higher substituted products was made more difficult by the hydrolysis of these products during solvent extraction from aqueous solution. Further work is required on the reaction between tetrafluoropyridazine and perfluorocyclohexene, but the isolation of the pyridazone (XXX) does indicate that the preparation of more highly substituted pyridazines may be possible. The main problem would appear to be the extraction of these products from the reaction mixture and not the relative reactivity of the olefin.

Preliminary reactions were also carried out using perfluorocyclohexa-1,4-diene (IV) and perfluorocyclobutene (III) in fluoride ion-initiated reactions with tetrafluoropyridazine. When tetrafluoropyridazine was heated with two molecular proportions of perfluorocyclohexa-1,4-diene (IV) in the presence of caesium fluoride and sulpholan in a stainless-steel tube, the only product obtained was isolated in small amount by solvent extraction from an aqueous solution of the reaction mixture. The solid product was purified by recrystallisation from ether/petroleum ether and shown to correspond to the dicyclohexenylpyridazine (XXXIV) by elemental analysis and mass spectrometry.



(IV) (XXXIV)

The possible structure of the product (XXXIV) is discussed in Chapter 10.

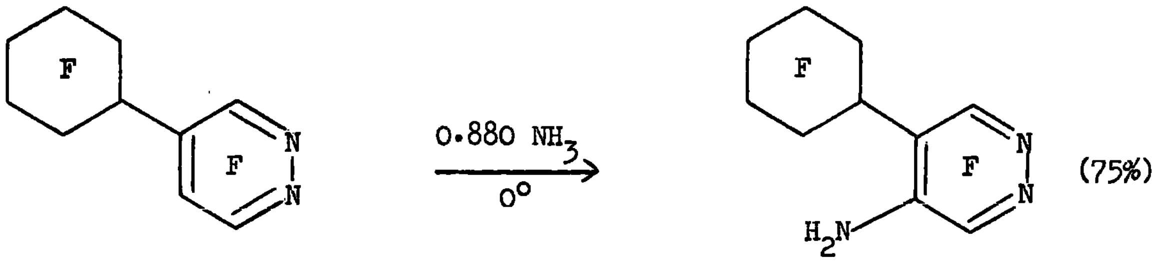
The fluoride ion-initiated reaction of tetrafluoropyridazine and perfluorocyclobutene (III) was unsuccessful when carried out in a sealed tube. Two reactions were carried out at ca. 120-130° using an excess of perfluorocyclobutene, one in a stainless-steel tube and the other in a nickel tube, but in each case the only major products were unchanged tetrafluoropyridazine and perfluorocyclobutene trimer (X). Future reactions involving tetrafluoropyridazine and perfluorocyclobutene would be best carried out at atmospheric pressure in which the substrate is stirred with caesium fluoride and sulpholan in an atmosphere of perfluorocyclobutene.

5.2 Reactions of Perfluoro-(4-cyclohexylpyridazine)

Perfluoro-(4-cyclohexylpyridazine) (XXIX) was the only compound isolated in reasonable yield from the preliminary fluoride ion-initiated reactions of tetrafluoropyridazine and perfluorocycloalkenes. It was found to be a fairly stable, colourless, viscous liquid, and several reactions were carried out with this compound, the most interesting of these being photolysis and pyrolysis.

5.2.1 Nucleophilic substitution with ammonia

Perfluoro-(4-cyclohexylpyridazine) (XXIX) was found to be very reactive towards aqueous ammonia, and 4-perfluorocyclohexyl-5-amino-3,6-difluoropyridazine (XXXI) was obtained in fairly high yield by addition of (XXIX) to aqueous ammonia at 0°.

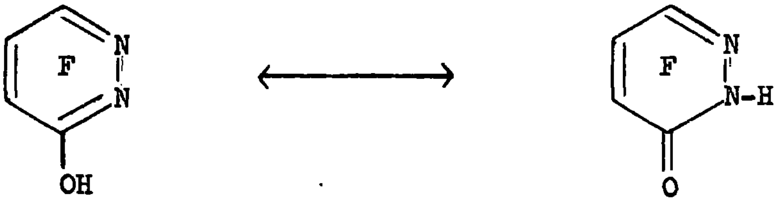


(XXIX) (XXXI)

The orientation of substitution of the amino group in (XXXI) was determined from ^{19}F n.m.r. data (see Chapter 10), and the normal mode of substitution was followed, the 4- and 5-positions of tetrafluoropyridazine having been shown to be the most reactive to nucleophilic attack by several nucleophiles.[109] Thus the presence of the perfluorocyclohexyl group did not have any unusual directive effect and the amino group was substituted for the remaining fluorine atom para to a nitrogen atom.

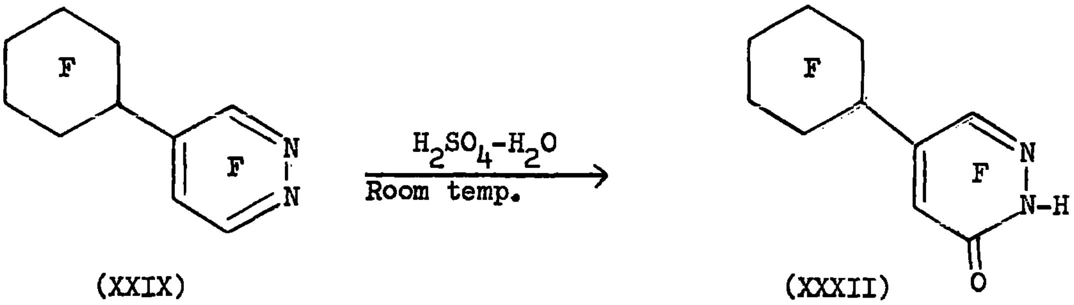
5.2.2 Reaction with sulphuric acid

Under strongly acidic conditions, nucleophilic attack on tetrafluoropyridazine by water leads to substitution of the fluorine atoms at C-3 and C-6[128] in preference to those at C-4 and C-5 which were previously shown to be more reactive towards nucleophilic reagents under basic conditions.[109] Also, the hydroxylation product of tetrafluoropyridazine has been shown to exist as the pyridazinone tautomer, rather than the hydroxypyridazine, the principal evidence for this being the presence of an N-H stretching band and



a carbonyl band in the i.r. spectrum.

When water was added slowly to perfluoro-(4-cyclohexylpyridazine) (XXIX) in concentrated sulphuric acid, 3,5-difluoro-4-perfluorocyclohexyl-1H-pyridazin-6-one (XXXII) was obtained in quantitative yield.

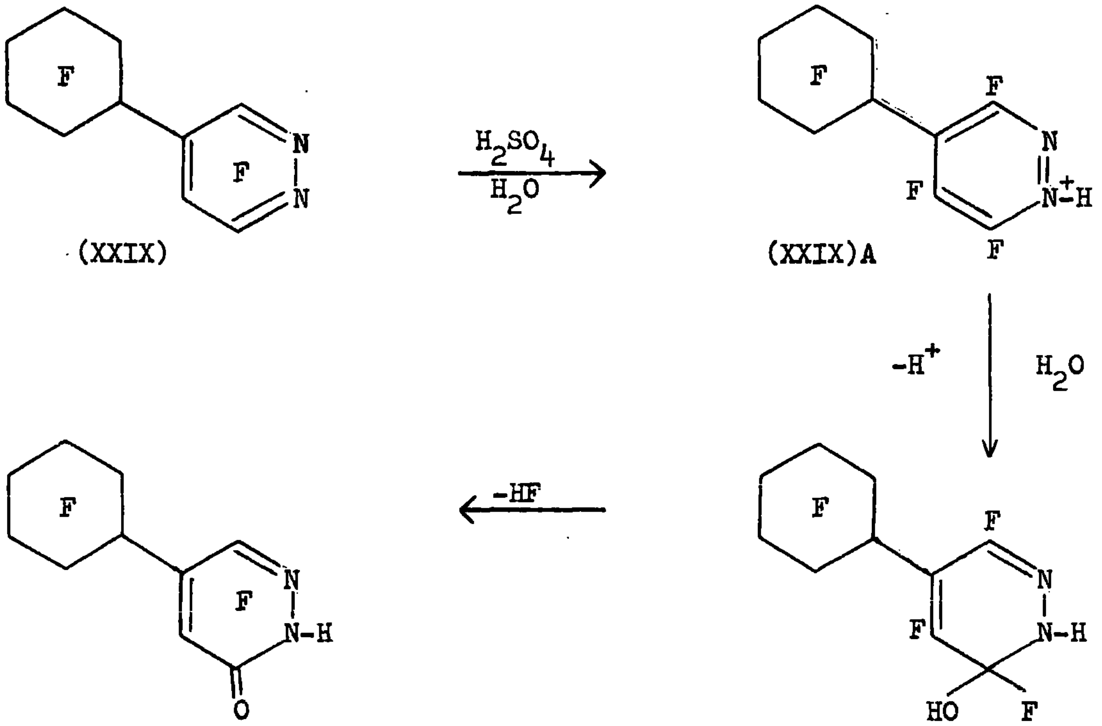


(XXIX) (XXXII)

The existence of (XXXII) as the pyridazinone tautomer was shown by the presence of N-H and carbonyl bands in the i.r. spectrum, and the structure of (XXXII) was confirmed by n.m.r. spectroscopy. The same pyridazone was also produced, autocatalytically, when perfluoro-(4-cyclohexylpyridazine) (XXIX) was exposed to atmospheric moisture.

Acid catalysis in nucleophilic attack on nitrogen heterocyclic compounds, which has been shown[129] to proceed by attack on the protonated cations, is well known, but is less expected in the very weakly basic perfluoro-series. However, substitution of heptafluoroquinoline[130] by adding nucleophilic reagents to its solution in concentrated sulphuric acid has been reported.

More recently, acid-catalysed nucleophilic substitution reactions have become a feature of polyfluorinated heterocyclic compounds, particularly with tetrafluoropyridazine and its derivatives,[128] and it has been suggested that these reactions involve nucleophilic attack on protonated polyfluoropyridazinium cations.[128] Thus the pyridazone (XXXII) may possibly be formed via the following mechanism,



(XXIX)

(XXIX)A

(XXXII)

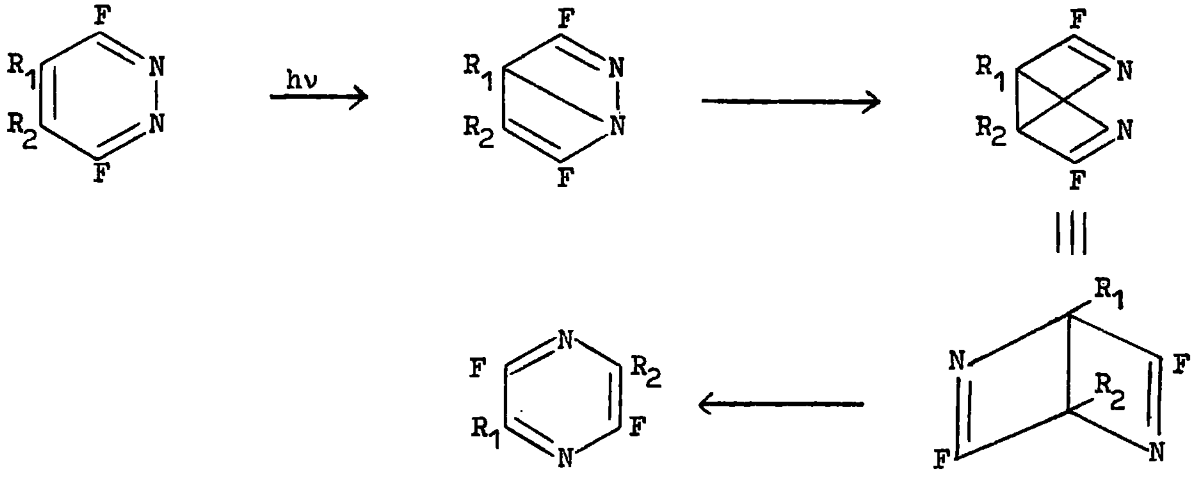
since it was suggested, from the result of acid hydrolysis of tetrafluoropyridazine, that both conjugation and electron-density effects could combine to lower the activation energy of the reaction path through the intermediate (XXIX)A, resulting in the observed attack at the position adjacent to the positively charged nitrogen atom.

Although nucleophilic substitution of tetrafluoropyridazine and its derivatives under basic conditions is complementary to that in acidic media, the observed difference in the orientation of substitution is not fully understood.

5.2.3 Photolysis of perfluoro-(4-cyclohexylpyridazine)

When perfluoro-(4-cyclohexylpyridazine) (XXIX) was irradiated with an unfiltered medium-pressure mercury lamp for ca. 6 days, perfluoro-(6-cyclohexylpyrazine) (XXXV) was obtained as the only product in 70% yield. No unchanged pyridazine (XXIX) was recovered and none of the corresponding pyrimidine derivative was detected in the photolysis product.

The photochemically-induced isomerisation of tetrafluoropyridazine to tetrafluoropyrazine has been described,[131] and a diazaprismane[132] intermediate was suggested in order to account for the 1,3-shift in the relative positions of the nitrogen atoms. However, it has recently been shown that[133] the photolysis of perfluoro-(4,5-bisisopropylpyridazine) yields, in addition to perfluoro-(2,5-bisisopropylpyrazine), a para-bonded valence isomer, and also that the pyrazine and the valence isomers cannot be obtained from the corresponding diazaprismane without prior rearrangement. The isolation of this intermediate confirms a mechanism, shown below, which was put forward to explain a range of rearrangement reactions of polyfluoropyridazine derivatives.[134]



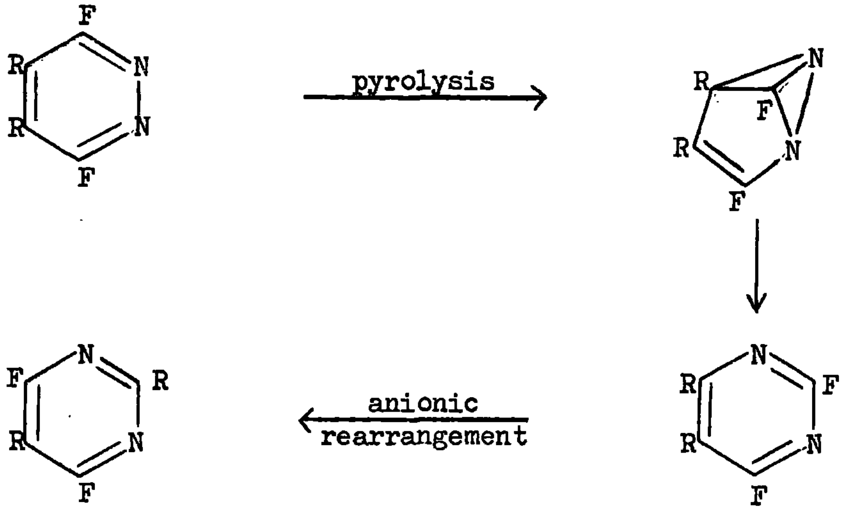
$[R_1 = R_2 = -CF(CF_3)_2]$

Although the isomerisation of perfluoro-(4-cyclohexylpyridazine) (XXIX) to perfluoro-(6-cyclohexylpyrazine) (XXXV) (where R_1 = F and R_2 = perfluoro-cyclohexyl-) may occur via the above mechanism, the presence of only one cyclohexyl substituent does not allow confirmation of this mechanism for the conversion of (XXXIX) to (XXXV). Since no pyrimidine could be detected in the photolysis product, however, it is unlikely that the corresponding diazabenzvalene is involved in the photochemical reaction.

The photochemical isomerisation of perfluoro-(4-cyclohexylpyridazine) (XXXIX) to the corresponding monosubstituted pyrazine derivative (XXXV) is interesting since the only previously reported photochemical isomerisation of a perfluoropyridazine system occurred with the bisheptafluoroisopropyl derivative.[131]

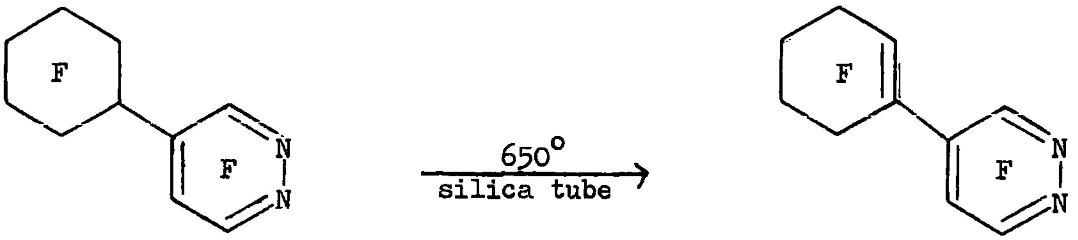
5.2.4 Attempted pyrolysis of perfluoro-(4-cyclohexylpyridazine)

In contrast to the isomerisation of tetrafluoropyridazine and its perfluoroalkyl derivatives to the corresponding pyrazine derivatives by u.v. irradiation, tetrafluoropyrimidine and its derivatives are obtained on pyrolysis.[131] It was suggested that this thermal isomerisation proceeds through a diazabenzvalene intermediate by fission of the N-N bond and re-aromatisation to the corresponding pyrimidine.



(R = F or iso-C_3F_7)

When perfluoro-(4-cyclohexylpyridazine) (XXIX) was passed over silica wool at 650°, this temperature being chosen as optimum after a series of small-scale preliminary reactions, a brown liquid was recovered and shown to consist of two components. Separation of the mixture afforded unchanged perfluoro-(4-cyclohexylpyridazine) and a white crystalline solid of which i.r. and ^{19}F n.m.r. data only were obtained before decomposition occurred. An attempt to recover any pure product, after decomposition, by vacuum distillation resulted in recovery of a small quantity of a colourless liquid which exhibited a strong molecular ion peak at $^{M}/e$ = 376 in the mass spectrum. This corresponds to perfluoro-(cyclohexenylpyridazine), and the previously obtained i.r. and ^{19}F n.m.r. data support this.



(XXIX) (XXXIII)

The structure given above for (XXXIII) is in accord with the n.m.r. spectrum. Thus the pyrolysis of perfluoro-(4-cyclohexylpyridazine) (XXIX) at 650° did not produce the corresponding pyrimidine derivative as expected, but instead the pyridazine ring remained intact, the cyclohexyl ring being partially defluorinated.

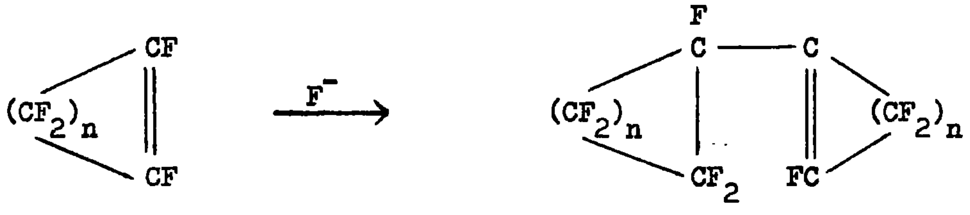
CHAPTER 6

REACTIONS OF THE OLIGOMERS OF PERFLUOROCYCLOALKENES

Introduction

In fluoride ion-initiated reactions involving polyfluoro-olefins with aromatic substrates, self-condensation of the olefin is often a major side-reaction. In fact, the readiness with which hexafluoropropene forms dimers and trimers in the presence of fluoride ion has enforced changes in technique in polyfluoroalkylation reactions in order to suppress the tendency for oligomerisation.

Self-condensation of perfluorocycloalkenes by fluoride ion occurred readily with perfluorocyclopentene and perfluorocyclobutene whereas perfluorocyclohexene required vigorous conditions, and the resulting products were of more interest than the oligomers of acyclic fluoro-olefins.

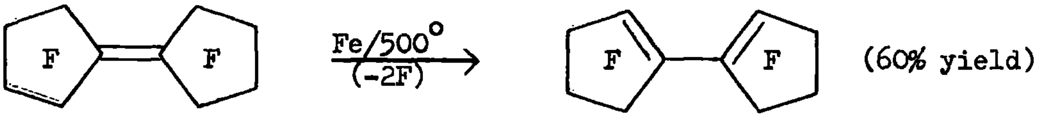


(dimer)

The dimer of perfluorocyclopentene was particularly interesting because of its novel structure, and the reactions of this and other oligomers are discussed. These include defluorination, oxidation, and nucleophilic substitution.

6.1 Defluorination

When perfluorocyclopentene dimer (VIII) was passed over iron at 350° a product other than unchanged starting material was shown to be present by chromatography. An increase in the proportion of this product was obtained by increasing the reaction temperature, and at 500°, a 100% conversion of (VIII) to perfluorobicyclopentenyl (IX) was realised.

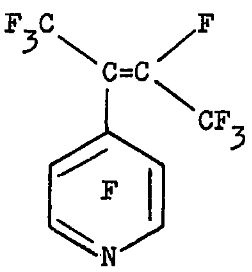


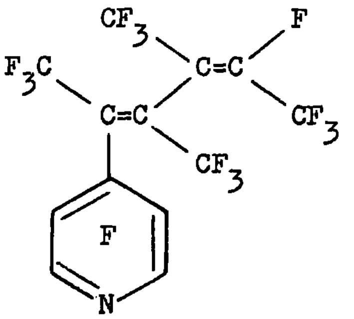
(VIII) (IX)

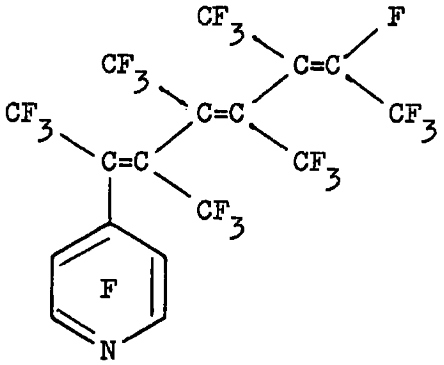
The ^{19}F n.m.r. spectrum of (IX) consisted of four absorptions with the following chemical shifts and integrated ratio:

109•9		113•2		122•1		132•8	p.p.m. (Ref. $CFCl_3$)
4	:	2	:	4	:	4	integration

and the structure given above for (IX) is in accord with the integrated n.m.r. spectrum. The u.v. spectrum contained an absorption with λ_{max} = 222mμ (close to the cut-out region of the solvent) and an extinction coefficient of 13,200. The expected value of the extinction coefficient for a conjugated olefinic system is appreciably higher than this, and it thus appears that perfluorobicyclopentenyl (IX) does not possess a conjugated system, the two cyclopentenyl rings being non-coplanar. Extinction coefficients of this order ($\approx$ 10,000) have also been obtained for systems in which a side-chain derived from hexafluorobut-2-yne is attached to a perfluorinated heterocycle, as in the compounds shown below.[83]

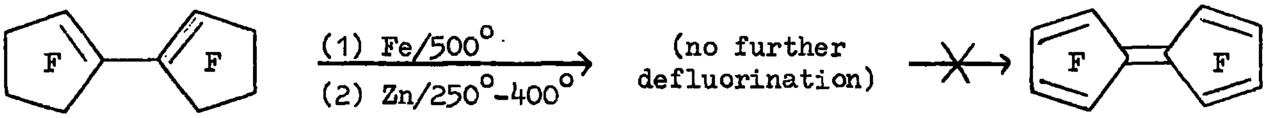






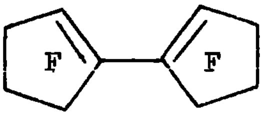
It was concluded that conjugation in these compounds is severely restricted since there is little variation in the u.v. spectra of the three products above and also in the corresponding derivatives of tetrafluoropyridazine. This also accounted for the highly unsaturated polymer $F\text{-}[C(CF_3)=C(CF_3)]_n$ being a greyish solid.

Perfluorobicyclopentenyl (IX) was found to be quite stable since attempts to remove fluorine to give a 'fulvalene-system' were unsuccessful. Reactions were carried out over iron at 500° and zinc[79] at 250°-400°, but in each case, (IX) was recovered unchanged.

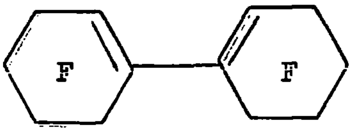


(IX)

Compound (IX) is comparable with the product (VII), a derivative of perfluorocyclohexene (I) (see section 4.1).

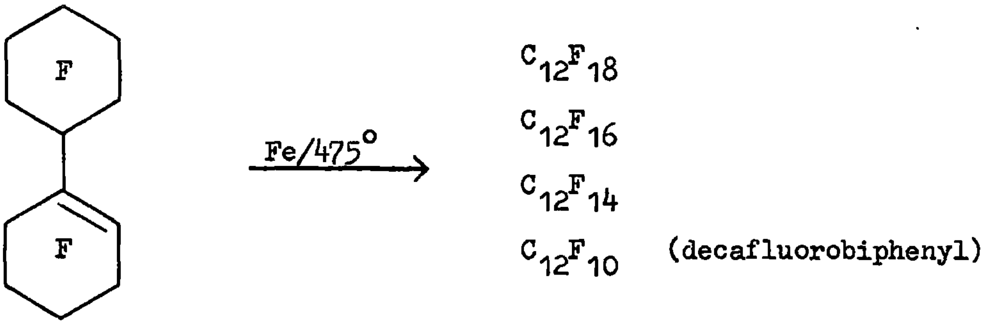


(IX)



(VII)

However, defluorination of perfluorocyclopentene dimer (VIII) gave (IX) and no other defluorinated derivatives, whereas a mixture of products corresponding to successive defluorination was obtained in small quantity from a preliminary reaction in which perfluoro-(1-cyclohexylcyclohexene) (VI) was passed over iron at 475°.

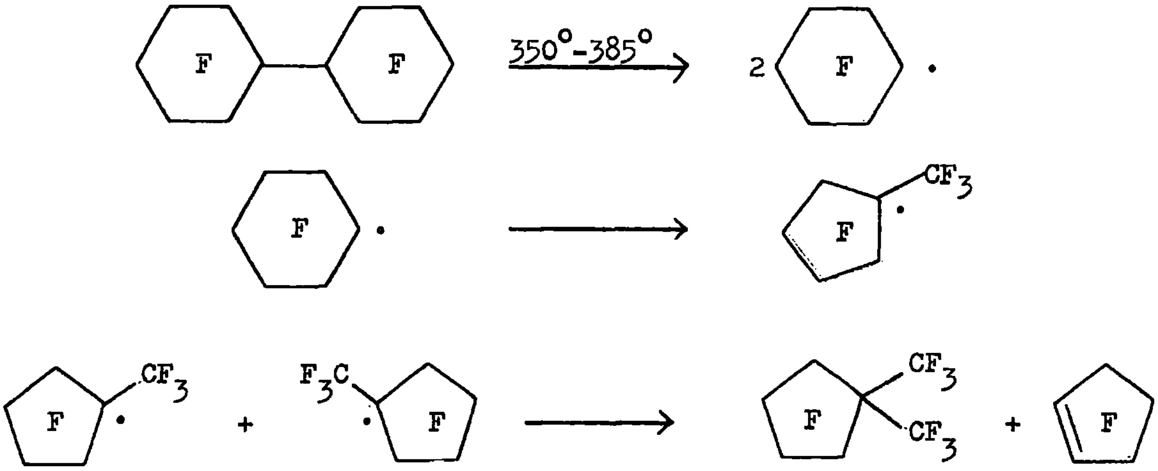


(VI)

The products in the mixture were identified by accurate mass spectral data. Decafluorobiphenyl was obtained alone in 45% yield when this reaction was repeated at a later date by passing (VI) over iron at 500°.

It can thus be seen that the removal of two fluorine atoms from perfluorocyclopentene dimer (VIII) gives a product which is stable to further defluorination, but fluorine can be removed more readily from perfluoro-(1-cyclohexylcyclohexene) (VI) to the extent that decafluorobiphenyl can be obtained as the only reaction product. Perfluorocyclobutene trimer (X) was not defluorinated to any siginificant extent by passage over iron at 475°.

Since (VI) can be considered as perfluorocyclohexenylcyclohexane it is feasible to contrast the aromatisation of (VI) with the attempted pyrolyses of similar compounds, i.e. perfluoroisopropylcyclohexane and perfluorobicyclohexyl. Tatlow and co-workers[135] found that the major products obtained from the pyrolysis of perfluoroisopropylcyclohexane over nickel at 600° were fluorinated cyclopentenes, and aromatisation to the corresponding perfluoro-αmethylstyrene occurred only to a small extent. They suggested that the failure of the attempted defluorination reaction was due to the intervention of a competing thermal reaction in the pyrolysis tube, producing undecafluorocyclohexyl radicals which can lose fluorine or isomerise to methylcyclopentyl radicals. Other workers[136] isolated perfluoro-1,1-dimethylcyclopentane from the pyrolysis of perfluorobicyclohexyl and suggested the following mechanism:



The formation of radicals by cleavage of the bond joining the two fragments in perfluoroisopropylcyclohexane and perfluorobicyclohexyl is due to the fact that the C-C bond joining two tertiary carbon atoms, as in these two compounds, is particularly weak.[137]

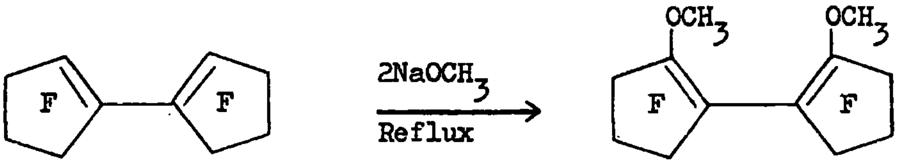
The presence of a cyclohexenyl group in perfluoro-(1-cyclohexylcyclohexene) (VI) prevents the linkage of two tertiary carbon atoms, and aromatisation to decafluorobiphenyl was the only process observed at 500°.

6.2 Nucleophilic Substitution

Investigations into the nucleophilic attack of perfluorobicyclopentenyl (IX) were carried out initially using methoxide ion as the nucleophile, but the perfluoroisopropyl anion was also used as the nucleophile since any products resulting from the 'polyfluoroalkylation' of perfluorobicyclopentenyl would be interesting.

6.2.1 Reaction of perfluorobicyclopentenyl with methoxide ion

Perfluorobicyclopentenyl (IX) was found to be very reactive towards nucleophilic attack by methoxide ion and, when (IX) was stirred with an equimolecular proportion of sodium methoxide in methanol, a mixture of the mono- and di-methoxy derivatives was obtained. The dimethoxy derivative was isolated in 95% yield when (IX) was refluxed with two molecular proportions of sodium methoxide in methanol.



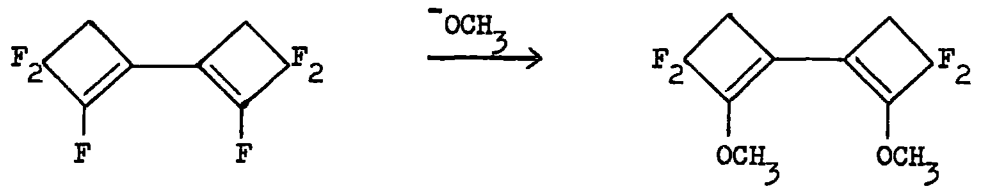
(IX) (XXXVI) (95%)

The structure given for (XXXVI) is in accord with the ^{19}F n.m.r. spectrum which contained three broad singlets of equal intensity and with the following chemical shifts:

107·2 116·3 131·9 p.p.m. (Ref. $CFCl_3$)

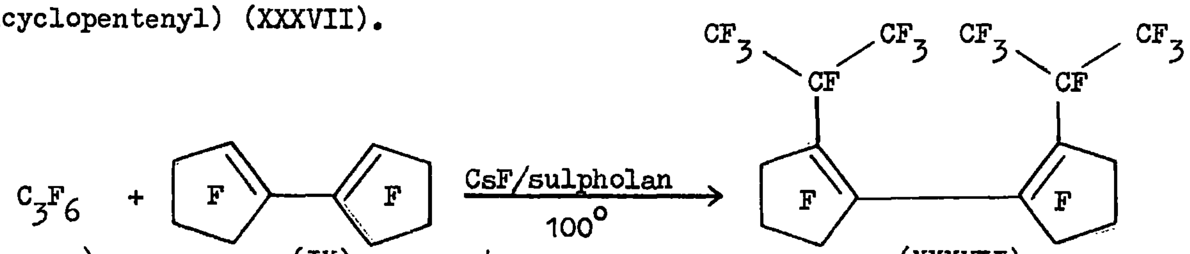
The non-planarity of (XXXVI) was indicated by the absence of any absorption in the u.v. spectrum of this compound.

The formation of a dimethoxy derivative of perfluorobicyclopentenyl (IX) under relatively mild conditions is indicative of the vinylic fluorine atoms being very reactive to nucleophilic attack. Park and co-workers[138] obtained similar results with hexafluorobicyclobutenyl and found that, as with perfluorocyclobutene, attack by alkoxide tends to give a diether at room temperature.



6.2.2 Fluoride ion-initiated reaction of perfluorobicyclopentenyl with hexafluoropropene

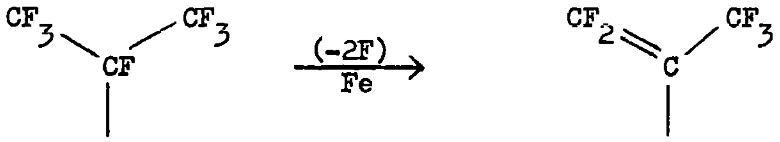
When perfluorobicyclopentenyl (IX) was stirred in the presence of caesium fluoride and sulpholan under an atmosphere of hexafluoropropene for 4-5 hours at 100°, a white crystalline solid was isolated from the reaction mixture by solvent extraction and shown to be perfluoro-(2,2'-di-isopropylbicyclopentenyl) (XXXVII).



(excess) (IX) atmos. pressure (XXXVII)

(35% yield)

The di-isopropyl compound (XXXVII) is interesting since the removal of fluorine from the side-chain could lead to a vinyl derivative or even cyclisation. The following conversion was effected when the side-chain was attached to a heterocyclic substrate,[124]

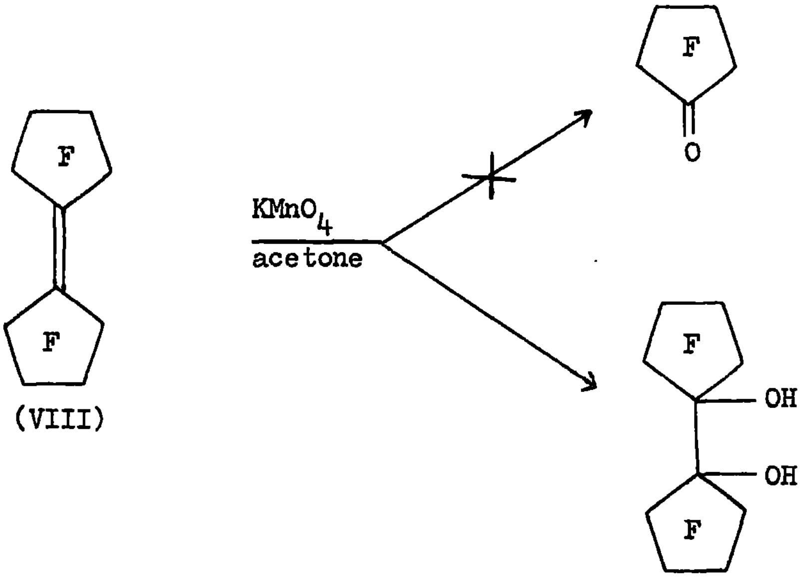


by passage over heated iron. When (XXXVII) was passed over iron at 480°, however, a 25% recovery of the starting material was obtained with no other products.

6.3 Oxidation of Perfluorocyclopentene Derivatives

6.3.1 Reaction of perfluorocyclopentene dimer with potassium permanganate

As further confirmation for the presence of an exocyclic double bond in perfluorocyclopentene dimer (VIII) an oxidation reaction was carried out using potassium permanganate/acetone in an unsuccessful attempt to produce perfluorocyclopentanone. The dimer (VIII) was stirred vigorously with a small excess of $KMnO_4$ in a large volume of acetone at room temperature. The only product isolated from this reaction was a white crystalline solid (N.B. perfluorocyclopentanone is a colourless liquid, b.pt. 24°[139]) which was shown to correspond to 1,1'-dihydroxyhexadecafluorobicyclopentyl (XXXVIII) by elemental analysis and i.r. spectroscopy.

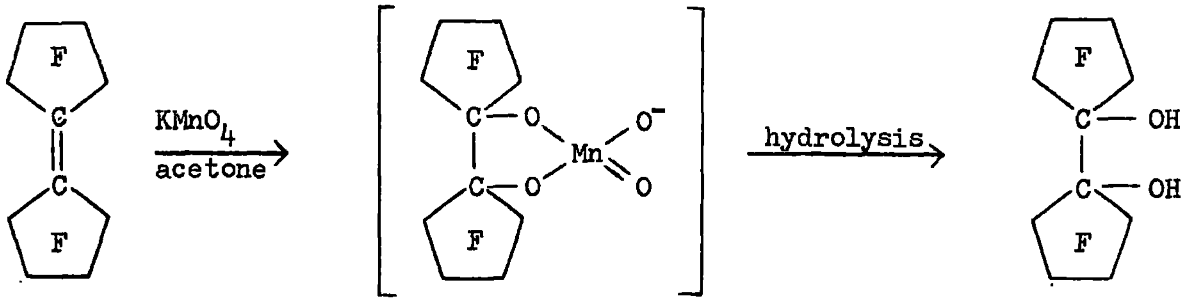


(VIII)

(XXXVIII)

(67%)

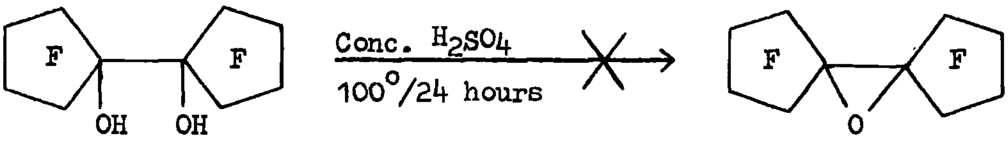
The probable mechanism for the hydroxylation of perfluorocyclopentene dimer (VIII) is as follows, proceeding via a cyclic intermediate.



(VIII) (XXXVIII)

This mechanism would account for cis hydroxylation in which both of the oxygen atoms come from the oxidising agent, and is well established for analogous hydrocarbon olefins.

In an attempt to dehydrate the dihydroxy compound (XXXVIII) to give the corresponding perfluoro-epoxide, it was heated with concentrated sulphuric acid in a sealed tube at 100° for 24 hours, but the resulting solid was shown by i.r. spectroscopy to be unchanged starting material.

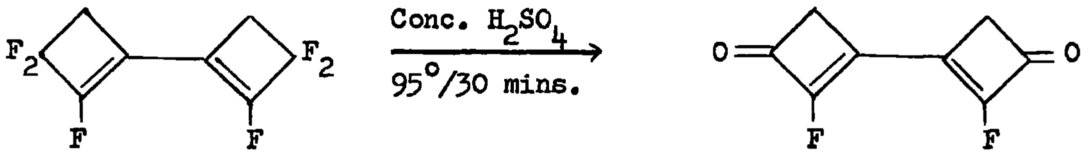


(XXXVIII)

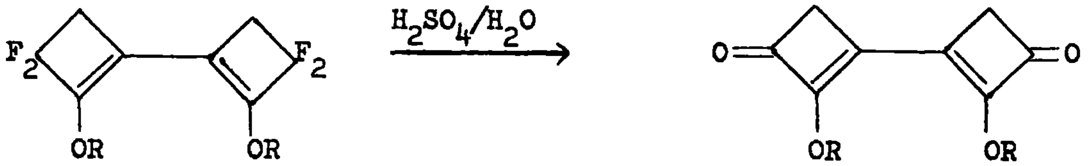
Further attempts to produce the epoxide would be best carried out using phosphorus pentoxide as the dehydrating agent.

6.4 Hydrolysis of Perfluorobicyclopentenyl Derivatives

Park and Frank[140,141] found that hexafluorobicyclobutenyl and its alkoxy derivatives were readily hydrolysed by concentrated sulphuric acid to the corresponding diketone derivatives by displacement of the allylic fluorine atoms,



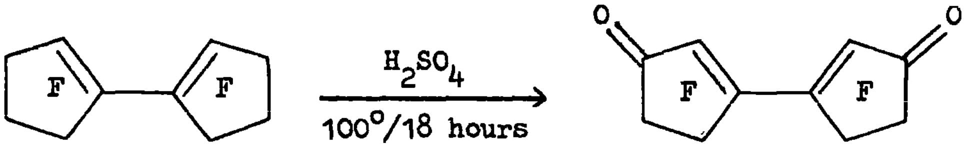
140



141

(R = CH_3, C_2H_5)

It was also shown earlier (section 6.2) that hexafluorobicyclobutenyl and perfluorobicyclopentenyl (IX) were similar in their reactivity towards nucleophilic attack by alkoxide ion. These observations led to an investigation into the reaction of perfluorobicyclopentenyl (IX) and its dimethoxy-derivative (XXXVI) with concentrated sulphuric acid. In each case, the reactant was heated with sulphuric acid in a sealed tube for 18 hours at 100°. After pouring into ice/water the products were isolated by solvent extraction with ether, and a white solid was obtained from both reactions. The product resulting from the hydrolysis of perfluorobicyclopentenyl (IX) was shown to correspond to the diketo-derivative (XXXIX) by elemental analysis and mass spectrometry.

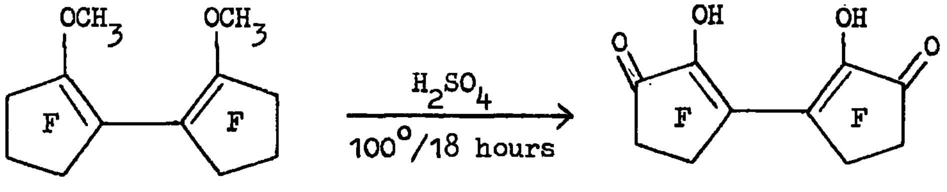


(IX) (XXXIX)

(35% yield)

The i.r. spectrum of (XXXIX) contained a strong absorption at 6·20μ due to the carbonyl groups and the u.v. spectrum consisted of a single absorption (broad) with $\lambda_{max.}$ = 263mμ (ϵ = 27,900).

Hydrolysis of 2,2'-dimethoxy-dodecafluorobicyclopentenyl (XXXVI), however, under identical conditions, gave an impure product whose mass spectrum exhibited a strong molecular ion peak at $^{M}/e$ 338, and this corresponds to the diketo-dihydroxy derivative (XL).

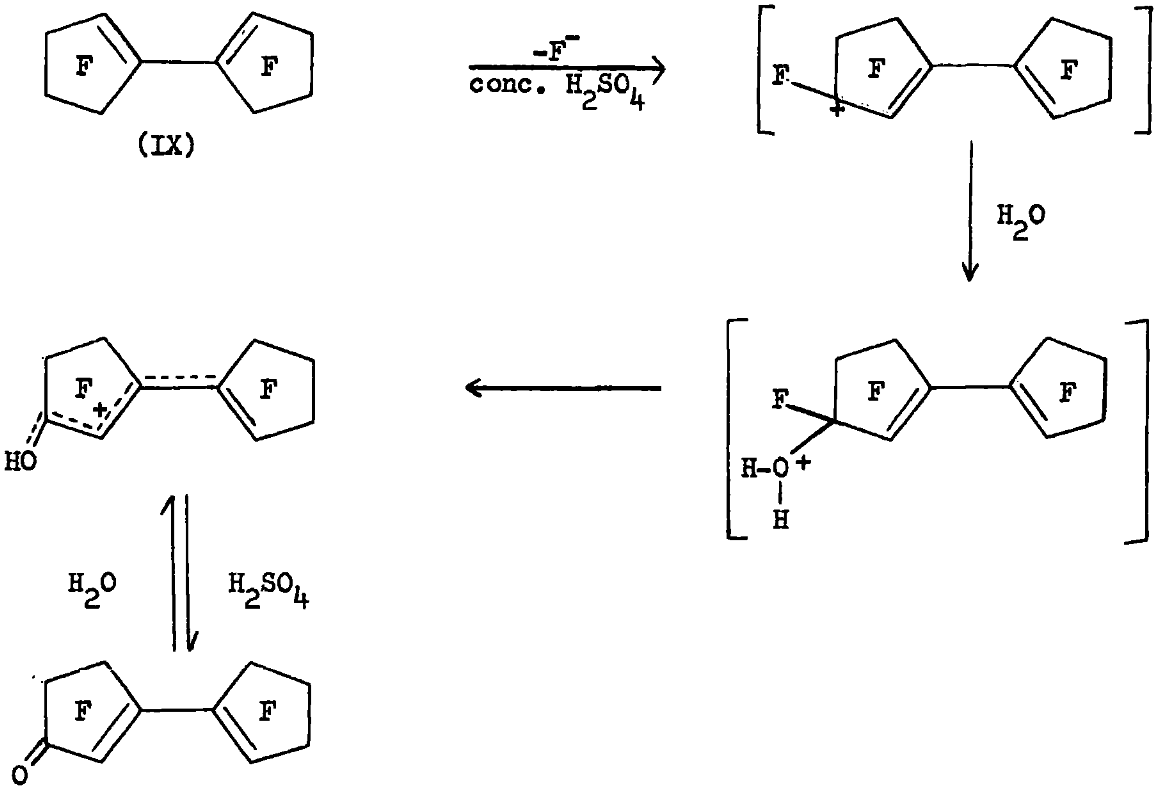


(XXXVI) (XL)

A strong peak at 6·33μ, due to the carbonyl groups was present in the i.r. spectrum of the product from this reaction, and the u.v. spectrum consisted of a single absorption (broad) with λ_{max} = 272mμ (ε = 27,600). The displacement of the methoxy groups at the vinyl positions by hydroxyl groups may be due to the relatively vigorous conditions of the reaction.

It must be noted that, although the products obtained from the hydrolysis of perfluorobicyclopentenyl and its dimethoxy derivative were not completely characterised, the data obtained on these compounds suggest the displacement of allylic fluorine atoms by a keto-group.

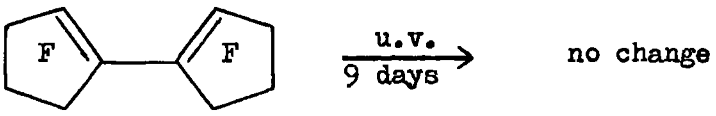
Park and Frank[140] proposed a mechanism for the sulphuric acid hydrolysis of the analogous cyclobutenes, and this involved the loss of fluoride ion at the allyl position giving a carbonium ion. In concentrated sulphuric acid this ion would be expected to be unstable and react with traces of water to give a hydrated carbonium ion, which can then lose hydrogen fluoride to give the stable protonated ketone. Application of this mechanism to the cyclopentene system would give the following stages.



6.5 Other Reactions of the Oligomers of Perfluorocycloalkenes

6.5.1 Irradiation with u.v. light

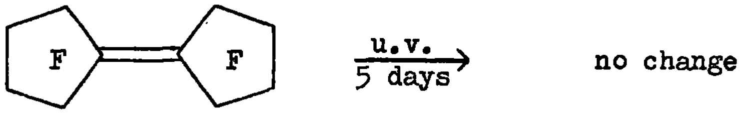
In order to establish whether perfluorobicyclopentenyl (IX) would rearrange on photolysis, a sample of (IX) was irradiated in a silica tube from a medium pressure u.v. lamp for 18 hours. No change occurred and the starting material was recovered. When this was repeated using a little benzophenone as photosensitizer and irradiating the compound for a much longer time (9 days), (IX) was recovered unchanged.



(IX)

This further substantiates the stability of the diene (IX), which was shown earlier (section 6.1) to be stable to defluorination.

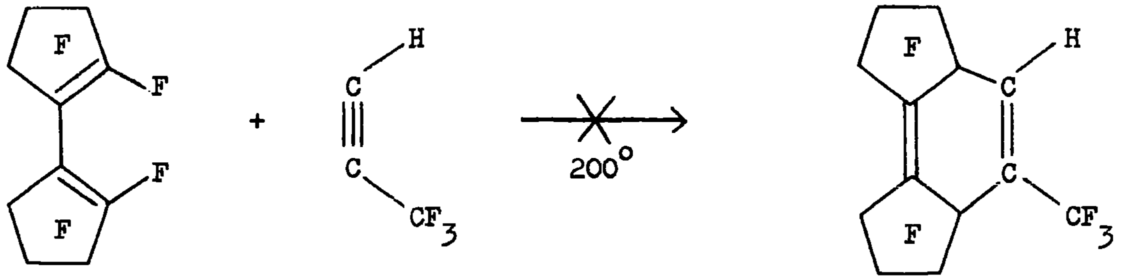
No change was observed when perfluorocyclopentene dimer (VIII) was irradiated with u.v. light under similar conditions.



It was also shown that perfluoro-(1-cyclohexylcyclohexene) (VI) and perfluorocyclobutene trimer (X) were stable to irradiation with u.v. light for 100 hours, and the recovered starting materials were confirmed by i.r. spectroscopy.

6.5.2 Attempted Diels-Alder reactions with perfluorobicyclopentenyl

Following the conclusions reached for the structure of perfluorobicyclopentenyl (IX), two reactions were carried out in which (IX) was used as a conjugated diene in a Diels-Alder reaction using (a) trifluoromethylacetylene and (b) ethylene[142] as the dienophile. In each case the reactants were heated together at 200°, but only starting material was recovered with no formation of a Diels-Alder adduct by the following possible route.



(IX)

This could be due to the difficulty with which (IX) adopts a cisoid conformation. Although these reactions were unsuccessful it must be remembered that only two compounds were employed as possible dienophiles and used under the same reaction conditions. This is by no means exhaustive, and further attempts to form Diels-Alder adducts are necessary.

EXPERIMENTAL

Reagents

The perfluoroheterocyclic compounds, pentafluoropyridine and tetrafluoropyridazine were prepared as described in the literature.[109,143]

Perfluorocyclobutene was obtained commercially from Peninsular Chem. Research Inc. Perfluorocyclohexa-1,4-diene was supplied by Imperial Smelting Corporation Ltd., and further quantities of this and the perfluorocyclohexa-1,3-diene were kindly donated by Dr. W.J. Feast. Perfluorocyclohexene was prepared by the dehydrofluorination of undecafluorocyclohexane,[144] the latter reagent being supplied by Imperial Smelting Corporation Ltd. The perfluorocyclohexene was stored over phosphorus pentoxide. Perfluorocyclopentene was prepared by the complete fluorination of perchlorocyclopentene,[51] the chloro-derivatives being synthesised according to the method of McBee.[145] The perfluorocyclopentene was purified by fractionation and stored in a sealed glass tube.

The caesium fluoride was reagent grade, dried by heating under high vacuum for 2-3 days, and stored in an oven at 150° until required. Any contaminated caesium fluoride was dissolved in water, neutralised (to remove any HF), and re-dried. Potassium fluoride (used mainly in the preparation of perfluorocyclopentene) 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 distillation, only the middle fractions, which were solid at room temperature, were retained and dried further by storage over molecular sieves (type IVA) at 40°.

Instrumentation

Infra-red spectra were recorded using Grubb-Parsons, type G.S.2A or 'Spectromaster' spectrometers, and a Perkin-Elmer 'Infracord' 137E spectrophotometer. 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 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, and certain solids were made into mulls with Nujol.

Ultra-violet spectra were recorded using a Unicam S.P.800 Spectrophotometer, and all values of $\lambda_{max.}$ are quoted in mμ. Solvents used were cyclohexane and ethanol (Spectrosol grade).

Proton (^{1}H) and fluorine (^{19}F) nuclear magnetic resonance spectra were recorded on a Perkin-Elmer R10 spectrometer and a Varian A56/60D spectrometer, both operating at 60 Mc/s and 56·4 Mc/s respectively. A variable temperature probe enabled spectra to be recorded at sample temperatures other than the standard temperature of the probe.

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

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 Varian 'Aerograph' instrument fitted with column 'A' or column 'O'.

CHAPTER 7

EXPERIMENTAL FOR CHAPTER 4

7.1 Reactions of Perfluorocycloalkenes with Fluoride Ion

7.1.1 Perfluorocyclohexene, C_6F_{10}

Three reactions were carried out using different reaction conditions.

(a) Perfluorocyclohexene (10g., 38·2 m.moles), caesium fluoride (5g., 32·8 m.moles), and sulpholan (30 mls.) were introduced into a nickel tube which was then sealed and rotated in an oil bath at 175°C for 40 hours. The tube was cooled, opened, and the volatile materials transferred under vacuum to a cold trap. The products (7·7g.) were distilled, and fractions collected up to 100° were shown by v.p.c. (column 'O' at 150°) to consist of unchanged perfluorocyclohexene with trace amounts of two components with longer retention times. Another fraction, collected up to 160°, consisted mainly of the two components with longer retention times and a small amount of unchanged starting material. The latter fraction was separated by prep. scale v.p.c. (Aerograph: column 'A' at 60°) to give only one of the unknown components in an amount sufficient for identification. This was shown to be the dimer of perfluorocyclohexene, $C_{12}F_{20}$, by comparison of the i.r. spectrum with that of an authentic sample isolated in reaction (b), and by mass spectrometry (M, 524).

(b) Reaction (a) was repeated using a longer reaction time. Perfluorocyclohexene (8g., 30·5 m.moles), caesium fluoride (3g., 19·7 m.moles), and sulpholan (40 mls.) were introduced into a nickel tube which was then sealed and rotated in an oil bath at 170° for 65 hours. The tube was colled, opened, and the volatile products transferred under vacuum to a cold trap. Analytical v.p.c. (G.D.B. - column 'A' at 50°) showed the mixture (6·5g.) to consist of three components, which were then separated by prep. scale v.p.c. (Aerograph:

column 'A' at 50°) and shown, in order of increasing retention time, to be:-

(i) unchanged perfluorocyclohexene (identified by i.r. spectroscopy);

(ii) perfluorobicyclohexenyl, $C_{12}F_{18}$, (Found: C, 29•3; F, 71•0%; M, 486. $C_{12}F_{18}$ requires C, 29•6; F, 70•4%; M, 486). $\lambda_{max.}$ (cyclohexane) = 276, (u.v. spectroscopy). (I.R. Spectrum No.2);

(iii) perfluoro-(1-cyclohexylcyclohexene), $C_{12}F_{20}$, b.pt. 161-162°/760 mm. (Found: C, 27•8; F, 72•9%; M, 524. $C_{12}F_{20}$ requires C, 27•5; F, 72•5%; M, 524). I.r. spectra of $C_{12}F_{20}$ were recorded in the liquid phase (I.R. Spectrum No.1a) and in the gas phase (I.R. Spectrum No.1b).

The yields of $C_{12}F_{18}$ and $C_{12}F_{20}$ were 57% and 19% respectively (based on a 85% conversion of perfluorocyclohexene).

(c) Perfluorocyclohexene (6•0g., 22•9 m.moles), caesium fluoride (3g., 19•7 m.moles) and sulpholan (40 mls.) were heated in a rotating nickel tube for 70 hours at 150°. After cooling the tube, the volatile products (4•7g.) were obtained by vacuum transfer from the reaction mixture and examined by v.p.c. (column 'A' at 150°) which showed them to consist of perfluoro-(1-cyclohexylcyclohexene) (98%) with trace amounts (2%) of perfluorobicyclohexenyl. The major product (yield 78%) was identified by i.r. spectroscopy and the minor component from the chromatographic retention time.

7.1.2 Perfluorocyclopentene, C_5F_8

Caesium fluoride (5g., 32•8 m.moles) and sulpholan (20 mls.) were introduced into a nickel tube. Perfluorocyclopentene (8•5g., 40•0 m.moles) was then condensed into the tube under vacuum and the tube sealed and rotated in an oil bath at 125°C for 40 hours. The tube was then cooled, opened, and the volatile products transferred under vacuum to a cold trap by heating the reaction mixture to 85°C. The products (7·3g.) were distilled over the range 120–130°C, and examination of the distillate by v.p.c. (column 'A' at 100°) showed this to be a single compound which was identified as perfluorocyclopentene dimer, $C_{10}F_{16}$, b.pt. 127°/760 mm. (Found: C, 28·2; F, 72·1%; M, 424. $C_{10}F_{16}$ requires C, 28·3; F, 71·7%; M, 424). (I.R. Spectrum No.3). The absolute yield of dimer was 86%.

Subsequent preparation of perfluorocyclopentene dimer (for further work) was carried out using shorter reaction times (20–24 hours). This and the use of smaller quantities of caesium fluoride (3g.) were not detrimental to the yield of the dimer.

7.1.3 Perfluorocyclobutene, C_4F_6

A nickel tube containing caesium fluoride (5g., 32·8 m.moles), sulpholan (20 mls.), and perfluorocyclobutene (10g., 61·7 m.moles) was sealed and rotated in an oil bath at 125°C for 24 hours. The tube was then cooled, opened, and the volatile products transferred to a cold trap by heating the reaction mixture to 85°C under vacuum. The volatile products (6·7g.) were distilled over the range 140–150°C, and examination of the distillate by v.p.c. (column 'A' at 100°C) showed this to be a single compound. The product, a colourless liquid, was identified as perfluorocyclobutene trimer, $C_{12}F_{18}$, b.pt. 151°/760 mm. (Found: C, 29·6; F, 70·7%; M, 486. $C_{12}F_{18}$ requires C, 29·6; F, 70·4%; M, 486). (I.R. Spectrum No.5). The absolute yield of trimer was 67%.

7.1.4 Perfluorocyclohexa-1,4-diene

(a) Perfluorocyclohexa-1,4-diene (2·0g., 8·9 m.moles), caesium fluoride

(0•5g., 3•3 m.moles) and sulpholan (2 mls.) were introduced into a small bore Carius tube which was sealed while cooled in liquid air. On reaching room temperature the materials in the tube became yellow and then orange. After standing overnight the contents of the tube were deep red in colour. The tube was then shaken on a vibroshaker for 24 hours at room temperature and, after allowing the contents to settle, three distinct layers were apparent, sulpholan (deep red), 1,4-diene (pale yellow) and caesium fluoride. The volatile material (2•0g.) was transferred from the tube under vacuum and shown to be unchanged perfluorocyclohexa-1,4-diene (quantitative recovery) by i.r. spectroscopy.

(b) Perfluorocyclohexa-1,4-diene (2•0g., 8•9 m.moles), caesium fluoride (1g., 6•6 m.moles) and sulpholan (2 mls.) were introduced into a small bore Carius tube which was then rotated in an oil bath for 24 hours at 80°. The volatile products were transferred under vacuum from the tube to a cold trap giving a colourless liquid (0•2g.). The i.r. spectrum of the liquid was identical to that of an authentic sample of perfluorocyclohexa-1,4-diene. Recovery of unchanged diene, 10%.

(c) Three Carius tubes, containing the following reactants, were sealed and allowed to stand in a vertical position for 48 hours at room temperature:

tube (i) - perfluorocyclohexa-1,4-diene (2•0g., 8•9 m.moles)
+ caesium fluoride (1•0g., 6•6 m.moles)
+ sulpholan (2 mls.),

tube (ii) - perfluorocyclohexa-1,4-diene (2•0g., 8•9 m.moles)
+ sulpholan (2 mls.),

tube (iii) - perfluorocyclohexa-1,4-diene (2•0g., 8•9 m.moles)
+ caesium fluoride (1•0g., 6•6 m.moles).

After this time, no change in colour was observed in tubes (ii) and (iii), but in tube (i) the sulpholan and caesium fluoride layers were deep red in colour and the diene layer colourless. The three tubes were then allowed to stand in an oil bath at 80° for 30 hours, and there was no apparent change in the contents of tubes (ii) and (iii). In tube (i), however, the sulpholan and caesium fluoride layers were now very dark in colour and the diene layer was reduced to ca. two-thirds of its original volume.

(d) A Carius tube containing perfluorocyclohexa-1,4-diene (3·0g., 13·4 m.moles), caesium fluoride (1·0g., 6·6 m.moles), and sulpholan (2 mls.) was rotated in an oil bath for 24 hours at 130°. No volatile products were recovered from the tube by distillation under vacuum. The materials in the tube were filtered, under nitrogen, through a sinter and the residual solid (1·0g.) pumped under vacuum while heated to remove any sulpholan. The i.r. spectrum of the solid (brown) contained four absorptions (broad) centred at 6·9, 8·1, 13·5, and 20·7μ, and elemental analysis showed the absence of carbon. The filtrate (sulpholan solution) was poured into water and the aqueous solution carefully extracted with small portions of ether. The extract was dried ($MgSO_4$) and carefully distilled. Only ether was obtained as the distillate leaving a small amount of a dark brown gum.

(e) A Carius tube containing perfluorocyclohexa-1,4-diene (2·0g., 8·9 m.moles), caesium fluoride (1·0g., 6·6 m.moles) and a few drops of sulpholan was rotated in an oil bath at 80° for 18 hours. The contents of the tube were deep red in colour, and the volatile material was transferred under vacuum to a cold trap. A colourless liquid was obtained (0·9g.) which was shown to be unchanged perfluorocyclohexa-1,4-diene (45% recovery) by i.r. spectroscopy.

The residues from this experiment were discarded since the reaction was carried out in order to determine the composition of the volatile products.

7.2 Fluoride Ion-initiated Reactions of Pentafluoropyridine and Perfluorocycloalkenes

7.2.1 Reactions of pentafluoropyridine with one molecular proportion of perfluorocyclohexene

(a) In a sealed glass tube

(i) Pentafluoropyridine (3·0g., 17·8 m.moles), perfluorocyclohexene (5·0g., 19·1 m.moles), caesium fluoride (3g., 19·7 m.moles), and sulpholan (15 mls.) were introduced into a Carius tube (100 ml.) which was then evacuated, sealed, and heated at 180° for 24 hours. The tube was cooled, opened to a vacuum system, and the volatile materials transferred under vacuum to a cold trap. Examination of the products (2·1g.) by v.p.c. (column 'A' at 150°) showed the presence of perfluorocyclohexene and pentafluoropyridine (approx. ratio 1:1) with a trace amount of a product with a longer retention time. The materials remaining in the tube were added to water (150 mls.) and the involatile products extracted with 2 x 50 ml. portions of ether. The extracts were combined, washed well with water, dried over $MgSO_4$, and the ether removed by fractionation. The remaining dark brown liquid was distilled under vacuum to give a colourless liquid which solidified on standing to white crystals (1·25g.). A brown residue remained in the distillation flask. The product was purified by sublimation under vacuum at room temperature and shown to be perfluoro-(4-cyclohexylpyridine), m.pt. 33·5-34·5° (Found: C, 30·3; F, 66·5%; M, 431. $C_{11}F_{15}N$ requires C, 30·6; F, 66·1%; M, 431). $\lambda_{max.}$ (cyclohexane) = 284, (ε = 4758). An approximate value for the yield of the monosubstituted product (based on the amount of pentafluoropyridine that had reacted) was 25% (65% conversion of pentafluoropyridine). The structure was confirmed by ^{19}F n.m.r. spectroscopy. (I.R. Spectrum No.6).

(ii) Pentafluoropyridine (3·1g., 18·3 m.moles), perfluorocyclohexene (5·1g., 19·5 m.moles), caesium fluoride (3g., 19·7 m.moles), and sulpholan (15 mls.) were introduced into a Carius tube, which was then evacuated, sealed, and shaken on a vibroshaker for 40 hours at 25°. The tube was cooled, opened to a vacuum system, and the volatile materials transferred under vacuum to a cold trap. Examination of the products (8·1g.) by v.p.c. (column 'A' at 100°) showed the presence of perfluorocyclohexene and pentafluoropyridine (almost quantitative recovery of starting materials) with no other products present.

(iii) Pentafluoropyridine (3·6g., 21·3 m.moles), perfluorocyclohexene (6·0g., 22·9 m.moles), caesium fluoride (5g., 32·8 m.moles), and sulpholan (20 mls.) were introduced into a Carius tube, which was then evacuated, sealed, and heated at 130° for 64 hours. The tube was cooled, opened to a vacuum system, and the volatile materials transferred under vacuum to a cold trap. Examination of the products (7·1g.) by v.p.c. (column 'A' at 100°) showed these to be unreacted starting materials. The materials remaining in the tube were added to 100 mls. water and the products extracted with 2 x 30 ml. portions of ether. The extracts were combined, washed several times with water, dried ($MgSO_4$), and the ether removed by fractionation. The extract was distilled under vacuum to give a white crystalline solid (0·3g.) which was shown to be perfluoro-(4-cyclohexylpyridine) by i.r. and ^{19}F n.m.r. spectroscopy. Approximate yield of product (estimated from the chromatogram) was 20% (with an approx. 15% conversion of pentafluoropyridine).

(iv) Reaction (i) was repeated but using a different method of work-up. Examination of the materials transferred under vacuum to a cold trap (1·5g.) by v.p.c. (column 'A' at 150°) showed the presence of perfluorocyclohexene and pentafluoropyridine with a small amount of the product whose retention time corresponded to that for perfluoro-(4-cyclohexylpyridine). The materials remaining in the flask were added to water (150 mls.) and the product extracted with ether. The extract was washed with water, dried ($MgSO_4$), and the solution concentrated by removing some of the ether by distillation. The product was then separated by prep. scale v.p.c. (Aerograph: column 'A' at 150°) to give a white solid (2·1g.), which was shown to be perfluoro-(4-cyclohexylpyridine) by i.r. and ^{19}F n.m.r. spectroscopy. Approximate yield of product (estimated by v.p.c.) was 45% (based on a 60% conversion of pentafluoropyridine).

(b) <u>In a stainless-steel autoclave</u>

(i) This was a preliminary reaction using a metal vessel and a new work-up procedure.

Pentafluoropyridine (3·0g., 17·8 m.moles), perfluorocyclohexene (5·0g., 19·1 m.moles), caesium fluoride (3g., 19·7 m.moles), and sulpholan (20 mls.) were introduced into the autoclave under dry nitrogen. The autoclave was sealed and shaken at 120° for 24 hours. The autoclave was then cooled, opened, and the products transferred under vacuum to a cold trap (the flask containing the glass wool being heated up to 80°). Examination of the products (5·0g.) by v.p.c. (column 'A' at 150°) showed the presence of perfluorocyclohexene, pentafluoropyridine, a major product, and traces of two components with short retention times. The unreacted starting materials were confirmed by comparison of the retention times with those of the original compounds, and the retention time of the major product was identical to that for perfluoro-(4-cyclohexylpyridine).

(ii) Pentafluoropyridine (3·0g., 17·8 m.moles), perfluorocyclohexene (5·0g., 19·1 m.moles), caesium fluoride (3g., 19·7 m.moles), and sulpholan (20 mls.) were introduced into the autoclave under dry nitrogen. The autoclave was sealed and shaken at 175° for 24 hours. After cooling, the autoclave was opened and the volatile products transferred under vacuum to a cold trap (the flask being heated up to 100°). Examination of the products (6·0g.) by v.p.c. (G.D.B., column 'A' at 150°) showed that 80% of the total peak area was due to the presence of perfluorocyclohexene, pentafluoropyridine, and perfluoro-(4-cyclohexylpyridine) in the ratio 5:10:85 respectively. The remaining 20% consisted of traces of short retention time components and a compound with a longer retention time than that of the monosubstituted pyridine. Separation of the mixture by prep. scale v.p.c. (Aerograph: column 'A' at 150°) gave pentafluoropyridine (confirmed by i.r. spectroscopy) and perfluoro-(4-cyclohexylpyridine) (3·5g.), m.pt. 33·5-34·5°, which was identifed by i.r. and ^{19}F n.m.r. spectroscopy. The yield of product (estimated from the chromatogram) was 65% (based on the amount of pentafluoropyridine that had reacted - 80% conversion). The compound with a longer retention time was present in too small an amount for separation by prep. scale chromatography.

Solvent extraction of the material remaining in the flask followed by vacuum distillation produced a black tar but no other products.

(c) <u>In a nickel tube</u>

Pentafluoropyridine (3·0g., 17·8 m.moles), perfluorocyclohexene (5·0g., 19·1 m.moles), caesium fluoride (3g., 19·7 m.moles), and sulpholan (20 mls.) were introduced into a nickel tube under dry nitrogen, the tube sealed, and rotated in an oil bath at 175° for 24 hours. The tube was then cooled, opened, and the products transferred under vacuum to a cold trap. The products (4·8g.) were examined by v.p.c. (G.D.B., column 'A' at 125°) and shown to consist of perfluorocyclohexene, pentafluoropyridine, and perfluoro-(4-cyclohexylpyridine) in the ratio 11:39:50 respectively, together with a small amount of a compound with a longer retention time. This represents a yield of 83% of the monosubstituted pyridine (40% conversion of pentafluoropyridine), estimated from the chromatogram. Solvent extraction from water gave no further products.

7.2.2 Reactions of pentafluoropyridine with an excess of perfluorocyclohexene

(a) Preparation of perfluoro-(2,4-dicyclohexylpyridine)

Pentafluoropyridine (3·0g., 17·8 m.moles), perfluorocyclohexene (10g., 38·2 m.moles), caesium fluoride (3g., 19·7 m.moles), and sulpholan (40 mls.) were introduced into a nickel tube which was then sealed and rotated in an oil bath for 65 hours at 170°. The tube was cooled and the volatile products (3·0g.) transferred under vacuum to a cold trap. Analytical v.p.c. (column 'A' at 100°) showed these to consist almost entirely of perfluoro-(1-cyclohexylcyclohexene) (see section 7.1.1) and perfluoro-(4-cyclohexylpyridine) with small amounts of unchanged pentafluoropyridine and perfluorocyclohexene. The products remaining after vacuum transfer of the volatile materials were poured into a large volume of water and extracted with ether. The extract was dried ($MgSO_4$), and the solvent removed under reduced pressure. The remaining dark brown residue was sublimed up to 80° under vacuum to give an orange-coloured solid, which was then recrystallised from petroleum ether (40/60). A white crystalline solid (2·0g.) was isolated, and shown to be <u>perfluoro-(2,4-dicyclohexylpyridine)</u>, m.pt. 78-79°. (Found: C, 29·3;

F, 68·9%; M, 693. $C_{17}F_{25}N$ requires C, 29·4; F, 68·5%; M, 693). $\lambda_{max.}$ (cyclohexane) = 279, (ϵ = 5381). Yield 15% (based on 95% conversion of pentafluoropyridine). (I.R. Spectrum No.7). The structure was confirmed by ^{19}F n.m.r. spectroscopy.

(b) Formation of perfluoro-(2,4,6-tricyclohexylpyridine)

Reaction (a) was repeated using pentafluoropyridine (3·0g., 17·8 m.moles), perfluorocyclohexene (10g., 38·2 m.moles), caesium fluoride (5g., 32·8 m.moles) and sulpholan (60 mls.), and the reactants heated in a nickel tube for 75 hours at 165°. After cooling, the volatile products (2·8g.) were transferred under vacuum to a cold trap, and shown by analytical v.p.c. (column 'A' at 150°) to consist of unchanged pentafluoropyridine (small amount) and two major products. The mixture was separated by prep. scale v.p.c. and the major products shown to be $C_{12}F_{18}$ (perfluorobicyclohexenyl) and perfluoro-(4-cyclohexylpyridine) by i.r. spectroscopy. The materials remaining after vacuum transfer were poured into a large volume of water and extracted with three portions of ether. The extracts were combined and washed with water, at which stage a small quantity of insoluble crystals were precipitated. These were isolated by filtration and sublimed under vacuum up to 110° to give a white crystalline solid (0·2g.). This was shown to be perfluoro-(2,4,6-tricyclohexylpyridine), m.pt. 112-114°. (Found: C, 29·2; F, 70·1%; M, 955. $C_{23}F_{35}N$ requires C, 28·9; F, 69·6%; M, 955). $\lambda_{max.}$ (cyclohexane) = 273, (ϵ = 4618). (I.R. Spectrum No.8). The structure was determined by ^{19}F n.m.r. spectroscopy. After isolation of this compound, the ether extract was dried ($MgSO_4$), and removal of the solvent left a dark brown viscous liquid. Sublimation under vacuum up to 120° followed by recrystallisation from petroleum ether (40/60) gave perfluoro-(2,4-dicyclohexylpyridine) (1·2g.), 10% yield, which was identified by i.r. spectroscopy.

7.2.3 Reaction of pentafluoropyridine and perfluorocyclohexene at atmospheric pressure

Two reactions were carried out in which the pentafluoropyridine, caesium fluoride, and sulpholan were introduced into a 250 ml. 3-necked flask fitted with a stirrer, water condenser, and a means of adding the olefin dropwise into the flask. The method used was to heat the contents of the flask to the required temperature and then introduce the olefin slowly with vigorous stirring (for quantities and reaction conditions, see Table 4). At the end of the reaction the products were transferred under vacuum to a cold trap and examined by v.p.c. (Gas Density Balance).

In both cases the reaction mixture consisted of unchanged starting materials (C_5F_5N and C_6F_{10}) and approximately 7% perfluoro-(4-cyclohexylpyridine) (estimated from the mole fractions calculated from the chromatogram).

7.2.4 Reactions of pentafluoropyridine with one molecular proportion of perfluorocyclopentene

Two reactions were carried out in metal vessels at different temperatures and using approximately equimolar amounts of the olefin and substrate (for quantities and reaction conditions, see Table 5). The olefin was condensed into the vessel in each case. After reaction, the autoclave/tube was cooled, opened, and the products transferred under vacuum to a cold trap.

(a) Examination of the products (3·2g.) by v.p.c. (G.D.B., column 'A' at 100°) showed a major component and two minor components with shorter retention times than pentafluoropyridine; pentafluoropyridine (ca. 65% of total peak area); and one component with longer retention time than penta-

Table 4

	C_5F_5N	C_6F_{10}	CsF	Sulpholan	Temp.	Time taken to add olefin	Means of adding olefin	Remaining reaction time
(a)	4·0g. (23·7 m.moles)	6·5g. (24·8 m.moles)	3g.	50 mls.	135°-140°	90 mins.	Dropping funnel	7 hours at 100°
(b)	4·0g. (23·7 m.moles)	7·0g. (26·7 m.moles)	3g.	80 mls.	120°-130°	45 mins.	Serum cap and syringe	2 hours at 130°

Table 5

Reaction	C_5F_5N	C_5F_8	CsF	Sulpholan	Reaction conditions
(i)	3·0g. (17·8 m.moles)	4·0g (18·9 m.moles)	3g.	20 mls.	Shaken in stainless-steel autoclave at 175° for 21 hours
(ii)	6·3g. (37·3 m.moles)	8·5g. (40·1 m.moles)	5·5g.	40 mls.	Rotated in nickel tube at 125° for 24 hours

fluoropyridine. Separation of the mixture by prep. scale v.p.c. enabled the isolation of 3 components:

(i) a colourless liquid whose i.r. spectrum showed strong absorption in the region 7·0–9·5 microns, and in the mass spectrum there was a well-defined molecular ion peak at $^{M}/e$ = 457 and significant fragmentation peaks at $^{M}/e$ = 438, 388, 350 and 300; the base peak in the spectrum occurred at $^{M}/e$ = 69,

(ii) a colourless liquid whose i.r. spectrum was identical to that of perfluorobicyclopentenyl,

(iii) pentafluoropyridine (identified by i.r. spectroscopy).

There was insufficient of the first component for further characterisation.

Solvent extraction of the remaining materials followed by vacuum distillation afforded a small quantity of a red oily liquid. Chromatography showed this to be essentially one component, with trace amounts of impurities, and of short retention time. It did not give a clear i.r. spectrum and little information could be obtained from its mass spectrum.

(b) Examination of the products (12g.) by v.p.c. (G.D.B., column 'A' at 80°) showed a mixture of a compound with a short retention time, pentafluoropyridine, and a major product. The mixture was distilled to separate the lower boiling component and starting material from the major product, the latter solidifying as it distilled over. The white crystalline solid was sublimed at room temperature and 0·005 mm. pressure to give needle-shaped crystals which were identified as <u>perfluoro-(4-cyclopentylpyridine)</u>, m.pt. 48·5-49·5° (Found: C, 31·3; F, 65·1%; M, 381. $C_{10}F_{13}N$ requires C, 31·5; F, 64·8%; M, 381). $\lambda_{max.}$ (cyclohexane) = 285, (ε = 4451).

Yield of product (based on 20% conversion of pentafluoropyridine), 70% (estimated from the chromatogram). The structure was confirmed by ^{19}F n.m.r. spectroscopy. (I.R. Spectrum No.9).

The liquid distillate was then separated by prep. scale v.p.c. and the two components isolated were identified as pentafluoropyridine and perfluorocyclopentene dimer by i.r. spectroscopy.

7.2.5 Reaction of pentafluoropyridine with an excess of perfluorocyclopentene

A nickel tube containing pentafluoropyridine (5·0g., 29·6 m.moles), perfluorocyclopentene (13·0g., 61·3 m.moles), caesium fluoride (5·0g., 32·8 m.moles), and sulpholan (40 mls.) was rotated in an oil bath at 130° for 21 hours. The tube was then cooled, opened, and the volatile products transferred under vacuum to a cold trap. The products were shown by v.p.c. (column 'A' at 140°) to be a mixture of perfluorocyclopentene dimer, pentafluoropyridine and perfluoro-(4-cyclopentylpyridine), but the proportion of dimer was relatively higher than in the product mixture obtained in the previous reaction (7.2.4 (b)).

7.2.6 Attempted preparation of perfluoro-(dicyclopentylpyridine)

A nickel tube containing pentafluoropyridine (2·0g., 11·9 m.moles), perfluorocyclopentene (7·4g., 34·9 m.moles), caesium fluoride (3g.) and sulpholan (50 mls.) was rotated in an oil bath for 48 hours at 175°. After cooling, the volatile products (7·0g.) were transferred under vacuum to a cold trap, and v.p.c. showed these to consist of the olefin dimer together with small amounts of unchanged pentafluoropyridine and the monosubstituted pyridine. The chromatogram showed the dimer to be the predominant component. Solvent extraction of the materials remaining after vacuum transfer gave no higher substitution products.

7.2.7 Reactions of pentafluoropyridine with an excess of perfluorocyclobutene

(a) In a sealed glass tube

Pentafluoropyridine (3•5g., 20•7 m.moles), caesium fluoride (3g., 19•7 m.moles) and sulpholan (20 mls.) were introduced into a Carius tube (100 ml.). Perfluorocyclobutene (6•3g., 38•9 m.moles) was condensed into the tube which was then evacuated, sealed, and shaken at 25° for 24 hours. The tube was opened to a vacuum system and the volatile materials transferred to a cold trap (0•6g.). The contents of the tube were then poured into 50 mls. water and the organic layer separated from the aqueous layer. The former was washed with water, dried ($MgSO_4$), and distilled over the range 76-142° giving 4•8g. products. The products were separated by prep. scale v.p.c. and shown to be unreacted pentafluoropyridine and perfluorocyclobutene trimer by i.r. spectroscopy.

When the above reaction was repeated by heating the reactants in a Carius tube at 130° for 48 hours, the olefin trimer was produced with almost quantitative recovery of pentafluoropyridine. There was also a small amount of a compound with a longer retention time (from v.p.c.)

(b) In a nickel tube

Two reactions were carried out in which the reactants were contained in a nickel tube, which was rotated in a heated oil bath (for quantities and reaction conditions, see Table 6).

Examination of the products by v.p.c. showed the mixture to consist, in

Table 6

Reaction	C_5F_5N	C_4F_6	CsF	Sulpholan	Temp. (°C)	Time	Wt. of volatile products
(a)	4·0g. (0·024 mole)	12·0g. (0·074 mole)	3·5g.	30 mls.	150	24 hours	13·0g.
(b)	3·0g. (0·018 mole)	15·0g. (0·093 mole)	3·0g.	30 mls.	180	16 hours	14·0g.

both cases, of perfluorocyclobutene trimer, unchanged pentafluoropyridine, and a small amount of a compound with a longer retention time. The mixtures were combined and separated by prep. scale v.p.c. (Aerograph: column 'A' at 100°). Perfluorocyclobutene trimer and pentafluoropyridine were identified by i.r. spectroscopy, and the product with a longer retention time was isolated in small quantity as a colourless liquid and shown to be perfluoro-(4-cyclobutylpyridine), b.pt. 154·5°/760 mm. (Found: C, 32·9; F, 63·4%; M, 331. $C_9F_{11}N$ requires C, 32·6; F, 63·1%; M, 331). $\lambda_{max.}$ (cyclohexane) = 284, (ε = 3718). (I.R. Spectrum No.11). The structure was determined by ^{19}F n.m.r. spectroscopy.

7.2.8 Reactions of pentafluoropyridine and perfluorocyclobutene at atmospheric pressure

(a) Using a flow system

Three reactions were carried out in which caesium fluoride and sulpholan were introduced into a 250 ml. flask under dry nitrogen. The flask was then evacuated at room temperature. When de-gassing of the solvent had ceased, perfluorocyclobutene was introduced into the system from a reservoir. The reaction mixture was then stirred and heated to reaction temperature, and pentafluoropyridine was introduced from a syringe through a serum cap. A circulating pump was then started and the hexafluorocyclobutene was bubbled slowly through a sinter into the reaction mixture for a specific time (for details of these reactions, see Table 7). Any unreacted olefin was recirculated by the pump. Solid CO_2 was used as the condenser coolant, and the formation of a vacuum at intervals due to the olefin reacting was compensated for by allowing a further quantity of the olefin into the system from the reservoir.

Table 7

Reaction	C_5F_5N	C_4F_6	CsF	Sulpholan	Reaction temp.	Reaction time	Products recovered by distillation under vacuum	C_4F_6 recovered
(i)	5·0g. (29·6 m.moles)	12·0g. (74·0 m.moles)	3g.	130 mls.	120°-130°	6 hours	7·4g.	6·1g.
(ii)	5·0g. (29·6 m.moles)	13·0g. (80·3 m.moles)	3g.	100 mls.	135°	5 hours	7·0g.	9·0g.
(iii)	5·0g. (29·6 m.moles)	10·5g. (60·8 m.moles)	5g.	120 mls.	140°	7 hours	5·5g.	5·4g.

N.B. In reactions (ii) and (iii) the olefin was diluted with N_2 before circulation

The reaction products were recovered from the reaction mixture by distillation under vacuum up to ca. 90°, and then analysed on the gas density balance. The residual perfluorocyclobutene was condensed out of the system and stored.

The ratio and yields of products obtained in these reactions are summarised in Table 8.

(b) Using a static system

Caesium fluoride (3g.) and sulpholan (50 mls.) were introduced, under dry nitrogen, into a conical flask (100 ml.) which was fitted with a gas inlet system and a water condenser on top of which was attached a rubber bladder which was employed as a reservoir for the gaseous olefin. After evacuation of the flask and de-gassing of the solvent, the flask was heated to the required temperature, and perfluorocyclobutene allowed into the system until atmospheric pressure was reached and the reservoir was partially inflated. Pentafluoropyridine (5·0g., 29·6 m.moles) was then added rapidly by means of a pipette, and the mixture stirred vigorously under an atmosphere of perfluorocyclobutene for 20 hours at 130°. The products were distilled under vacuum from the reaction mixture (as in (a)), and the ratio and respective yields of products (estimated by v.p.c.) were almost identical to those obtained in reaction (a) (ii).

7.2.9 Reactions involving perfluorocyclohexa-1,4-diene

(a) Reactions in sealed glass tubes

(i) Pentafluoropyridine (6·0g., 35·6 m.moles), perfluorocyclohexa-1,4-diene (4·0g., 17·9 m.moles), caesium fluoride (5g., 32·8 m.moles) and sulpholan (20 mls.) were placed in a Carius tube which was then evacuated, sealed, and shaken on a vibroshaker at 25° for 24 hours. The tube was opened into a

Table 8

Reaction	Temp.	Products recovered by distillation under vacuum					% conversion of C_5F_5N	% yield of $C_9F_{11}N$ (based on C_5F_5N consumed)
		Wt.	Composition by weight					
			Butene dimers C_8F_{12}	Butene trimers $C_{12}F_{18}$	C_5F_5N	$C_9F_{11}N$		
(i)	120°-130°	7·4g.	0·4g.	2·1g.	4·4g.	0·5g.	12	43
(ii)	135°	7·0g.	0·8g.	1·3g.	4·1g.	0·8g.	18	48
(iii)	140°	5·5g.	-	-	4·5g.	1·0g.	10	100

N.B. Product ratios were calculated assuming the minor components of short retention time to be perfluorocyclobutene dimers.

vacuum system and the volatile materials collected (2·3g.). Examination by v.p.c. (column 'A' at 100°) showed these to be 94% unreacted pentafluoropyridine. The contents of the tube were poured into water (100 mls.) and extracted with 2 x 25 ml. portions of ether. The extracts were combined, washed with water, dried ($MgSO_4$), and the ether removed by fractionation. The extract (deep red liquid) was then distilled, and two fractions collected over the ranges 38-64° and 104-172° (1·0g.). The first fraction was shown by v.p.c. to be pentafluoropyridine and unchanged diene in approx. equal amounts. Examination of the second fraction by v.p.c. showed this to consist of two products, with retention times longer than that of pentafluoropyridine, in approx. ratio 50:50. In the mass spectrum of this fraction (insufficient for separation of the products) strong peaks were present at $^M/e$, 393 (monosubstituted pyridine, $C_{11}F_{13}N$) and $^M/e$, 617 (disubstituted pyridine, $C_{17}F_{21}N$).

(ii) Pentafluoropyridine (6·0g., 35·6 m.moles), perfluorocyclohexa-1,4-diene (4·5g., 20·1 m.moles), caesium fluoride (5g., 32·8 m.moles) and sulpholan (20 mls.) were shaken in a sealed glass (Carius) tube at 25° for 40 hours. The products collected by transfer under vacuum into a cold trap (8·8g.) were examined by v.p.c. and shown to consist of unreacted pentafluoropyridine and two products with longer retention times (as in reaction (i)). Separation by prep. scale v.p.c. afforded a white crystalline solid (0·8g.), m.pt. 38·5-39·5°, which was shown by elemental analysis and mass spectrometry to correspond to the <u>'disubstituted' pyridine</u>, $C_{17}F_{21}N$ (Found: C, 33·4; F, 64·4%; M, 617. $C_{17}F_{21}N$ requires C, 33·1; F, 64·7%; M, 617). $\lambda_{max.}$ (cyclohexane) = 279, (ε = 3640). Approx. yield 15%. (I.R. Spectrum No.14). The orientation of substitution of this compound and its possible structure is discussed in Chapter 10. Throughout the experimental section it will be convenient to denote it as $C_{17}F_{21}N$.

The retention time of the other product was shown in later experiments to correspond to that for the monosubstituted pyridine.

(iii) Pentafluoropyridine (3·0g., 17·8 m.moles), perfluorocyclohex-1,4-diene (8·0g., 35·7 m.moles), caesium fluoride (5g., 32·8 m.moles), and sulpholan (20 mls.) were shaken in a Carius tube on a vibroshaker at 25° for 24 hours. The tube was then opened and the contents poured into water. Solvent extraction with ether gave unreacted starting materials.

(b) Reactions in a stainless-steel autoclave

Three reactions were carried out in which the materials were shaken in the autoclave at fairly high temperatures (for quantities and reaction conditions, see Table 9). In each case the volatile products were transferred under vacuum and collected in a cold trap.

(i) Examination of the volatile products by v.p.c. (G.D.B., column 'A' at 150°) showed the mixture to contain pentafluoropyridine, a product with slightly longer retention time than pentafluoropyridine, and a component with a much longer retention time. The two products were separated by prep. scale v.p.c. (Aerograph: column 'A' at 150°). The first product was a colourless liquid and shown to be perfluoro-(4-cyclohexenylpyridine), b.pt. 168-169°/760 mm. (Found: C, 33·5; F, 63·1%; M, 393. $C_{11}F_{13}N$ requires C, 33·6; F, 62·8%; M, 393). $\lambda_{max.}$ (cyclohexane) = 277, (ϵ = 4520). (I.R. Spectrum No.13). The second product was a colourless liquid which was not fully characterised. In the mass spectrum of this compound there was a fairly strong molecular ion peak at $^{M}/e$ = 371, and relatively intense fragmentation peaks at $^{M}/e$ = 352, 302, 224, 205, 186, 167, 155 and 117. The base peak of the spectrum occurred at $^{M}/e$ = 271. The i.r. spectrum contained absorptions in the range 7·5-8·5µ

Table 9

Reaction	C_5F_5N	C_6F_8(1,4–)	CsF	Sulpholan	Temp. (°C)	Time	wt. of volatile products
(i)	4·5g. (26·6 m.moles)	3·0g. (13·4 m.moles)	3g.	20 mls.	175	24 hours	4·4g.
(ii)	4·5g. (26·6 m.moles)	3·0g. (13·4 m.moles)	3g.	20 mls.	120	24 hours	4·3g.
(iii)	3·0g. (17·8 m.moles)	4·0g. (17·9 m.moles)	3g.	20 mls.	160	24 hours	3·0g.

(aliphatic fluorine) and, in addition, a broad band in the region 8·5-9·1µ.

The yield of perfluoro-(4-cyclohexenylpyridine) in this reaction was 23% (estimated from the chromatogram).

Solvent extraction of the materials remaining after vacuum transfer of the volatile products gave a trace amount of a green liquid (insufficient for identification) leaving a tarry residue behind.

(ii) The volatile products were examined by v.p.c. (G.D.B., column 'A' at 150°) and shown to consist of pentafluoropyridine and two major products in the ratio 55:33:12 respectively. The products were separated by prep. scale v.p.c. and identified as perfluoro-(4-cyclohexenylpyridine), $C_{11}F_{13}N$ and $C_{17}F_{21}N$ by i.r. spectroscopy. The yields of $C_{11}F_{13}N$ and $C_{17}F_{21}N$ were 28% and 7% respectively (based on the pentafluoropyridine consumed).

Solvent extraction of the remaining materials gave a small amount of a green liquid (as in reaction (i)) which gave a molecular ion peak at $^{M}/e$ = 841 in the mass spectrum. This corresponds to $C_{23}F_{29}N$ (i.e. the 'tri-substituted' pyridine).

(iii) Analytical v.p.c. (G.D.B., column 'A' at 150°) showed the volatile products to consist of pentafluoropyridine, perfluoro-(4-cyclohexenylpyridine), and the unidentified product (isolated in reaction (i)) in the ratio 40:22:38 respectively (from retention time). This corresponds to a yield of 16% for the perfluoro-(4-cyclohexenylpyridine) (estimated from the chromatogram and based on the amount of pentafluoropyridine that had reacted).

Solvent extraction of the involatile materials gave no other products but a gummy residue remained after vacuum distillation of the extract.

(c) Reactions in a nickel tube

Three reactions were carried out in which the materials were rotated in a nickel tube in a heated oil bath (for quantities and reaction conditions, see Table 10). In each case the volatile products were transferred under vacuum and collected in a cold trap.

(i) The products were shown by v.p.c. to consist of pentafluoropyridine, perfluoro-(4-cyclohexenylpyridine), and $C_{17}F_{21}N$ in the ratio 66:24:10 respectively. This corresponds to yields of 50% and 14% for the $C_{11}F_{13}N$ and $C_{17}F_{21}N$ respectively (estimated from the chromatogram - G.D.B.), calculated from the pentafluoropyridine consumed.

(ii) Examination of the products by v.p.c. (G.D.B., column 'A' at 100^{o}) indicated a mixture containing pentafluoropyridine (60%), perfluoro-(4-cyclohexenylpyridine) (16%), and $C_{17}F_{21}N$ (23%). This represents a 90% recovery of pentafluoropyridine, and high yields of the two major products based on the amount of pentafluoropyridine that had reacted.

(iii) Only 1•5g. of products were collected by vacuum transfer, and examination by v.p.c. (G.D.B., column 'A' at 100^{o}) showed this to be a mixture of pentafluoropyridine (52%), perfluoro-(4-cyclohexenylpyridine) (25%), and $C_{17}F_{21}N$ (20%), with trace amounts of components with short retention times.

In reactions (i) and (iii) solvent extraction of the involatile materials was carried out but a trace amount of a green liquid (obtained previously) was the only product isolated.

7.2.10 Fluoride ion-initiated reaction of pentafluoropyridine and perfluorocyclohexa-1,3-diene

Pentafluoropyridine (5•0g., 29•6 m.moles), perfluorocyclohexa-1,3-diene

Table 10

Reaction	C_5F_5N	C_6F_8(1,4-)	CsF	Sulpholan	Temp. (°C)	Time	wt. of volatile products
(i)	3·0g. (17·8 m.moles)	4·0g. (17·9 m.moles)	3g.	20 mls.	125	24 hours	4·0g.
(ii)	6·0g. (35·6 m.moles)	8·0g. (35·7 m.moles)	5g.	40 mls.	50	50 hours	9·0g.
(iii)	1·5g. (8·9 m.moles)	6·0g. (26·8 m.moles)	3g.	20 mls.	125	24 hours	1·5g.

(7·0g., 31·2 m.moles), caesium fluoride (5g., 32·8 m.moles), and sulpholan (30 mls.) were introduced into a nickel tube which was then sealed and rotated in an oil bath at 150° for 26 hours. The tube was cooled, opened, and the products transferred under vacuum to a cold trap. Examination of the products (4·5g.) by v.p.c. showed the presence of two components, and separation by prep. scale v.p.c. gave pentafluoropyridine (identified by i.r. spectroscopy) and perfluoro-(4-cyclohexenylpyridine) (30% yield/30% conversion of pentafluoropyridine - estimated from the chromatogram). The latter was confirmed by i.r. and mass spectroscopy, and the ^{19}F n.m.r. spectrum of this product was identical with that of the monosubstituted compound obtained by the reaction of pentafluoropyridine and octafluorocyclohexa-1,4-diene, the isomer of the 1,3-diene.

7.2.11 Comparative reactions of pentafluoropyridine with perfluorocyclohexa-1,3- and -1,4-dienes

Two reactions were carried out in which the respective diene (5·0g., 22·3 m.moles) and pentafluoropyridine (7·5g., 44·5 m.moles) were heated in a rotating nickel tube in the presence of caesium fluoride (3g.) and sulpholan (40 mls.). Both reactions were carried out with the heterocycle in excess, and after reaction, the tubes were allowed to cool and the products transferred under vacuum to a cold trap. The product mixture in each reaction was shown by v.p.c. (G.D.B., column 'A' at 100°) to consist of unreacted pentafluoropyridine, perfluoro-(4-cyclohexenylpyridine) and $C_{17}F_{21}N$ in the mole ratios given in Table 11. In each reaction any materials remaining, after vacuum transfer of the volatile products, were extracted with ether after pouring into a large excess of water. This produced a dark brown residue from which no further products were obtained.

Table 11

Reactants	Mole ratios of products		
	C_5F_5N :	$C_{11}F_{13}N$:	$C_{17}F_{21}N$
C_5F_5N + C_6F_8(1,4-)	3·6 :	0·5 :	0·2
C_5F_5N + C_6F_8(1,3-)	3·9 :	0·6 :	0·2

7.2.12 Reaction of pentafluoropyridine and perfluorocyclohexa-1,4-diene at atmospheric pressure

Pentafluoropyridine (3·0g., 17·8 m.moles), caesium fluoride (3g.) and sulpholan (60 mls.) were introduced into a 250 ml. 3-necked flask fitted with a stirrer, water condenser, and a serum cap and syringe (for adding the olefin). The contents of the flask were heated to 120° and the olefin added dropwise to the vigorously stirred mixture over a period of 110 mins. The mixture was then maintained at 130° with stirring for a further 2 hours. The products (2·4g.) were transferred under vacuum to a cold trap and examination by v.p.c. showed a mixture of unchanged pentafluoropyridine (62%), $C_{11}F_{13}N$ (19%), and $C_{17}F_{21}N$ (19%). This represents a 50% conversion of pentafluoropyridine, and yields of less than 10% of the two products (estimated from the chromatogram).

7.2.13 Comparative fluoride ion-initiated reactions of pentafluoropyridine and perfluorocyclohexa-1,4-diene in sulpholan and tetraglyme

Two reactions were carried out simultaneously in which pentafluoropyridine (2·5g., 14·8 m.moles), perfluorocyclohexa-1,4-diene (3·5g., 15·6 m.moles) and caesium fluoride (3g.) were heated in a rotating nickel tube for 22 hours at

130° in the presence of 40 mls. (a) sulpholan and (b) tetraglyme. The volatile products, transferred from the tube under vacuum, were compared for each reaction using v.p.c. In both reactions the recovery of pentafluoropyridine was the same, but the amount of $C_{11}F_{13}N$ formed was less with tetraglyme than with sulpholan, and there was no $C_{17}F_{21}N$ formed in the reaction in tetraglyme, whereas $C_{17}F_{21}N$ was produced with sulpholan as solvent although to a smaller extent than the formation of $C_{11}F_{13}N$.

7.3 Reactions of Perfluorocycloalkylpyridines

7.3.1 Nucleophilic substitution with methoxide ion

The following reactions were carried out using methoxide ion (CH_3O^-) as the nucleophilic reagent, and the perfluorocycloalkylated pyridines were treated with either a solution of sodium in methanol or a standard solution of sodium methoxide.

(a) Preparation of 4-perfluorocyclohexyl-2-methoxy-3,5,6-trifluoropyridine

To a refluxing solution of perfluoro-(4-cyclohexylpyridine) (0·45g., 1·04 m.moles) in dry methanol (40 mls.) was added a solution of sodium (0·027g., 1·17 m.moles) in dry methanol (10 mls.) over a period of 25 mins. The addition was carried out under dry nitrogen with stirring, and the solution was heated under reflux for a further 18 hours. The reaction mixture was then allowed to cool, poured into water (300 mls.) and the aqueous mixture extracted twice with methylene chloride. The combined extracts were dried ($MgSO_4$), and removal of the solvent left a white solid which was sublimed at 25-35° and 0·02 mm., and shown to be 4-perfluorocyclohexyl-2-methoxy-3,5,6-trifluoropyridine, (0·4g., 87% yield), m.pt. 45-46°. (Found: C, 32·2; H, 0·62; F, 60·2%; M, 443. $C_{12}H_3F_{14}NO$ requires C, 32·5; H, 0·67; F, 60·0%;

M, 443). $\lambda_{max.}$ (cyclohexane) = 303, (ε = 5498). (I.R. Spectrum No.15). V.p.c. (column 'O' at 200^{o}) and mass spectrometry indicated the presence of a trace amount of the di-methoxy derivative. The structure of the mono-methoxy compound was confirmed by n.m.r. spectroscopy.

(b) Preparation of 4-perfluorocyclohexyl-2,6-dimethoxy-3,5-difluoropyridine

Reaction (a) was repeated using perfluoro-(4-cyclohexylpyridine) (0•43g., 1•00 m.moles) in dry methanol (40 mls.) and a solution of sodium (0•050g., 2•17 m.moles) in dry methanol (10 mls.). Solvent extraction with methylene chloride gave a white solid which was sublimed at 50^{o} and 0•02 mm., and shown to be pure v.p.c. (column 'O' at 200^{o}). The product was identified as 4-perfluorocyclohexyl-2,6-dimethoxy-3,5-difluoropyridine, (0•45g., 99% yield), m.pt. 58-60^{o}. (Found: C, 34•4; H, 0•91; F, 54•6%; M, 455. $C_{13}H_6F_{13}NO_2$ requires C, 34•3; H, 1•32; F, 54•3%; M, 455). $\lambda_{max.}$ (cyclohexane) = 317, (ε = 5784). (I.R. Spectrum No.16).

(c) Preparation of 2,4-perfluorodicyclohexyl-6-methoxy-3,5-difluoropyridine

To a refluxing solution of perfluoro-(2,4-dicyclohexylpyridine) (0•25g., 0•36 m.moles) in dry methanol (50 mls.) was added a solution of sodium (0•008g., 0•35 m.moles) in dry methanol (10 mls.) over a period of 20 mins., with stirring. The mixture was heated under reflux with stirring for a further 18 hours. After cooling, the mixture was poured into water (500 mls.) and extracted with two portions of methylene chloride. The extract was dried ($MgSO_4$), and removal of the solvent left a pale yellow oil which was shown by v.p.c. (column 'O' at 200^{o}) to be essentially one component. The product was identified as 2,4-perfluorodicyclohexyl-6-methoxy-3,5-difluoropyridine, (0•2g., 80% yield). (Found: C, 30•7; H, 0•52; F, 64•6%; M, 705. $C_{18}H_3F_{24}NO$

requires C, 30·6; H, 0·42; F, 64·7%; M, 705). $\lambda_{max.}$ (cyclohexane) = 288, (ε = 4804). (I.R. Spectrum No.17). The orientation of substitution was shown by n.m.r. spectroscopy.

(d) <u>Preparation of 4-perfluorocyclopentyl-2-methoxy-3,5,6-trifluoropyridine</u>

To a stirred solution of perfluoro-(4-cyclopentylpyridine) (0·32g., 0·84 m.mole) in dry methanol (30 mls.) was added 8 mls. 0·1M solution of sodium methoxide (0·80 m.moles) over a period of 15 mins., with stirring, at room temperature. The mixture was then refluxed with stirring for a further 3 hours. The mixture was poured into water (500 mls.) and extraction with methylene chloride afforded a pale yellow liquid (v.p.c. pure) which was shown to be <u>4-perfluorocyclopentyl-2-methoxy-3,5,6-trifluoropyridine</u>, (0·25g., 76% yield), b.pt. > 200°/760 mm. (Found: C, 33·9; H, 1·15; F, 57·6%; M, 393. $C_{11}H_3F_{12}NO$ requires C, 33·6; H, 0·76; F, 58·0%; M, 393). $\lambda_{max.}$ (cyclohexane) = 304, (ε = 4860). (I.R. Spectrum No.18).

(e) <u>Preparation of 4-perfluorocyclobutyl-2-methoxy-3,5,6-trifluoropyridine</u>

To a stirred solution of perfluoro-(4-cyclobutylpyridine) (0·25g., 0·76 m.moles) in dry methanol (30 mls.) was added 8 mls. 0·1M solution of sodium methoxide (0·80 m.moles) over a period of 30 mins., with stirring, at room temperature. The mixture was then stirred under reflux for a further 2 hours, cooled, poured into water (500 mls.), and extraction of the aqueous solution with methylene chloride gave a light brown liquid (b.pt. > 160°/760 mm.). This was shown to be one component by v.p.c. and identified as <u>4-perfluorocyclobutyl-2-methoxy-3,5,6-trifluoropyridine</u>, (0·15g., 58% yield). (Found: C, 34·9; H, 1·18; F, 55·7%; M, 343. $C_{10}H_3F_{10}NO$ requires C, 35·0; H, 0·87; F, 55·4%; M, 343). $\lambda_{max.}$ (cyclohexane) = 305, (ε = 4444). (I.R. Spectrum No.19).

The orientation of substitution of the methoxy group in the products from reactions (d) and (e) was confirmed by n.m.r. spectroscopy.

(f) Reactions of perfluoro-(4-cyclohexenylpyridine) with one molecular proportion of sodium methoxide

Three reactions were carried out in which perfluoro-(4-cyclohexenylpyridine) was treated with an equimolar proportion of sodium methoxide solution (for quantities and reaction conditions, see Table 12). In each case the requisite amount of sodium in dry methanol was added to a stirred solution of the fluorocarbon in dry methanol. After each reaction the methanol solution was poured into a large volume of water and extracted with methylene chloride in the usual way.

In reactions (i) and (ii) a mixture of three products was obtained (shown by v.p.c.), and shown by i.r. and mass spectroscopy to be mono- and di-methoxy derivatives.

From reaction (iii) a pale yellow liquid was isolated (v.p.c. pure) and shown to be monomethoxy-perfluoro-(4-cyclohexenylpyridine), (0·3g., 86% yield), b.pt. > 200°/760 mm. (Found: C, 35·3; H, 1·1; F, 56·6%; M, 405. $C_{12}H_3F_{12}NO$ requires C, 35·6; H, 0·74; F, 56·3%; M, 405). $\lambda_{max.}$ (cyclohexane) = 275, (ε = 3797). (I.R. Spectrum No.20).

(g) Reaction of perfluoro-(4-cyclohexenylpyridine) with two molecular proportions of sodium methoxide

To a stirred solution of perfluoro-(4-cyclohexenylpyridine) (0·30g., 0·76 m.mole) in dry methanol (30 mls.) at room temperature was added 15 mls.

Table 12

Reaction	$C_{11}F_{13}N$	wt. of sodium in 10 mls. methanol	Reaction conditions
(i)	0·403g. (1·03 m.moles) in 40 mls. CH_3OH	0·025g. (1·09 m.moles)	$NaOCH_3$ solution added over a period of 30 mins. to refluxing solution of $C_{11}F_{13}N$, and mixture stirred under reflux for a further 4 hours.
(ii)	0·302g. (0·77 m.moles) in 30 mls. CH_3OH	0·016g. (0·70 m.moles)	$NaOCH_3$ solution added over a period of 25 mins. to stirred solution of $C_{11}F_{13}N$ at room temperature, and mixture stirred under reflux for a further 30 mins.
(iii)	0·339g. (0·86 m.moles) in 30 mls. CH_3OH	0·021g. (0·91 m.moles)	$NaOCH_3$ solution added over a period of 10 mins. to stirred solution of $C_{11}F_{13}N$ at room temperature, and mixture stirred at room temperature for a further 60 mins.

0·1M solution of sodium methoxide (1·50 m.moles) over a period of 15 mins., and the solution stirred for a further 90 mins., at room temperature. Extraction of the product with methylene chloride gave a pale yellow oil (v.p.c. pure) which was shown to be dimethoxy-perfluoro-(4-cyclohexenylpyridine), (0·25g., 78% yield). (Found: C, 37·7; H, 1·63; F, 50·3%; M, 417. $C_{13}H_6F_{11}NO_2$ requires C, 37·4; H, 1·44; F, 50·1%; M, 417). $\lambda_{max.}$ (cyclohexane) = 275, (ε = 3190). (I.R. Spectrum No.21).

For a discussion of the orientation of substitution of the methoxy group(s) in the derivatives of perfluoro-(4-cyclohexenylpyridine), see Chapter 10.

(h) Reaction of perfluoro-(4-cyclohexenylpyridine) with methanol

Perfluoro-(4-cyclohexenylpyridine) (0·37g., 0·94 m.moles) was refluxed with 20 mls. dry methanol for 4 hours. Extraction from water using methylene chloride in the usual way gave 0·34g. of a pale yellow liquid, which was shown by v.p.c. (Gas Density Balance) to consist of unchanged perfluoro-(4-cyclohexenylpyridine) and its mono-methoxy derivative (isolated previously) in the approximate ratio 1:1·5 respectively. This represents a 55% yield of the latter compound.

(i) Reactions of $C_{17}F_{21}N$ with sodium methoxide

Several reactions were carried out with $C_{17}F_{21}N$ (see Table 13), using the method as for the above reactions.

When reaction (ii) was repeated a pale yellow oil was isolated (one major product with $>$ 90% of total peak area on the chromatogram), and shown to be the mono-methoxy derivative of $C_{17}F_{21}N$, (0·28g., 89% yield). (Found: C, 34·0; H, 0·52; F, 60·5%; M, 629. $C_{18}H_3F_{20}NO$ requires C, 34·3; H, 0·48; F, 60·4%; M, 629). $\lambda_{max.}$ (cyclohexane) = 278, (ε =3634). (I.R. Spectrum No.22).

Table 13

Reaction	$C_{17}F_{21}N$ in 30 mls. CH_3OH	wt. of sodium in 10 mls. CH_3OH	Time taken to add $NaOCH_3$ solution at room temperature	Additional stirring at room temp.	Products (shown by v.p.c. and mass spectrometry).		
					methoxy-derivatives		
					mono-	:	di-
(i)	0·304g. (0·49 m.moles)	0·012g. (0·52 m.moles)	45 mins.	60 mins.	75	:	25
(ii)	0·333g. (0·54 m.moles)	0·012g. (0·52 m.moles)	30 mins.	10 mins.	85	:	15
(iii)	0·283g. (0·46 m.moles)	0·023g. (1·00 m.moles)	30 mins.	60 mins.	40	:	60

7.3.2 Defluorination of perfluorocycloalkylpyridines

The following reactions were carried out using the same procedure as in section 9.1, and heated iron filings as the defluorinating agent.

(a) Perfluoro-(4-cyclohexylpyridine), $C_{11}F_{15}N$

$C_{11}F_{15}N$ (0·5g.) was passed over iron heated to ca. 460°. The product (0·25g.) was a white solid (v.p.c. pure), m.pt. 96-97° (literature 94-100°), whose i.r. spectrum was identical to that of perfluoro-(4-phenylpyridine).[68] The molecular weight ($C_{11}F_9N$ requires M, 317) was confirmed by mass spectrometry, and the yield of $C_{11}F_9N$ was 70% (100% conversion of $C_{11}F_{15}N$).

(b) Perfluoro-(2,4-dicyclohexylpyridine), $C_{17}F_{25}N$

$C_{17}F_{25}N$ (0·3g.) was passed over iron heated to 450°. The product (0·1g.) was a colourless viscous oil which was shown by v.p.c. (column 'O' at 200°) to consist of two components. The mass spectrum of the liquid contained two fairly strong molecular ion peaks at $^{M}/e$, 541 ($C_{17}F_{17}N$) and 465 ($C_{17}F_{13}N$), together with less intense peaks at $^{M}/e$, 655 ($C_{17}F_{23}N$), 617 ($C_{17}F_{21}N$), and 579 ($C_{17}F_{19}N$). On standing for an appreciable time, a solid crystallised out from the liquid and this exhibited a molecular ion peak at M, 465 ($C_{17}F_{13}N$) in the mass spectrum.

(c) Perfluoro-(4-cyclohexenylpyridine), $C_{11}F_{13}N$

$C_{11}F_{13}N$ (1·3g.) was passed over iron at 450°. The products (0·8g.) were shown to consist of two components in approx. ratio 10:1. Separation of the mixture gave unchanged $C_{11}F_{13}N$ (90% - identified by i.r. spectroscopy) and a white solid, m.pt. 96°, which was shown to be perfluoro-(4-phenylpyridine) by i.r. and mass spectroscopy.

(d) Preparation of perfluoro-(4-cyclopentenylpyridine)

Perfluoro-(4-cyclopentylpyridine) (0·5g.) was passed over iron at ca. 460°. The product was a colourless liquid (pure by v.p.c.) and shown to be perfluoro-(4-cyclopentenylpyridine), (0·2g., 45% yield), b.pt. 161·5°/760 mm. (Found: C, 34·7; F, 60·3%; M, 343. $C_{10}F_{11}N$ requires C, 35·0; F, 60·9%; M, 343). $\lambda_{max.}$ (cyclohexane) = 274, (ε = 2818). (I.R. Spectrum No.10). Conversion of perfluoro-(4-cyclopentylpyridine), 100%.

(e) Preparation of perfluoro-(4-cyclobutenylpyridine)

Perfluoro-(4-cyclobutylpyridine) (0·35g.) was passed over iron at 450°. The product was a colourless liquid (present in very small quantity) which was identified as perfluoro-(4-cyclobutenylpyridine), (Found: C, 37·2; F, 58·1%; M, 293. C_9F_9N requires C, 36·9; F, 58·4%; M, 293). (I.R. Spectrum No.12).

7.3.3 Attempted photolysis of perfluoro-(2,4,6-tricyclohexylpyridine)

Perfluoro-(2,4,6-tricyclohexylpyridine) (0·1g.) was dissolved in 1·5g. pentafluoropyridine (as solvent) and introduced into a small bore silica tube, which was then evacuated, sealed, and irradiated with u.v. light for 95 hours. After this time the pentafluoropyridine was removed by vacuum transfer and shown to be unchanged by i.r. spectroscopy. The solid remaining (0·1g.) was shown to be unchanged starting material by melting-point data and i.r. spectroscopy.

7.4 Fluoride Ion-initiated Reactions of Perfluoro-(4-isopropylpyridine) and Perfluorocycloalkenes

7.4.1 Reaction with perfluorocyclohexene

Perfluoro-(4-isopropylpyridine) (3·0g., 9·4 m.moles), perfluorocyclohexene (6•5g., 24•8 m.moles), caesium fluoride (5g.) and sulpholan (60 mls.) were heated in a rotating nickel tube for 64 hours at 165°. The volatile products were transferred under vacuum to a cold trap, and examination by v.p.c. showed a multicomponent mixture. The mixture (5•0g.) was distilled under vacuum (0•02-0•03 mm.), and the products distilling up to 85° collected, leaving a solid (1•2g.) in the distillation flask. The solid was recrystallised from petroleum ether (40/60) and shown to be perfluoro-(4-isopropyl-2,6-dicyclohexylpyridine), m.pt. 120-122°. (Found: C, 28•4; F, 69•8%; M, 843. $C_{20}F_{31}N$ requires C, 28•5; F, 69•9%; M, 843). $\lambda_{max.}$ (cyclohexane) = 271, (ε = 4080). (I.R. Spectrum No.24).

The distillate mixture was then separated by prep. scale v.p.c. to give the following fractions (in order of increasing retention times):

(i) a colourless liquid which was shown to be a mixture of perfluoro-(1-cyclohexylcyclohexene) ($C_{12}F_{20}$) and perfluorobicyclohexenyl ($C_{12}F_{18}$) by mass spectrometry;

(ii) a small quantity of unchanged perfluoro-(4-isopropylpyridine) (identified by i.r. spectroscopy);

(iii) a colourless liquid (0•5g.) which was shown to be perfluoro-(2-cyclohexyl-4-isopropylpyridine), b.pt. 203°/760 mm. (Found: C, 28•6; F, 69•0%; M, 581. $C_{14}F_{21}N$ requires C, 28•9; F, 68•7%; M, 581). $\lambda_{max.}$ (cyclohexane) = 274, (ε = 5437). (I.R. Spectrum No.23).

The materials remaining after vacuum transfer were poured into a large volume of water and extracted with ether. The extracts were dried ($MgSO_4$), and removal of the solvent left a dark viscous residue, which was sublimed at 90-125°/0·01-0·03 mm. to give a yellow solid. This was recrystallised from petroleum ether (40/60) giving perfluoro-(4-isopropyl-2,6-dicyclohexylpyridine) (0·5g. - identified by i.r. spectroscopy).

The approximate yields of perfluoro-(2-cyclohexyl-4-isopropylpyridine) and perfluoro-(4-isopropyl-2,6-dicyclohexylpyridine) were 25% in each case (estimated from the chromatogram).

7.4.2 Reaction with perfluorocyclopentene

Perfluoro-(4-isopropylpyridine) (3·0g., 9·4 m.moles), perfluorocyclopentene (8·0g., 37·8 m.moles), caesium fluoride (5g.) and sulpholan (60 mls.) were heated in a rotating nickel tube for 24 hours at 150°. The volatile materials were transferred under vacuum to a cold trap, and examination of the products (8·1g.) by v.p.c. (column 'O' at 100°) showed the presence of two components. Separation by prep. scale v.p.c. (Aerograph: column 'A' at 100°) afforded two colourless liquids, which were identified as unreacted perfluoro-(4-isopropylpyridine) and perfluorocyclopentene dimer by i.r. spectroscopy. In the mass spectrum of the product mixture before separation there was a small peak at $^{M}/e$, 531 (corresponding to the monocyclopentyl-substituted isopropylpyridine).

Solvent extraction of the involatile materials gave a dark brown viscous liquid (2g.) but no further products were obtained on sublimation.

7.4.3 Reaction with perfluorocyclohexa-1,4-diene

Perfluoro-(4-isopropylpyridine) (3·2g., 10·1 m.moles), perfluorocyclohexa-1,4-diene (4·4g., 19·7 m.moles), caesium fluoride (3g.) and sulpholan (50 mls.) were heated in a rotating nickel tube for 24 hours at 130°. Work-up of the reaction mixture gave 85% recovery of perfluoro-(4-isopropylpyridine) (identified by i.r. spectroscopy).

CHAPTER 8

EXPERIMENTAL FOR CHAPTER 5

8.1 Fluoride Ion-initiated Reactions of Tetrafluoropyridazine and Perfluorocycloalkenes

8.1.1 Reactions involving perfluorocyclohexene

(a) Using 1 molecular proportion of perfluorocyclohexene

Two reactions were carried out in which equimolar quantities of tetrafluoropyridazine and perfluorocyclohexene were heated in the presence of caesium fluoride and sulpholan in a stainless steel autoclave (for quantities and reaction conditions, see Table 14).

The products were recovered by vacuum transfer from the autoclave into a cold trap. Examination by v.p.c. (column 'O' at 200°) showed that in reaction (i) a mixture of unchanged perfluorocyclohexene and tetrafluoropyridazine and a product of longer retention time was obtained. In the mass spectrum of this mixture there was a peak at $^{M}/e$, 414 which corresponds to the monosubstituted derivative of pyridazine. The material recovered from reaction (ii) was shown by v.p.c. to be one component (a colourless viscous liquid), and identified as perfluoro-(4-cyclohexylpyridazine), b.pt. 200°/760 mm. (Found: C, 29·1; F, 64·7%; M, 414. $C_{10}F_{14}N_2$ requires C, 29·0; F, 64·3%; M, 414). $\lambda_{max.}$ (cyclohexane) = 230 and 272, (ε = 7403 and 6963). (I.R. Spectrum No.25). Yield of product, 70% (100% conversion of tetrafluoropyridazine).

When reaction (ii) was repeated, the materials remaining after vacuum transfer of the volatile product were poured into water and extracted in the usual way with ether. In this way a yellow-brown solid (1·0g.) was recovered, and this was dissolved in hot benzene with a little ethanol added. On cooling, a pale brown solid crystallised out, and this was shown by i.r.

Table 14

Reaction	$C_4F_4N_2$	C_6F_{10}	CsF	Sulpholan	Temp. (°C)	Time	Wt. of products recovered
(i)	2·0g. (13·2 m.moles)	3·5g. (13·4 m.moles)	2g.	25 mls.	80	19 hours	4·3g.
(ii)	1·5g. (9·9 m.moles)	2·8g. (10·7 m.moles)	2g.	25 mls.	110	19 hours	2·8g.

spectroscopy to be the corresponding dicyclohexylpyridazone which was characterised fully in the following reaction.

(b) Using 2 molecular proportions of perfluorocyclohexene

Tetrafluoropyridazine (1·0g., 6·6 m.moles), perfluorocyclohexene (3·7g., 14·1 m.moles), caesium fluoride (2g.) and sulpholan (25 mls.) were introduced into a stainless-steel autoclave which was then shaken for 22 hours at 120°. The autoclave was opened and the volatile materials transferred under vacuum to a cold trap. The product mixture (1·8g.) was shown by v.p.c. to consist of unchanged C_6F_{10}, a trace amount of tetrafluoropyridazine, and the monosubstituted pyridazine (45% yield) (from retention times). The remaining materials were poured into water and extracted with ether, the extract dried ($MgSO_4$), and removal of the solvent left a brown solid (1·5g.). Sublimation of the solid at 200° and 0·005 mm. gave a yellow crystalline solid which melted at ca. 260°. No chromatographic analysis was possible, but, in the mass spectrum of the solid, molecular ion peaks were present at $^M/e$ = 676, 674 and 938 corresponding to the disubstututed pyridazine, its monohydroxy derivative, and the trisubstituted pyridazine respectively. The solid was dissolved in hot benzene (containing a little ethanol) and, on cooling, a pale yellow crystalline solid (0·2g.) was obtained. This was filtered from the mother liquid, dried by pumping under vacuum, and shown to be a,b-perfluorodicyclohexyl-c-fluoro-1H-pyridazin-d-one, m.pt. 302°. (Found: N, 4·00; H, 0·49; F, 65·1%; M, 674. $C_{16}HF_{23}N_2O$ requires N, 4·15; H, 0·15; F, 64·8%; M, 674). $\lambda_{max.}$ (ethanol) = 243 and 305 (broad), (ε = 8243 and 5707). (I.R. Spectrum No.30). Absorptions due to the $\rangle$C=O and $\rangle$N-H vibrations were present at 3·3 and 6·3μ respectively in the i.r.

spectrum of the solid, but a correct elemental analysis for carbon could not be obtained. Insufficient of this compound was obtained for n.m.r. studies.

8.1.2 Reaction with perfluorocyclohexa-1,4-diene

Tetrafluoropyridazine (2·0g., 13·2 m.moles), octafluorocyclohexa-1,4-diene (6·0g., 26·8 m.moles), caesium fluoride (2g.), and sulpholan (25 mls.) were shaken in a stainless-steel autoclave for 20 hours at 120°. Vacuum transfer of the materials from the tube at high temperature (105°) gave a mixture of sulpholan and a high melting solid. Water was then added to the mixture to dissolve the sulpholan and the product was extracted from the aqueous solution with ether. The extract was dried ($MgSO_4$), and removal of the solvent followed by pumping under vacuum left a brown 'crystalline' solid. Recrystallisation of the crude solid from ether/petroleum ether afforded a cream crystalline solid (0·5g.) which was identified as perfluoro-(dicyclohexenylpyridazine), m.pt. 152-154°. (Found: C, 31·9; F, 63·3%; M, 600. $C_{16}F_{20}N_2$ requires C, 32·0; F, 63·3%; M, 600). $\lambda_{max.}$ (ethanol) = 227·5, 259 (infl.) and 301 (broad), (ε = 4950, 3200 and 4709). (I.R. Spectrum No.27). For a discussion of the structure of this compound, see Chapter 10. Solvent extraction of the remaining materials of this reaction yielded a dark brown polymeric gum (4g.).

8.1.3 Reactions involving perfluorocyclobutene

(a) Tetrafluoropyridazine (2·0g., 13·2 m.moles), perfluorocyclobutene (5·0g., 30·9 m.moles), caesium fluoride (2g.) and sulpholan (20 mls.) were shaken in a stainless-steel autoclave at 130° for 19 hours. After cooling, the volatile products were transferred under vacuum to a cold trap, and examination of the mixture (3·5g.) by v.p.c. showed this to consist almost entirely of perfluorocyclobutene trimer and unchanged tetrafluoropyridazine.

Solvent extraction of the involatile products gave a dark brown gum (3g.).

(b) Reaction (a) was repeated by heating tetrafluoropyridazine (3·0g., 19·7 m.moles), perfluorocyclobutene (7·0g., 43·2 m.moles), caesium fluoride (3g.) and sulpholan (40 mls.) in a rotating nickel tube in an oil bath at 125° for 20 hours. The volatile products (4·4g.), removed by vacuum transfer, consisted mainly of perfluorocyclobutene trimer and unchanged tetrafluoropyridazine together with a small amount of a product of longer retention time.

8.2 Reactions of Perfluoro-(4-cyclohexylpyridazine)

8.2.1 Reaction with ammonia

5 mls. 0·880 ammonia was stirred in a small conical flask which was immersed in ice. Perfluoro-(4-cyclohexylpyridazine) (2·0g.) was added slowly to the ammonia solution. A yellow-brown solid was precipitated almost immediately, and this was filtered, washed with water, and recrystallised from aqueous ethanol to give a pale brown crystalline solid (1·5g.). This was identified as 4-perfluorocyclohexyl-5-amino-3,6-difluoropyridine, m.pt. 191° (Found: C, 29·6; H, 0·79; F, 60·5%; M, 411. $C_{10}H_2F_{13}N_3$ requires C, 29·2; H, 0·5; F, 60·1%; M, 411). $\lambda_{max.}$ (ethanol) = 241 and 286·5 (broad), (ε = 7911 and 6360). (I.R. Spectrum No.28). The yield of the amino-derivative was 75%.

8.2.2 Reaction with sulphuric acid

Perfluoro-(4-cyclohexylpyridazine) (0·5g.) in concentrated sulphuric acid (10 mls.) was treated dropwise with water (40 mls.) during 40 mins. with vigorous stirring; the addition was regulated to keep the temperature below 60°. The mixture was stirred for a further 2·5 hours at ca. 25° and then extracted with 2 x 50 ml. portions of ether. The extract was washed with saturated sodium sulphate solution and dried ($MgSO_4$), and removal of the solvent left a white powdery solid (0·50g.). This was recrystallised from benzene to give a white crystalline solid which was identified as 3,5-difluoro-4-perfluorocyclohexyl-1H-pyridazin-6-one, m.pt. 251° (d). (Found: C, 28·8; H, 0·34; F, 59·9%; M, 412. $C_{10}HF_{13}N_2O$ requires C, 29·1; H, 0·24; F, 60·0%; M, 412). $\lambda_{max.}$ (ethanol) = 241 and 276 (broad), (ε = 8900 and 5600). (I.R. Spectrum No.29). Yield of pyridazone 100%.

8.2.3 Photolysis of perfluoro-(4-cyclohexylpyridazine)

Perfluoro-(4-cyclohexylpyridazine) (0·6g.) was placed in a small silica tube and irradiated with u.v. light for 138 hours. The resulting brown liquid (0·4g.) was removed from the tube with a pipette and purified by vacuum distillation to give a colourless liquid. The product was shown to be pure by v.p.c. (column 'O' at 170°), having a shorter retention time than that of the starting material, and identified as perfluoro-(6-cyclohexylpyrazine), (Found: C, 28·7; F, 64·4%; M, 414. $C_{10}F_{14}N_2$ requires C, 29·0; F, 64·3%; M, 414). $\lambda_{max.}$ (ethanol) = 276, (ε = 7478). (I.R. Spectrum No.31). Yield of monosubstituted pyrazine, 70%. The structure was confirmed by ^{19}F n.m.r. spectroscopy.

8.2.4 Attempted pyrolysis of perfluoro-(4-cyclohexylpyridazine)

Three preliminary reactions were carried out at different temperatures in order to find an optimum temperature for the pyrolysis of perfluoro-(4-cyclohexylpyridazine). A small quantity of perfluoro-(4-cyclohexylpyridazine) was passed through a silica tube packed with silica wool using a steady flow of dry nitrogen and the products collected in a cold trap (for quantitites and conditions, see Table 15).

Table 15

Temp. (°C)	Wt. of $C_{10}F_{14}N_2$	N_2 flow (mls./min.)	Wt. of products	Composition of products (from analytical v.p.c.)
500°	0·5g.	100	0·2g.	(i) Unchanged $C_{10}F_{14}N_2$ + (ii) major product with slightly shorter retention time + (iii) minor component (low b.pt.)
600°	0·5g.	50	0·25g.	No unchanged $C_{10}F_{14}N_2$ + two components with shorter retention times + component (iii) as above
700°	0·5g.	100	0·15g.	No unchanged $C_{10}F_{14}N_2$ + two major components of shorter retention times

Perfluoro-(4-cyclohexylpyridazine) (3·1g.) was passed through the silica tube at 650° using a flow of nitrogen (50-100 mls./min.). The product, a brown liquid (1·4g.), was collected in a cold trap and shown by v.p.c. to consist of two components having slightly different retention times. Separation of the mixture by prep. scale v.p.c. (Aerograph: column 'O' at 120°) gave a colourless liquid, which was shown to be recovered perfluoro-(4-cyclohexylpyridazine) by i.r. spectroscopy, and a white crystalline solid, m.pt. 37-38°. I.r. and ^{19}F n.m.r. spectra of the solid were obtained but it decomposed to a brown liquid before elemental analysis and mass spectral data could be acquired. A small quantity of a colourless liquid was recovered after decomposition by vacuum distillation. (Found: M, 376. $C_{10}F_{12}N_2$

requires M, 376). $\lambda_{max.}$ (ethanol) = 242·5 and 292 (infl.), (ε = 5926 and 1995). The i.r., n.m.r. and mass spectral data obtained showed the product to be perfluoro-(4-cyclohexenylpyridazine). (I.R. Spectrum No.26).

CHAPTER 9

EXPERIMENTAL FOR CHAPTER 6

9.1 Defluorination Reactions

The standard procedure employed in these reactions was to pass the compound to be defluorinated through a silica tube (ca. 12" in length), containing a suitable defluorinating agent (coarse iron filings or zinc dust/ shavings were used in this work), by means of a steady flow of nitrogen and application of the requisite amount of heat to the compound. The defluorination tube was heated by a cylindrical heater and the products were collected in a cold trap. The average contact time was approx. 0·5 min.

9.1.1 Defluorination of perfluorocyclopentene dimer, $C_{10}F_{16}$

Perfluorocyclopentene dimer was passed in the vapour phase through a silica tube containing coarse iron filings. The reaction was carried out over a range of temperatures (see Table 16) and the products collected in a cold trap.

Table 16

Temp. °C	$C_{10}F_{16}$	Products
350°	2·0g.	1·3g. - approx. 60% conversion to $C_{10}F_{14}$
450°	1·3g.	0·8g. - 90% conversion to $C_{10}F_{14}$
500°	1·5g.	0·8g. - 100% conversion to $C_{10}F_{14}$

The product obtained was a colourless liquid corresponding to $C_{10}F_{14}$, and shown to be perfluorobicyclopentenyl, b.pt. 128°/760 mm. (Found: C, 30·9; F, 69·4%; M, 386. $C_{10}F_{14}$ requires C, 31·1; F, 68·9%; M, 386). $\lambda_{max.}$

(cyclohexane) = 222 and $\varepsilon_{max.}$ = 13,200 (u.v. spectroscopy). The yield of product at 500° was 60%. (I.R. Spectrum No.4).

9.1.2 Attempted defluorination of $C_{10}F_{16}$ over zinc

Perfluorocyclopentene dimer (1·0g.) was passed through a tube containing a mixture of zinc dust and shavings at 460°. No product was collected in the cold trap.

9.1.3 Attempted defluorination of perfluorobicyclopentenyl, $C_{10}F_{14}$

Perfluorobicyclopentenyl (0·8g.) was passed over coarse iron filings at 500° but the material recovered (0·6g.) was shown to be unchanged $C_{10}F_{14}$ by comparison of its i.r. spectrum.

9.1.4 Attempted defluorination of $C_{10}F_{14}$ over zinc

Perfluorobicyclopentenyl was passed through a tube packed with a mixture of zinc dust and shavings at various temperatures (see Table 17).

Table 17

Temp. °C	$C_{10}F_{14}$	Products
250°	1·0g.	0·8g. - unchanged starting material
300°	0·7g.	0·5g. - unchanged starting material
400°	0·8g.	Insufficient product for identification

The material recovered in each case was shown to be unchanged $C_{10}F_{14}$ by a comparison of its i.r. spectrum.

9.1.5 Defluorination of perfluoro-(1-cyclohexylcyclohexene), $C_{12}F_{20}$

Perfluorocyclohexene dimer (0•8g.) was passed over heated iron filings at 475° using a steady flow of nitrogen (50–60 mls./min.) and heating the sample to ca. 60°. The products (0•5g.) were collected in a cold trap, and shown by v.p.c. to consist of four major components, one having a fairly long retention time. The mass spectrum of the mixture (too small an amount for separation) indicated the presence of derivatives obtained by the successive defluorination of $C_{12}F_{20}$, giving 'molecular ion' peaks at $^{M}/e$ = 524 (some unchanged dimer), 486 ($C_{12}F_{18}$), 448 ($C_{12}F_{16}$), 410 ($C_{12}F_{14}$), and 334 ($C_{12}F_{10}$).

Reaction 9.1.5 was later repeated by passing 1•2g. $C_{12}F_{20}$ over iron filings at 500°, and a white crystalline solid (0•35g., v.p.c. pure) was collected, m.pt. 61-63°. This was shown by i.r. and mass spectroscopy to be decafluorobiphenyl, $C_{12}F_{10}$.

9.1.6 Attempted defluorination of perfluorocyclobutene trimer, $C_{12}F_{18}$

Perfluorocyclobutene trimer (2•5g.) was passed over iron at 450–475° and the products (1•7g.) examined by v.p.c. In addition to unchanged trimer (ca. 95% of the product mixture) trace amounts of other components were present, and 'molecular ion' peaks corresponding to defluorinated derivatives of $C_{12}F_{18}$ could be seen in the mass spectrum of the mixture, i.e. $^{M}/e$ = 448 ($C_{12}F_{16}$), 410 ($C_{12}F_{14}$), and 372 ($C_{12}F_{12}$).

9.2 Nucleophilic Substitution Reactions using Sodium Methoxide

9.2.1 Perfluorobicyclopentenyl, $C_{10}F_{14}$

(a) Reaction of $C_{10}F_{14}$ with 2 molecular proportions of methoxide ion

To a stirred solution of perfluorobicyclopentenyl (0•40g., 1•04 m.moles) in 25 mls. dry methanol at room temperature was added 25 mls. (2•5 m.moles) of a 0·1M solution of sodium methoxide over a period of 25 mins. The mixture was then stirred under reflux for a further 4 hours. After cooling, the solution was poured into water (500 mls.) and extracted with two portions of methylene chloride. The extracts were combined, dried ($MgSO_4$), and removal of the solvent left a pale yellow liquid (0·40g.) which solidified slowly on standing to give a white crystalline solid. This was shown to be <u>2,2'-dimethoxy-dodecafluorobicyclopentenyl</u>, m.pt. 52-53°. (Found: C, 35·4; H, 1·00; F, 55·1%; M, 410. $C_{12}H_6F_{12}O_2$ requires C, 35·1; H, 1·46; F, 55·6%; M, 410). Yield of dimethoxy derivative 95%. (I.R. Spectrum No.32).

(b) <u>Attempted preparation of the monomethoxy derivative of $C_{10}F_{14}$</u>

Two reactions were carried out using one molecular proportion of sodium methoxide solution (for quantities and reaction conditions, see Table 18). In each case the requisite amount of sodium methoxide solution was added to a stirred solution of the fluorocarbon in dry methanol.

<u>Table 18</u>

Reaction	$C_{10}F_{14}$	0·1M sodium methoxide solution (mls.)	Reaction conditions
(i)	0·47g. (1·22 m.moles) in 30 mls. methanol	10 (1·00 m.moles)	NaOMe solution added over a period of 20 mins. to stirred solution of $C_{10}F_{14}$ at room temp., and mixture stirred at room temp. for a further 90 mins.
(ii)	0·50g. (1·30 m.moles) in 30 mls. methanol	13 (1·30 m.moles)	NaOMe solution added over a period of 15 mins. to stirred solution of $C_{10}F_{14}$ at room temp., and mixture stirred under reflux for a further 75 mins.

After each reaction the methanol solution was poured into a large volume of water and extracted with methylene chloride in the usual way.

In reaction (i), 0·5g. pale yellow liquid was recovered and shown by analytical v.p.c. (column 'O' at 150°) to consist of the mono- and di-methoxy derivatives in approx. ratio 40:60 respectively with a trace of unreacted $C_{10}F_{14}$.

In reaction (ii), 0·5g. pale yellow liquid was recovered and this was shown by v.p.c. to be mainly the dimethoxy derivative (ca. 80% of the total area of the chromatogram) with small amounts of the monomethoxy compound and unreacted $C_{10}F_{14}$. On cooling, solidification occurred and it was possible to extract a white crystalline solid. This was confirmed as the dimethoxy derivative by i.r. and mass spectrometry.

9.3 Fluoride Ion-initiated Reaction of Perfluorobicyclopentenyl with Hexafluoropropene

Caesium fluoride (1g., 6·6 m.moles) and sulpholan (15 mls.) were introduced under dry nitrogen into a 50 ml. flask fitted with a water condenser. The flask was then evacuated at room temperature. When degassing of the solvent had ceased, hexafluoropropene was allowed into the system until atmospheric pressure was reached and a bladder attached to the top of the water condenser was partially inflated. Perfluorobicyclopentenyl (1·2g., 3·11 m.moles) was introduced into the flask from a pipette when the reaction mixture had reached the reaction temperature (100°). The mixture was then heated with stirring at this temperature, under an atmosphere of hexafluoropropene, for 4½ hours.

After this time the reservoir of hexafluoropropene had collapsed and a partial vacuum was indicated in the system. The volatile materials (0·7g.)

were then transferred under vacuum to a cold trap. Analytical v.p.c. showed these to consist of hexafluoropropene dimers and trimers (ca. 90%), a trace of perfluorobicyclopentenyl, and a product of longer retention time (ca. 10%).

The remaining materials were extracted from water (150 mls.) with 3 x 50 ml. portions of ether. The extracts were dried ($MgSO_4$) and removal of the solvent left a yellow-orange solid. This was sublimed at 0·05 mm. and 50° to give a white solid (0·75g.), which was then recrystallised from ether/petroleum ether giving white needle-shaped crystals. The compound was identified as perfluoro(2,2'-di-isopropylbicyclopentenyl), m.pt. 54-55°. (Found: C, 27·8; F, 71·7%; M, 686. $C_{16}F_{26}$ requires C, 28·0; F, 72·0%; M, 686). (I.R. Spectrum No.33). Yield of $C_{16}F_{26}$ was 35% (based on quantitative conversion of perfluorobicyclopentenyl).

The preparation of a further quantity of perfluoro-(2,2'-di-isopropylbicyclopentenyl) in a subsequent experiment showed that the product with a longer retention time in the mixture of volatile products was perfluoro-(2,2'-di-isopropylbicyclopentenyl).

9.3.1 Attempted defluorination of perfluoro-(2,2'-di-isopropylbicyclopentenyl).

Perfluoro-(2,2'-di-isopropylbicyclopentenyl) (0·4g.) was passed over iron filings heated to 480° in a silica tube. A white solid (0·1g.) was collected in a cold trap after 2 hours, and this was shown to be pure by v.p.c. (column 'O' at 125°). The i.r. spectrum of the product was identical to that of the starting material.

9.4 Oxidation of Perfluorocyclopentene Dimer, $C_{10}F_{16}$

Potassium permanganate (0·5g., 3·2 m.moles) and dry ($MgSO_4$) acetone (200 mls.) were placed in a 500 ml. 3-necked flask fitted with a stirrer, water condenser, and small dropping funnel. The $KMnO_4$/acetone solution was stirred vigorously and the $C_{10}F_{16}$ (1·2g., 2·8 m.moles) was added to the stirred solution over a period of 30 mins. No initial exothermic reaction was apparent but the solution turned brown. The mixture was stirred at room temperature for a further 18 hours, 200 mls. distilled water added, and the mixture stirred. Sulphur dioxide was then passed through the solution until it was decolourised, and the acetone removed under reduced pressure. The remaining aqueous solution was extracted with two portions of ether, the extracts dried ($MgSO_4$), and removal of the solvent left a pale yellow liquid which solidified on standing (0·8g.). This was sublimed to give a white crystalline solid, which was identified as 1,1'-dihydroxy-hexadecafluorobicyclopentyl, m.pt. 62-64°. (Found: C, 26·4; H, 0·65; F, 66·2%. $C_{10}H_2F_{16}O_2$ requires C, 26·2; H, 0·44; F, 66·4%). Yield of dihydroxy derivative 67%. (I.R. Spectrum No.34).

9.5 Hydrolysis of Perfluorobicyclopentenyl Derivatives

9.5.1 Reaction of perfluorobicyclopentenyl with concentrated sulphuric acid

Perfluorobicyclopentenyl (1·0g., 2·6 m.moles) and concentrated sulphuric acid (5 mls.) were introduced into a small bore Carius tube which was then sealed and rotated in an oil bath at 100° for 18 hours. The tube was then opened and the contents poured into ice/water, allowed to reach room temperature, and the aqueous solution extracted with two portions of ether. The extracts were dried ($MgSO_4$) and removal of the solvent left a pale orange liquid (1•1g.) which was shown to be mainly starting material by analytical v.p.c. (column 'O' at 125°). Unchanged starting material was transferred under vacuum to another flask leaving a white solid (0•3g.) which was then purified by sublimation at 0•4 mm. and 100°, and identified as the diketo-derivative of perfluorobicyclopentenyl, m.pt. 120-122°. (Found: C, 34•8; F, 56•0%; M, 342. $C_{10}F_{10}O_2$ requires C, 35•1; F, 55•6%; M, 342). Although the correct elemental analysis was obtained for this compound there was also a fairly intense molecular ion peak at $^M/e$ = 362 ($C_{10}F_{11}O_2H$) in the mass spectrum of the solid. Yield of $C_{10}F_{10}O_2$ = 35%.

9.5.2 Reaction of 2,2'-dimethoxy-dodecafluorobicyclopentenyl with concentrated sulphuric acid

2,2'-Dimethoxy-dodecafluorobicyclopentenyl (0•2g., 0•5 m.moles) and concentrated sulphuric acid (5 mls.) were introduced into a Carius tube and heated at 100° for 18 hours (as in 9.5.1). After cooling, the tube was opened and the contents poured into ice/water and allowed to reach room temperature. The aqueous solution was then extracted with two portions of ether, the extracts dried ($MgSO_4$), and removal of the solvent left a cream solid which was sublimed at 0•02 mm. and 60° to give a white crystalline solid (0•15g.), m.pt. 178-180°. There was an intense molecular ion peak at $^M/e$ = 338 in the mass spectrum, corresponding to $C_{10}F_8O_2(OH)_2$, the diketo-dihydroxy derivative of perfluorobicyclopentenyl. A strong carbonyl absorption was present at 6•35μ in the i.r. spectrum of this solid, but there was no significant absorption in the 2•0-5•0μ region corresponding to $-OCH_3$.

9.6 Photolytic Reactions

9.6.1 Perfluorocyclopentene dimer, $C_{10}F_{16}$

$C_{10}F_{14}$ (1·0g.) was placed in a small bore silica tube and a trace of benzophenone was added as photosensitiser. The tube was sealed and irradiated under a u.v. lamp for 113 hours, after which time the tube was cooled, opened, and the products transferred under vacuum to a cold trap. A colourless liquid (0·6g.) was obtained and shown to be unchanged $C_{10}F_{14}$ by v.p.c. and i.r. spectroscopy.

9.6.2 Perfluorobicyclopentenyl, $C_{10}F_{14}$

Three reactions were carried out in small bore silica tubes which were irradiated under a u.v. lamp (for quantities and reaction times, see Table 19).

Table 19

Reaction	$C_{10}F_{14}$	Benzophenone	Time of irradiation with u.v. light
(i)	1·0g.	None	18 hours
(ii)	1·0g.	Trace	14·5 hours
(iii)	1·0g.	Trace	290 hours

It was shown by v.p.c. and i.r. spectroscopy that, in all three reactions, the material recovered was unchanged $C_{10}F_{14}$.

9.6.3 Perfluorocyclobutene trimer, $C_{12}F_{18}$

0·5g. perfluorocyclobutene trimer was irradiated with u.v. light for 100 hours in a silica tube. The product was shown to be unchanged trimer by i.r. spectroscopy.

9.6.4 Perfluoro-(1-cyclohexylcyclohexene), $C_{12}F_{20}$

$C_{12}F_{20}$ (0·8g.) was introduced into a small silica tube which was then sealed under vacuum and placed under a u.v. lamp for 102 hours. The tube was then cooled (liquid air), opened, and the products (0·6g.) transferred under vacuum to a cold trap. The product was pure (v.p.c.) and the i.r. spectrum was identical to that of perfluoro-(1-cyclohexylcyclohexene), the starting material.

9.7 Attempted Diels-Alder Reactions with $C_{10}F_{14}$ (perfluorobicyclopentenyl)

9.7.1 Using trifluoromethylacetylene

Perfluorobicyclopentenyl (0·9g., 2·33 m.moles) was introduced into a Carius tube and a few drops of dipentene (radical inhibitor) added. Trifluoromethylacetylene (0·5g., 5·3 m.moles) was condensed into the tube which was then evacuated, sealed, and heated for 15 hours at 205°. The tube was cooled, opened, and the excess acetylene allowed to expand into a large glass bulb. The remaining material in the tube was then transferred under vacuum to a cold trap leaving some dark 'tarry' material behind. Analytical v.p.c. (column 'A' at 100°) showed the product (0·5g.) to be one compound, which was identified as unchanged $C_{10}F_{14}$ by i.r. spectroscopy.

9.7.2 Using ethylene

Perfluorobicyclopentenyl (1·0g., 2·6 m.moles) was introduced into a large Carius tube. Ethylene (0·4g.) was condensed into a cold finger and then allowed to expand into an evacuated 500 ml. flask. The pressure of this weight of ethylene was recorded, and then the gas was allowed to condense into the cooled, evacuated Carius tube until the pressure in the flask decreased to the level corresponding to the introduction of 0·1g. (3·57 m.moles) ethylene. The tube was then sealed and heated at 200° for 21 hours. After this time, the tube was cooled and the unchanged ethylene was allowed to expand into the flask. The pressure recorded indicated ca. 92% recovery of ethylene. The liquid remaining in the tube (0·9g.) was removed, and v.p.c. and i.r. spectroscopy showed this to be unchanged $C_{10}F_{14}$.

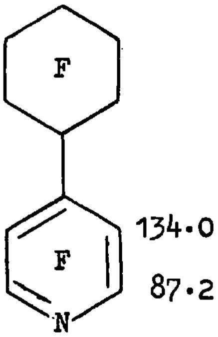
CHAPTER 10

NUCLEAR MAGNETIC RESONANCE DATA

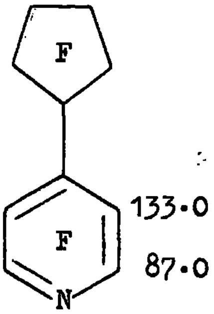
10.1 Perfluorocycloalkylpyridines and Their Derivatives

10.1.1 Perfluoro-monocycloalkylated pyridines

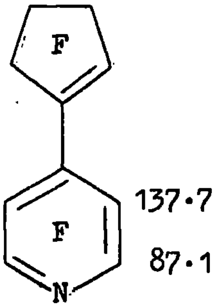
On introducing a perfluorocycloalkyl group into pentafluoropyridine the resulting ^{19}F n.m.r. spectra became complex but it was possible to assign the shifts due to the pyridine ring fluorine atoms (see below).



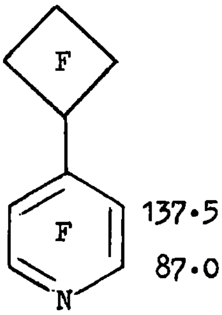
(XI)



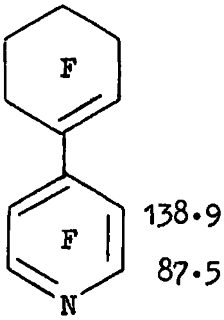
(XIV)



(XV)



(XVI)

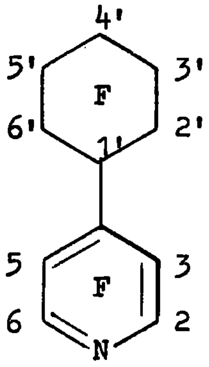
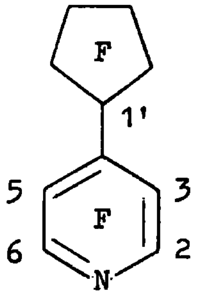
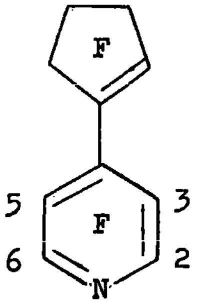


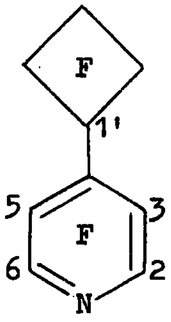
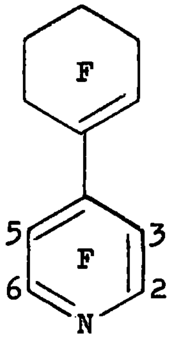
(XVIII)

The orientation of substitution in perfluoro-(4-cyclohexylpyridine) (XI) was confirmed using double resonance techniques,[146] and the assignments in (XI) were made by comparison with the spectra of perfluoro-(4-isopropylpyridine) and perfluoromethylcyclohexane. From the n.m.r. spectra of the other cycloalkylated pyridines the shifts due to the ring fluorine atoms (2,6) were easily assigned, but those due to the (3,5) fluorine atoms were more difficult to establish. The chemical shifts of the perfluoro-monocycloalkylated pyridines are given in Table 20.

Table 20

^{19}F n.m.r. spectra of perfluoro-monocycloalkylated pyridines

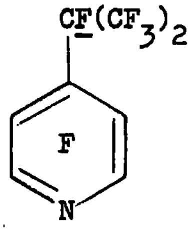
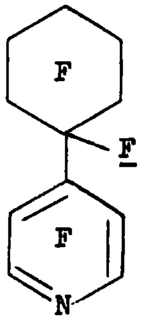
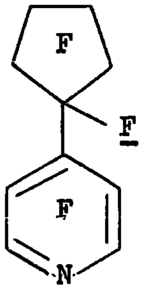
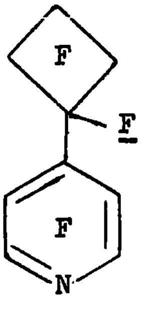
Compound	Chemical shift (p.p.m.)	Assignment (where possible)
 (XI) (in benzene)	87·2 134·0 180·8 119·0 113·7 124·1 128·6 123·7 128·6 135·7 140·7 119·7 124·6 139·6 144·6	F(2,6) F(3,5) F(1') Fa(2',6') Fe(2',6') Fa(3',5') Fe(3',5') Fa(4') Fe(4')
 (XIV)	87·0 116·2 121·1 127·7 128·9 130·2 131·2-134·8 167·9	F(2,6) F(3,5) F(1')
 (XV)	87·1 107·8 116·1 120·3 131·2 137·7	F(2,6) F(3,5)

Compound	Chemical shift (p.p.m.)	Assignment (where possible)
 (XVI)	87·0 125·2 125·7 129·4 129·7 130·9 132·3 132·5 135·2 136·3 137·5 167·1	F(2,6) F(3,5) F(1')
 (XVIII)	87·5 108·9 113·5 119·8 120·2 134·3 138·9	F(2,6) F(3,5)

The above spectra were recorded as solutions in CCl_4 except where stated

The position of the double bond in the cycloalkenyl ring of (XV) and (XVIII) was shown by the absence of an absorption in the n.m.r. spectrum due to a tertiary fluorine atom in these substituents. A signal at high field in (XIV) and (XVI) was assigned to this fluorine atom by comparison with perfluoro-(4-cyclohexylpyridine) (XI) and perfluoro-(4-isopropylpyridine) (see Table 21).

Table 21

Compound	Chemical shift of F(1') (p.p.m.)
	176·3
 (XI)	180·8
 (XIV)	167·9
 (XVI)	167·1

The substituent chemical shifts for the perfluorocycloalkyl groups are comparable with those for the perfluoroisopropyl group (see Table 22).

Table 22

Substituent	Effect of substituent in 4-position of C_5F_5N on neighbouring fluorine atoms (p.p.m.)	
	F(6)	F(3)
perfluoroisopropyl	-0·5	-26·1
perfluorocyclohexyl-	-0·7	-28·4
perfluorocyclopentyl-	-0·9	-29·4
perfluorocyclopentenyl-	-0·8	-24·7
perfluorocyclobutyl-	-0·9	-24·9
perfluorocyclohexenyl-	-0·4	-23·5

Perfluoro-(4-cyclohexylpyridine) (XI) can be considered as a substituted cyclohexane, and in the perfluorocyclohexanes monosubstitution usually results in the substituted molecule existing in a preferred 'chair' conformation at room temperature[147] with the substituent occupying an equatorial position. A 'fixed' conformer of this type would give three different pairs of non-equivalent geminal fluorine nuclei. Also, the two fluorine atoms on each carbon are themselves non-equivalent because they occupy equatorial and axial positions. The n.m.r. spectra of perfluoro-(4-cyclohexylpyridine) (XI) and perfluoromethylcyclohexane are closely similar, differing only in the resonances due to the perfluoromethyl and tetrafluoropyridyl substituents.

Variable temperature ^{19}F n.m.r. studies on perfluoroalkylpyridines led to the identification of rotational isomers,[127,148,149] for example, at room temperature the spectra of perfluoroisopropylpyridines exhibit broad resonances but the spectra are very temperature dependent, and at approximately -40° quite sharp lines are obtained. Using a variable temperature probe, spectra of perfluoro-(4-cyclohexylpyridine) (XI) were obtained over the temperature range -10° to $+140^{\circ}$ and the signals due to the F(3,5) and F(1'), in particular, observed. There was no significant change in the spectrum on varying the temperature, but a slight uniform variation in the chemical shifts was observed (see Table 23).

Table 23

Chemical shifts of perfluoro-(4-cyclohexylpyridine) in p.p.m.

Temp.	F(2,6)	F(3,5)	F(1')
-10°	90·4	135·4	182·8
0°	90·5	135·6	182·8
40°	90·3	135·4	182·0
80°	90·2	135·2	181·3
120°	89·8	134·6	180·5
140°	88·8	133·9	178·8

Acetone was employed as the solvent for the low temperature spectra, but spectra at temperatures lower than -10° could not be obtained due to the compound solidifying in the solvent.

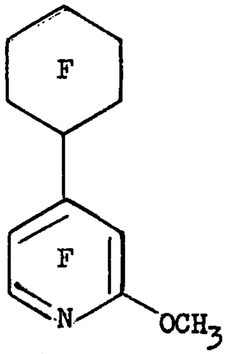
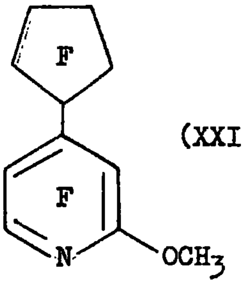
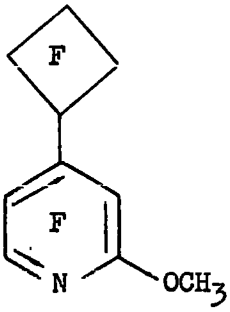
Variable temperature spectra over a similar range were also recorded for perfluoro-(4-cyclopentylpyridine) (XIV) and perfluoro-(4-cyclobutylpyridine) (XVI), but there was no significant variation with temperature in both cases.

10.1.2 Methoxy derivatives of perfluorocycloalkylpyridines

The chemical shifts of the monomethoxy derivatives of perfluoro-(4-

cyclohexyl), -(4-cyclopentyl), and -(4-cyclobutyl) pyridines are given in Table 24. The spectra were recorded as solutions in CCl_4.

Table 24

Compound	Chemical shift (p.p.m.)	Assignment (where possible)
 (XX) ^1H: -4·03 p.p.m.	90·7	F(6)
	115·5	
	120·4	
	121·3	
	124·5	
	125·2	
	126·2	
	130·2	
	134·3	F(3)
	136·8	
	140·3	
	141·7	
	145·3	
	146·7	F(5)
 (XXIII) ^1H: -4·07 p.p.m.	91·3	F(6)
	116·6	
	121·5	
	128·2	
	129·1	
	130·5	
	132·8	F(3)
	145·5	F(5)
 (XXIV) ^1H: -4·08 p.p.m.	91·1	F(6)
	124·6	
	125·1	
	129·7	
	130·0	
	131·3	
	131·7	
	133·9	
	134·8	
	136·2	F(3)
	149·2	F(5)
	167·2	F(1')

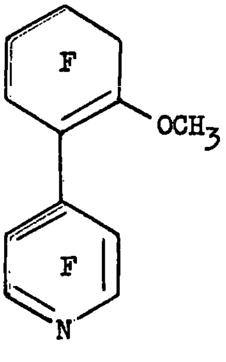
Substitution of the methoxy group in the 2-position was clearly shown by the good agreement between the observed and calculated substituent chemical shifts. The effect of introducing a methoxyl group at C-2 on the 3-, 5- and 6-fluorine chemical shifts has been determined[77] for tetrafluoro-2-methoxypyridine as being 0, +11, and +4 p.p.m. respectively. The shifts arising from the ring fluorines in (XX), (XXIII), and (XXIV) were compared with the calculated values for the introduction of a methoxy group at C-2 in (XI), (XIV), and (XVI), using the ortho-, meta-, and para- effects for a C-2 methoxyl group mentioned above. The results are given in Table 25.

Table 25

Chemical shifts of ring fluorines in p.p.m. (ref. $CFCl_3$)

		3-	5-	6-
(XX)	Observed	134·3	145·3	90·7
	Calculated	134·7	145·7	90·9
(XXIII)	Observed	132·8	145·5	91·3
	Calculated	133·0	144·0	91·0
(XXIV)	Observed	136·2	149·2	91·1
	Calculated	137·5	148·5	91·0

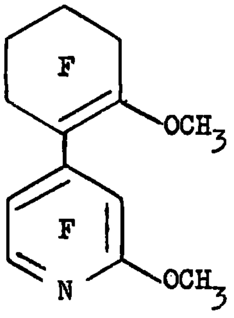
10.1.3 Methoxy derivatives of perfluoro-(4-cyclohexenylpyridine)



(XXV)

Chemical shift (p.p.m.)	Assignment
89·1	F(2,6)
139·0	F(3,5)

The chemical shifts of the F(2,6) and F(3,5) were essentially unchanged by the introduction of a methoxy group into perfluoro-(4-cyclohexenylpyridine) (XVIII), whereas the resonance due to the F(6) in the 2-methoxy derivatives of (XI), (XIV) and (XVI) was an overlapping doublet of doublets (J_{FF} = 21 and 30 c.p.s.). Also the proton n.m.r. consisted of a doublet (J_{HF} = 3 c.p.s.) centred at -3·75 (downfield from $(CH_3)_4Si$), the corresponding signal in the other 2-methoxy-4-perfluorocycloalkylpyridines occurring at 4·0. The ^1H n.m.r. spectrum of nonafluoro-1-methoxy-cyclohexene consisted of a doublet (J_{HF} = 4 c.p.s.) centred at 3·8.[38]



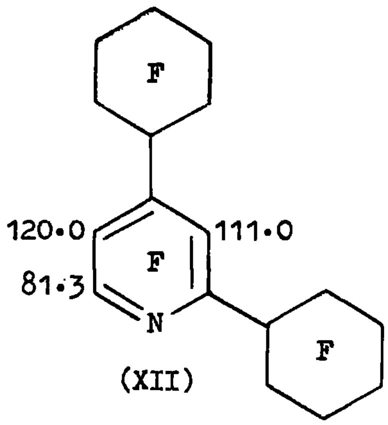
(XXVI)

Chemical shift (p.p.m.)	Assignment
91·0	F(6)
140·2	F(3)

The ^1H n.m.r. spectrum consisted of a doublet centred at -3·70 and a singlet at -3·97 (downfield from $(CH_3)_4Si$), indicating the existence of the two methoxy groups in different environments.

10.1.4 Perfluoro-(2,4-dicyclohexylpyridine)

A methoxy group was shown to substitute in the 2-position of perfluoro-(4-cyclohexylpyridine) (XI), and on this basis the second cyclohexyl group in (XII) must enter at C-2 since entry ortho to the 4-substituent would be even less likely than with a methoxy group, for steric reasons.



(XII)

The assignments in (XII) are supported by the substituent chemical shifts which are comparable with those for perfluoro-(2,4-di-isopropylpyridine) (see Table 26).

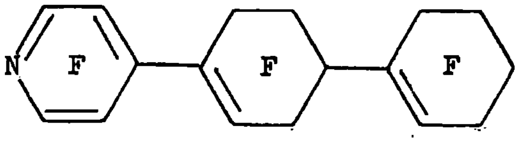
Table 26

Substituent	Effect of the 2-substituent on neighbouring F atoms (p.p.m.)		
	3-	5-	6-
perfluoroisopropyl- *	-22·8	-12·4	-5·4 [72]
perfluorocyclohexyl- **	-22·6	-14·0	-5·9

* the 4-substituent is perfluoroisopropyl

** the 4-substituent is perfluorocyclohexyl

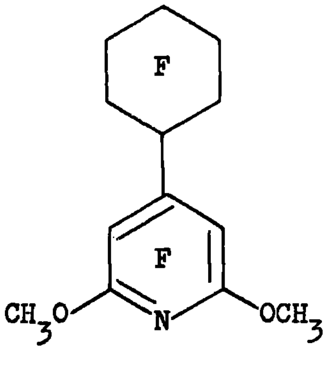
The product (XIX) obtained from the reaction of pentafluoropyridine with perfluorocyclohexa-1,4-diene (IV) corresponded to a disubstituted compound, $C_{17}F_{21}N$. The ^{19}F n.m.r. spectrum, however, was very complex, but it was easy to assign a low field signal at 86·8 p.p.m. (ref. $CFCl_3$) to the F(2) or F(2,6) of the pyridine ring. From a consideration of the substituent chemical shifts, this is more likely to be due to the F(2,6), and that (XIX) is not a disubstituted compound. The signal at 133·8 was assigned to the F(3,5) of the pyridine ring. It is possible, therefore that (XIX) has the following structure,



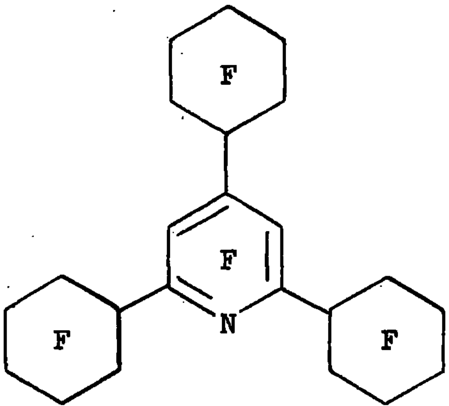
(XIX)

The absence of an absorption due to a tertiary fluorine in the cycloalkenyl ring(s) is in accord with the above structure.

10.1.5 Tri-substituted pyridine derivatives



(XXI)

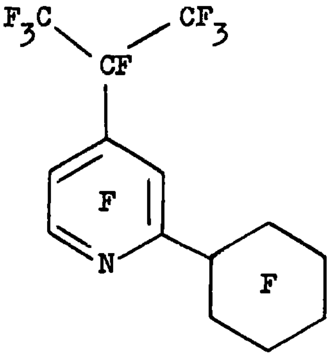


(XIII)

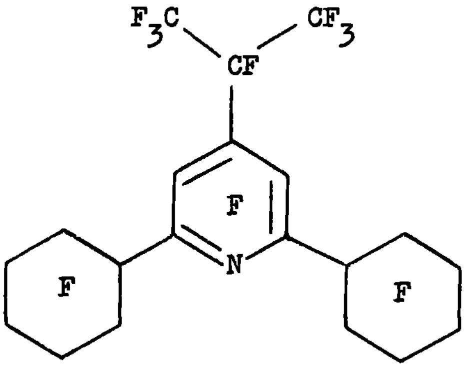
^{1}H n.m.r.
(ref. $(CH_3)_4Si$): Singlet at -4·02 p.p.m.

The above structures are in accord with the absence of a signal due to the F(6) of the pyridine ring in both spectra.

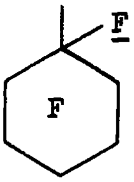
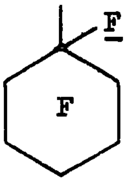
10.1.6 Perfluorocyclohexyl derivatives of perfluoro-(4-isopropylpyridine)



(XXVII)

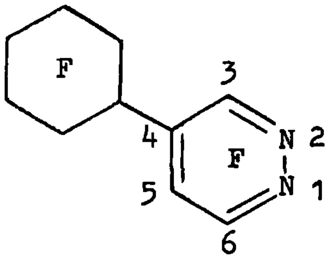


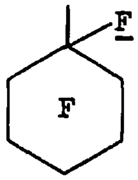
(XXVIII)

Chemical shift (ref.$CFCl_3$) p.p.m.	Assignment	Chemical shift (ref.$CFCl_3$) p.p.m.	Assignment
71·7	$-CF(C\underline{F}_3)_2$	74·5	$-CF(C\underline{F}_3)_2$
81·8	F(6)		
113·0	F(3)	182·1	
119·0	F(5)		
179·8	$-C\underline{F}(CF_3)_2$		
182·5			

The effect of a perfluorocyclohexyl group in the 2-position of perfluoro-(4-isopropylpyridine) on the neighbouring fluorines (substituent chemical shift) is -21·5 (3), -15·4 (5), and -4·9 (6). There was no signal due to the F(6) in the spectrum of (XXVIII), which confirms that the second perfluorocyclohexyl group is substituted at this position.

10.2 Perfluorocycloalkylpyridazines and Their Derivatives

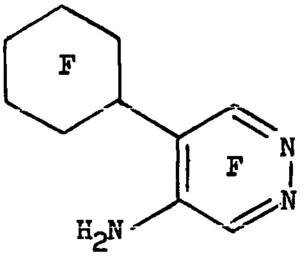


Chemical shift (ref.$CFCl_3$) p.p.m.	Assignment
74·7	F(6)
98·2 (doublet of doublets, J_{FF} = 24 and 33 c.p.s.)	F(3)
114·3	F(5)
182·3	

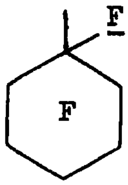
The substituent chemical shifts for the perfluorocyclohexyl and perfluoroisopropyl groups (relative to tetrafluoropyridazine^{109}) are given in Table 27.

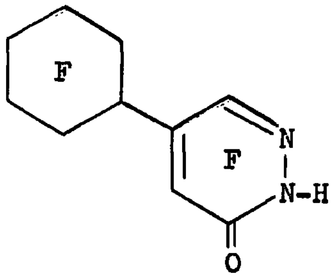
Table 27

Substituent	Effect of substituent in 4-position of tetrafluoropyridazine on neighbouring fluorine atoms (p.p.m.)			
	F(3)	F(5)	F(6)	
perfluoroisopropyl-	+3·2	-29·3	-23·0	82
perfluorocyclohexyl-	+7·6	-29·9	-15·9	

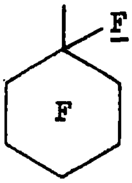


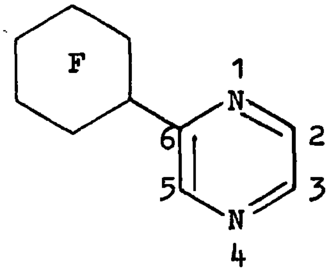
(XXXI)

Chemical shift (ref.$CFCl_3$) p.p.m.	Assignment
73·3	F(6)
96·1 (doublet, J_{FF} = 31 c.p.s.)	
180·5	

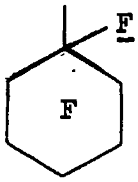


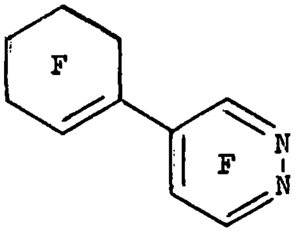
(XXXII)

Chemical shift (ref.$CFCl_3$) p.p.m.	Assignment
95·8 (doublet, J_{FF} = 19 c.p.s.)	F(3)
111·8	F(5)
179·3	



(XXXV)

Chemical shift (ref.$CFCl_3$) p.p.m.	Assignment
76·4	F(5)
83·5 (doublet, J_{FF} = 19 c.p.s.)	F(2)
93·4 (doublet of doublets, J_{FF} = 20 c.p.s.)	F(3)
184·6	



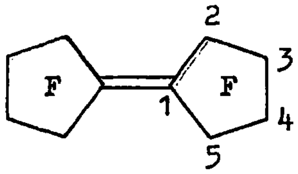
(XXXIII)

Intensity	Chemical shift (ref.$CFCl_3$) p.p.m.	Assignment
1	78·2	F(6)
1	96·3 (doublet of doublets, J_{FF} = 26 and 32 c.p.s.)	F(3)
2	107·8	
1	109·8	
1	117·5	F(5)
2	119·4	
4	133·8	

There was no signal due to a tertiary F atom in the spectrum of (XXXIII).

The n.m.r. spectrum of the product corresponding to perfluoro-(dicyclohexenylpyridazine), $C_{16}F_{20}N_2$ (XXXIV), contained resonances at 79·8 and 93·4 p.p.m. which could be assigned to the F(6) and F(3) atoms respectively, but the spectrum was too complex to determine the presence or not of a signal due to the F(5) atom. Thus it was not possible to determine whether (XXXIV) was a disubstituted compound or possessed a structure analogous to $C_{17}F_{21}N$ (XIX) in the pyridine series.

10.3 Oligomers of Perfluorocycloalkenes and Their Derivatives

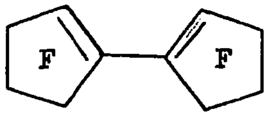


(VIII)

(neat liquid)

Two singlets of equal intensity:-

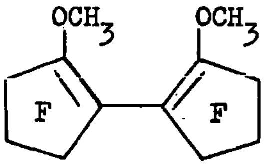
110·1 p.p.m.	F(2,5)
136·1 p.p.m.	F(3,4)



(IX)

(neat liquid)

Chemical shift p.p.m.	Relative intensity	Appearance
109·9	4	Triplet (J_{FF} = 15 c.p.s.)
113·2	2	Pentet of doublets (J_{FF} = 3·5 and 14 c.p.s.)
122·1	4	Doublet (J_{FF} = 7 c.p.s.)
132·8	4	Unresolved multiplet



(XXXVI)

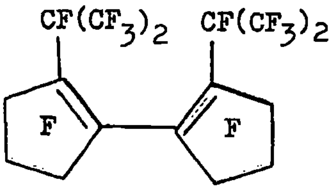
(in CCl_4)

Three broad singlets of equal intensity:-

107·2 p.p.m.

116·3 p.p.m.

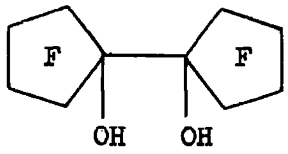
131·9 p.p.m.



(XXXVII)

(neat liquid at 90°)

Chemical shift p.p.m.	Assignment	Appearance
75·1	$-CF(C\underline{F}_3)_2$	Broad unresolved doublet
105·7		Doublet (J_{FF} = 16 c.p.s.)
107·4		Unsymmetrical triplet
110·6		Doublet (J_{FF} = 16 c.p.s.)
112·3		Unsymmetrical triplet
114·3		Doublet (J_{FF} = 20 c.p.s.)
115·2		
119·2		Doublet (J_{FF} = 20 c.p.s.)
119·9		
136·6		Quartet (J_{FF} = 6 c.p.s.)
137·3		Octet (J_{FF} = 2·5 c.p.s.)
176·1	$-C\underline{F}(CF_3)_2$	Broad singlet

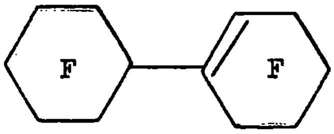


(XXXVIII)

(in CCl_4)

Contained 8 resonances with the following chemical shifts:-

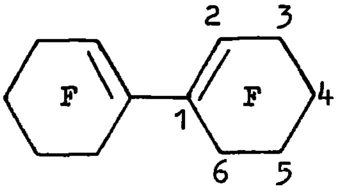
114·7, 118·4, 119·2, 122·8, 128·2, 130·2, 132·5 and 134·8 p.p.m.



(VI)

(in ether)

Spectrum complex but typical of a substituted cyclohexane system. The signal at 181·9 was assigned to the tertiary fluorine atom, and the remaining resonances had the following chemical shifts:- 98·3, 105·6, 113·1, 114·5, 118·6, 120·0, 123·7, 125·4, 128·2, 133·6, 135·8, 140·0, 141·1 and 144·7 p.p.m.



(VII)

(in ether)

Chemical shift (p.p.m.)	Relative intensity	Assignment
110·7	4	F(2)
113·2	2	
122·2	4	
136·2	8	

(X)

(neat liquid)

Chemical shift (p.p.m.)	Relative intensity
91·8	1
111·8	2
114·7	2
117·0	2
121·0	2
122·3	4
127·9	2
129·1	1
129·7	1
173·0	1

CHAPTER 11

MASS SPECTROMETRIC STUDIES ON PERFLUOROCYCLOALKENES AND PERFLUOROALKYLPYRIDINES

Introduction

The mass spectrum of an organic molecule is obtained by bombarding the compound under investigation with a beam of electrons of medium energy in a high vacuum. The ions produced are separated into a spectrum according to their mass to charge ratio ($^m/e$) and the relative abundance of each ion species is recorded by the mass spectrometer.

By using a high resolution mass spectrometer, it is possible to separate the positive ions corresponding to CO, H_2CN, $CH_2{=}CH_2$ and N_2, for example, all of which have the same integral mass (28), but whose exact masses are different. Hence these instruments can provide the exact elemental analysis of every ion in the spectrum, and this data can be of vital importance in structural analysis.

When a gaseous organic molecule, for example ABC, is bombarded with electrons, the following interactions may occur:

$$ABC + e \longrightarrow ABC^{+} + 2e$$

$$ABC^{+} \longrightarrow \begin{cases} AB^{+} + C \\ BC^{+} + A \\ A^{+} + BC \quad \text{etc.} \end{cases}$$

and a fragmentation pattern is produced which is characteristic of the compound being studied. Such ionisations only occur if the electron beam energy (normally 70eV) is equal to, or higher than, the ionisation potential of the particular molecule. The pattern will contain all possible combinations of atoms A, B and C, including ions of the type AC^{+}, formed by decomposition of the molecular ion and subsequent rearrangement processes.

Rearrangement processes yield ions corresponding to groups not present as such in the molecule, and it is the presence of these ions which produces difficulties when correlating the mass spectrum of a compound with its structure.

Although a great deal of information has been obtained from the mass spectra of hydrogen-containing organic molecules, enabling structural determination, little has been done to date on the mass spectrometry of highly fluorinated organic compounds. The early work in this field has been reported in a review by Majer.[150]

11.1 Experimental

Spectra were recorded on an A.E.I. M.S.9 double focussing mass spectrometer, and ions were produced under the following conditions:

Ionising electron beam voltage = 70eV.
Trap current (i.e. electron beam voltage) = 10 µamps.
Ion repeller voltage = -2 to +4 volts.
Source temperature = 190^{o} to 210^{o}.

Spectra for abundance measurements were recorded using a resolution of 1 part in 1,000 and a source pressure not so high that sparking of the high voltage employed in the source occurred.

11.1.1 Presentation of data

Mass spectral data are frequently presented in tabular form, listing the mass number of the peaks and their intensities. The latter are expressed in relation to the most intense peak of the spectrum (often referred to as the 'base peak'), which is assigned an arbitrary value of 100. For the comparison of individual spectra, the relationship between the intensity of the given peak and the total intensity of the spectrum, i.e. the sum of the intensities of all the peaks, is important. The intensity of a peak, in per cent of the 'total ionisation' (Σ), then indicates the extent to which the initially formed molecular ions decompose to this fragment ion. For any comparisons one has to ensure that the mass range over which the peak intensities were summed is the same for all compounds to be compared. The lowest mass of this range is thus indicated as a subscript, e.g. Σ_{31} signifies the sum of the intensities of all peaks from $^{m}/e$ 31 to the molecular weight (or peak of highest mass in the spectrum). The metastable ions are listed in a separate table.

11.1.2 Calculation of abundances

For ions containing monoisotopic elements the abundances are determined easily from the peak heights produced by the ions in the low resolution spectra. Thus if A^+ is of peak height 4 arbitrary units (a.u.), B^+ 3 a.u., C^+ 2 a.u., and D^+ 1 a.u., then the abundance of A^+ as a percentage of the total ion current is 40%.

Allowance has been made for the presence of ^{13}C when calculating the abundances of ions in terms of the percentage of the total ion current. The natural abundance of ^{13}C is 1% and for ions containing n carbon atoms, n% of the ions will contain a ^{13}C atom. Thus the abundances of ions containing a large number of carbon atoms will be underestimated if the effects of the ^{13}C are neglected. The ^{13}C isotope contribution to an ion is calculated using the formula:-

$$\%\ \text{length of}\ ^{13}C\ \text{isotope peak relative to}\ ^{12}C\ \text{peak}$$

$$= \frac{1{\cdot}1 \times \text{no. of C atoms in ion}\ \%}{100} + \frac{0{\cdot}36 \times \text{no. of N atoms in ion}\ \%}{100}$$

and the abundance compared with the observed value.

Some of the compounds studied, i.e. perfluorocycloalkenes and their derivatives, gave spectra containing ions whose composition could be assigned without the use of accurate mass measurements. For these compounds tables of the composition of the ions in decreasing molecular weight and their abundances, as a percentage of the total ion current, are given. All peaks less than 2% of the length of the base peak are omitted if the molecular ion is of reasonable intensity. The composition of the ions in the spectra of the substituted perfluoropyridines could not be determined uniquely without the use of accurate mass measurements, and in this case the most intense single ion in the spectrum was chosen as the base peak and all abundances less than 5% of the base peak were omitted. The mass to charge ratio of each ion is given and its abundance expressed as the percentage intensity relative to that of the base peak which is considered to be 100%.

11.1.3 Metastable ions

Simple inspection of a mass spectrum does not reveal the pathway(s) by which a particular ion is formed since the usual peaks in a spectrum indicate only the $^{m}/e$ and abundance of the ions formed. The fragmentation pattern of the positive ions can be elucidated by the help of metastable ions. These are small diffuse ions which usually appear at a non-integral mass number in the spectrum, and such metastable ions are associated with ion fragmentations which occur in the field free space of a sector instrument. The mass m*, at which such ions are recorded, can be simply related to the mass of the parent ion m_1 and the mass of the daughter ion m_2 by the following equation:[151]

$$m^* = \frac{(m_2)^2}{m_1}$$

The difference between m_1 and m_2 determines the mass and composition of the neutral fragment lost in a decomposition process. Kinetic energy is lost with the neutral fragment resulting from the decomposition and this gives rise to a broad peak of low intensity, i.e. a 'metastable peak'. The equation given above will not hold if dissociation occurs with a release of internal energy.[152]

The absence of a metastable transition does not rule out a particular reaction pathway, nor does the presence of a 'metastable' show that its reaction is the only one of importance which is involved in the decomposition of the particular parent ion or the formation of the particular daughter ion.

Tables of m* values that occur for various values of m_1 and m_2 ($m_1 \leqslant 500$ and $500 \geqslant m^* \geqslant 1$) are of help in the assignment of metastables.[153]

11.2 Discussion of Experimental

11.2.1 Perfluorocycloalkenes

A series of perfluorocycloalkenes was the first group of compounds to be studied in detail by mass spectrometry. Those examined were perfluorocyclohexene, -cyclohexa-1,3-diene, -cyclohexa-1,4-diene, -cyclopentene, and -cyclobutene, and, although the mass spectra of some of these olefins have been reported by Majer,[150] a study of the series as a whole was justified since compounds studied subsequently can be considered as tetrafluoropyridyl-substituted derivatives of the above olefins. The study was further justified by the presence of metastable ions that were not reported by Majer.

The mass spectra (i.e. the abundance of ions relative to the base peak and the relative ion intensities) of five perfluorocycloalkenes are listed in Tables 28 and 29. Hexafluorobenzene is included for the purposes of comparison. It can be seen from the table that the molecular ion peak is about one-half of the size of the base peak in each case with the exception of perfluorocyclohexene, where the molecular ion is less abundant. The molecular ion of hexafluorobenzene forms the base peak.

The major ions in the spectrum of perfluorocyclohexene in order of decreasing abundances are $C_4F_6^+$, $C_6F_9^+$, $C_3F_3^+$, and $C_6F_{10}^+$, and the base peak at $^m/e$, 162 ($C_4F_6^+$) corresponds to the loss of C_2F_4 from the molecular ion.

Table 28

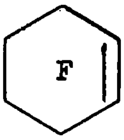
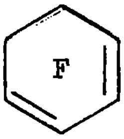
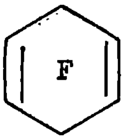
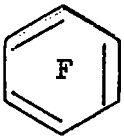
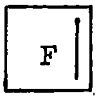
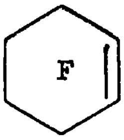
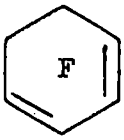
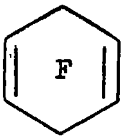
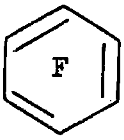
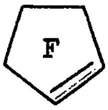
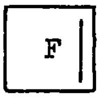
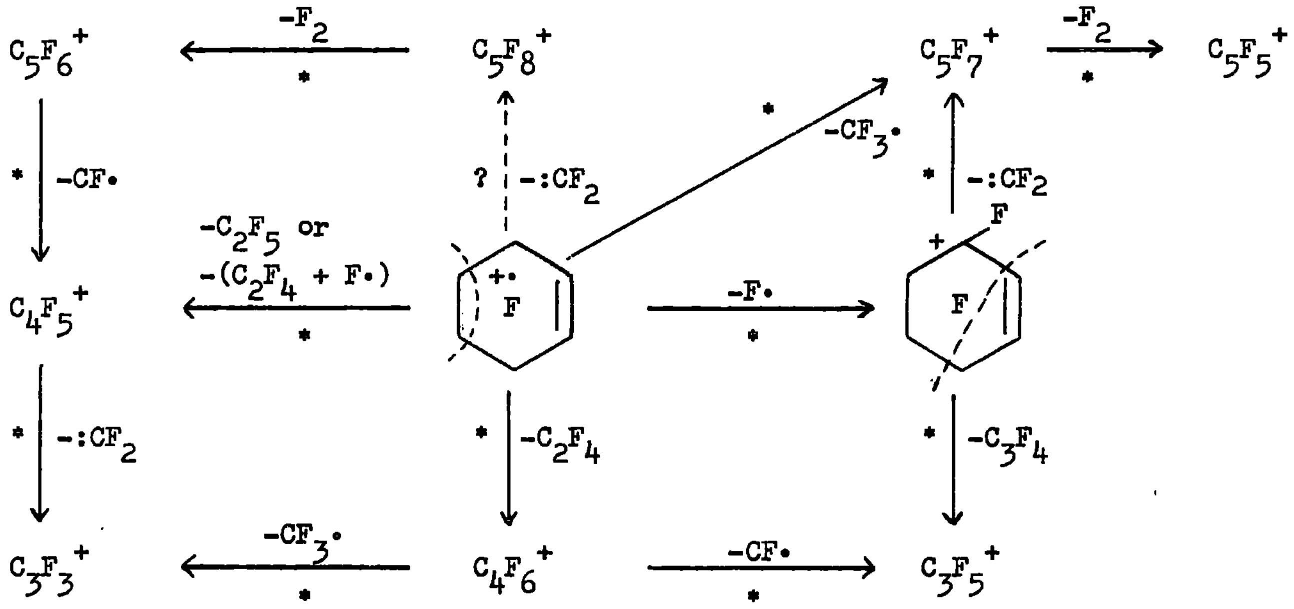
Ion	$^m/_e$	Relative Abundances					
							
C_6F_{10}	262	19					
C_6F_9	243	59					
C_6F_8	224		52	46			
C_6F_7	205		46	49			
C_6F_6	186		11	10	100		
C_6F_5	167				22		
C_6F_4	148				2		
C_5F_8	212	5				51	
C_5F_7	193	27	6			62	
C_5F_6	174	2	32	33			
C_5F_5	155	10	100	100	21		
C_5F_4	136		3	3	13		
C_5F_3	117	4	19	18	83		
C_5F_2	98		4	5	13		
C_5F	79		4	4	11		
C_4F_6	162	100	20	4		83	46
C_4F_5	143	31	10			51	20
C_4F_4	124	10	44	37	3	11	2
C_4F_3	105	4	10	6	4	6	
C_4F_2	86	2	6	6	7	3	
C_3F_5	131	22	8	3		5	3
C_3F_4	112	9	5	3		17	24
C_3F_3	93	54	36	23	29	100	100
C_3F_2	74	9	11	8	8	18	7
C_3F	55	3	5		5	8	3
C_2F_5	119						2
C_2F_4	100	7	4			7	4
C_2F_3	81					3	
C_2F_2	62					4	5
CF_3	69	36	41	26	9	21	8
CF_2	50	2				14	
CF	31	16	26	22	40	42	25
C_3	36		3		2	4	

Table 29

Composition of ion	Ion Intensities					
						
C_6F_{10}	4·3					
C_6F_9	14·2					
C_6F_8		10·7	11·8			
C_6F_7		9·1	12·5			
C_6F_6		2·1	2·4	27·3		
C_6F_5				6·4		
C_6F_4				0·5		
C_5F_8	1·1				10·3	
C_5F_7	6·1	1·2			12·5	
C_5F_6	0·5	6·5	8·5			
C_5F_5	2·3	20·0	24·9	5·3		
C_5F_4		0·5	0·7	3·8		
C_5F_3	0·9	3·6	4·2	22·5		
C_5F_2		0·8	1·2	3·8		
C_5F		0·8	1·0	2·8		
C_4F_6	23·7	3·7	1·0		16·5	19·2
C_4F_5	7·7	2·8			10·3	7·8
C_4F_4	2·3	8·8	9·2	0·8	2·1	0·8
C_4F_3	0·9	1·9	1·4	1·0	1·1	
C_4F_2	0·5	1·2	1·4	1·8	0·6	
C_3F_5	5·0	1·5	0·7		0·9	1·2
C_3F_4	2·0	0·9	0·7		3·3	9·4
C_3F_3	12·2	6·7	5·4	7·4	19·6	40·7
C_3F_2	2·0	2·5	1·9	2·0	3·5	2·7
C_3F	0·7	0·9		1·3	1·5	1·2
C_2F_5						0·8
C_2F_4	1·6	0·8			1·3	1·6
C_2F_3					0·6	
C_2F_2					0·7	1·9
CF_3	8·1	7·7	6·1	2·3	4·0	3·1
CF_2	0·5				2·6	
CF	3·6	4·9	5·2	10·2	7·9	9·8

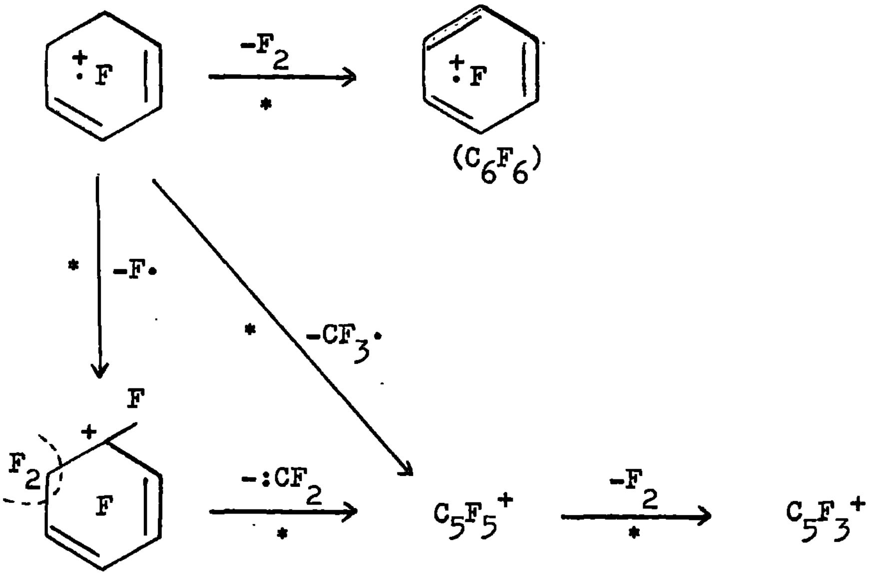


<u>Fragmentation of the molecular ion of perfluorocyclohexene</u>

The main dissociative process results in the formation of $C_4F_6^+$ but simultaneous fragmentation also occurs to give the ions $C_3F_3^+$ and $C_3F_5^+$.

Majer[150] reported that, in cyclic C_6 compounds, the size of the fragment forming the base peak, i.e. the number of carbon atoms which it contains, increases as the unsaturation in the ring is increased, and it has been shown that in all the cyclohexenes containing fluorine atoms the base peak is due to an ion containing four carbon atoms. This can be seen from the data in Table 28, where the base peak in perfluorocyclohexene is due to an ion containing four carbon atoms, while the base peak in the perfluorocyclohexadienes is provided by an ion with five carbon atoms. Also, aromatic fluorine compounds, such as hexafluorobenzene, which can be considered as a hexafluorocyclohexatriene, have the molecular ion peak containing six carbon atoms as the base peak.

The most abundant ions in the spectra of the perfluorocyclohexadienes are $C_5F_5^+$, $C_6F_8^+$, and $C_6F_7^+$ (1,3-) and $C_5F_5^+$, $C_6F_7^+$, and $C_6F_8^+$ (1,4-), in decreasing order of intensity. The base peak at $^m/e$, 155 ($C_5F_5^+$) is formed by the loss of CF_3 from the molecular ion.

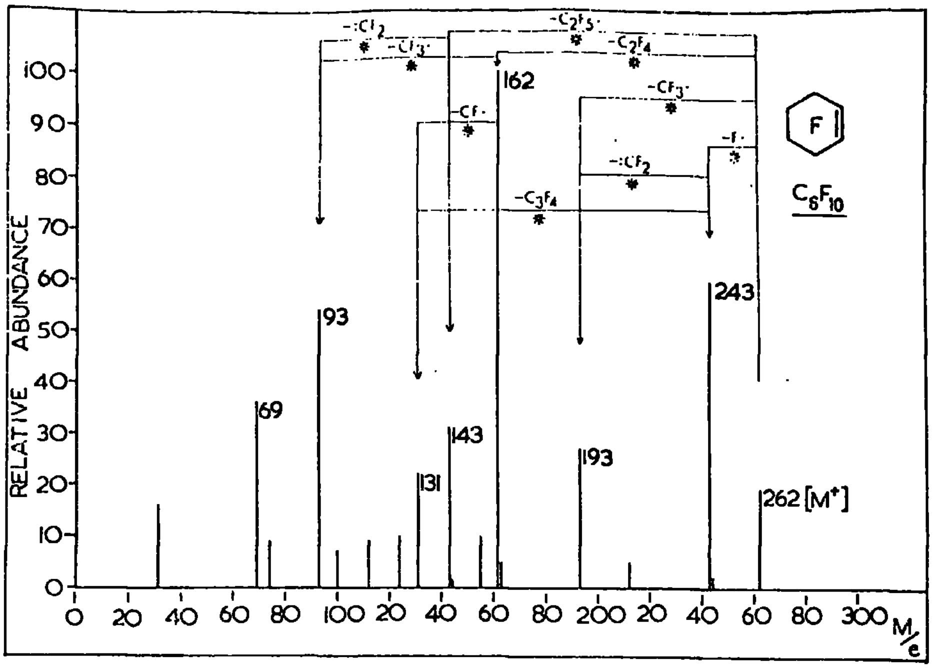


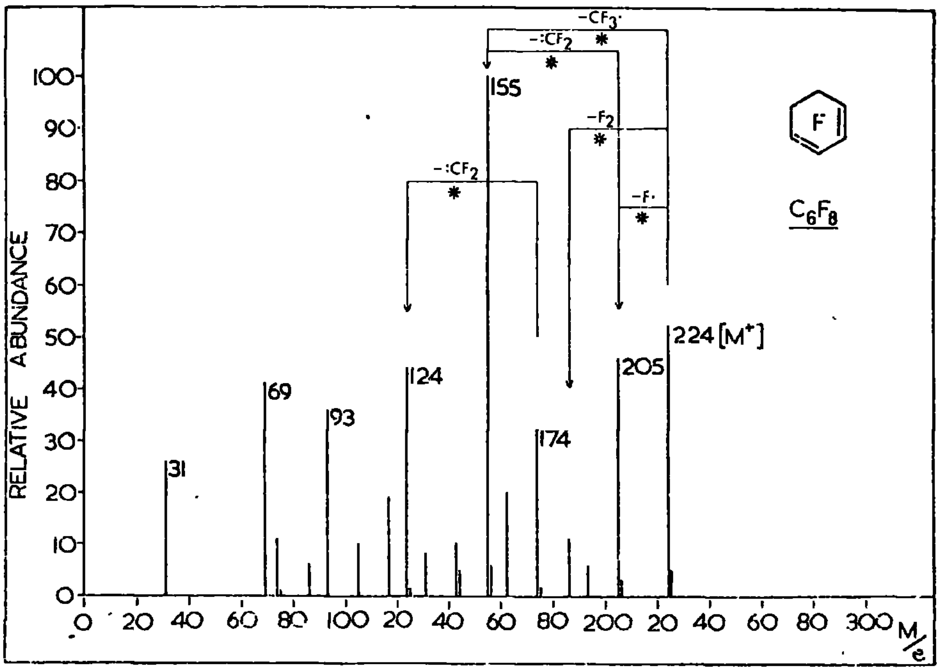
Fragmentation of the molecular ion of perfluorocyclohexa-1,3-diene

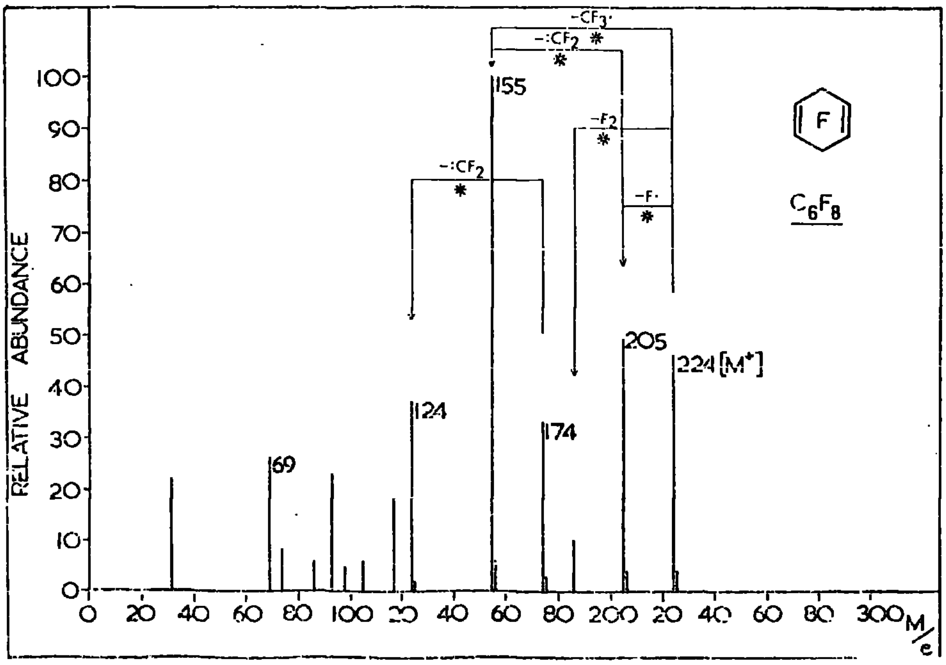
A relatively minor fragmentation of interest is the loss of F_2 from the molecular ion to give C_6F_6. The fragmentation of the 1,4-isomer proceeds in an identical manner.

The spectra of the two isomeric dienes are very similar although a significant difference in the relative abundances of the $C_4F_6^+$ ($^m/e$, 162) and $C_4F_5^+$ ($^m/e$, 143) ions can be seen. Assuming these ions to have cyclic structures, then this difference may be explained on a structural basis, since it would be easier to form these ions from the 1,3-diene because of its structure, whereas a rearrangement process would be required with the 1,4-diene.

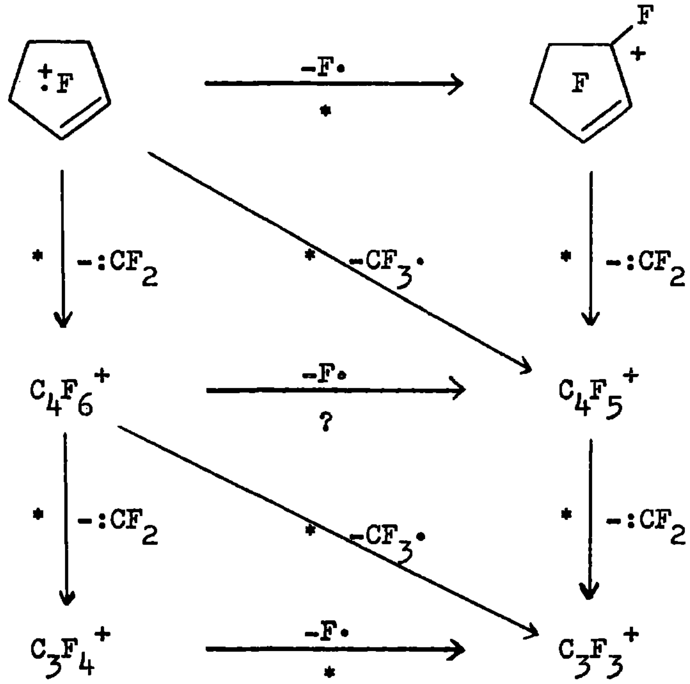
The relative abundances of the major ions and the fragmentation processes produced on electron impact are illustrated diagrammatically on page 208.


RELATIVE ABUNDANCE
100
90
80
70
60
50
40
30
20
10
0
0 20 40 60 80 100 20 40 60 80 200 20 40 60 80 300
M/e
-:CF2
-CF3·
-C2F5·
-C2F4
-CF3·
-CF·
-:CF2
-F·
-C3F4
162
93
69
143
131
193
243
262 [M+]
F
C6F10


RELATIVE ABUNDANCE
100
90
80
70
60
50
40
30
20
10
0
0 20 40 60 80 100 20 40 60 80 200 20 40 60 80 300
M/e
-CF3·
-:CF2
-F2
-:CF2
-F·
155
224 [M+]
205
124
69
93
174
31
F
C6F8


RELATIVE ABUNDANCE
100
90
80
70
60
50
40
30
20
10
0
0 20 40 60 80 100 20 40 60 80 200 20 40 60 80 300
M/e
-CF3·
-:CF2
-F2
-:CF2
-F·
155
205
224 [M+]
124
174
69
F
C6F8

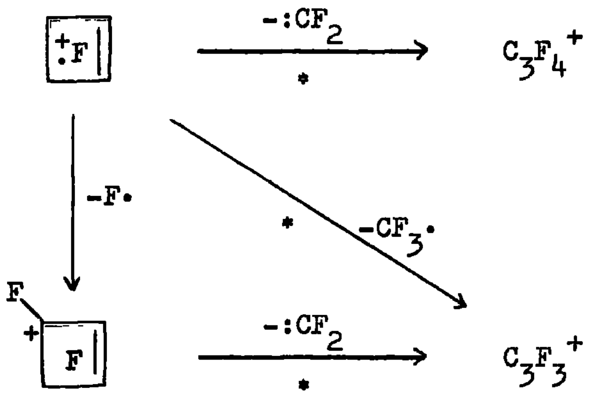
The base peak in the spectrum of perfluorocyclopentene and perfluorocyclobutene is due to the ion $C_3F_3^+$, this being formed by the loss of $C_2F_5^+$ and CF_3^+ from the respective molecular ions of these two compounds. The major ions in the spectrum of perfluorocyclopentene in order of decreasing abundance are $C_3F_3^+$, $C_4F_6^+$, $C_5F_7^+$, $C_5F_8^+$, and $C_4F_5^+$.



Fragmentation of the molecular ion of perfluorocyclopentene

The loss of an allylic fluorine atom from the carbon atom adjacent to the double bond in the molecular ion of perfluorocyclopentene would afford a structure for the $C_5F_7^+$ ion which would facilitate delocalisation of the positive charge in the ring. The metastable ions in the spectrum of C_5F_8 show that the $C_3F_3^+$ ion is formed by successive loss of $:CF_2$ and F• radicals, although there may be a direct loss of C_2F_5• without a metastable transition.

The most abundant ions in the spectrum of perfluorocyclobutene are $C_3F_3^+$ and $C_4F_6^+$ in decreasing order of intensity. The loss of CF_3 from the molecular ion results in the formation of the $C_3F_3^+$ ion, which forms the base peak of the spectrum.

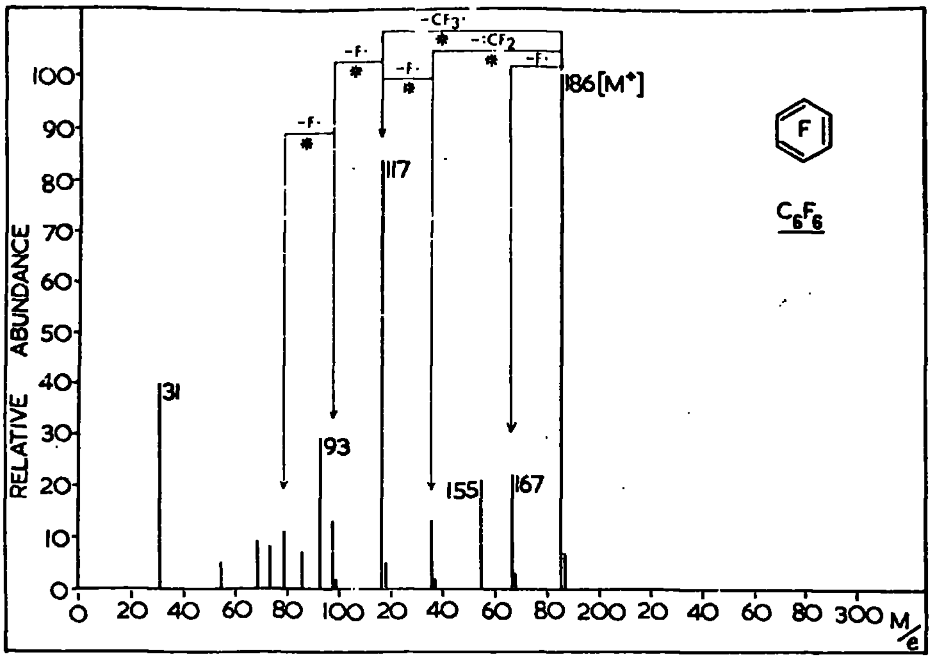


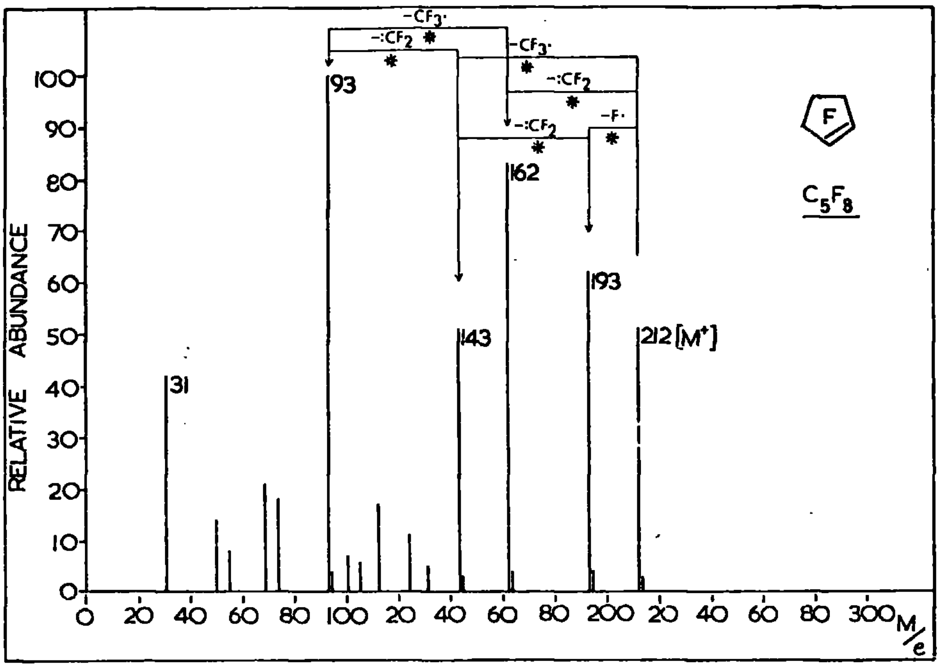
Fragmentation of the molecular ion of perfluorocyclobutene

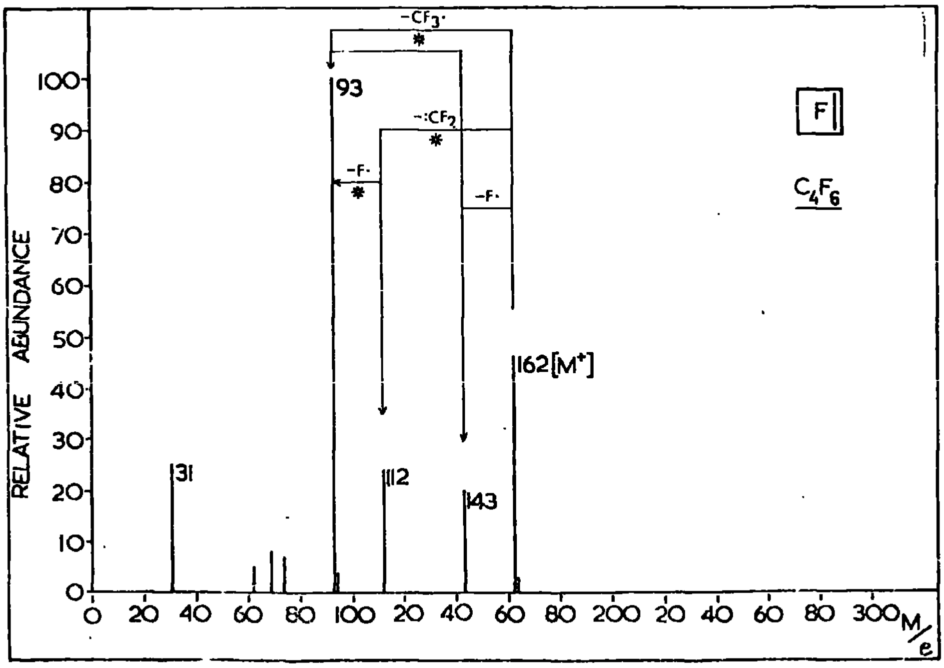
Diagrammatic representation of the relative abundances of the ions and modes of fragmentation are shown on page 211.

In all the spectra of the perfluorocycloalkenes it can be seen that the loss of a fluorine radical (F•) from the molecular ion to give the ion $(M-F)^+$ is a major fragmentation process, although this is not always supported by the presence of a metastable transition. In fact, in each case the ion $(M-F)^+$ is the second most abundant ion in the spectrum. It is also interesting to note that the second most abundant ion in the spectrum of hexafluorobenzene has the formula $C_5F_3^+$ and is formed by the loss of CF_3• from the molecular ion. The composition of this ion suggests that a rearrangement process occurs following the loss of CF_3• from the molecule of hexafluorobenzene, and the structure of the resulting ion might probably contain acetylenic linkages since a cyclic structure is very unlikely.

When, in the spectra of the perfluorocycloalkenes, a fragmentation involves the loss of a carbon atom, it is not certain whether the resulting ion has a cyclic or straight-chain structure.


RELATIVE ABUNDANCE
0
10
20
30
40
50
60
70
80
90
100
0 20 40 60 80 100 20 40 60 80 200 20 40 60 80 300 M/e
31
93
117
155
167
186[M⁺]
-CF₃·
-:CF₂
-F·
-F·
-F·
-F·
*
F
C₆F₆


RELATIVE ABUNDANCE
0
10
20
30
40
50
60
70
80
90
100
0 20 40 60 80 100 20 40 60 80 200 20 40 60 80 300 M/e
31
93
143
162
193
212[M⁺]
-CF₃·
-:CF₂
-CF₃·
-:CF₂
-:CF₂
-F·
*
F
C₅F₈


RELATIVE ABUNDANCE
0
10
20
30
40
50
60
70
80
90
100
0 20 40 60 80 100 20 40 60 80 200 20 40 60 80 300 M/e
31
93
112
143
162[M⁺]
-CF₃·
-:CF₂
-F·
-F·
*
F
C₄F₆

11.2.2 Perfluoroalkylpyridines

A mass spectral analysis of a series of perfluoroalkylpyridines was carried out to obtain information on the mode of fragmentation of these compounds, and in particular, to see if cleavage of the bond joining the tetrafluoropyridyl and perfluorocycloalkyl substituent occurred to give the corresponding perfluorocycloalkene as a fragment ion. Also, it was interesting to compare the fragmentation of the perfluorocycloalkenylpyridines with the corresponding perfluorocycloalkenes to see if the tetrafluoropyridyl group was acting as an inert substituent. Perfluoro-isopropylpyridines were included in the study to help elucidate the fragmentation of the perfluorocyclohexyl derivatives of perfluoro-(4-isopropylpyridine).

It must be noted that the compounds studied are numbered conveniently for discussion in this section and are not necessarily the same numbers as given to the same compounds in previous sections of this thesis. Also, with the exception of the perfluoroisopropylpyridines, the preparation of which is referenced, all the compounds were prepared as described in Chapter 7.

Mass spectra of perfluoroalkylpyridines [$^{m}/e$ values; relative abundance (% of base peak) in parentheses]

All peaks > 5% of the base peak (arbitrarily 100%), and certain others of diagnostic value < 5%, are recorded.

Perfluoro-(4-cyclohexylpyridine) (i)

432(13), 431(100), 412(9), 263(7), 262(77), 231(18), 224(8), 212(8), 200(12), 181(9), 162(6), 131(25), 117(6), 100(15), 93(6), 69(50), 31(6).

Perfluoro-(2,4-dicyclohexylpyridine) (ii)

694(9), 693(43), 674(19), 525(18), 524(100), 493(11), 462(18), 324(7), 274(8), 262(4), 255(6), 224(8), 131(40), 119(6), 100(17), 69(47).

Perfluoro-(2,4,6-tricyclohexylpyridine) (iii)

956(12), 955(45), 937(6), 936(23), 787(24), 786(100), 755(10), 748(9), 724(13), 586(8), 524(6), 181(6), 131(80), 119(13), 100(27), 93(6), 69(72), 31(6).

Perfluoro-(4-cyclohexenylpyridine) (iv)

393(33), 374(29), 324(8), 293(29), 286(7), 274(34), 255(12), 243(6), 225(10), 224(100), 205(12), 193(7), 186(7), 179(5), 155(6), 148(6), 141(6), 131(9), 124(11), 117(8), 100(9), 93(14), 69(47), 31(12).

$C_{17}F_{21}N$ (v)

618(20), 617(100), 598(20), 448(6), 398(6), 360(3), 131(8), 100(3), 69(30).

Perfluoro-(4-cyclopentylpyridine) (vi)

382(10), 381(83), 362(8), 263(9), 262(100), 231(12), 224(8), 212(14), 200(8), 193(7), 181(9), 162(8), 131(35), 117(9), 100(20), 93(7), 69(46), 31(9).

Perfluoro-(4-cyclobutylpyridine) (vii)

332(4), 331(36), 262(40), 242(8), 232(9), 231(100), 224(6), 212(9), 200(5), 193(5), 181(34), 162(18), 131(16), 124(6), 117(16), 100(26), 93(9), 69(43), 43(6), 31(16).

Perfluoro-(4-cyclopentenylpyridine) (viii)

344(12), 343(100), 324(31), 293(23), 275(6), 274(54), 255(9), 243(6), 225(9), 224(94), 193(8), 131(4), 124(9), 117(9), 93(11), 69(25), 43(6), 31(13).

Perfluoro-(4-cyclobutenylpyridine) (ix)

294(5), 293(44), 274(32), 264(7), 243(6), 225(9), 224(95), 219(35), 193(15), 179(4), 148(6), 131(27), 124(10), 119(9), 117(10), 100(16), 98(6), 93(14), 69(100), 43(6), 31(21).

Perfluoro-(4-isopropylpyridine) (x)[154]

319(66), 300(14), 250(18), 231(5), 200(100), 100(5), 69(70), 31(6).

Perfluoro-(2,4-diisopropylpyridine) (xi)[154]

470(3), 469(25), 451(6), 450(44), 400(46), 351(11), 350(100), 281(14), 262(11), 231(9), 69(64).

Perfluoro-(2,4,6-triisopropylpyridine) (xii)[154]

620(5), 619(30), 601(13), 600(76), 551(14), 550(84), 501(15), 500(100), 462(7), 431(8), 412(12), 381(6), 117(6), 69(95).

Perfluoro-(2-cyclohexyl-4-isopropylpyridine) (xiii)

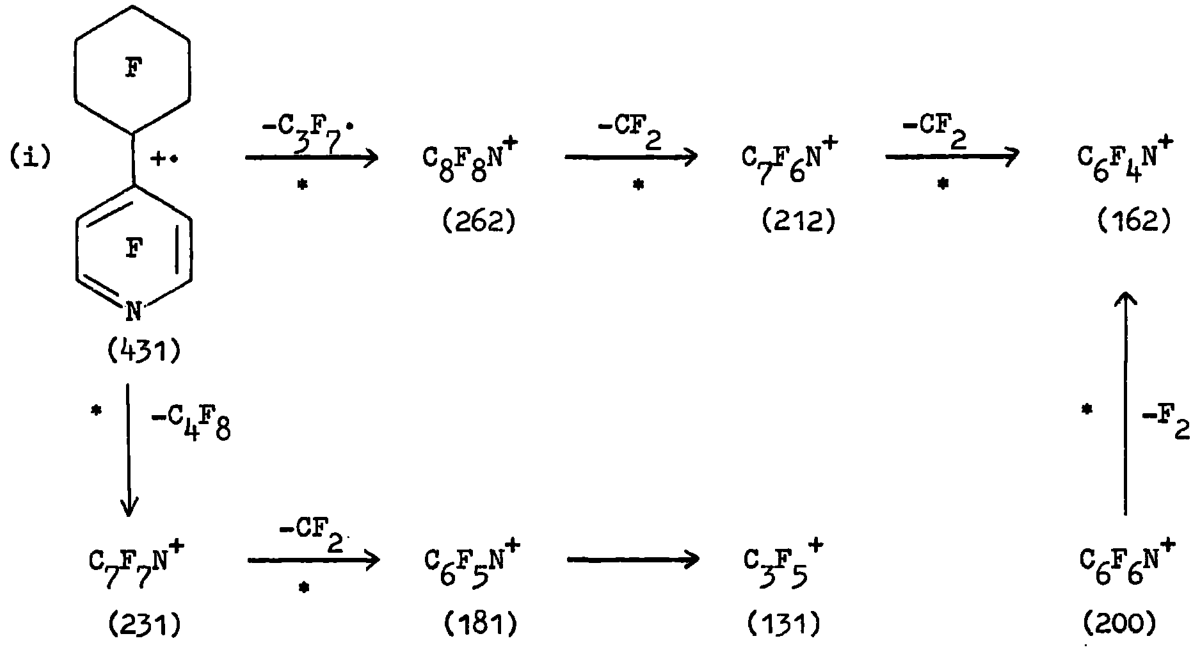
582(11), 581(66), 563(8), 562(46), 512(7), 462(14), 413(16), 412(100), 381(14), 350(22), 343(18), 324(7), 312(6), 274(6), 262(13), 224(7), 131(34), 100(11), 69(55).

Perfluoro-(2,6-dicyclohexyl-4-isopropylpyridine) (xiv)

844(11), 843(44), 825(8), 824(34), 675(20), 674(100), 643(9), 612(12), 412(3), 343(6), 224(6), 131(54), 100(11), 69(52).

It was seen earlier (section 11.2.1) that the molecular ion of a particular perfluorocycloalkene gave a fairly intense peak in the mass spectrum, and in general, the molecular ion of the perfluoroalkylpyridines was also of relatively high intensity and in some cases formed the base peak. In all of the perfluoroalkylpyridines, an initial fragmentation was the loss of fluoride ion from the molecular ion, although this was not always supported by an appropriate metastable ion.

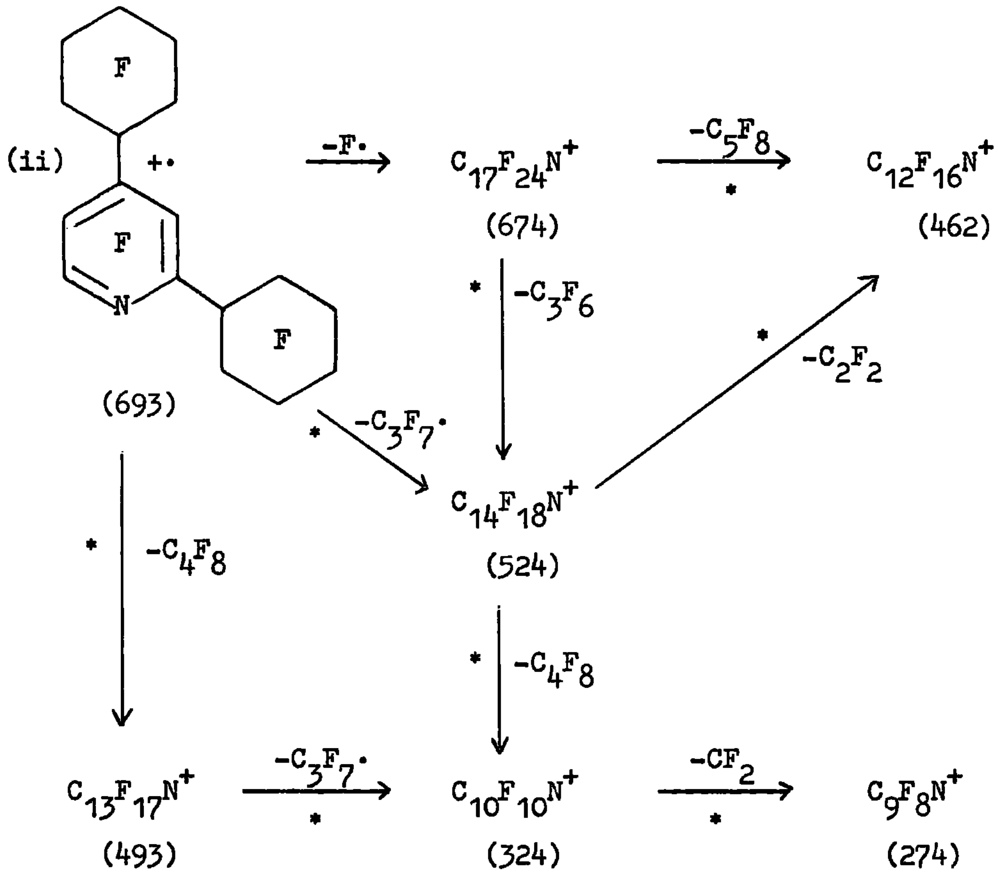
Scheme 1 shows the fragmentation of perfluoro-(4-cyclohexylpyridine) (i). The base peak is due to the molecular ion, and the second most intense peak, at $^m/e$ 262, was shown by accurate mass measurement to be formed by loss of C_3F_7 from the molecular ion. The loss of C_3F_7 forms the main fragmentation of perfluorocyclohexane[150] and this suggests that fragmentation of the cyclohexyl substituent forms the main dissociative process in the mass spectrum of (i).



Scheme 1

Scheme 2 shows the fragmentation of perfluoro-(2,4-dicyclohexylpyridine) (ii). The molecular ion is the third most abundant ion in the spectrum of (ii), and the base peak, at $^m/e$ 524, is formed by loss of C_3F_7 from the molecular ion.

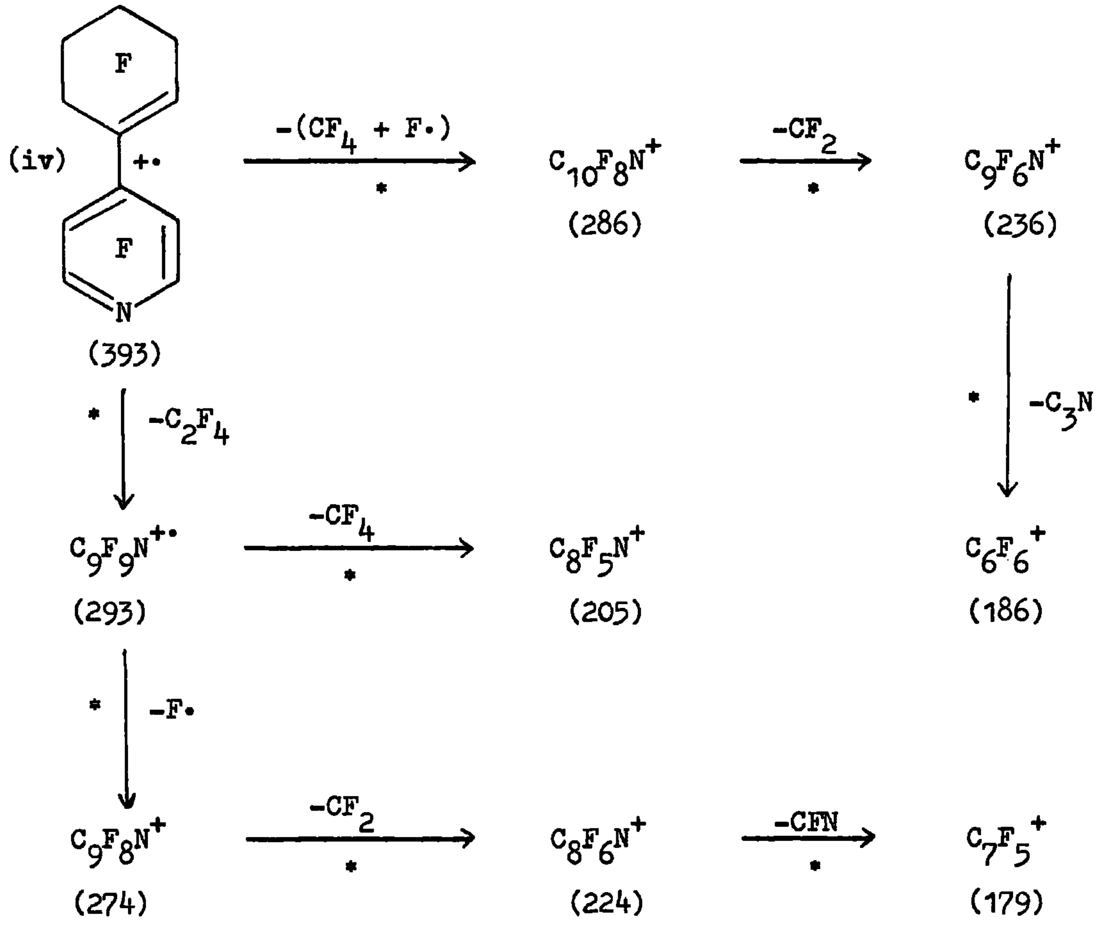
Additional fragmentations, after the loss of fluoride ion from (ii), may be due to the presence of a second cyclohexyl substituent, although the order in which the 2- and 4-substituents fragment is unknown.



Scheme 2

The molecular ion of perfluoro-(2,4,6-tricyclohexylpyridine) (iii) also fragments in the manner shown in Scheme 2, the base peak being formed by the loss of C_3F_7 from the molecular ion. The most abundant ions in the mass spectrum of (iii) are in the same order of intensity as the corresponding ions in the spectrum of (ii), and fragmentation of a cyclohexyl substituent is the major breakdown process. An additional peak corresponding to the loss of F_2 from the base peak ion in the spectrum of (iii) may be due to the presence of an additional cyclohexyl substituent in the molecular ion of (iii).

The base peak in the mass spectrum of perfluoro-(4-cyclohexenylpyridine) (iv) is formed by the loss of $C_3F_7\cdot$ from the molecular ion, as in perfluoro-(4-cyclohexylpyridine) (i), but the molecular ion of (iv) is only the fourth most abundant ion in the spectrum. The manner in which the molecular ion of (iv) fragments is shown in Scheme 3.

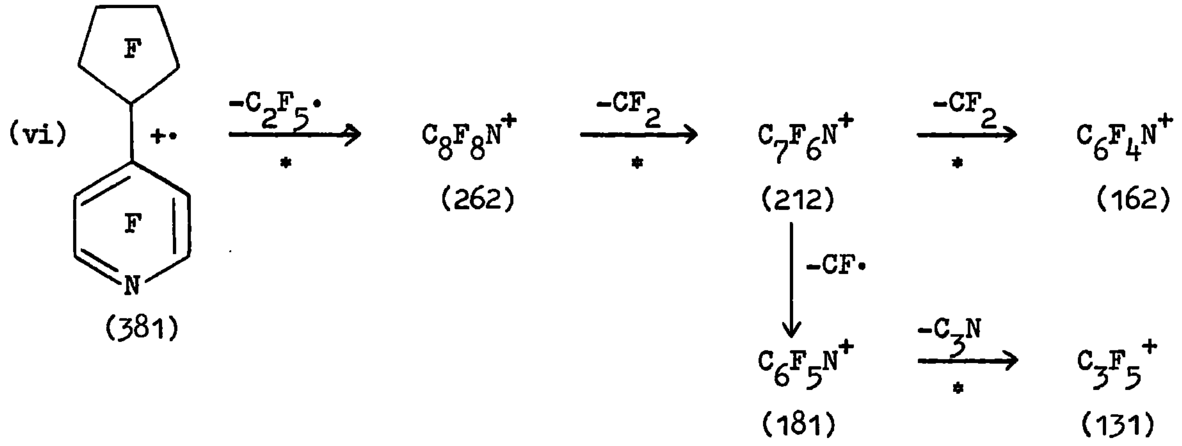


Scheme 3

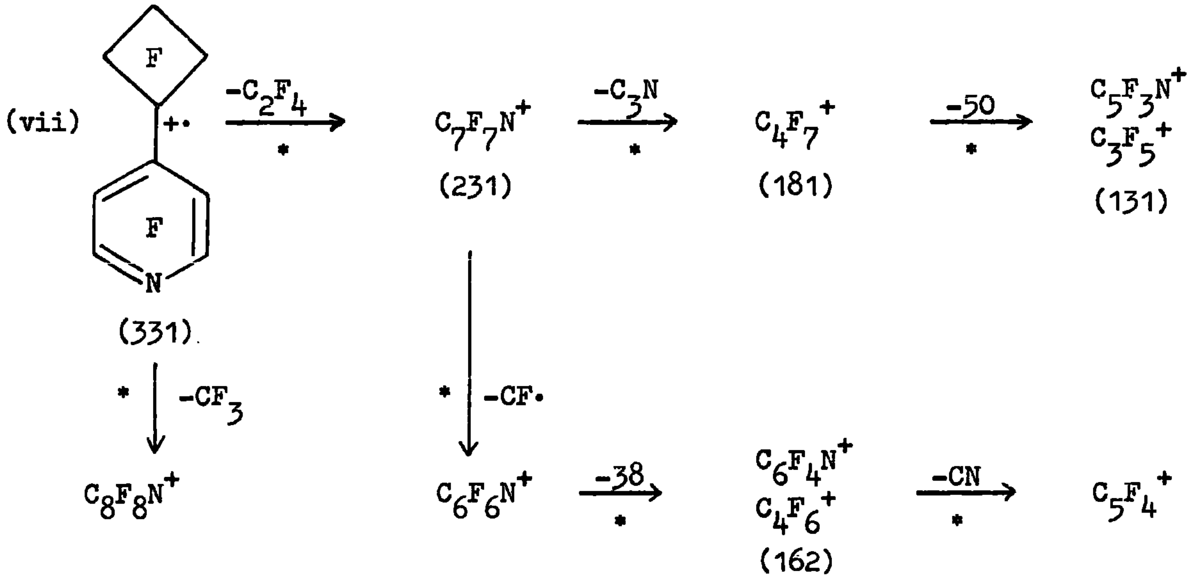
The intensities of the ions $C_{11}F_{12}N^+$, $C_9F_9N^+$, and $C_9F_8N^+$ are similar to that of the molecular ion. The base peak was shown to contain nitrogen by accurate mass measurements and this is supported by the loss of CFN from this ion to give $C_7F_5^+$.

The initial fragmentation of $C_{17}F_{21}N$ (v) follows Scheme 3, but the loss of C_3F_7 from the molecular ion of (v) gives a minor ion, whereas the corresponding ion in the spectrum of (iv) formed the base peak. The molecular ion of $C_{17}F_{21}N$ formed the base peak, and $C_{17}F_{20}N^+$ and CF_3^+ were the only other ions having significant intensities.

The fragmentations of perfluoro-(4-cyclopentylpyridine) (vi) and perfluoro-(4-cyclobutylpyridine) (vii) are shown in Schemes 4 and 5 respectively. The base peaks in the spectra of (vi) and (vii) are formed by the loss of $C_2F_5\cdot$ and C_2F_4, respectively, from their molecular ions, whereas the molecular ion formed the base peak in the spectrum of (i), the major fragmentation of (i) being the loss of $C_3F_7\cdot$ from the molecular ion.



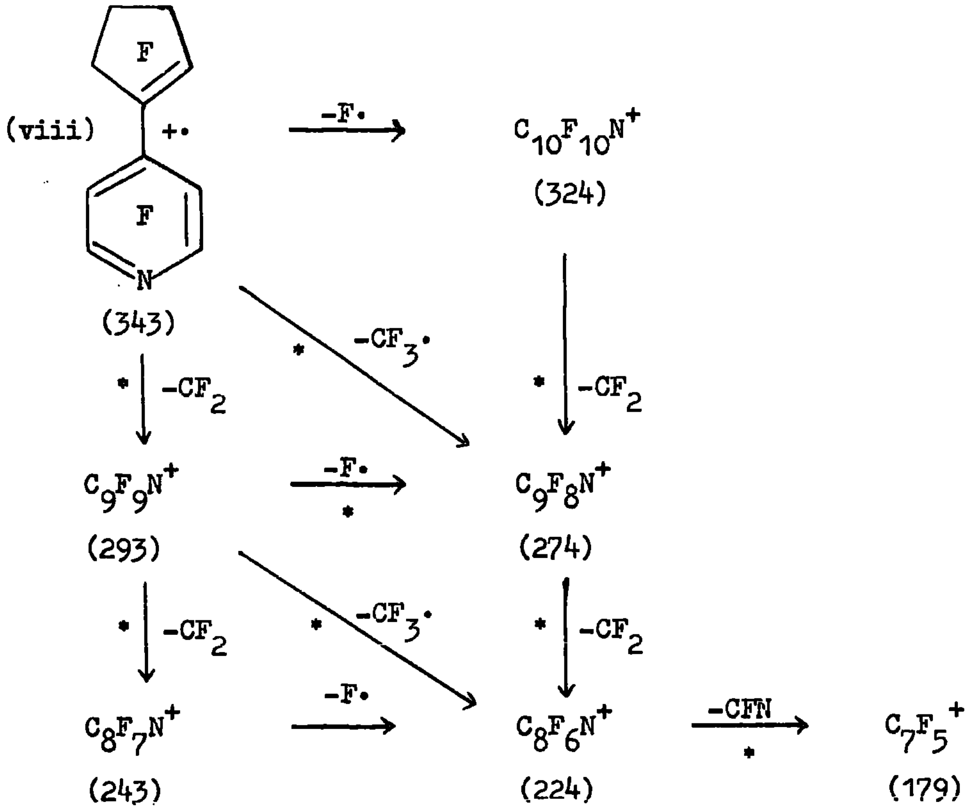
Scheme 4



Scheme 5

Accurate mass measurements on perfluoro-(4-cyclobutylpyridine) (vii) showed the presence of two ions for $^m/e$ 162 and 131, and the occurrence of a doublet at $^m/e$ 162 probably shows that cleavage of the bond between the tetrafluoropyridyl and perfluorocyclobutyl substituents occurs to some extent giving perfluorocyclobutene as a fragment ion.

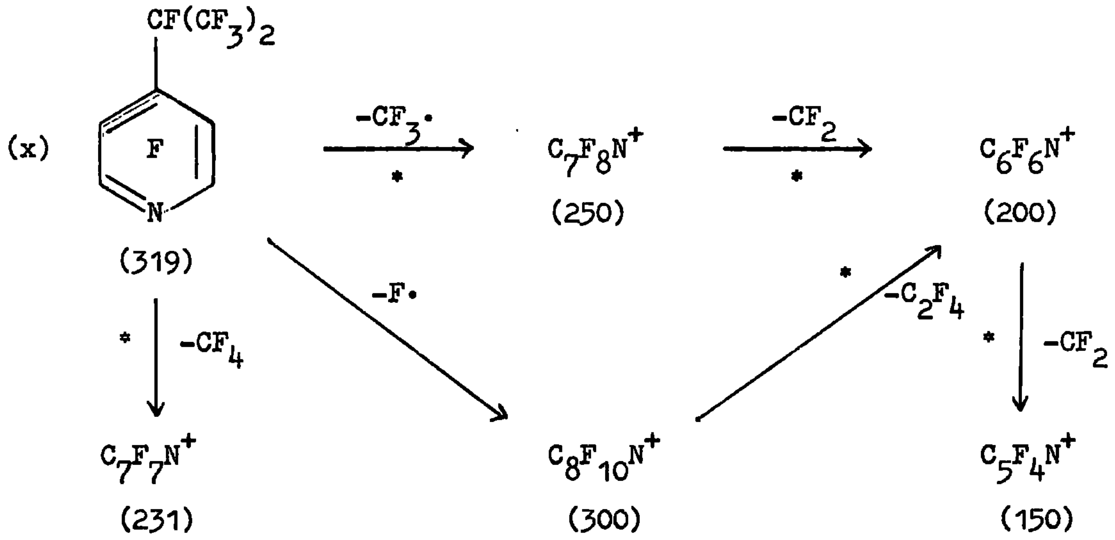
Fragmentation of perfluoro-(4-cyclopentenylpyridine) (viii) is shown in Scheme 6. The molecular ion forms the base peak although the relative abundance of the ion $C_8F_6N^+$ ($^m/e$ 224) is 95%. The same ion, having the same relative intensity, is present in the spectrum of perfluoro-(4-cyclobutenylpyridine) (ix), and also formed the base peak in the spectrum of perfluoro-(4-cyclohexenylpyridine) (iv) (see Scheme 3).



Scheme 6

Fragmentation of the molecular ions of (iv), (viii) and (ix) leads to the ion $C_8F_6N^+$ ($^m/e$ 224), and the presence of the appropriate metastable peak shows that this ion then loses CFN, in each case, to give the ion $C_7F_5^+$. Also, since similar fragmentations occur in the corresponding olefins, perfluoro-cyclo-hexene, -pentene, and -butene (see 11.2.1), the tetrafluoropyridyl group in (iv), (viii) and (ix) may be acting as an inert substituent. A fairly intense peak at $^m/e$ 219 corresponding to the loss of C_3F_2 from the molecular ion of perfluoro-(4-cyclobutenylpyridine) (ix) was not confirmed by the appropriate metastable ion.

The base peak in the mass spectrum of perfluoro-(4-isopropylpyridine) (x) is formed by the loss of $C_2F_5\cdot$ from the molecular ion, and Scheme 7 shows the fragmentation of (x).

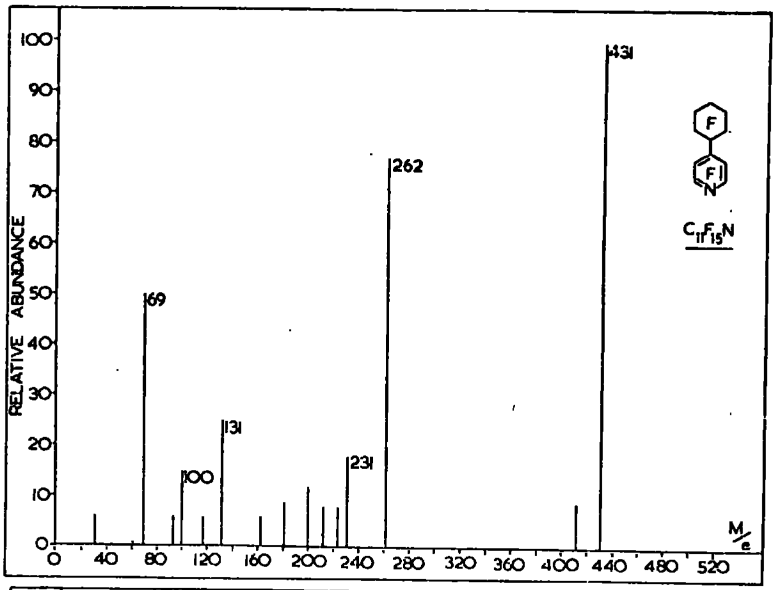


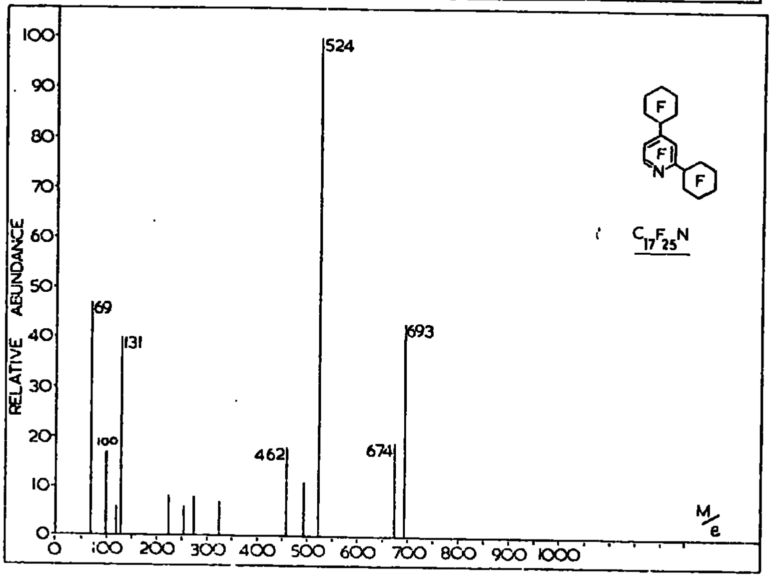
Scheme 7

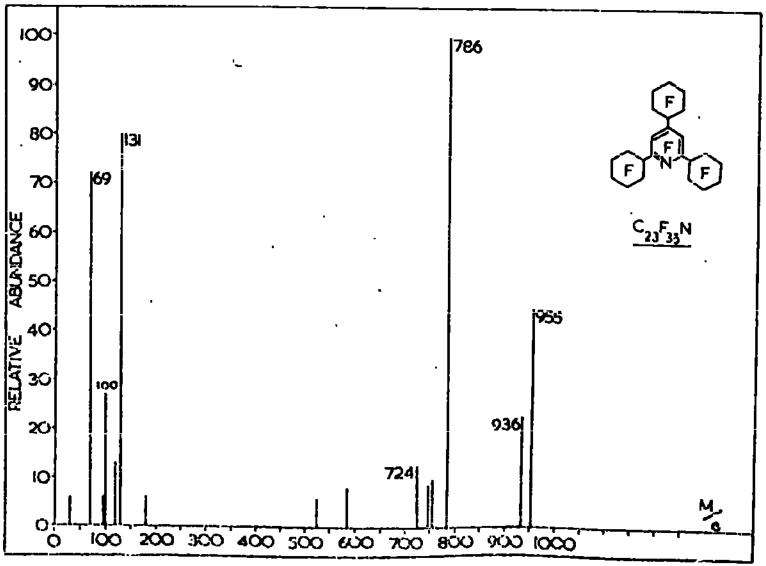
Fragmentation of the molecular ions of perfluoro-(2,4-diisopropylpyridine) (xi) and perfluoro-(2,4,6-triisopropylpyridine) (xii) also follows Scheme 7, and in both cases the base peak is formed by loss of $C_2F_5\cdot$ from the molecular ion, as in (x).

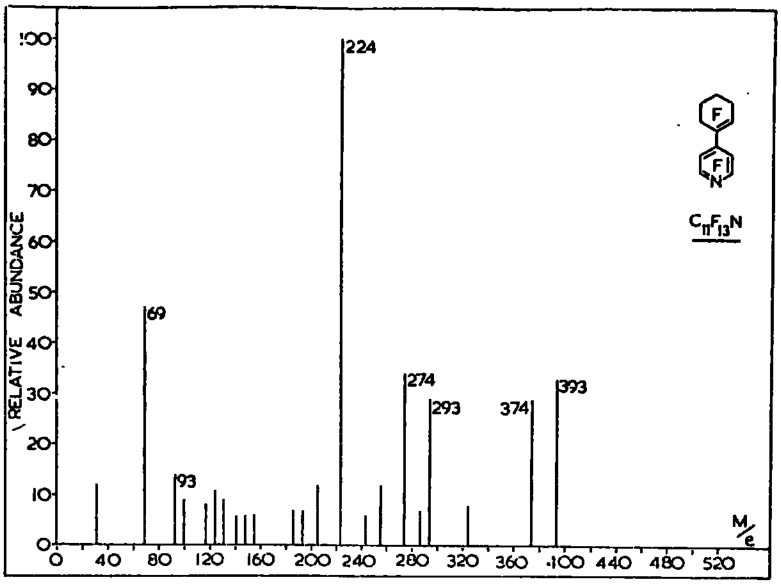
The base peak in perfluoro-(2-cyclohexyl-4-isopropylpyridine) (xiii) and perfluoro-(2,6-dicyclohexyl-4-isopropylpyridine) (xiv) is formed, in both cases, by loss of $C_3F_7\cdot$ from the corresponding molecular ion, and the fragmentation of (xiii) is similar to that of perfluoro-(2,4-dicyclohexylpyridine) (ii) (see Scheme 2). This suggests that initial fragmentation of the 2-cyclohexyl substituent occurs in (xiii), and may be due to additional stabilisation of the resulting fragment ion by the adjacent nitrogen atom.

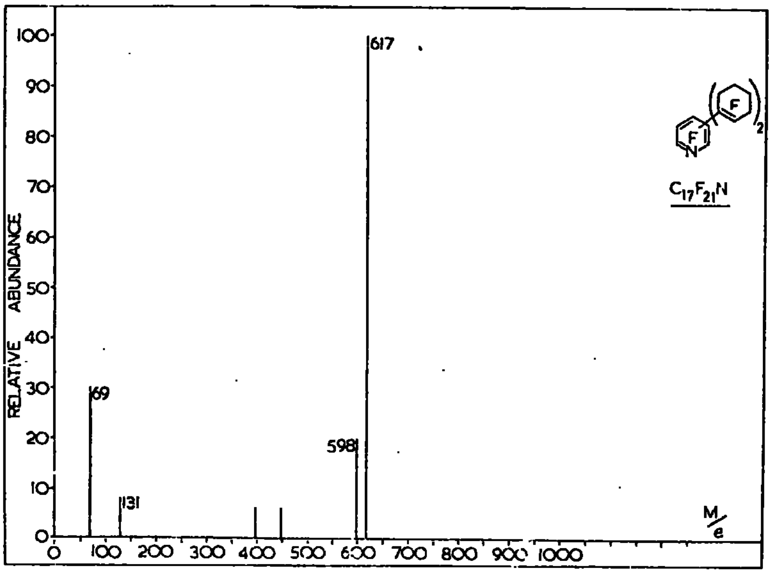
Relative Abundances of Perfluoroalkylpyridines








RELATIVE ABUNDANCE
100
90
80
70
60
50
40
30
20
10
0
224
69
93
274
293
374
393
M/e
0
40
80
120
160
200
240
280
320
360
400
440
480
520
F
F
N
$C_{11}F_{13}N$


RELATIVE ABUNDANCE
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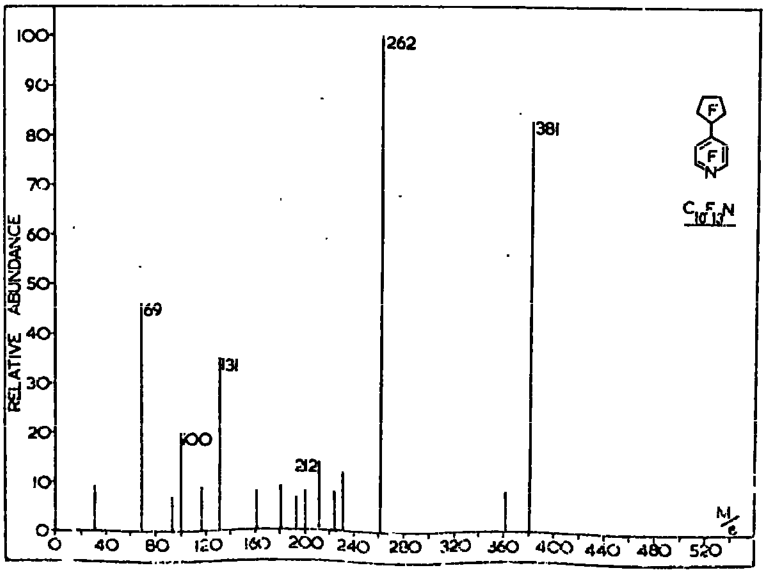
90
80
70
60
50
40
30
20
10
0
617
69
131
598
M/e
0
100
200
300
400
500
600
700
800
900
1000
F
F
N
2
$C_{17}F_{21}N$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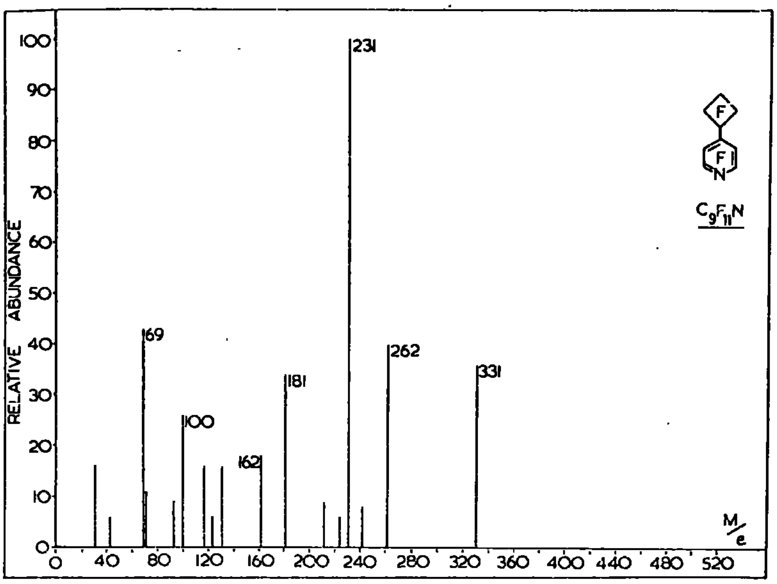
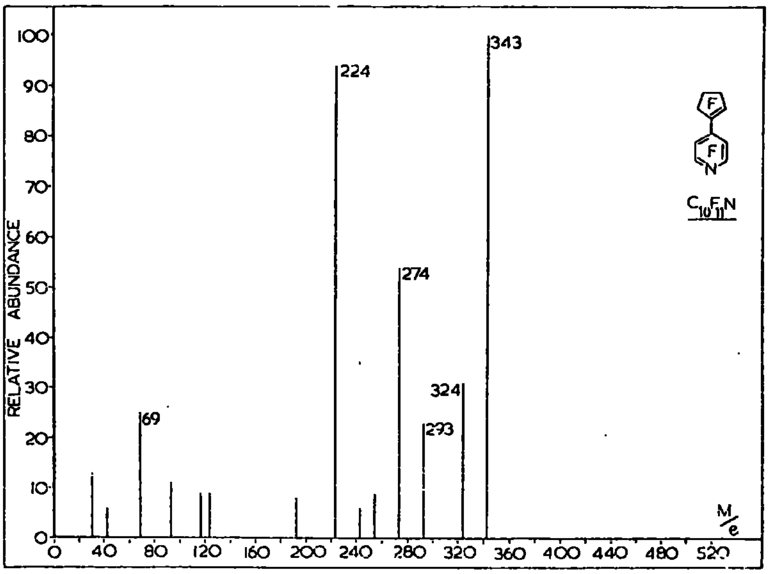
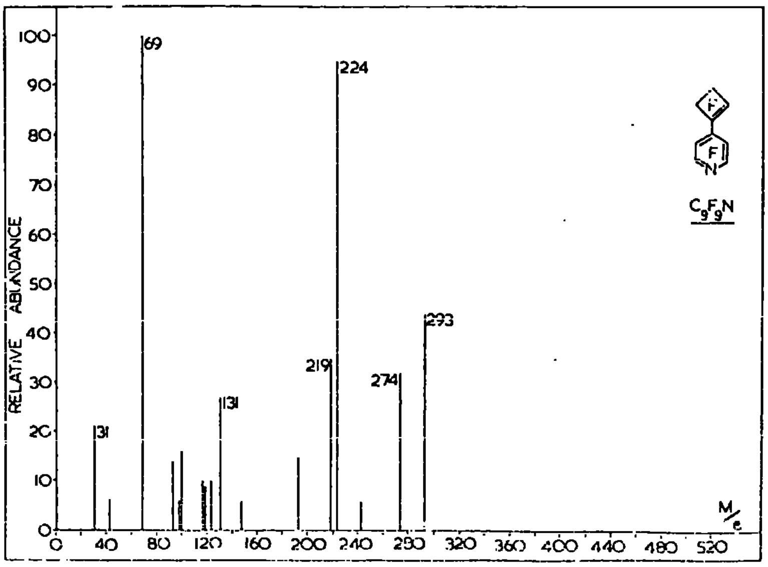
90
80
70
60
50
40
30
20
10
0
262
381
69
131
100
212
M/e
0
40
80
120
160
200
240
280
320
360
400
440
480
520
F
F
N
$C_{10}F_{13}N$


RELATIVE ABUNDANCE
100
90
80
70
60
50
40
30
20
10
0
231
69
262
181
331
100
162
M/e
0 40 80 120 160 200 240 280 320 360 400 440 480 520
F
F
N
$C_9F_{11}N$


RELATIVE ABUNDANCE
100
90
80
70
60
50
40
30
20
10
0
343
224
274
324
69
293
M/e
0 40 80 120 160 200 240 280 320 360 400 440 480 520
F
F
N
$C_{10}F_{11}N$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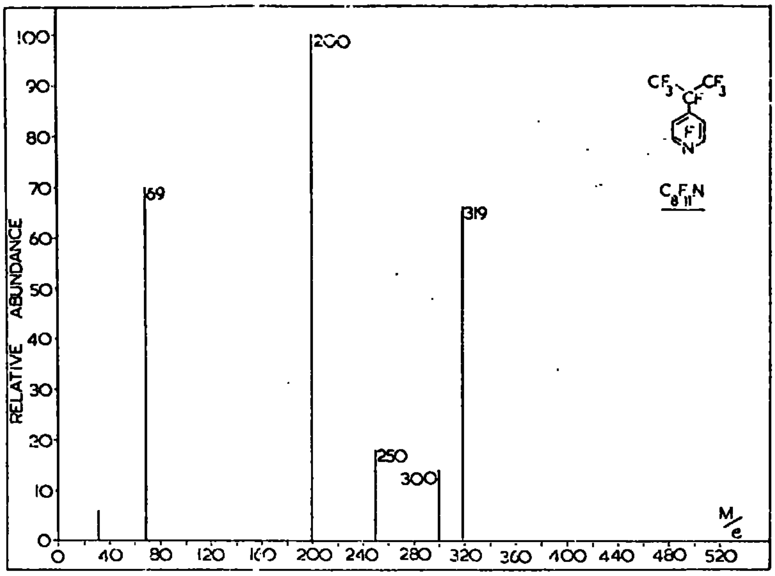
90
80
70
60
50
40
30
20
10
0
69
224
293
219
274
131
31
M/e
0 40 80 120 160 200 240 280 320 360 400 440 480 520
F
F
N
C_9F_9N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30
40
50
60
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80
90
100
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M/e
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80
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200
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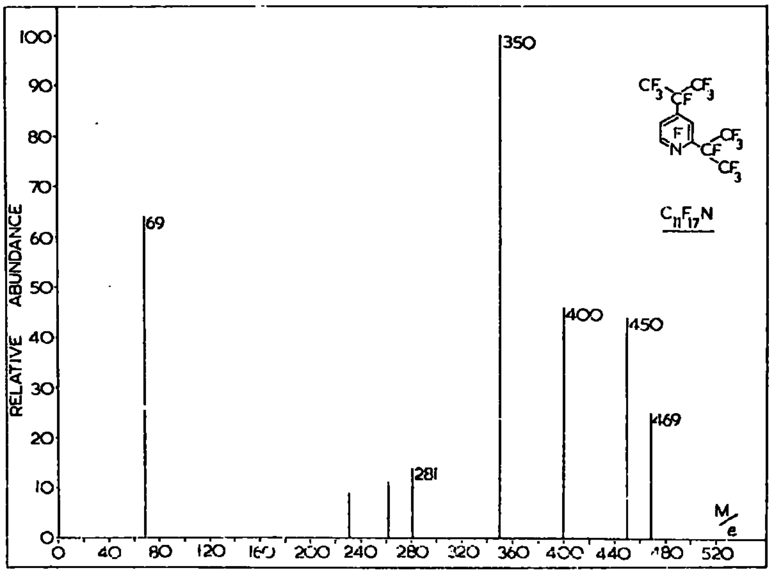
360
400
440
480
520
CF3
CF
CF3
F
N
C8F11N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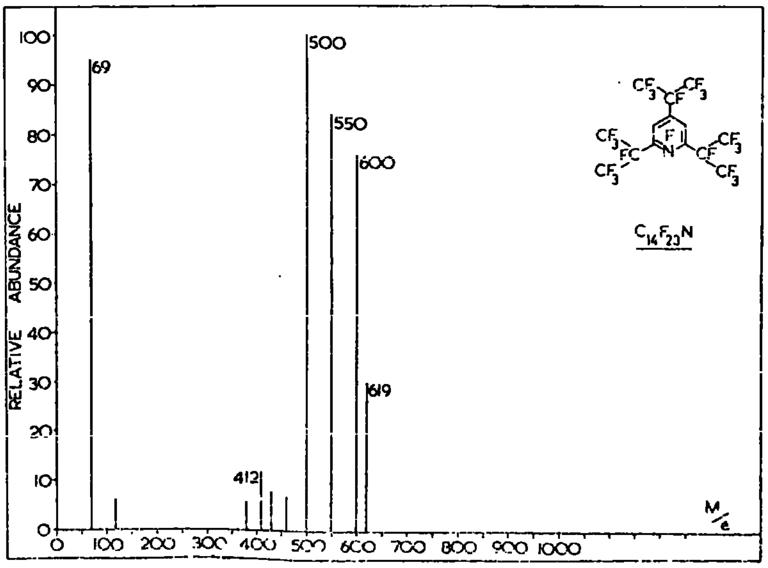
10
20
30
40
50
60
70
80
90
100
69
281
350
400
450
469
M/e
0
40
80
120
160
200
240
280
320
360
400
440
480
520
CF3
CF
CF3
F
N
CF
CF3
CF3
C11F17N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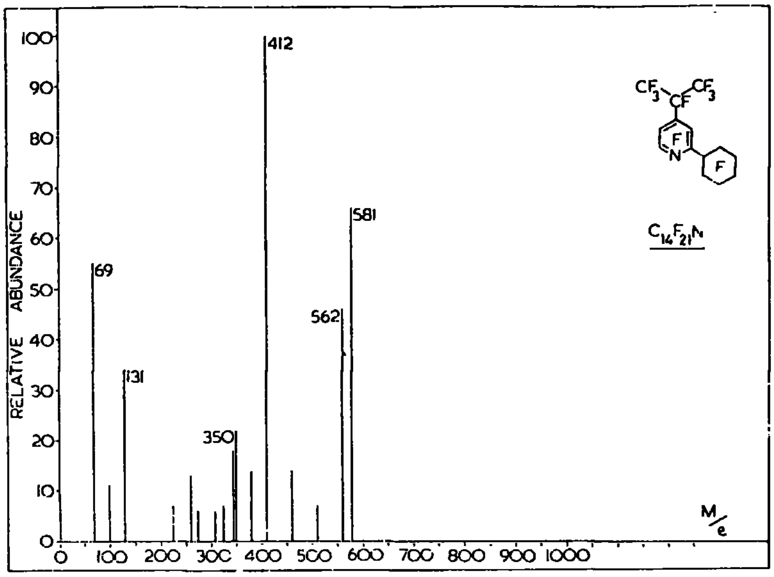
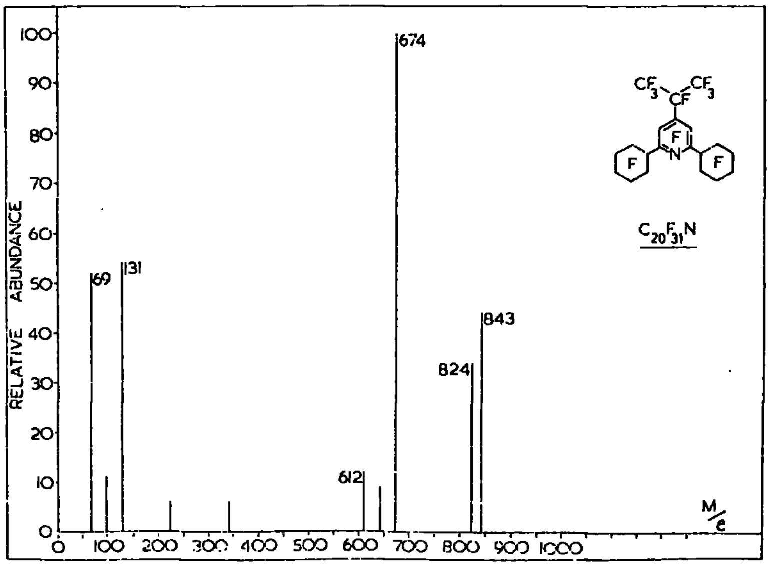
0
10
20
30
40
50
60
70
80
90
100
69
412
500
550
600
619
M/e
0
100
200
300
400
500
600
700
800
900
1000
CF3
CF
CF3
CF3
FC
CF3
F
N
CF
CF3
CF3
C14F23N


RELATIVE ABUNDANCE
0
10
20
30
40
50
60
70
80
90
100
69
131
350
412
562
581
M/e
0
100
200
300
400
500
600
700
800
900
1000
CF3
CF
CF3
F
N
F
$C_{14}F_{21}N$


RELATIVE ABUNDANCE
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10
20
30
40
50
60
70
80
90
100
69
131
612
674
824
843
M/e
0
100
200
300
400
500
600
700
800
900
1000
CF3
CF
CF3
F
N
F
F
$C_{20}F_{31}N$

APPENDIX 1

Metastable Ions and Accurate Mass Measurements determined in the Mass Spectrometric Studies on Perfluorocycloalkenes and Perfluoroalkylpyridines

Metastable ions observed in the spectra of Perfluorocycloalkenes

Perfluorocyclohexene

Observed $^m/e$	Calculated $^m/e$	Transition
225•0	225•4	262 ⟶ 243
153•3	153•3	243 ⟶ 193
143•0	142•8	212 ⟶ 174
142•2	142•2	262 ⟶ 193
124•0	124•5	193 ⟶ 155
117•0	117•5	174 ⟶ 143
105•9	105•9	162 ⟶ 131
100•2	100•2	262 ⟶ 162
96•5	96•5	212 ⟶ 143
77•4	78•0	262 ⟶ 143
70•6	70•6	243 ⟶ 131
60•5	60•5	143 ⟶ 93
53•4	53•4	162 ⟶ 93

Perfluorocyclohexa-1,3-diene

Observed $^m/e$	Calculated $^m/e$	Transition
188•3	187•7	224 ⟶ 205
155•0	154•5	224 ⟶ 186
125•8	126•2	162 ⟶ 143
117•1	117•1	205 ⟶ 155
107•3	107•3	224 ⟶ 155
88•3	88•4	174 ⟶ 124
	88•3	155 ⟶ 117

Perfluorocyclohexa-1,4-diene

Observed $^m/e$	Calculated $^m/e$	Transition
155·0	154·5	224 → 186
117·2	117·1	205 → 155
107·2	107·3	224 → 155
88·3	88·4	174 → 124
	88·3	155 → 117

Perfluorobenzene

Observed $^m/e$	Calculated $^m/e$	Transition
100·7	100·7	136 → 117
99·5	99·4	186 → 136
82·0	82·1	117 → 98
73·5	73·6	186 → 117
63·7	63·7	98 → 79

Perfluorocyclopentene

Observed $^m/e$	Calculated $^m/e$	Transition
123·8	123·8	212 → 162
106·0	106·0	193 → 143
96·5	96·5	212 → 143
77·3	77·4	162 → 112
	77·2	112 → 93
60·4	60·5	143 → 93
53·4	53·4	162 → 93

Perfluorocyclobutene

Observed $^m/e$	Calculated $^m/e$	Transition
77•2	77•2	112 ⟶ 93
	77•4	162 ⟶ 112
60•5	60•5	143 ⟶ 93
53•4	53•4	162 ⟶ 93

Metastable ions observed in the spectra of Perfluoroalkylpyridines

Perfluoro-(4-cyclohexylpyridine) (i)

Observed $^m/e$	Calculated $^m/e$	Transition
255•0	254•8	412 ⟶ 324
231•1	231•8	324 ⟶ 274
226•0	225•9	431 ⟶ 312
220•0	220•0	312 ⟶ 262
183•0	183•1	274 ⟶ 224
171•6	171•5	262 ⟶ 212
159•4	159•3	431 ⟶ 262
142•0	141•9	231 ⟶ 181
131•1	131•2	200 ⟶ 162
123•8	123•8	212 ⟶ 162
94•8	94•8	181 ⟶ 131

Perfluoro-(4-cyclohexenylpyridine) (iv)

Observed $^m/e$	Calculated $^m/e$	Transition
280•8	280•6	374 ⟶ 324
267•5	268•2	305 ⟶ 286
256•3	256•3	293 ⟶ 274
248•7	248•7	374 ⟶ 305
231•8	231•8	324 ⟶ 274
218•5	218•5	393 ⟶ 293
208•0	208•1	393 ⟶ 286
206•5	206•5	243 ⟶ 224
201•0	201•5	293 ⟶ 243
194•6	194•7	286 ⟶ 236
183•1	183•1	274 ⟶ 224
171•5	171•5	293 ⟶ 224
165•0	164•9	255 ⟶ 205
162•0	161•9	198 ⟶ 179
158•0	157•9	374 ⟶ 243
146•5	146•6	236 ⟶ 186
143•1	143•0	224 ⟶ 179
135•4	135•7	255 ⟶ 186
124•4	124•5	193 ⟶ 155
117•2	117•2	205 ⟶ 155

$C_{17}F_{21}N$ (v)

Observed $^m/e$	Calculated $^m/e$	Transition
433•5	433•2	617 ⟶ 517
403•0	404•0	498 ⟶ 448
402•5	401•9	617 ⟶ 498
388•0	388•3	517 ⟶ 448
354•0	353•6	448 ⟶ 398
343•0	342•0	379 ⟶ 360
336•0	335•7	598 ⟶ 448
325•5	325•6	398 ⟶ 360
321•0	320•6	448 ⟶ 379
316•0	316•1	410 ⟶ 360
304•5	304•3	398 ⟶ 348
289•8	289•3	448 ⟶ 360
272•0	272•0	398 ⟶ 329
267•0	266•9	360 ⟶ 310

Perfluoro-(4-cyclopentylpyridine) (vi)

Observed $^m/e$	Calculated $^m/e$	Transition
220•0	220•0	312 ⟶ 262
207•1	207•4	362 ⟶ 274
180•2	180•2	381 ⟶ 262
171•6	171•5	262 ⟶ 212
142•0	142•2	262 ⟶ 193
124•0	123•8	212 ⟶ 162
95•0	94•8	181 ⟶ 131

Perfluoro-(4-cyclobutylpyridine) (vii)

Observed $^m/_e$	Calculated $^m/_e$	Transition
220•0	220•0	312 ⟶ 262
207•2	207•4	331 ⟶ 262
191•1	191•5	262 ⟶ 224
173•2	173•2	231 ⟶ 200
171•6	171•5	262 ⟶ 212
161•5	161•3	231 ⟶ 193
	161•2	331 ⟶ 231
149•8	149•7	231 ⟶ 186
141•9	141•9	231 ⟶ 181
131•0	131•2	200 ⟶ 162
114•0	114•1	162 ⟶ 136
94•9	94•9	162 ⟶ 124
	94•8	181 ⟶ 131

Perfluoro-(4-cyclopentenylpyridine) (viii)

Observed $^m/_e$	Calculated $^m/_e$	Transition
256•1	256•3	293 ⟶ 274
250•5	250•3	343 ⟶ 293
231•8	231•8	324 ⟶ 274
219•0	219•0	343 ⟶ 274
206•5	206•5	243 ⟶ 224
201•0	201•5	293 ⟶ 243
183•0	183•1	274 ⟶ 224
171•4	171•2	293 ⟶ 224
164•9	164•8	255 ⟶ 205

Observed $^{m}/e$	Calculated $^{m}/e$	Transition
161·9	161·8	198 ⟶ 179
146·0	146·2	343 ⟶ 224
143·0	143·1	224 ⟶ 179
135·3	135·2	162 ⟶ 148
124·0	124·5	193 ⟶ 155
66·6	66·8	205 ⟶ 117

Perfluoro-(4-cyclobutenylpyridine) (ix)

Observed $^{m}/e$	Calculated $^{m}/e$	Transition
256·1	256·3	293 ⟶ 274
237·5	237·2	274 ⟶ 255
215·0	215·5	274 ⟶ 243
206·6	206·5	243 ⟶ 224
183·1	183·1	274 ⟶ 224
171·4	171·2	293 ⟶ 224
162·0	161·8	198 ⟶ 179
143·0	143·1	224 ⟶ 179
135·2	135·2	224 ⟶ 174
107·4	107·5	143 ⟶ 124
84·5	84·7	148 ⟶ 112
78·3	78·7	174 ⟶ 117

Perfluoro-(4-isopropylpyridine) (x)

Observed $^{m}/e$	Calculated $^{m}/e$	Transition
196·0	195·9	319 ⟶ 250
167·7	167·3	319 ⟶ 231
160·0	160·0	250 ⟶ 200

Observed $^m/e$	Calculated $^m/e$	Transition
142·0	141·9	231 ⟶ 181
133·3	133·3	300 ⟶ 200
112·5	112·5	200 ⟶ 150
66·7	66·7	150 ⟶ 100

Perfluoro-(2,4-diisopropylpyridine) (xi)

Observed $^m/e$	Calculated $^m/e$	Transition
356·0	355·6	450 ⟶ 400
341·0	341·2	469 ⟶ 400
306·2	306·3	400 ⟶ 350
272·2	272·3	450 ⟶ 350
257·2	257·1	350 ⟶ 300
238·2	238·5	331 ⟶ 281
225·8	225·6	350 ⟶ 281
220·2	220·0	312 ⟶ 262
190·0	189·9	281 ⟶ 231
178·2	178·5	350 ⟶ 250
171·3	171·5	262 ⟶ 212
142·0	141·9	231 ⟶ 181

Perfluoro-(2,4,6-triisopropylpyridine) (xii)

Observed $^m/e$	Calculated $^m/e$	Transition
488·7	488·8	619 ⟶ 550
454·5	454·5	550 ⟶ 500
436·8	436·9	600 ⟶ 512
416·8	416·8	512 ⟶ 462

Observed $^m/e$	Calculated $^m/e$	Transition
402•0	402•2	462 ⟶ 431
386•5	386•3	481 ⟶ 431
371•5	371•5	500 ⟶ 431
367•8	367•5	462 ⟶ 412
337•0	336•7	431 ⟶ 381
320•0	320•0	500 ⟶ 400
304•8	304•0	431 ⟶ 362
285•6	285•6	412 ⟶ 343
250•2	250•3	343 ⟶ 293
220•0	220•0	312 ⟶ 262
212•0	211•8	324 ⟶ 262
172•0	171•7	217 ⟶ 193

Accurate mass measurements

Compound	Measured Mass	Calculated Mass	Formula
Perfluoro-(4-cyclohexylpyridine) (i)	230•9913	230•9919	C_7F_7N
	180•9965	180•9951	C_6F_5N
	161•9976	161•9967	C_6F_4N
	130•9912	130•9920	C_3F_5
Perfluoro-(2,4-dicyclohexylpyridine) (ii)	461•9777	461•9775	$C_{12}F_{16}N$
	273•9922	273•9903	C_9F_8N

Compound	Measured Mass	Calculated Mass	Formula
Perfluoro-(4-cyclohexenylpyridine) (iv)	292•9886	292•9886	C_9F_9N
	285•9904	285•9902	$C_{10}F_8N$
	223•9929	223•9935	C_8F_6N
	204•9940	204•9950	C_8F_5N
	185•9911	185•9904	C_6F_6
$C_{17}F_{21}N$ (v)	359•9870	359•9871	$C_{13}F_{10}N$
Perfluoro-(4-cyclopentylpyridine) (vi)	161•9976	161•9967	C_6F_4N
	130•9914	130•9920	C_3F_5
Perfluoro-(4-cyclobutylpyridine) (vii)	261•9908	261•9903	C_8F_8N
	230•9916	230•9919	C_7F_7N
	180•9875	180•9888	C_4F_7
	161•9928	161•9904	C_4F_6
	161•9931	161•9967	C_6F_4N
	Peak at 162 a doublet		
	130•9950	130•9920	C_3F_5
		130•9983	C_5F_3N
	Peak at 131 a doublet		
Perfluoro-(4-cyclopentenylpyridine) (viii)	292•9886	292•9886	C_9F_5N
	223•9936	223•9935	C_8F_6N

Compound	Measured Mass	Calculated Mass	Formula
Perfluoro-(4-isopropylpyridine) (x)	199·9934	199·9935	C_6F_6N
	180·9888	180·9888	C_4F_7
	149·9964	149·9967	C_5F_4N
	99·9936	99·9936	C_2F_4
Perfluoro-(2,4-diisopropylpyridine) (xi)	349·9852	349·9839	$C_9F_{12}N$
	180·9946	180·9951	C_6F_5N
Perfluoro-(2,4,6-triisopropylpyridine) (xii)	499·9751	499·9743	$C_{12}F_{18}N$
	430·9782	430·9791	$C_{11}F_{15}N$
Perfluoro-(2-cyclohexyl-4-isopropylpyridine) (xiii)	349·9832	349·9839	$C_9F_{12}N$
Perfluoro-(2,6-dicyclohexyl-4-isopropylpyridine) (xiv)	673·9649	673·9647	$C_{17}F_{24}N$
	642·9656	642·9663	$C_{16}F_{23}N$
	635·9684	635·9679	$C_{17}F_{22}N$
	611·9683	611·9679	$C_{15}F_{22}N$

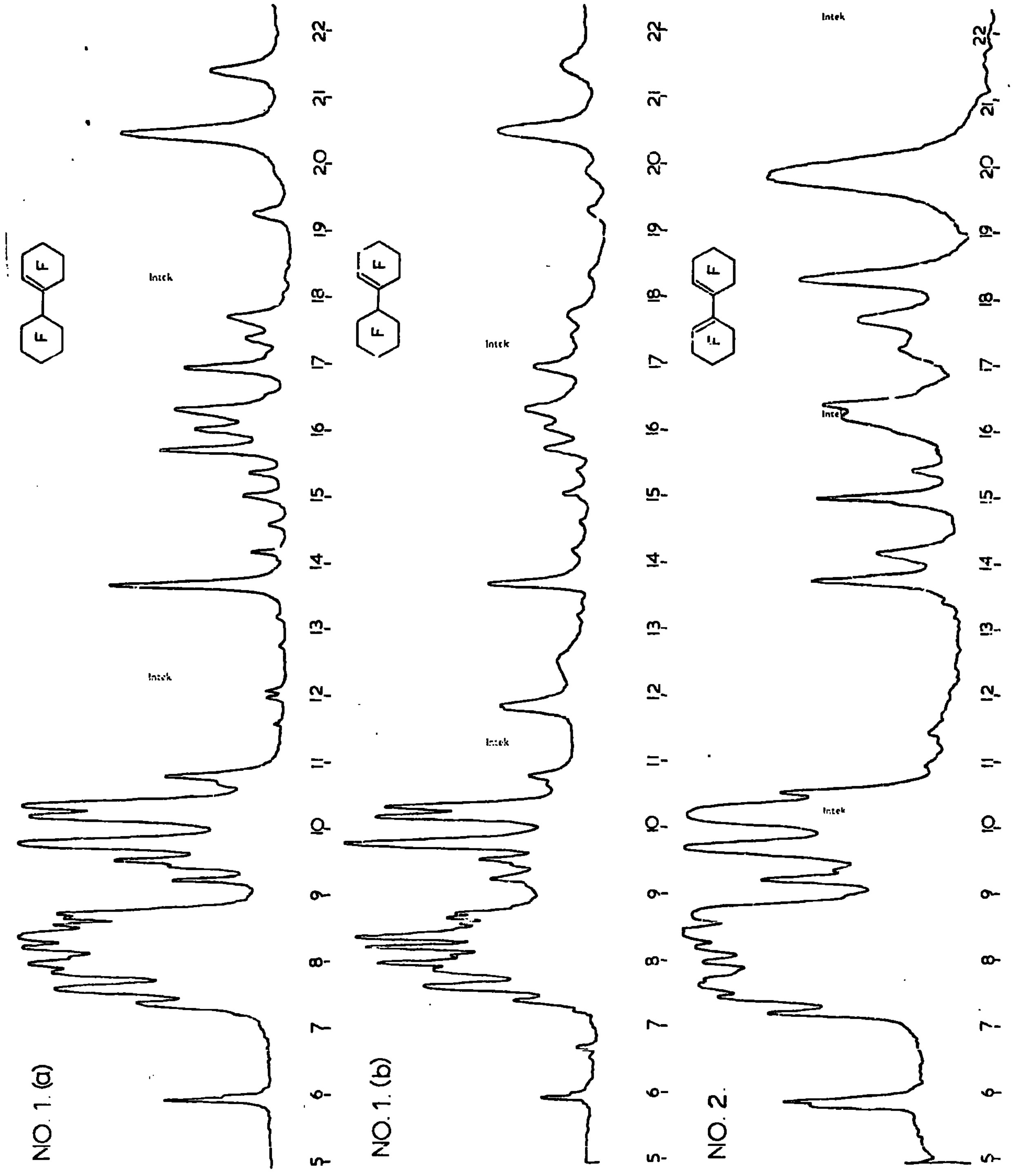
APPENDIX 2

Infra-red spectra

Solid samples were recorded as KBr discs and liquid samples as contact films between KBr plates.

Spectrum No.	Compound	
1(a)	Perfluoro-(1-cyclohexylcyclohexene)	(l)
1(b)	Perfluoro-(1-cyclohexylcyclohexene)	(g)
2	Perfluorobicyclohexenyl	(l)
3	Perfluorocyclopentene dimer	(l)
4	Perfluorobicyclopentenyl	(l)
5	Perfluorocyclobutene trimer	(l)
6	Perfluoro-(4-cyclohexylpyridine)	(s)
7	Perfluoro-(2,4-dicyclohexylpyridine)	(s)
8	Perfluoro-(2,4,6-tricyclohexylpyridine)	(s)
9	Perfluoro-(4-cyclopentylpyridine)	(s)
10	Perfluoro-(4-cyclopentenylpyridine)	(l)
11	Perfluoro-(4-cyclobutylpyridine)	(l)
12	Perfluoro-(4-cyclobutenylpyridine)	(l)
13	Perfluoro-(4-cyclohexenylpyridine)	(l)
14	$C_{17}F_{21}N$	(s)
15	4-Perfluorocyclohexyl-2-methoxy-3,5,6-trifluoropyridine	(s)
16	4-Perfluorocyclohexyl-2,6-dimethoxy-3,5-difluoropyridine	(s)
17	2,4-Perfluorodicyclohexyl-6-methoxy-3,5-difluoropyridine	(l)
18	4-Perfluorocyclopentyl-2-methoxy-3,5,6-trifluoropyridine	(l)
19	4-Perfluorocyclobutyl-2-methoxy-3,5,6-trifluoropyridine	(l)
20	Monomethoxy-perfluoro-(4-cyclohexenylpyridine)	(l)

Spectrum No.	Compound	
21	Dimethoxy-perfluoro-(4-cyclohexenylpyridine)	(l)
22	Monomethoxy derivative of $C_{17}F_{21}N$	(l)
23	Perfluoro-(2-cyclohexyl-4-isopropylpyridine)	(l)
24	Perfluoro-(2,6-dicyclohexyl-4-isopropylpyridine)	(s)
25	Perfluoro-(4-cyclohexylpyridazine)	(l)
26	Perfluoro-(4-cyclohexenylpyridazine)	(s)
27	$C_{16}F_{20}N_2$	(s)
28	4-Perfluorocyclohexyl-5-amino-3,6-difluoropyridazine	(s)
29	3,5-Difluoro-4-perfluorocyclohexyl-1H-pyridazin-6-one	(s)
30	a,b-Perfluorodicyclohexyl-c-fluoro-1H-pyridazin-d-one	(s)
31	Perfluoro-(6-cyclohexylpyrazine)	(l)
32	2,2'-Dimethoxy-dodecafluorobicyclopentenyl	(s)
33	Perfluoro-(2,2'-bisisopropylbicyclopentenyl)	(s)
34	1,1'-Dihydroxy-hexadecafluorobicyclopentyl	(s)



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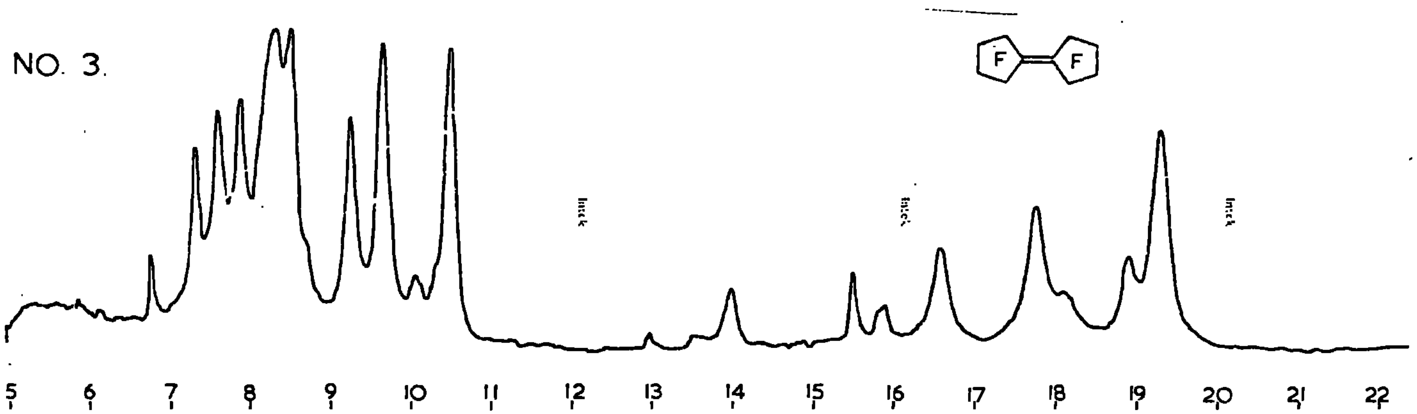
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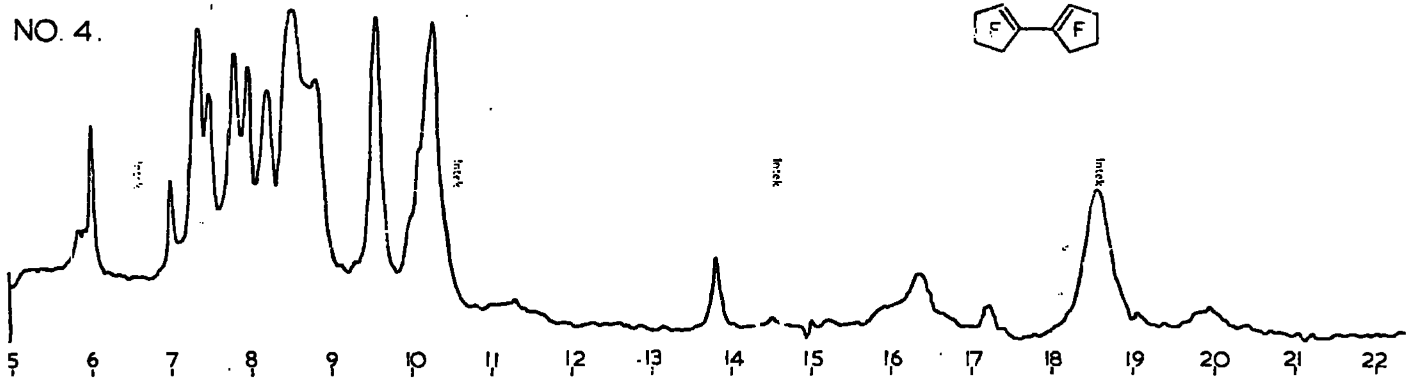
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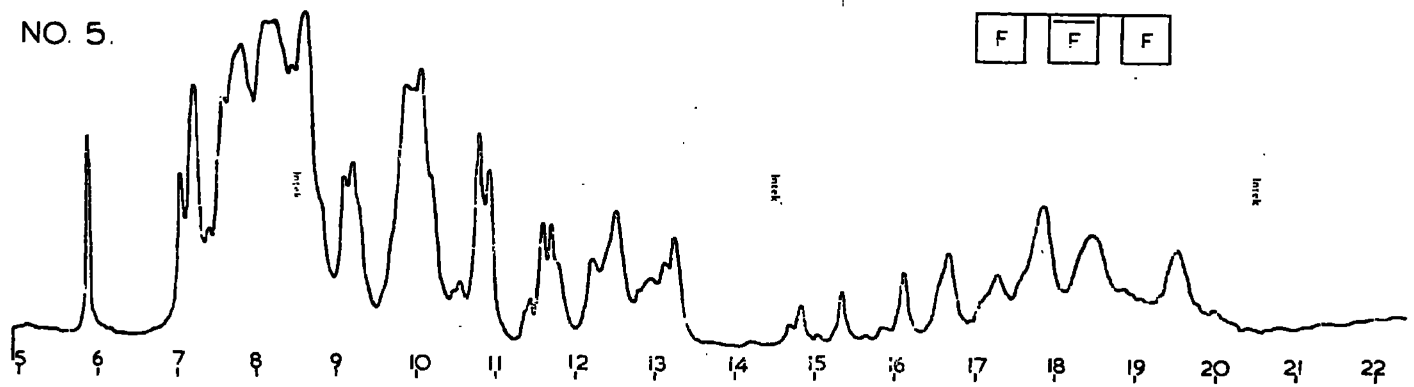
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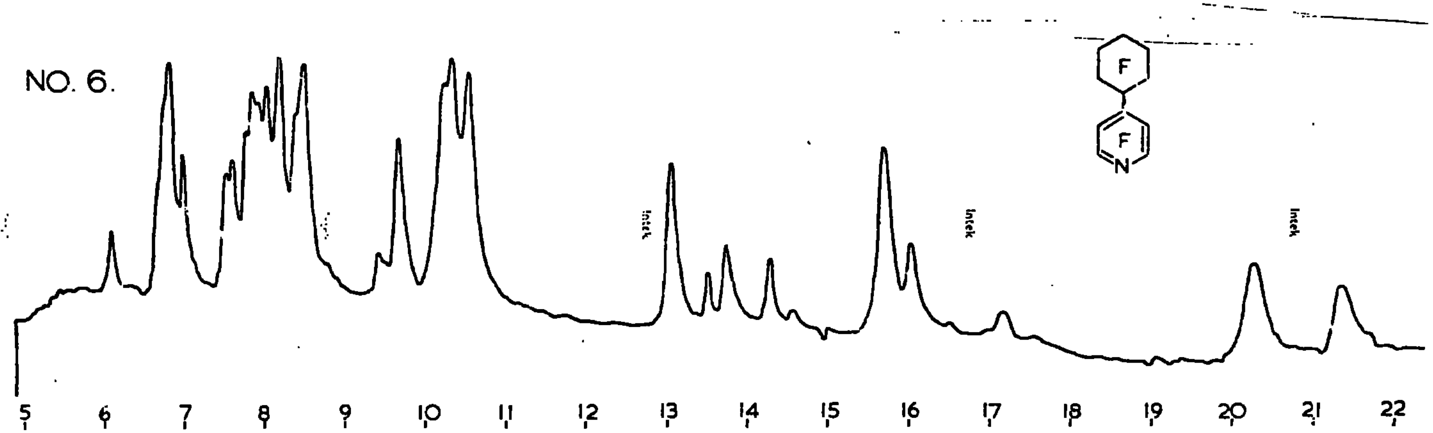
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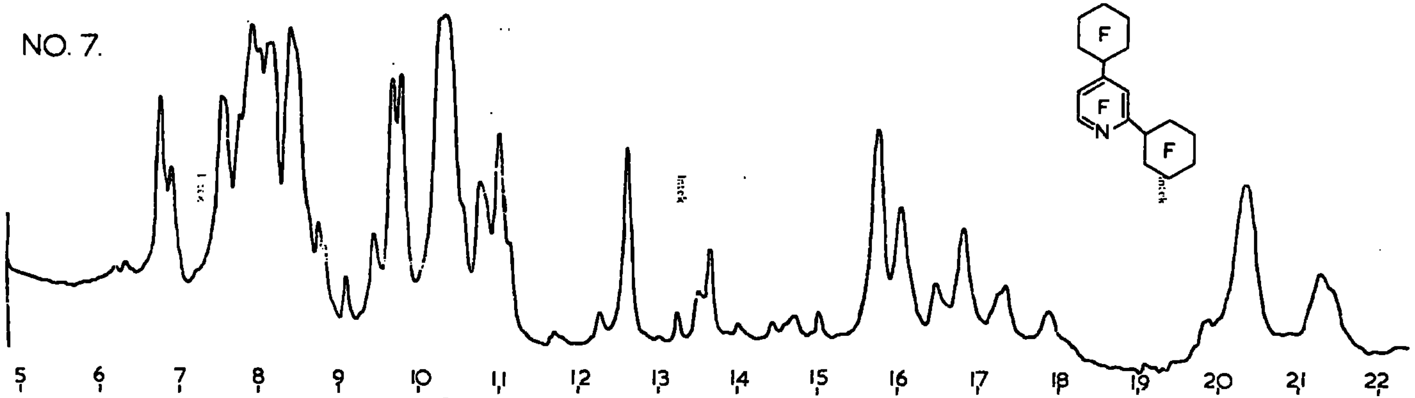
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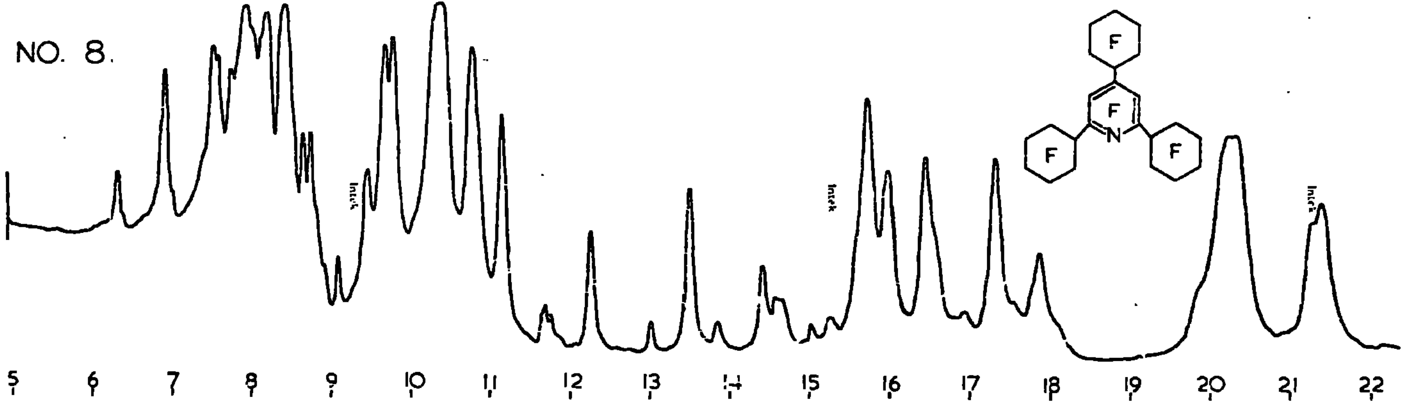
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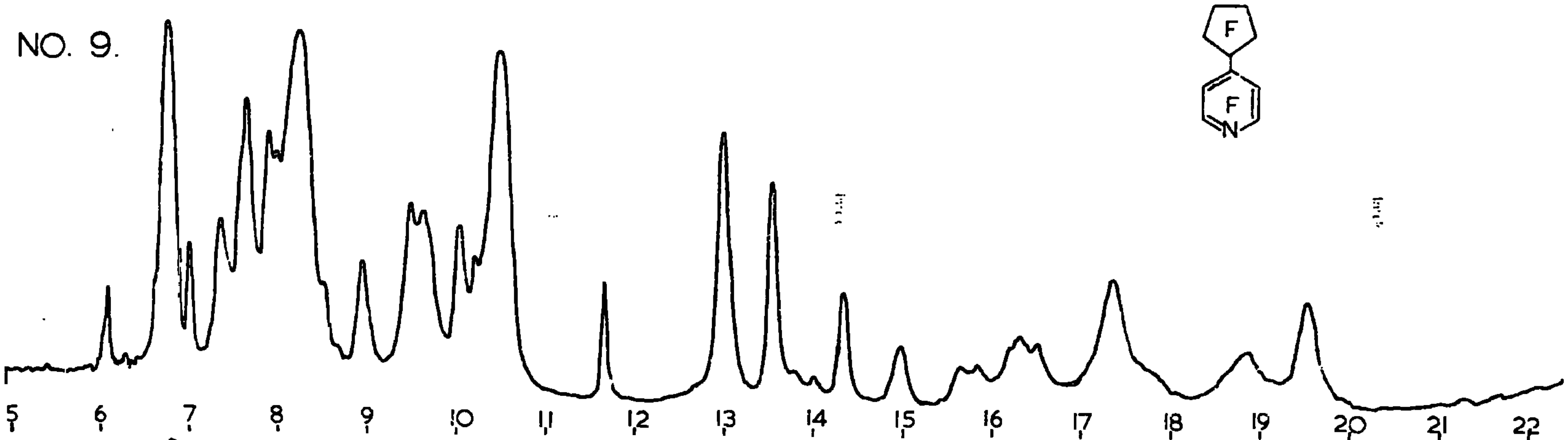
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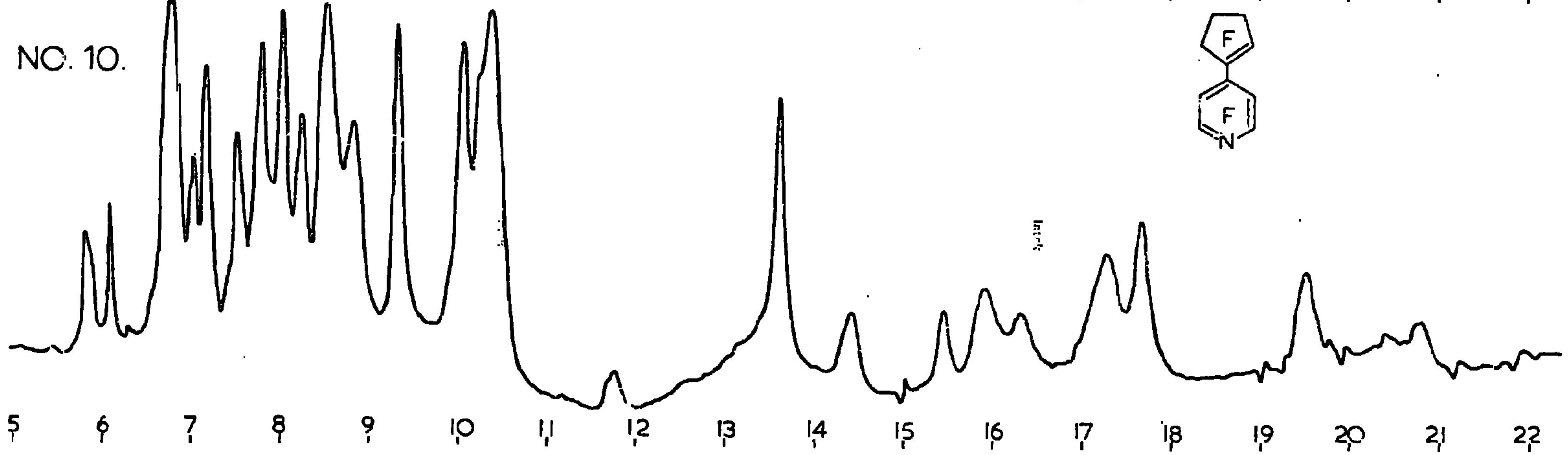
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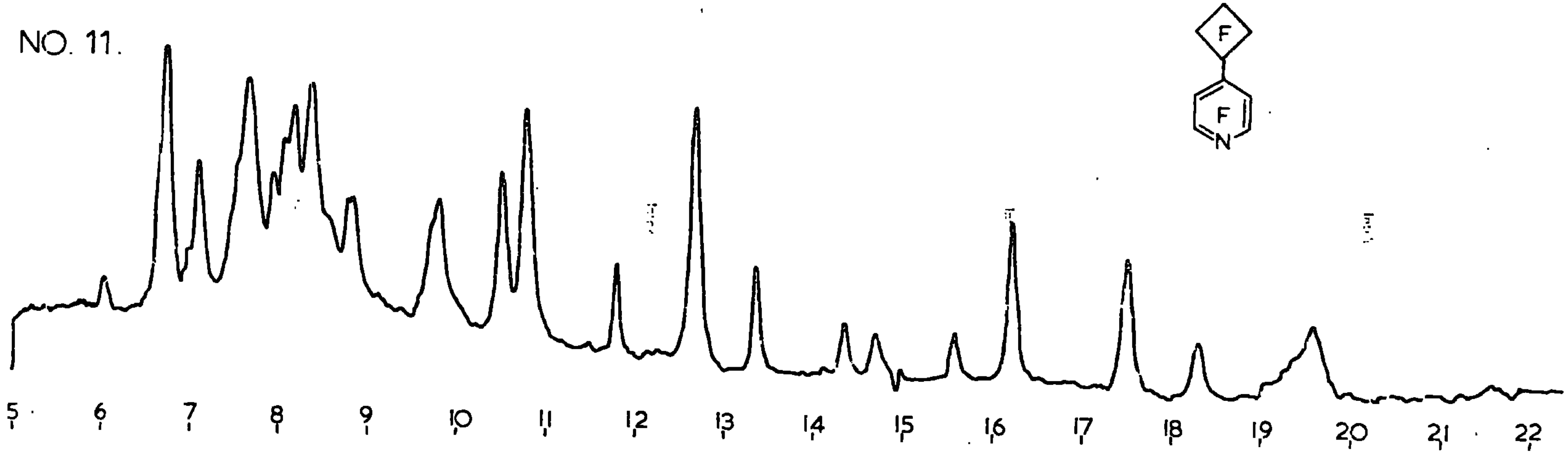
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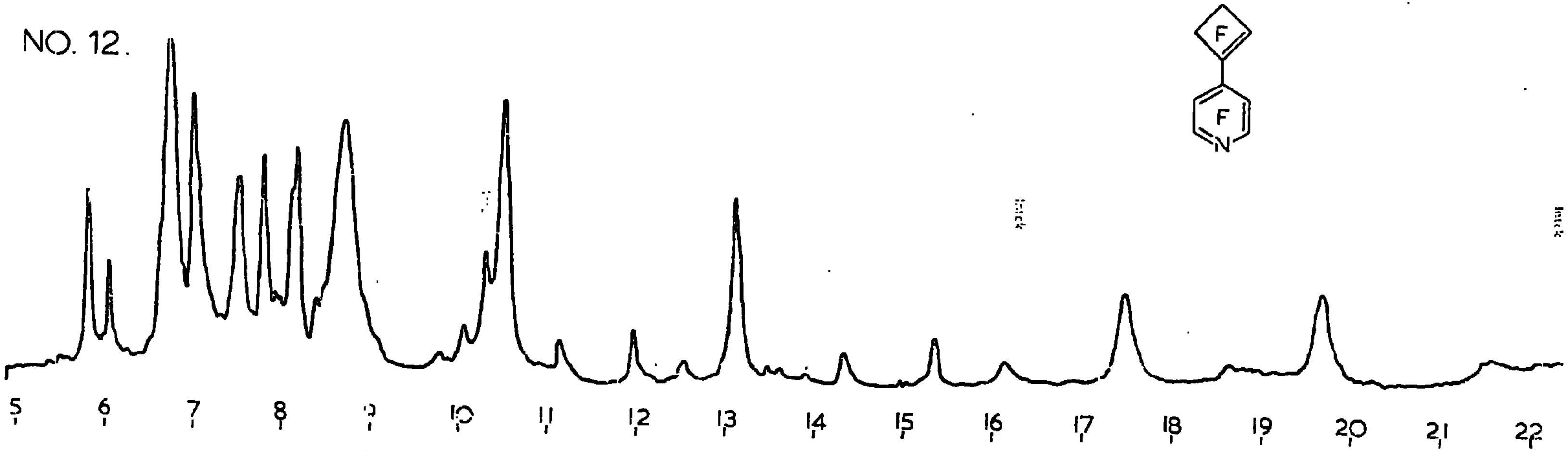
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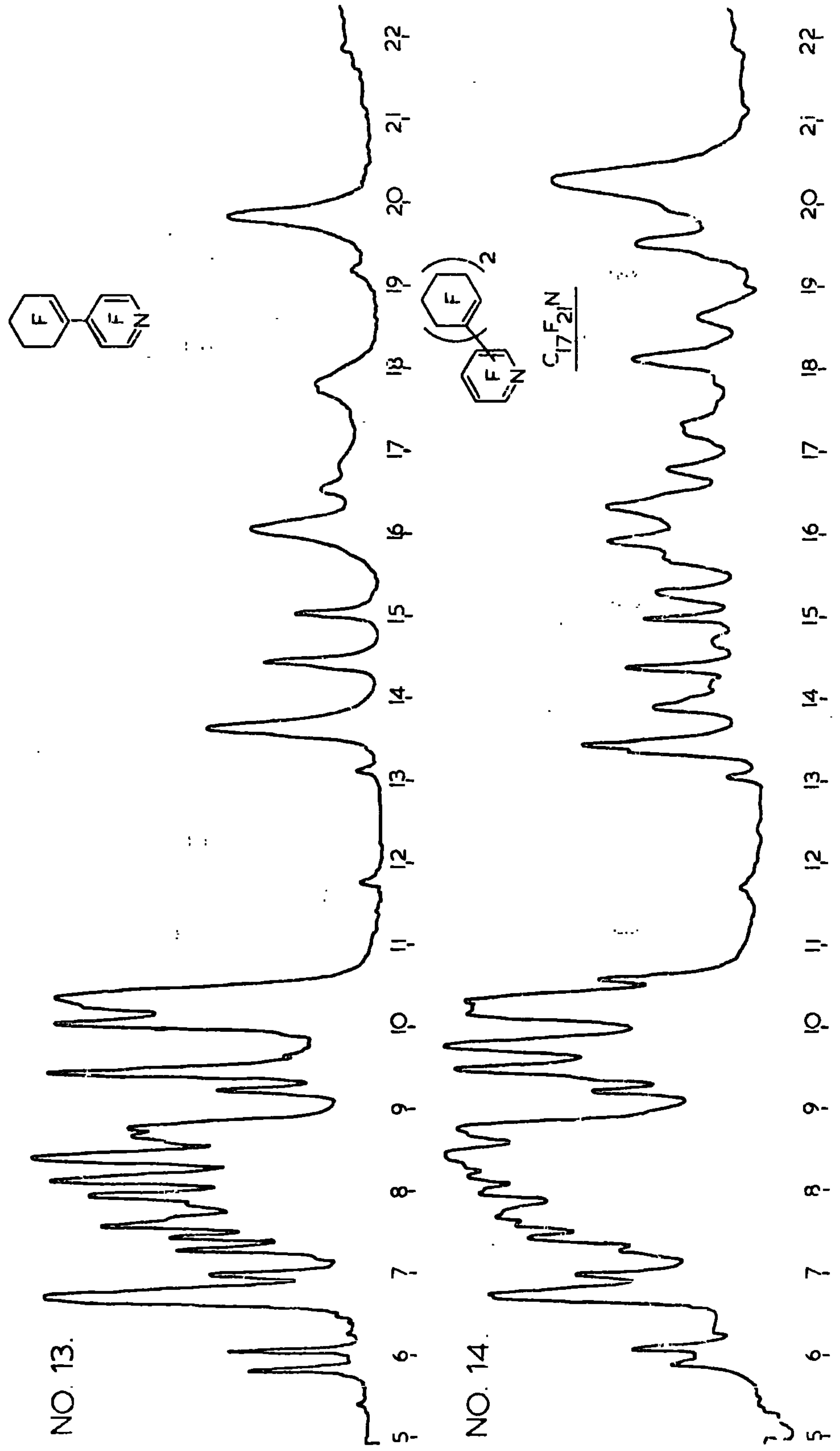
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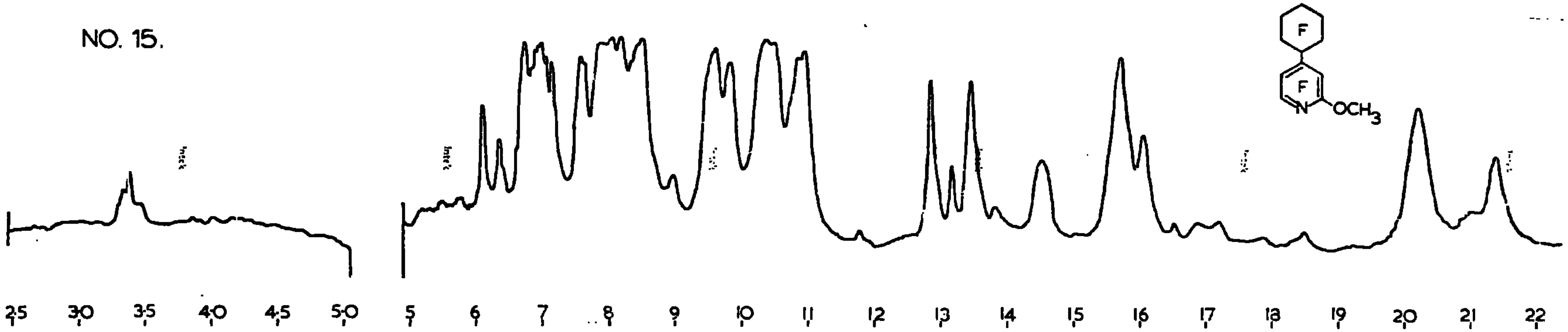

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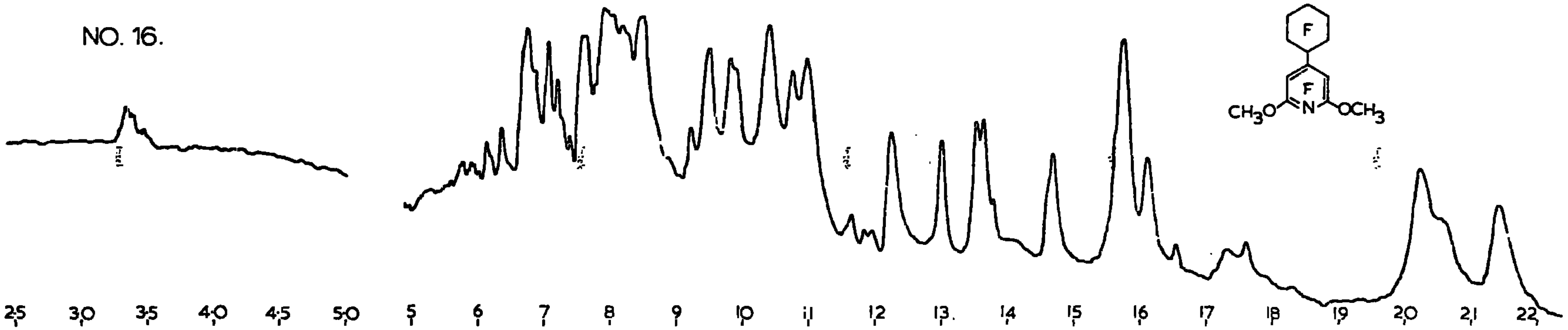

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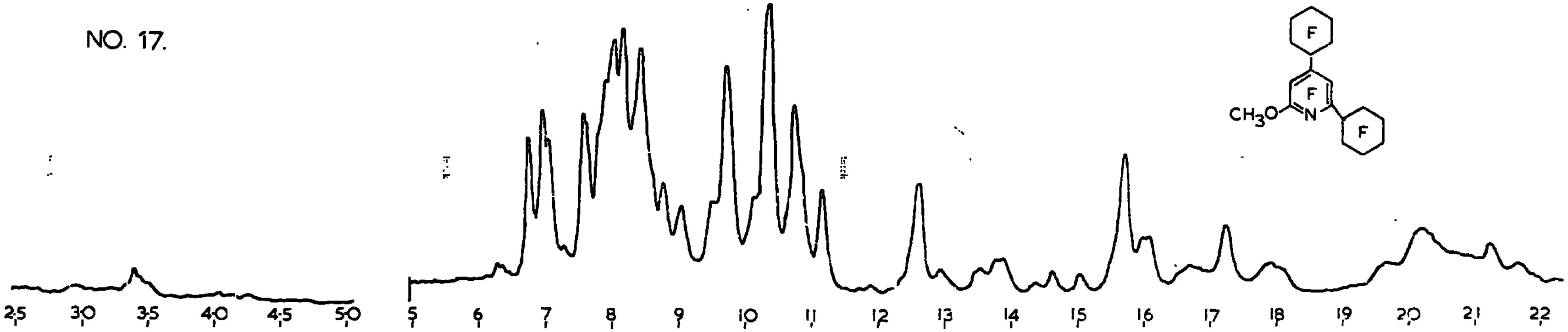

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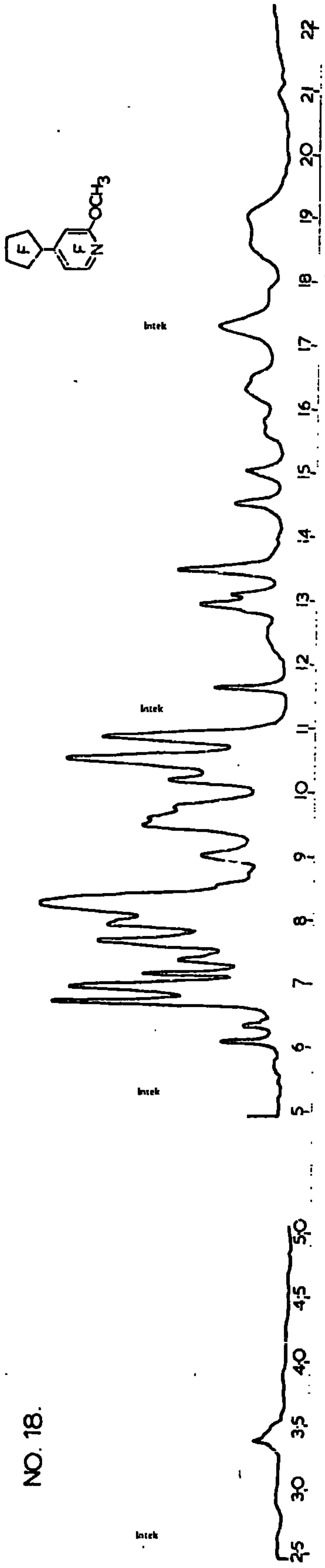
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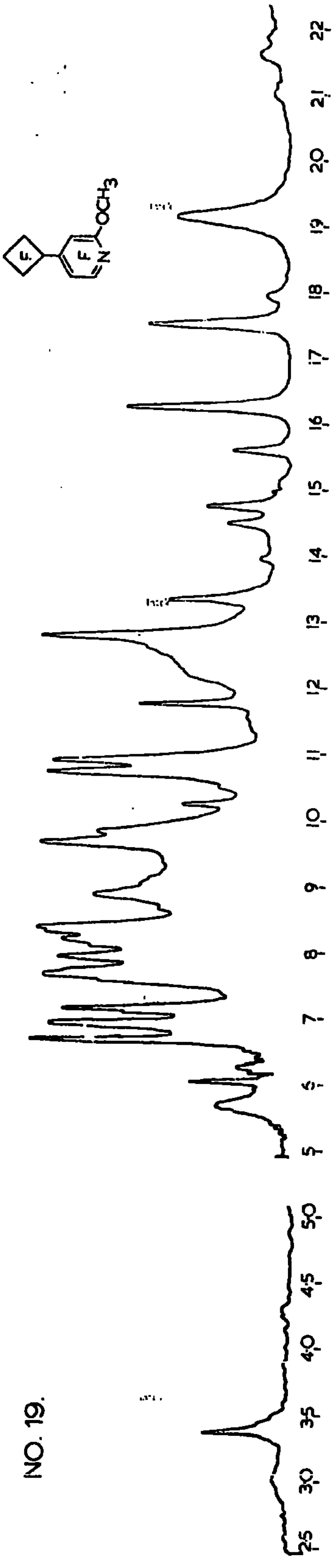
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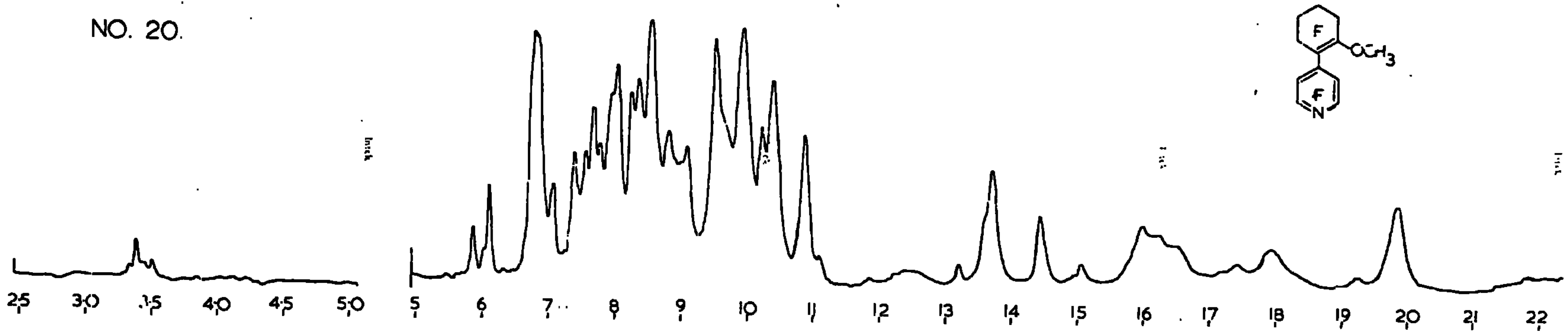

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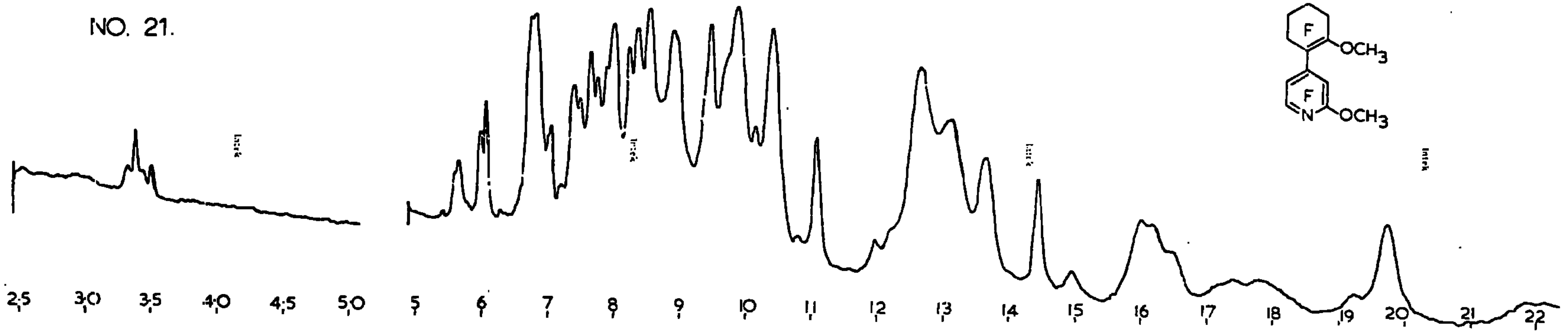

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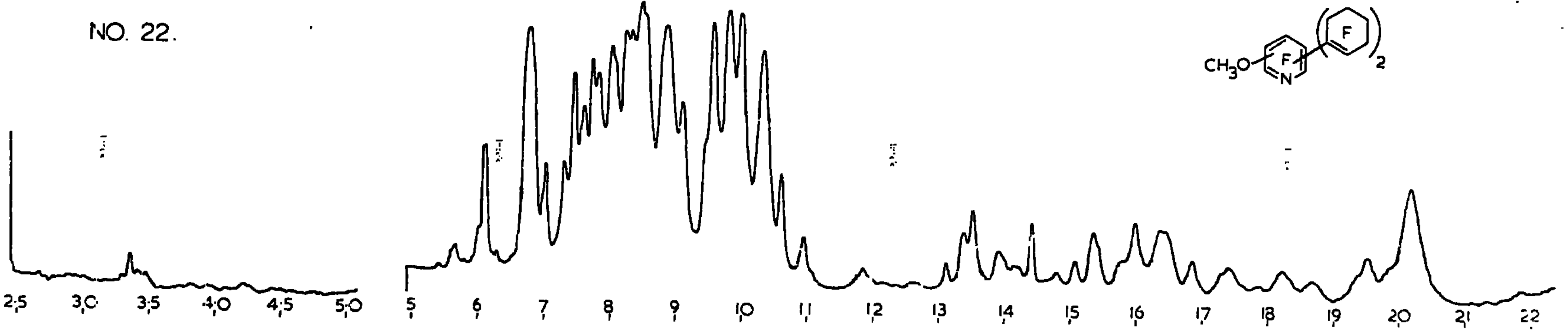

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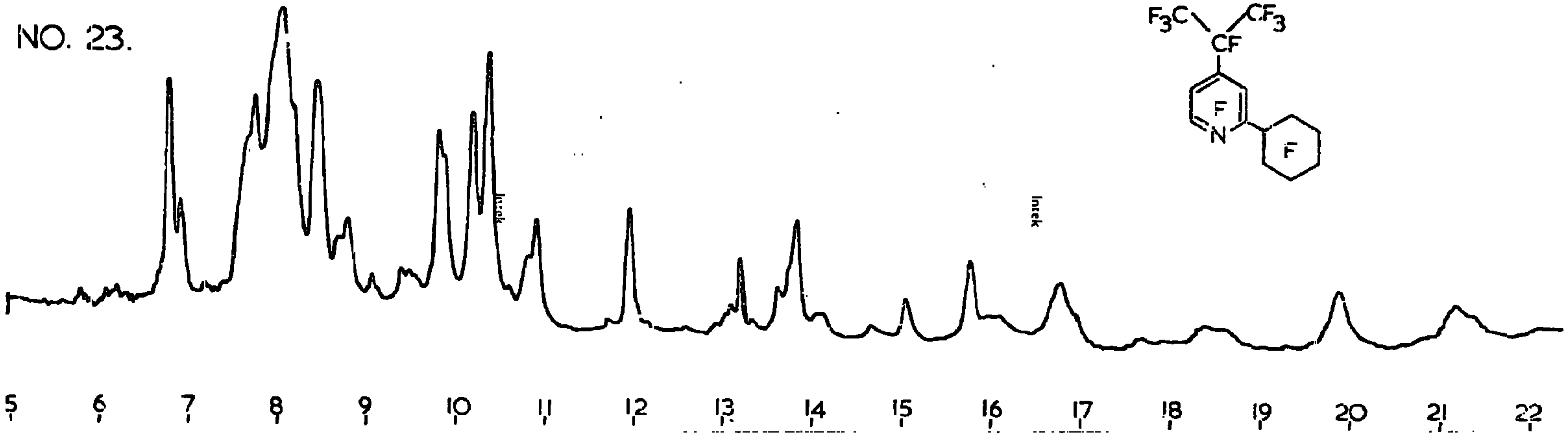
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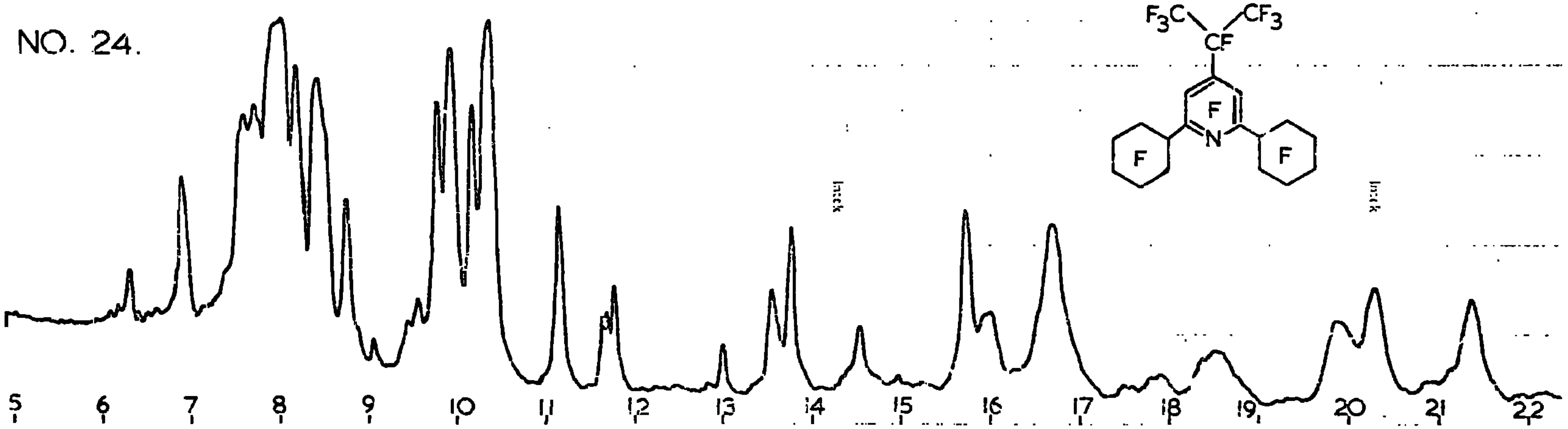
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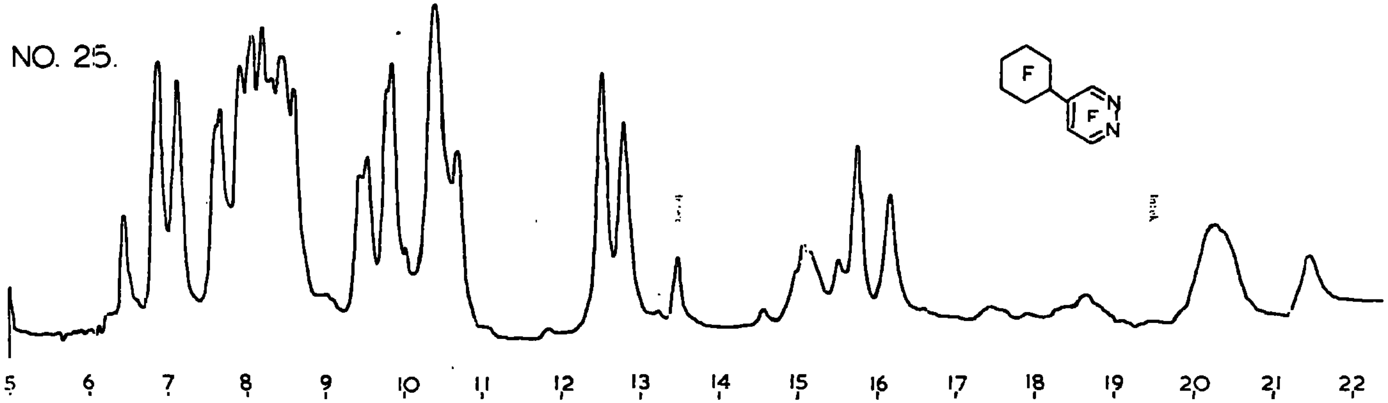

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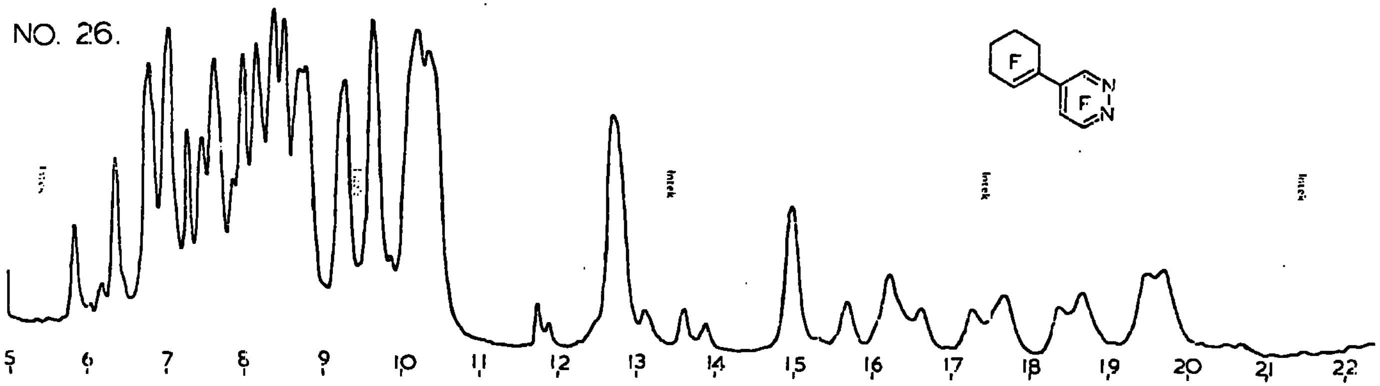

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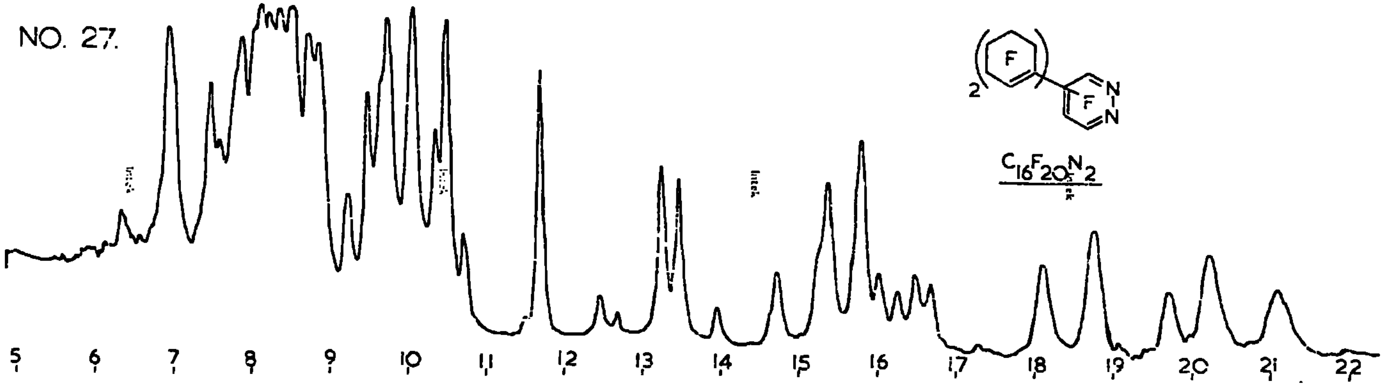

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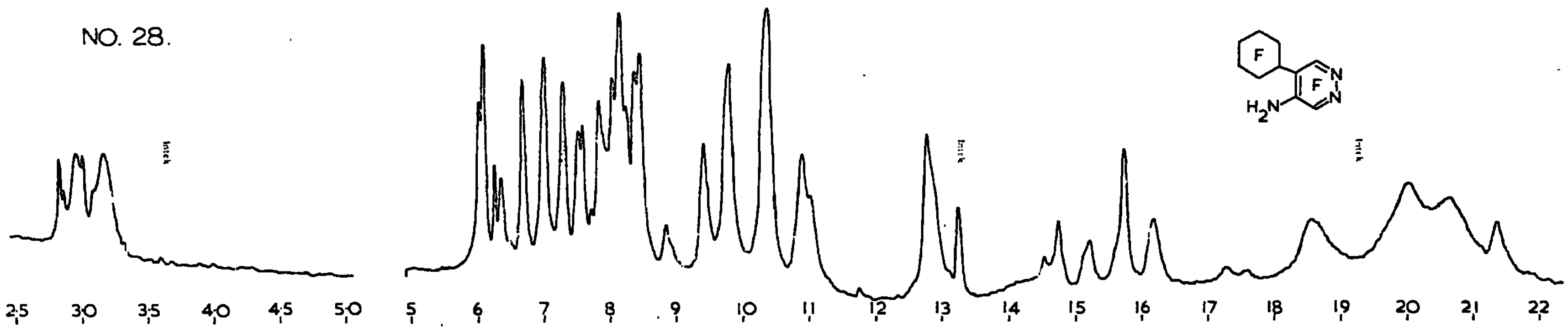

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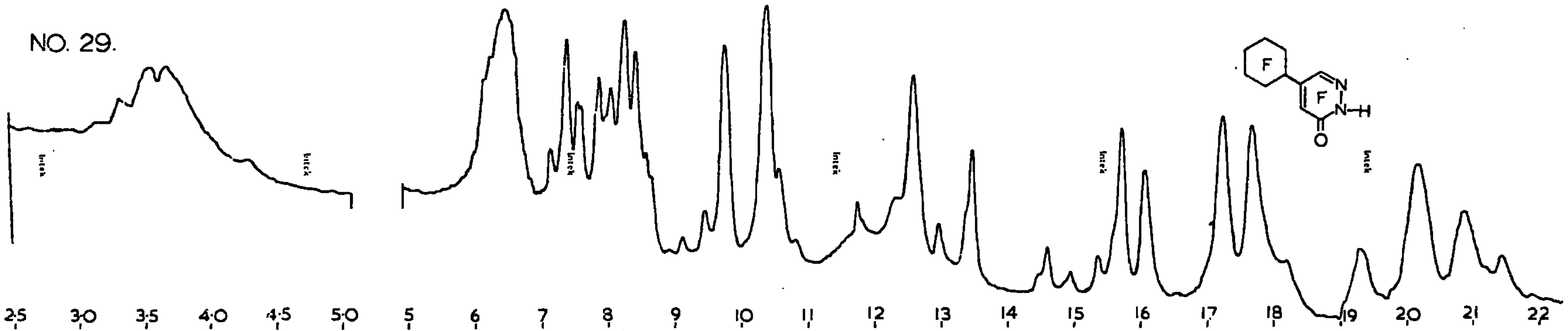

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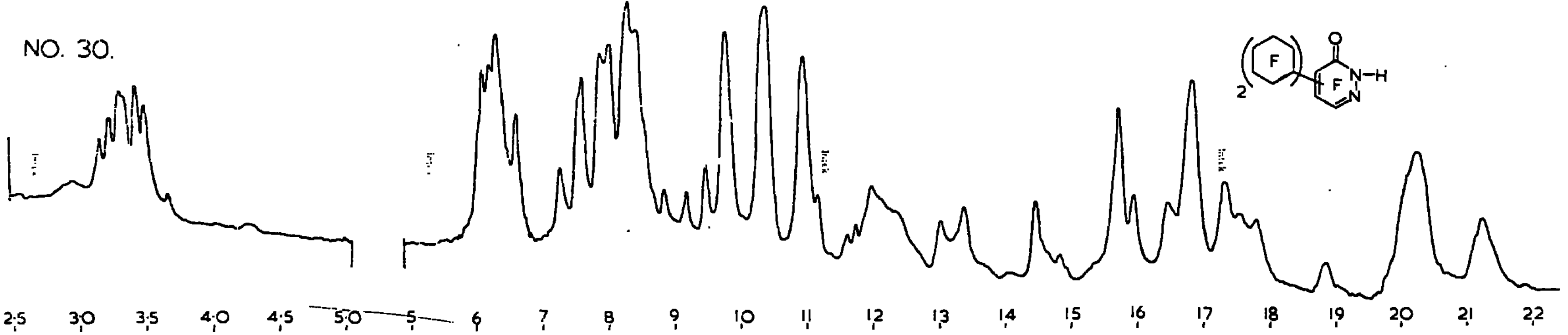

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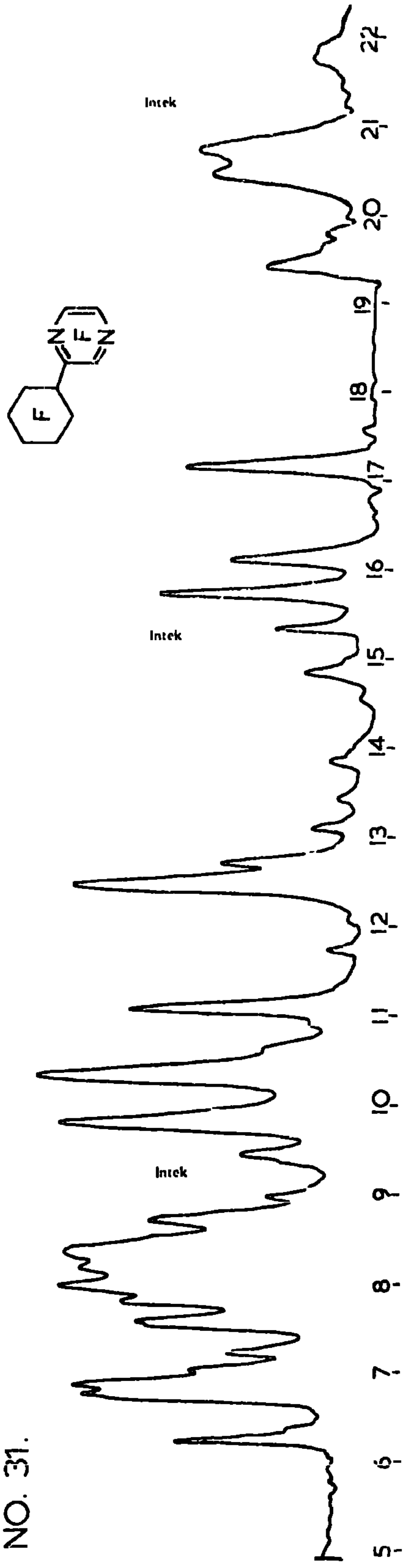
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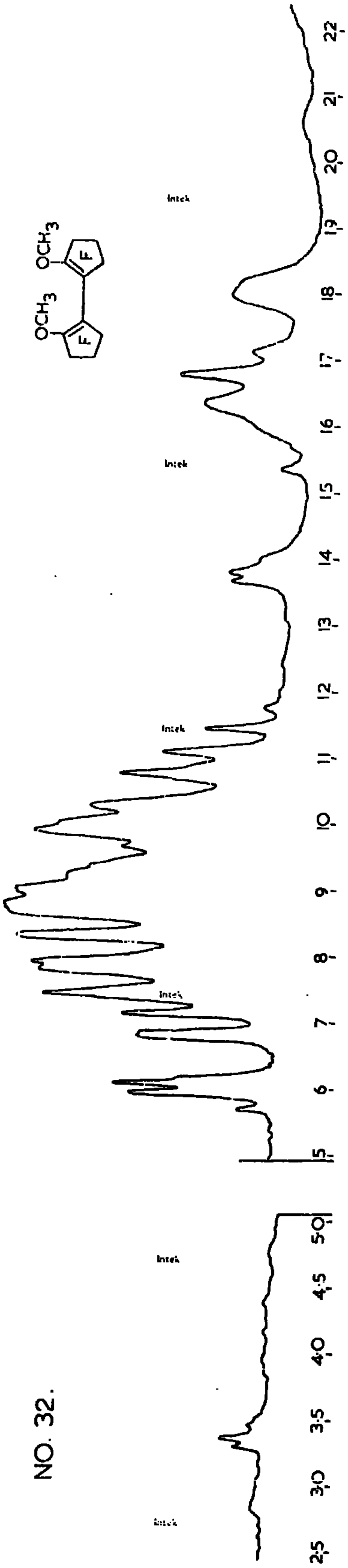

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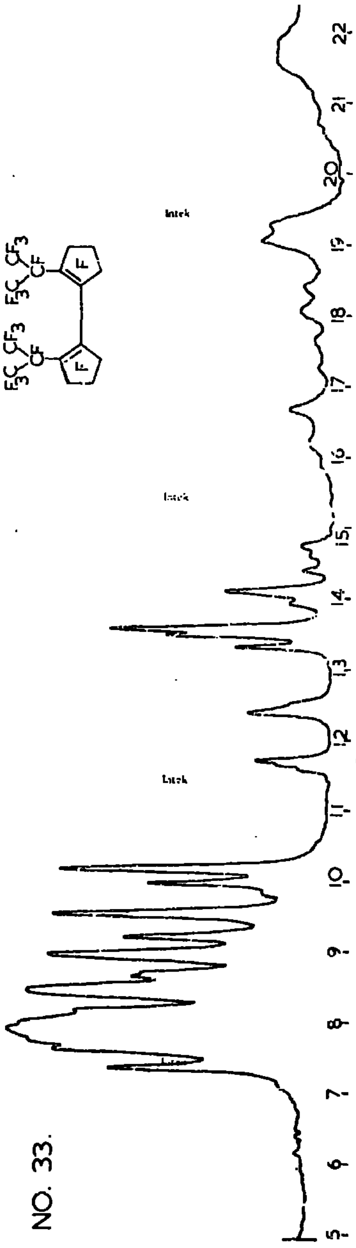

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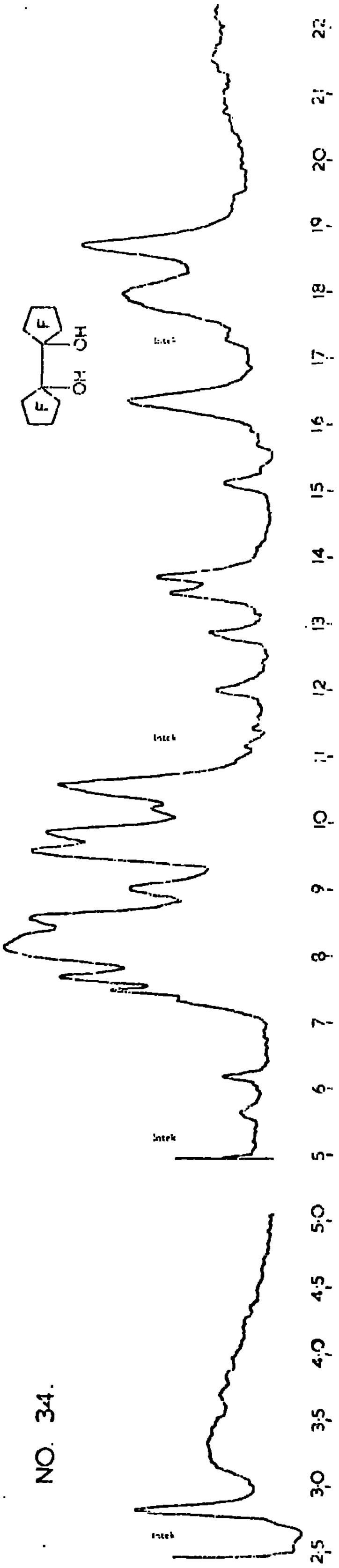

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