The fluorination of polyfluoroazabenzenes

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UNIVERSITY OF DURHAM

A THESIS

entitled

THE FLUORINATION OF POLYFLUOROAZABENZENES

Submitted by

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(St. Cuthbert's Society)

A candidate for the degree of Doctor of Philosophy

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Finally, may I also thank the Science Research Council for a maintenance award.

MEMORANDUM

The work described in this thesis was carried out in the University of Durham between October 1973 and October 1976. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

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

R.D. Chambers, R.D. Hercliffe and W.K.R. Musgrave, J.Chem.Soc., Chem Comms., 1978, 305.

R.D. Chambers, R.D. Hercliffe and R. Middleton, J.Chem.Soc., Chem. Comm., 1978, 306.

ABSTRACT

In this thesis the results of a series of fluorinations of polyfluoroazabenzenes with a 50:50 mixture of CoF_3 and CaF_2 are described. Perfluoro-4-isopropyl, -2,4-di-isopropyl, -3-methyl and -4-methylpyridines reacted by the addition of two or four fluorine atoms to give high yields of -azacyclodienes and -monoenes. The observed products were thought to represent the thermodynamically more stable dienes and a mechanism is proposed for their formation. Pyrimidines exhibited a variety of behaviours in that a diene resulted from perfluoro-4,6-di-isopropylpyrimidine, 5-chlorotrifluoropyrimide behaved more like tetrafluoropyrmidine in that dimers were produced whilst perfluoro-4-isopropylpyrimidine gave a complicated mixture of fragmentation products. Perfluoro-4,5- and 4,6-di-isopropylpyridazines both gave products resulting from the loss of nitrogen whilst a diene was obtained in high yield upon fluorinating perfluoro-2,5-di-isopropylpyrazine. Cyanuric fluoride was resistant to fluorination.

Some direct fluorinations have been performed but only tetrafluoropyrimidine and perfluoro-4,5-di-isopropylpyridazine were reactive, the former producing a dimer the latter products due to loss of nitrogen.

Some of the new perfluoropolyazacyclodienes have been reacted with a variety of nucleophilic reagents and whilst imino fluorines were readily substituted imines bearing perfluoroisopropyl were resistant to reaction. Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene has a very labile fluorine at C-2 compared with the one at C-3 and it is thought that polarisation of the imine bond by nitrogen is responsible for this.

Several of the new dienes have been subjected to photolysis and ring opening and fragmentation reactions were observed. Products with isolated double bonds were not reactive.

GLOSSARY

The following terms and conventions have been followed throughout the text:

1. F within a ring denotes all unmarked bonds within the molecule are to fluorine.

2. H.V.H.M.F. = high valency heavy metal fluoride.

3. A.H.F. = anhydrous hydrogen fluoride.

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CHAPTER 1

THE DIRECT FLUORINATION OF ORGANIC COMPOUNDS

1.1 Introduction

Various techniques for fluorinating organic molecules have been developed over the years and they can be divided into two broad classes:-

(1) Techniques which involve reaction of the organic compound with fluorine gas directly;

(2) Techniques which involve the reaction of the organic compound with a fluorine containing species in which the labile fluorine is bonded to a different element. These latter are called indirect techniques and are described, with an emphasis on CoF_3, in Chapter 2.

1.2 Thermodynamics of Direct Fluorination

Compared with reactions between organic compounds and chlorine, reactions with fluorine are characteristically violent and often proceed explosively or with combustion. Special techniques to moderate the reaction often have to be employed as a result. The table of enthalpy changes, presented below, illustrates this point.

The data in Table 1.1 indicate that a large amount of energy is released when fluorine is reacted with an organic compound as a result of the low dissociation energy of molecular fluorine and the strength of the bonds formed.

TABLE 1.1

Enthalpy changes during halogenation reactions

Process	Enthalpy change Kjoules $mole^{-1}$	Reference
1 Dissociation of Fluorine $F_2 \rightarrow 2F\cdot$	+ 155	1
2 Dissociation of Chlorine $Cl_2 \rightarrow 2Cl\cdot$	+ 254	1
3 Formation of $\geq C-F$ bond	- 439	2
4 Formation of $\geq C-Cl$ bond	- 340	2
5 Formation of H-F bond	- 565	2
6 Formation of H-Cl bond	- 438	2
7 Addition of F_2 to $>C=C<$ $F_2 + >C=C< \rightarrow >CF-CF<$	- 421	3
8 Addition of Cl_2 to $>C=C<$ $Cl_2 + >C=C< \rightarrow >CCl-CCl<$	- 147	3
9 Substitution of $\geq C-H$ by F_2 $F_2 + \geq C-H \rightarrow \geq C-F + HF$	- 410	1
10 Substitution of $\geq C-H$ by Cl_2 $Cl_2 + \geq C-H \rightarrow \geq C-Cl + HCl$	- 107	1

The energy released is sufficient to rupture $\geq C-H$ and $\geq C-C\leq$ bonds. Therefore, unless extremely efficient methods of conducting this energy away from the site of reaction are employed, fluorination reactions result in complicated mixtures of fragmentation products and tarry polymers.

1.3 Proposed Mechanisms for Direct Fluorination Reactions

Fluorine usually reacts with organic compounds by a radical chain mechanism, similar to that observed when organic compounds are chlorinated in the presence of ultra-violet radiation. The evidence for the intermediacy of radicals is:-

a) dimerisations and oligomerisations are common, especially when the fluorination is performed in a condensed phase.[4]

e.g. $CCl_2 = CCl_2 \xrightarrow[F_2]{0^{o}C} C_4F_2Cl_2$ and other products;[4]

b) reactions are catalysed by light;[5]

c) reactions are inhibited by free radical inhibitors such as oxygen.[6]

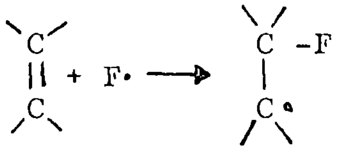
One major difference between chlorinations and fluorinations is the fact that fluorinations proceed very readily in the absence of ultra-violet radiation and at very low temperatures. In spite of the low dissociation energy of fluorine, only a small number of radicals can be produced, thermally, at room temperature.[7]

$$F_2 \longrightarrow 2F\cdot \qquad K_{eq} = 10^{-20}$$ Ref: 7

Whether this is sufficient to initiate the reaction has been a subject for debate.[7,8,9] The proposed initiation steps are:-

$$F_2 \longrightarrow 2F\cdot$$

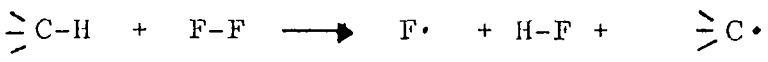
$$\geq C{-}H \;+\; F\cdot \longrightarrow \;\geq C\cdot \;+\; HF$$



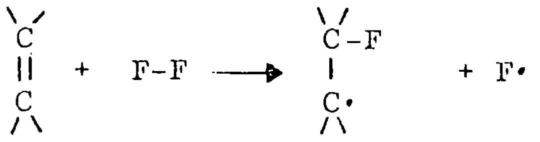
etc. Ref: 8

The activation energy of the hydrogen abstraction step is very low, and it has been argued that, because of this, such low fluorine atom concentrations are sufficient for initiation.[8]

However, Miller has suggested alternative initiation processes in which a molecule of fluorine, as opposed to an atom, reacts with either a $\geq C{-}H$ bond, for substitution reactions, or with a double bond, for addition reactions.[9] Radicals are generated in both processes:-



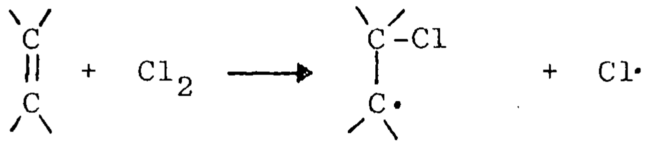
ΔH = 17Kj.mole^{-1}



ΔH = -5Kj.mole^{-1}

Ref: 9

Thermodynamically, both processes are quite reasonable, and the data are consistent with the fact that fluorine is significantly more reactive with olefins than is chlorine.[9]



ΔH = + 94.5 Kj.mole^{-1}

Ref: 9

Rogers studied the kinetics of the reaction between gaseous fluorine and the olefins perfluorobut-2-ene and 2,3-dichlorohexafluorobut-2-ene and found that the order of reaction, with respect to fluorine, was consistent with a bimolecular initiation step.[10,11] This was firm evidence for Miller's earlier proposals. Semenov did a theoretical study of the reaction of fluorine with olefins, and also argued for the bimolecular process.[7]

1.4 Experimental Techniques for Direct Fluorination

1.4A Direct fluorination in the liquid phase

Many successful fluorinations have been performed by passing fluorine, or a mixture of fluorine and an inert gaseous diluent, into cold dilute solutions of an organic compound. By stirring vigorously, a reasonable degree of thermal homogeneity can be achieved, although Tedder has said that, as the solubility of fluorine in organic solvents is low, most of the reaction must occur inside bubbles in the gas phase, or at the interface, and the temperature of such environments may be significantly higher than that of the solvent.[12] Therefore, there is a degree of uncertainty about the reaction temperature of liquid-phase fluorinations.

The solvent must be **reaso**nably inert to fluorine and, in this respect, the chlorofluoroalkanes have proven superior to other solvents, when sufficient quantities of substrates can be dissolved in them.

The apparatus in Figure 1.1, which Miller designed illustrates how many of the difficulties of direct liquid phase fluorination can be overcome.[13]

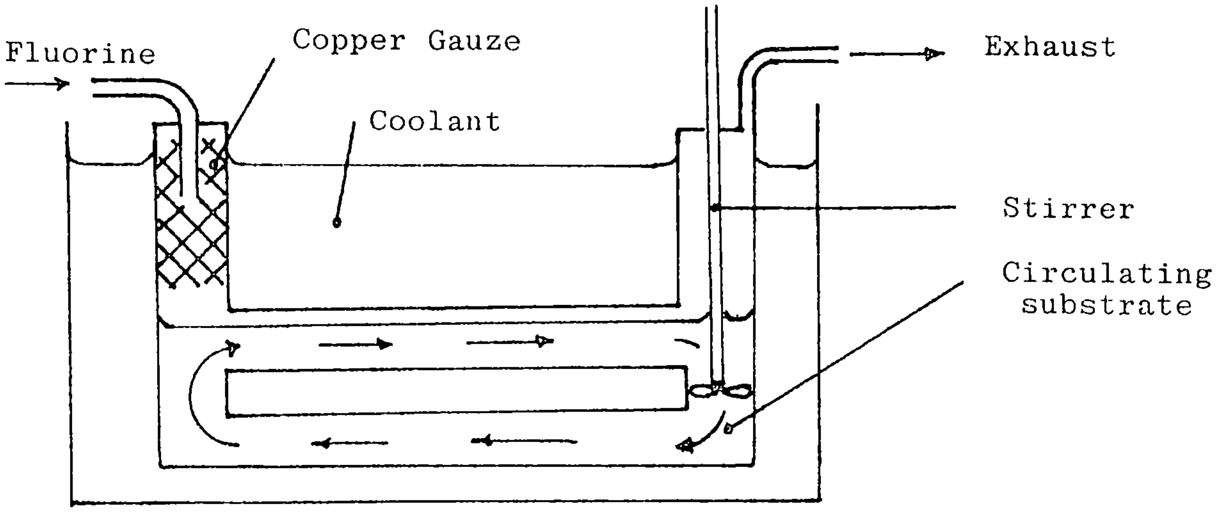


Figure 1.1 Ref: 13

It consisted of a rectangular loop of brass tubing, to which was added an inlet and an outlet tower. The material to be fluorinated (either neat or in solution) was caused to circulate in the loop by a paddle, whilst the fluorine was passed over the liquid surface, counter to the current. The whole apparatus was immersed in a cooling bath.

Many examples of reactions performed by direct fluorination in the liquid phase will be found in Sections 1.5 to 1.8.

Coupling reactions are common when this technique is used, since radicals are produced in a condensed phase.

1.4B Jet fluorination

Bigelow performed a series of successful direct fluorinations by reacting gaseous substrates with fluorine in a turbulent nitrogen jet.[14] The jet speed was set to exceed that of the flame speed, so that reaction occurred in an homogenised mixture instead of the localised area of a flame front. In this way, heat was efficiently dissipated. Hexafluoroethane (1) was obtained in 85% yield from ethane and no fragmentation or polymerisation products were detected.[15]

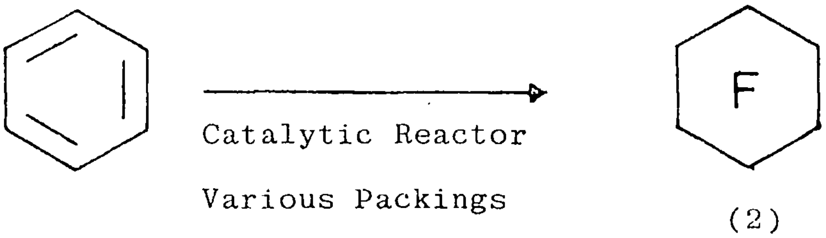
$$C_2H_6 \xrightarrow[\text{Jet fluorination}]{F_2/N_2} \underset{(1)}{C_2F_6} + HF$$

85%

Ref: 15

1.4C Catalytic fluorination

Another early technique, was to employ reactors filled with metal shot for the reaction of organic substrates in the vapour phase with fluorine. It is uncertain whether the success of the method is simply due to heat dissipation by the shot, or, as has been suggested, because the reaction occurs at the metal surfaces via a catalytic process involving high valency fluorides formed there.[16] This seems unlikely, however, as Musgrave and Smith found that yields of perfluorocyclohexane (2) from benzene varied little when a series of different surfaces were employed.[17]



(2)

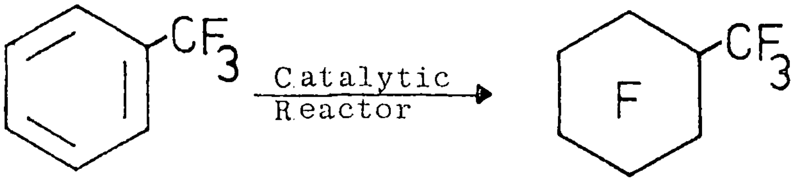
Ref: 17

Silver[18] and cobalt[12] fluorides are active fluorinating agents at the temperature of these reactions, but these metals did not appear to be more active as packings than copper turnings.

Using this technique, Cady et al. were able to prepare perfluoroheptane (3) in 62% yield from n-heptane[16] and, in contrast to fluorination in condensed phases, the vapour phase reaction of trifluoromethylbenzene (4) gave perfluoromethylcyclohexane (50) in good (85%) yield.[19]

$$n\text{-}C_7H_{16} \xrightarrow[\text{Reactor}]{\text{Catalytic}} n\text{-}C_7F_{16}$$

(3) 62% Ref: 16



(4) (5) 85% Ref: 19

Polymerisation sometimes occurs in catalytic fluorinations and, if it is extensive enough, material condenses onto the 'catalyst' surfaces and reduces the efficiency of heat dissipation. However at higher reaction temperatures such deposits are quickly degraded. Bigelow observed hexafluoroethane (6) and heptafluoropropane (7) as well as carbon tetrafluoride, when he fluorinated methane.[20]

$$CH_4 \xrightarrow{F_2} CF_4 + \underset{(6)}{C_2F_6} + \underset{(7)}{C_3F_8}$$

Ref: 20

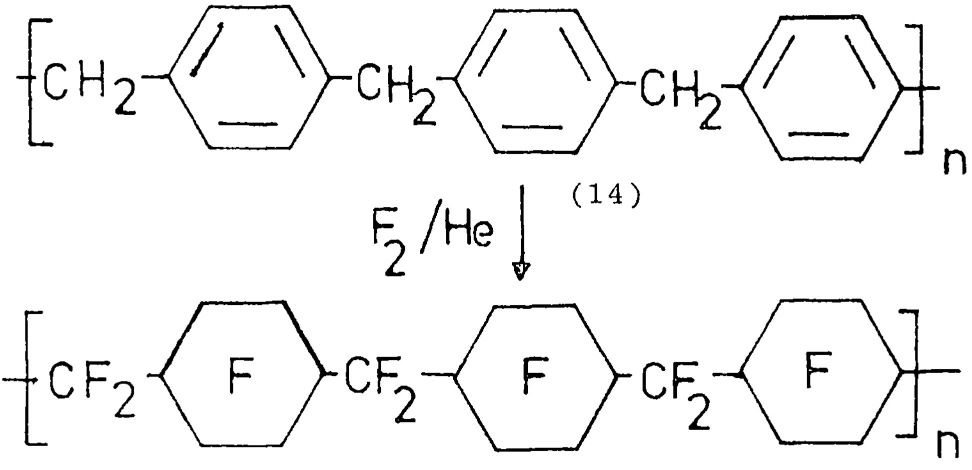
1.4D The fluorination of solids - the 'La Mar' process

Margrave and Lagow reacted a wide range of solids by exposing them to an atmosphere of helium containing low concentrations of fluorine which resulted in high yields of the corresponding saturated perfluoro analogues. Both organic and inorganic compounds were reacted. They rationalised their results by suggesting that the fluorine took so long to reach a reactive site, whilst diffusing through the helium and the solid lattice, that the energy released by previous reactions was well dissipated and hence species with sufficient kinetic energy to rupture $\geq C-C \leq$ bonds would not be generated.[21]

As the amount of fluorine incorporated into the lattice increased, the concentration of fluorine in the helium was also increased to maintain the rate of reaction. It was found that complete reaction, as determined by elemental analysis of the final product, was not possible beyond a few millimetres from the solid surface, unless the solid was reacted in a finely divided state, or as a thin film.

The method has been used to convert hydrocarbon polymers into perfluoro polymers. Thus, poly-p-xylylene (14), in the form of a powder, was fluorinated by this method, using a helium diluent.[22] The concentration of fluorine was increased successively until, after six days, it constituted 95% of the atmosphere. According to elemental analysis, the yield of the saturated perfluoro analogue (15) of the original polymer was 99%.

e.g.



(14)

Ref: 22

(15)

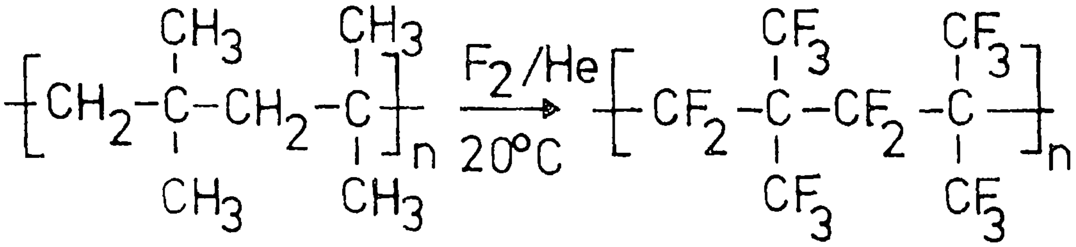
The possibility that polyethylenes, and other polymers, could be given extremely inert surfaces by treatment with fluorine suggests potential for major commercial exploitation of this technique.

Polyethylene (8), polypropylene and polystyrene have all been successfully treated.[23] It has been reported that the softening temperature of polyvinylfluoride films rises sharply to above 300°C when they gain a fluorine content in excess of 50%,[24] whilst polyethylene films treated this way have increased oil resistance.[25]

$$-[CH_2-CH_2]-_n \xrightarrow{F_2/He} -[CF_2-CF_2]-_n$$

Ref: 23

Even highly branched compounds like polyisobutylene (9) gave yields of the perfluoro derivative (10) as high as 95%.[22]



$$-\!\left[CH_2-\overset{CH_3}{\underset{CH_3}{C}}-CH_2-\overset{CH_3}{\underset{CH_3}{C}}\right]_n- \xrightarrow[20^{\circ}C]{F_2/He} -\!\left[CF_2-\overset{CF_3}{\underset{CF_3}{C}}-CF_2-\overset{CF_3}{\underset{CF_3}{C}}\right]_n-$$

(9) (10)

Ref: 22

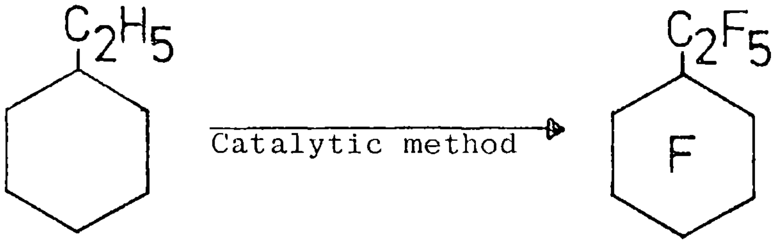
1.5 The Direct Fluorination of Alkanes

Alkanes have been fluorinated by all four of the direct methods described. In general, yields of the perfluoro analogues are reasonable for straight chains but become poor if the skeleton is very branched. Monofluorides have been prepared by liquid phase fluorination whereas fully saturated derivatives are more easily prepared by the catalytic and jet techniques. It has been shown that fluorine atoms inhibit the substitution of adjacent hydrogens, so that in long chains, e.g. lubricants, it is very difficult to remove the final traces of hydrogen by direct fluorination.[26]

1. $n\text{-}C_7H_{16} \xrightarrow{\text{Catalytic method}} n\text{-}C_7F_{16}$ 62% Ref: 17

2. $C_2H_6 \xrightarrow{\text{Jet reactor}} C_2F_6$ 83% Ref: 16

3.



13% Ref: 26

1.6 Direct Fluorination of Alkenes

Bockemüller was the first to successfully fluorinate an alkene in the liquid phase, when he treated tetrachloroethylene (11) with fluorine diluted with carbon dioxide.[27]

$$\underset{(11)}{CCl_2 = CCl_2} \xrightarrow[-80^{\circ}C\ CCl_4]{F_2/CO_2} \underset{1.2\%}{CFCl_3} + \underset{26\%}{CFCl2CFCl_2} + \underset{1.7\%}{CCl_3CFCl_2} + \underset{8.5\%}{C_4F_2Cl_8}$$

Ref: 27

Dimerisation was a major reaction and some migration of chlorine atoms occurred.

Miller later also obtained a dimer (12) when he added fluorine to s-dichlorodifluoroethylene (13) and hence he proposed a free-radical mechanism, in spite of the low reaction temperature.[34]

$$\underset{(13)}{CFCl = CFCl} + F_2 \longrightarrow CF_2Cl - CFCl\cdot + F\cdot$$

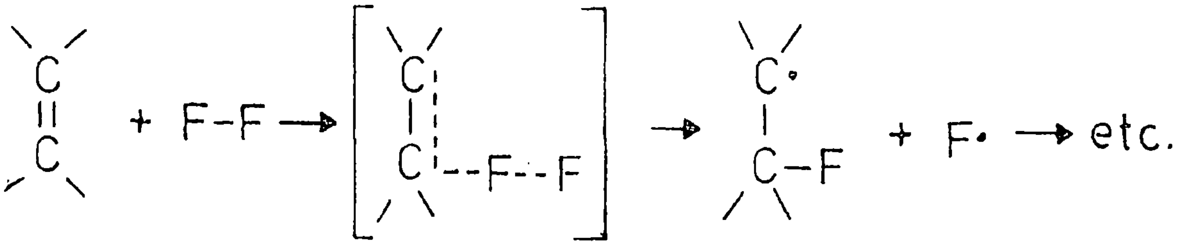
$$2CF_2Cl - CFCl\cdot \longrightarrow \underset{(12)}{(CF_2Cl - CFCl)_2}$$

$$CF_2Cl - CFCl\cdot + F\cdot \longrightarrow CF_2Cl - CF_2Cl$$

$$\underline{\text{Overall}}\ CFCl = CFCl \xrightarrow[\text{No solvent}]{\text{Neat } F_2} \underset{(12)\quad 30\%}{(CF_2Cl - CFCl)_2} + \underset{17\%}{CF_2Cl - CF_2Cl}$$

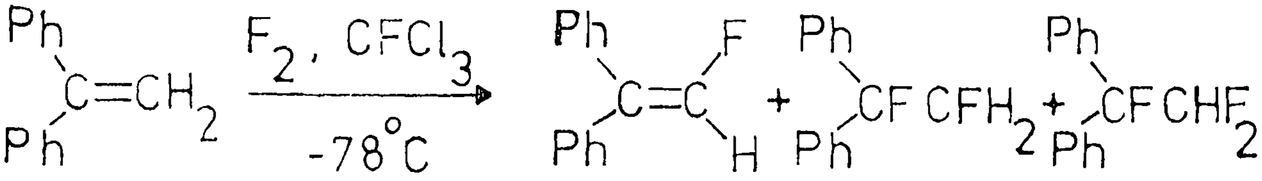
Ref: 28

It was on the basis of this and other reactions that Miller proposed the bimolecular initiation referred to earlier. A non-polar four-centred transition stage was envisaged:-



Ref: 28

This contrasts with the ionic mechanism later proposed for the addition of fluorine to the olefin (14).[29]



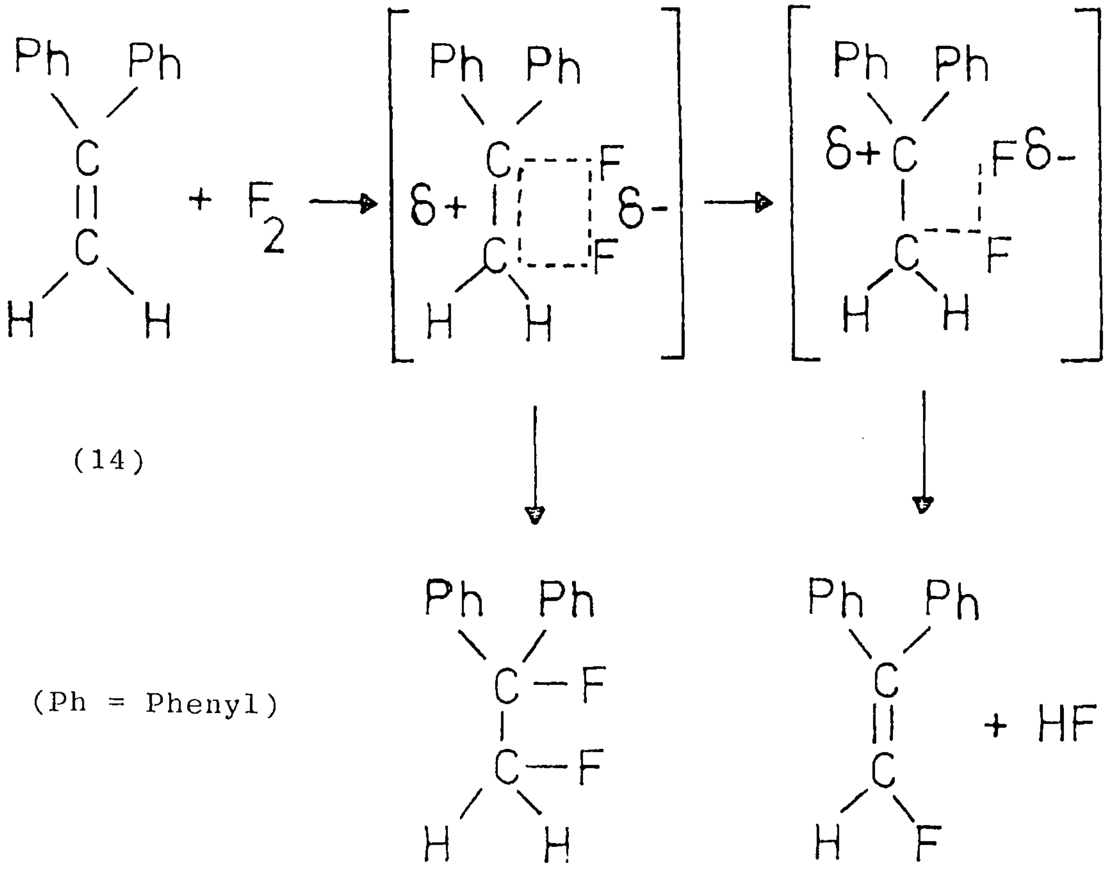
(14) (16) (17) (15)

78% 14% 8%

(Ph = Phenyl)

Ref: 29

It was shown that the trifluoride (15) is formed by the addition of fluorine to (16) exclusively and that olefin (16) itself, is unlikely to have formed by the loss of HF from (17). This was accounted for by the following mechanism :-



(14)

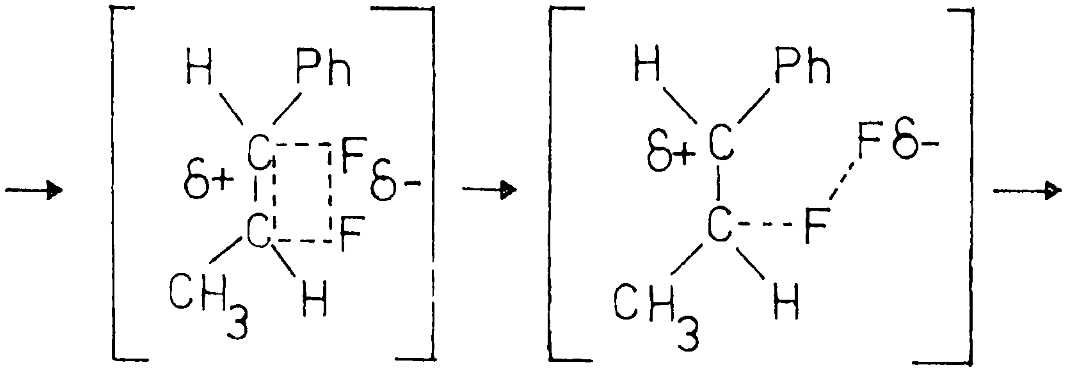
(Ph = Phenyl)

(17)

(16)

Ref: 29

Later, Merritt fluorinated cis- and trans-propenylbenzenes in a series of solvents, and was able to show that the mode of addition was predominantly syn in both cases, consistent with complex (18).[30] Reaction in methanol resulted in an addition reaction as well as formation of the difluoride. The addition was stereospecific and was presented as evidence for the formation of (19)



(18) (19)

Ref: 30

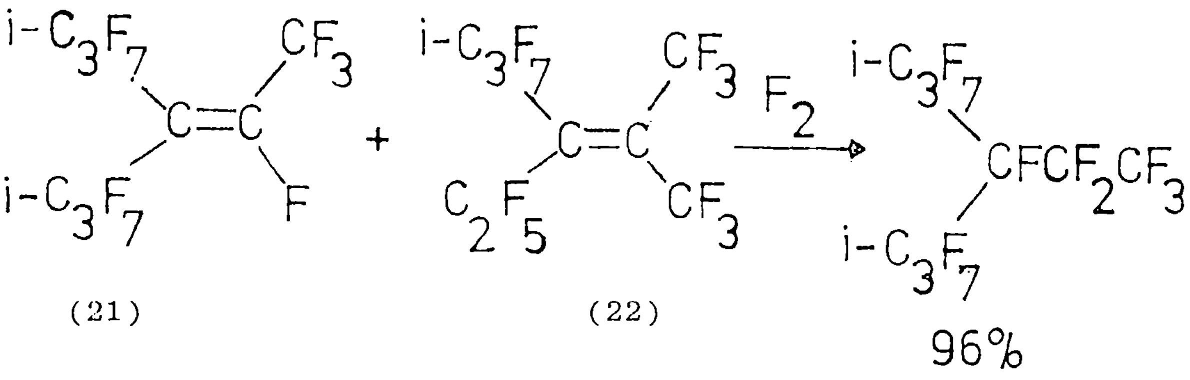
Radical fluorinations in the liquid phase were employed during the 1939 war, as a route to oligomeric perfluorocarbon lubricants. Perfluorobutadiene (20) gave good yields of viscous oligomers.[13]

$$CF_2 = CF\text{-}CF = CF_2 + F_2 \longrightarrow C_8F_{18} + C_{12}F_{26} + C_{16}F_{34} + C_{28}F_{58}$$

(20)

Ref: 13

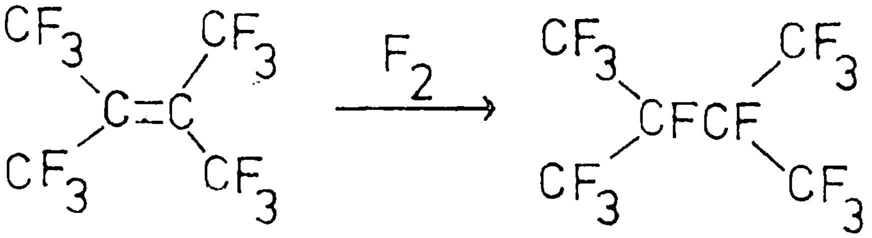
Direct fluorination of perfluoroolefins is less exothermic than of hydrogen rich olefins, and hence, is more easily controlled. Recently, Von Halasz patented a fluorination of perfluorononene isomers (21) and (22) in which he does not use a diluent.[31]



(21) (22)

Ref: 31

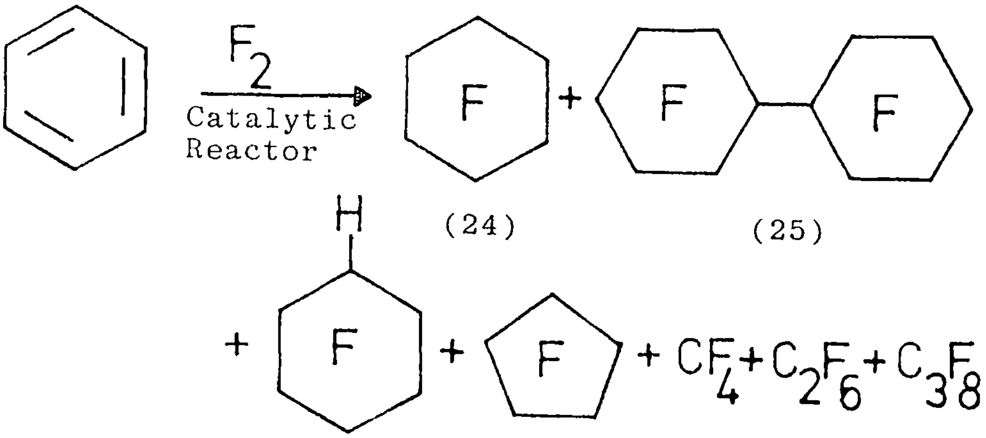
No oligomerisation was reported. Similarly, perfluoro-2,3-dimethyl-2-butene (23) failed to dimerise upon fluorination.[32]



1.7 Direct Fluorination of Aromatic Systems

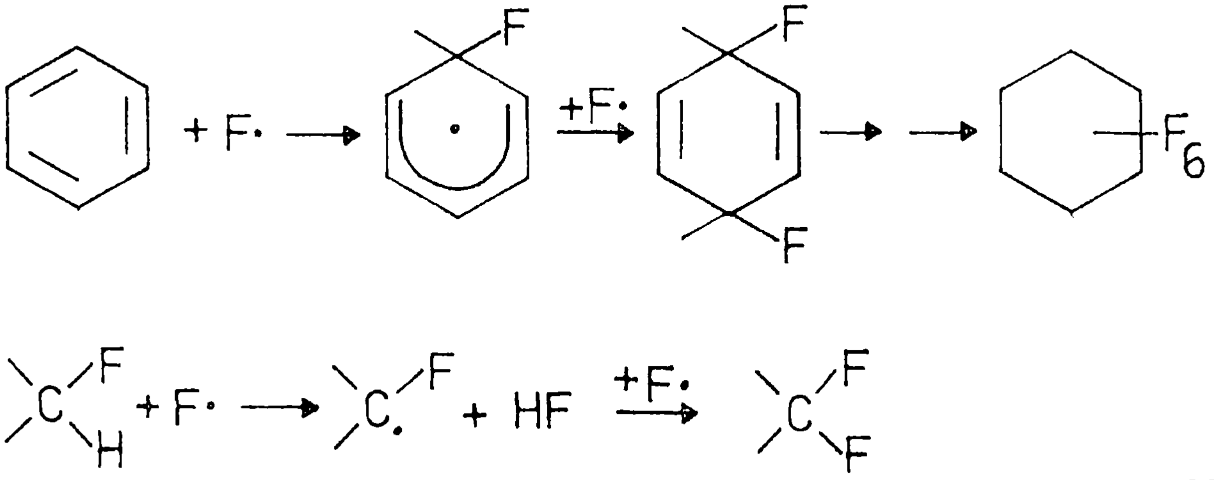
1.7A The fluorination of benzene

Bigelow fluorinated benzene in a catalytic reactor packed with copper gauze and obtained a complicated mixture containing dodecafluorocyclohexane (24) and some bi-undecafluorocyclohexyl (25) amongst the major products.[33] No aromatic products were produced, and the other products consisted of saturated fragments and some ring contracted compounds.



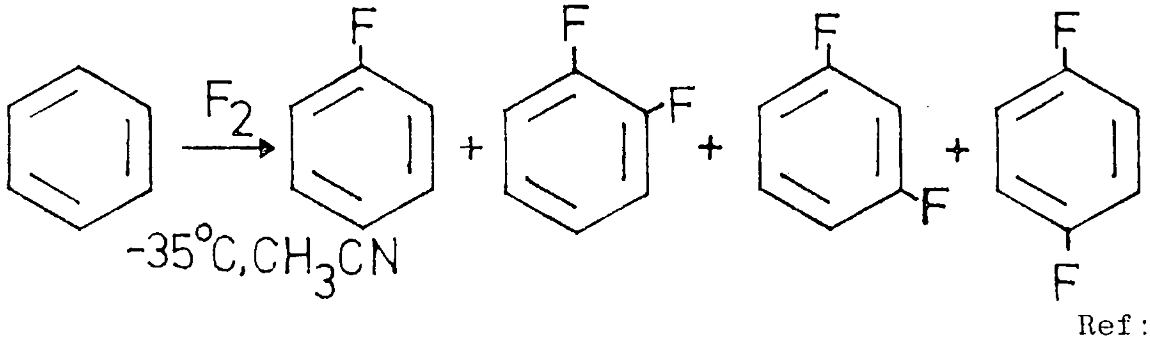
(24) (25) Ref: 33

He postulated a radical mechanism involving addition reactions followed, in the later stages, by substitution reactions:-



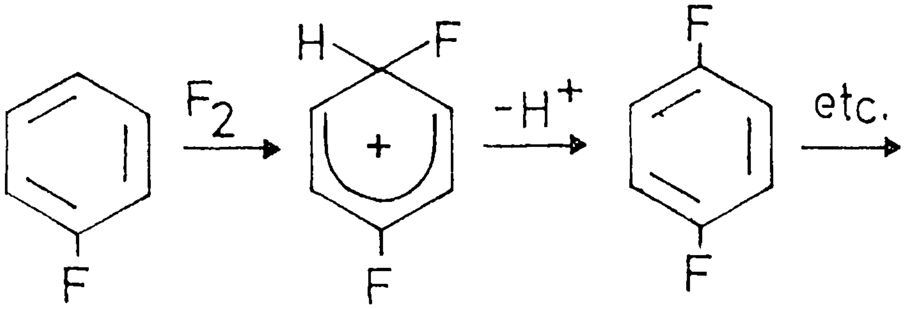
Ref: 33

Grakauskas, however, did produce aromatic substitution products when he reacted benzene, as a 6% solution in acetonitrile at -35°C with fluorine[34] in the molar ratio of 1 part benzene to 0.7 of fluorine. Some polymeric material was also produced:



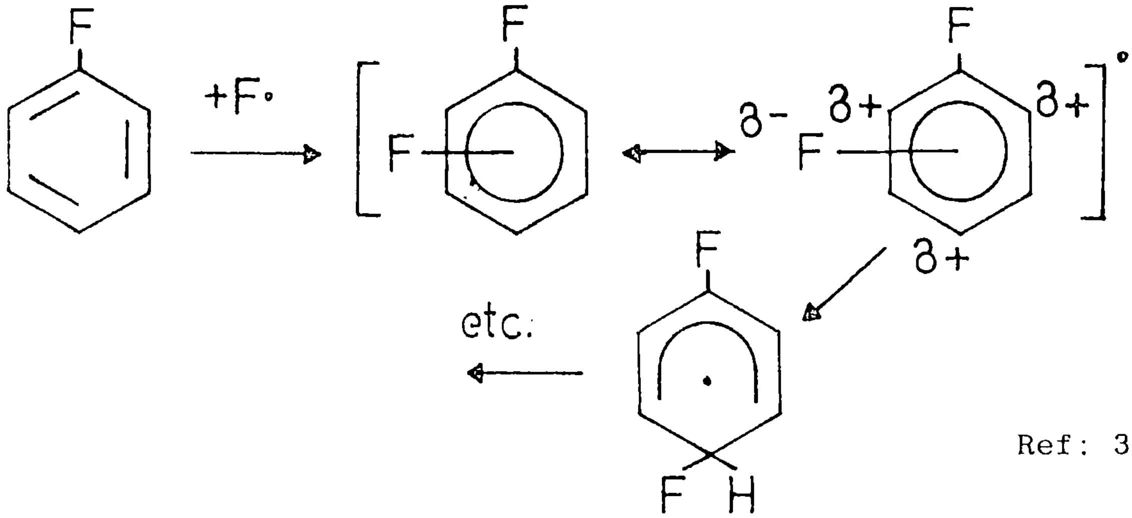
Ref: 34

The difluorobenzenes were found to be in the ratio 1:4:5 for meta:ortho:para. Similar selectivity was found in the reactions of toluene and nitrobenzene which led Grakauskas to propose an electrophilic ionic mechanism:



Ref: 34

In spite of this, Vasek and Sams suggested a radical mechanism for Grakauskas' fluorination, on the basis of their experiments with cold fluorine plasmas.[35,36] They showed that the reaction of fluorobenzene (26) and bromobenzene with fluorine atoms produced in a glow discharge of molecular fluorine, at 0°C, gives aromatic species as major components of the product. They also demonstrated that the fluorine atom was more selective than previously supposed, e.g. in the reaction of bromobenzene to form fluorobromobenzene the isomer ratio is in the order para>ortho>meta. The yield of para product is about three times that of the meta and therefore the reactivity of the para position is statistically six times that of one of the meta's. These observations are rationalised in a proposed mechanism in which a charge transfer complex forms an intermediate:-

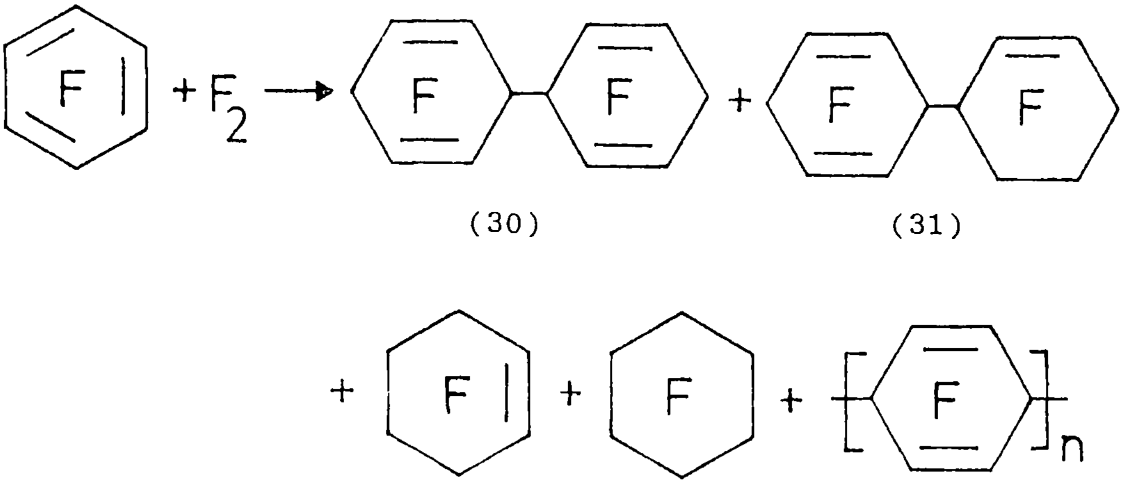


Ref: 35

The complex then collapses to yield a radical intermediate, substituted in the same positions as in an electrophilic substitution. Knunyants et al. obtained similar results by fluorinating nitrobenzene with fluorine diluted with nitrogen at -5°C.[37] They also related the selectivity of the fluorine atom to its electrophilicity.

1.7B Direct fluorination of halobenzenes

The fluorination of halobenzenes is, in general, easier to control than that of hydrogen containing benzenes. Both Tatlow[38] and Grakauskas[39] have performed liquid phase fluorinations of hexafluorobenzene (27). Dimeric (30), (31) and polymeric products were produced with smaller amounts of perfluorocyclohexene (28) and perfluorocyclohexane (29). The conditions used by the latter worker were more forcing and, as a result, his products were more saturated and included perfluorobicyclohexyl.

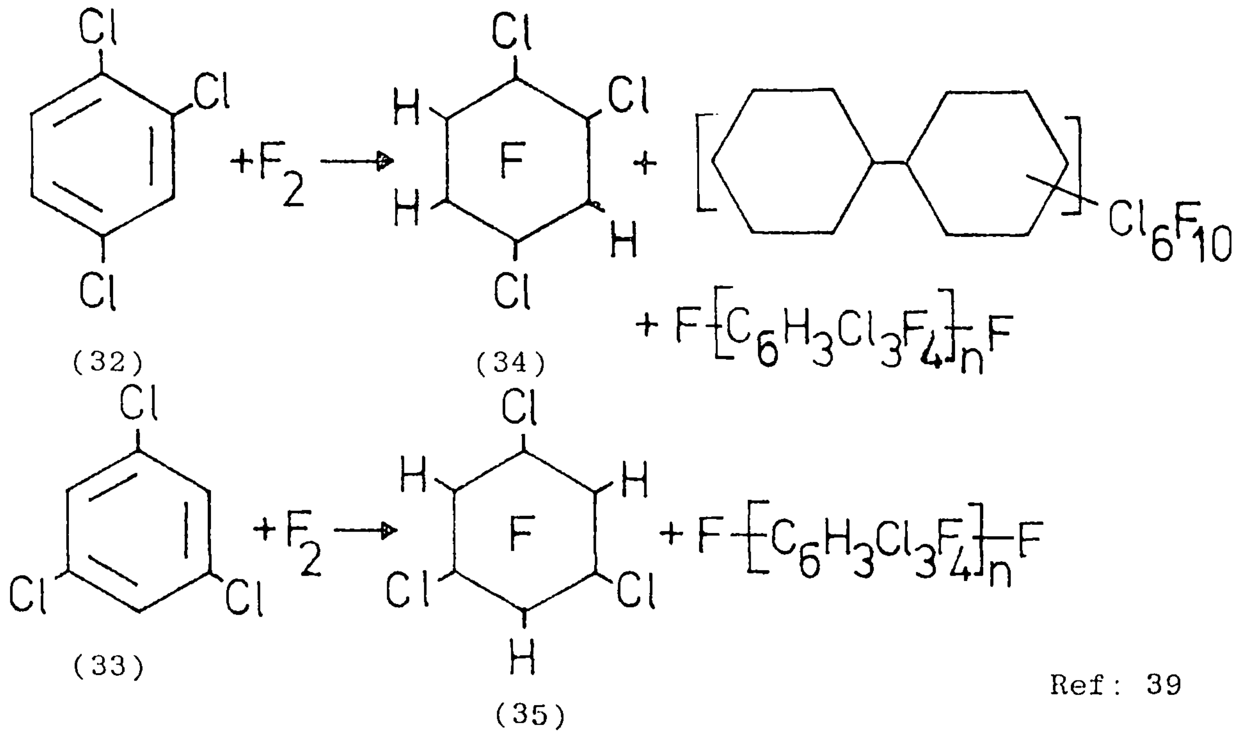


(30) (31)

(28) (29) (n > 2) Ref: 48

Grakauskas reported two explosions whilst fluorinating hexafluorobenzene (27) but Tatlow achieved smooth reaction. The need to eliminate oxygen containing species from the fluorine used in order to reduce losses of material due to the formation of acid fluoride side-products was stressed by the latter. The oxygen containing species were supposed to originate from moisture ingressed into the electrolyte of the cell used to generate the fluorine and Tatlow described precautions designed to eliminate electrolyte moisture.

Brooke et al.[40] and, later, Grakauskas[39] reported that hexachlorobenzene (29) reacted very easily with fluorine to produce a single product, analysing for $C_6F_6Cl_6$. Grakauskas further reported the fluorination of 1,2,4- and 1,3,5-trichlorobenzenes (32) and (33), which reacted smoothly by addition, rather than substitution reactions, as indicated gravimetrically.[39] The products from (32) were identified as the cyclohexane (34) and a dimer or mixture of dimers, analysing for $C_{12}Cl_6F_{10}$ and identified spectroscopically as one or more bicyclohexyls. Polytrichlorotetrafluorocyclohexenes were also detected. 1,3,5-trichlorobenzene (33) behaved similarly, giving the 1,2,3,4,5,6-hexafluoro adduct (35) as the major product, with some decafluorohexachlorobicyclohexyls and some polytrichlorotetrafluorocyclohexenes as well.



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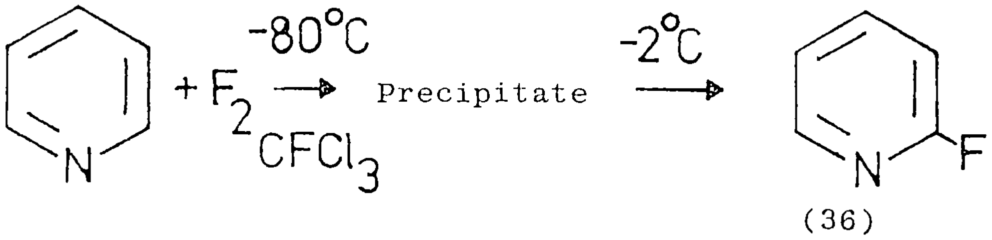
1.7C The Direct Fluorination of Aza-aromatics

Meinert reacted pyridine with fluorine, diluted with nitrogen, in $CFCl_3$ solution at -80°C, and obtained a precipitate which exploded at -2°C to give 2-fluoropyridine (36).[41]



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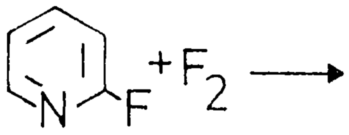
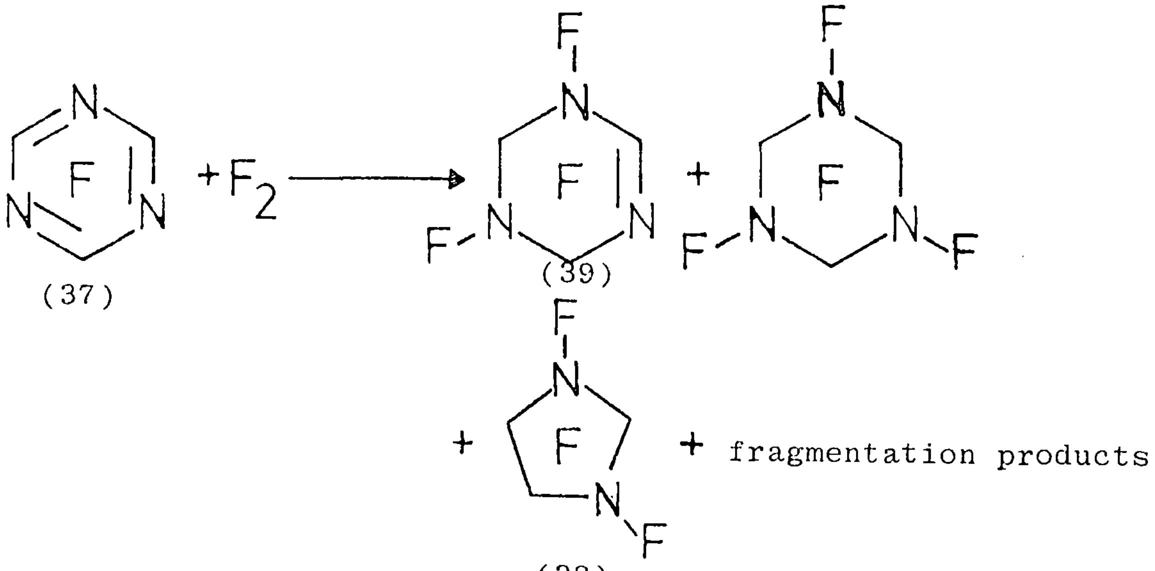
(36) itself was exhaustively fluorinated by Banks in a jet

reactor.[42] Extensive fragmentation occurred and several oxygen containing products were detected.



NF_3, CF_4, C_2F_6, COF_2, CO_2, SiF_4, $(CF_3)_2CHF$, $C_2F_5CHF_2$, $(CF_3)_2NF$, $CF_3N{=}CF_2$, $(CF_3)_2NH$, CF_3NCO, $CF_3N{=}CFCF_3$, $(CF_3)_2N{-}N(CF_3)_2$, CF_3COF, C_2F_5COF + other products. Ref: 42

Bigelow fluorinated cyanuric fluoride (37) in both a jet and a catalytic reactor.[43] An earlier attempt was made by Young with silver II fluoride, but he recovered mainly starting material.[44] However, Bigelow observed smooth reactions. The reaction was performed at a variety of temperatures, and high yields of cyclic products were obtained at low temperature and mainly fragmentation products at higher temperatures.

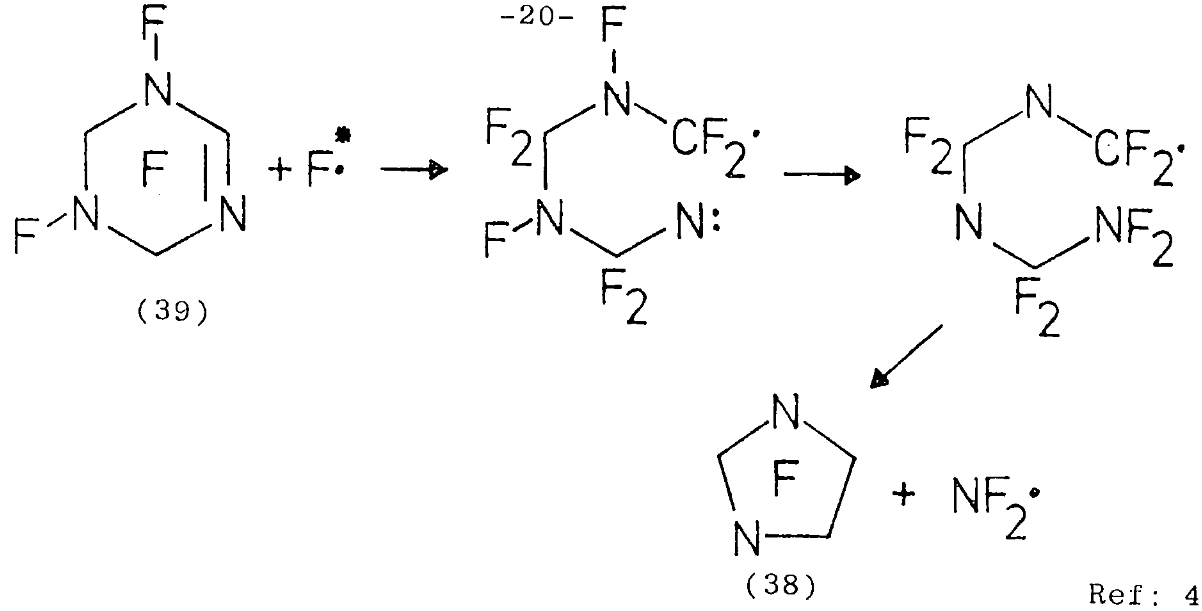


(37) (39) (38)

Ref: 43

The largest fragments were the perfluoroazaalkanes:- $CF_3NFCF_2NFCF_2NF_2$, $CF_3NFCF_2NFCF_3$ and $CF_3NFCF_2NF_2$.

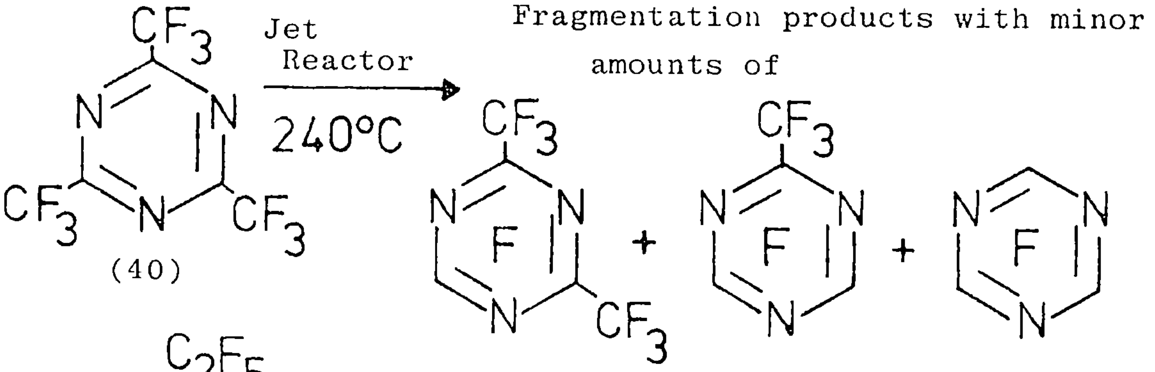
The diazacyclopentane (38) was thought to result from the triazacyclohexene (39) thus:



Ref: 43

where F.* is a fluorine atom of sufficient energy to dissociate the double bond.

Young reported that perfluorotrialkyl-s-triazines were even more resistant to AgF_2 than cyanuric fluoride.[44] This was confirmed by Bigelow who, on reacting the tris (trifluoromethyl)-(40) and tris (pentafluoroethyl)-(41) derivatives in a jet reactor, was unable to produce addition products.[45] At elevated temperatures, fragmentation was the main reaction and the only other components in the product were recovered starting material and products due to the loss of substituent perfluoroalkyl groups.



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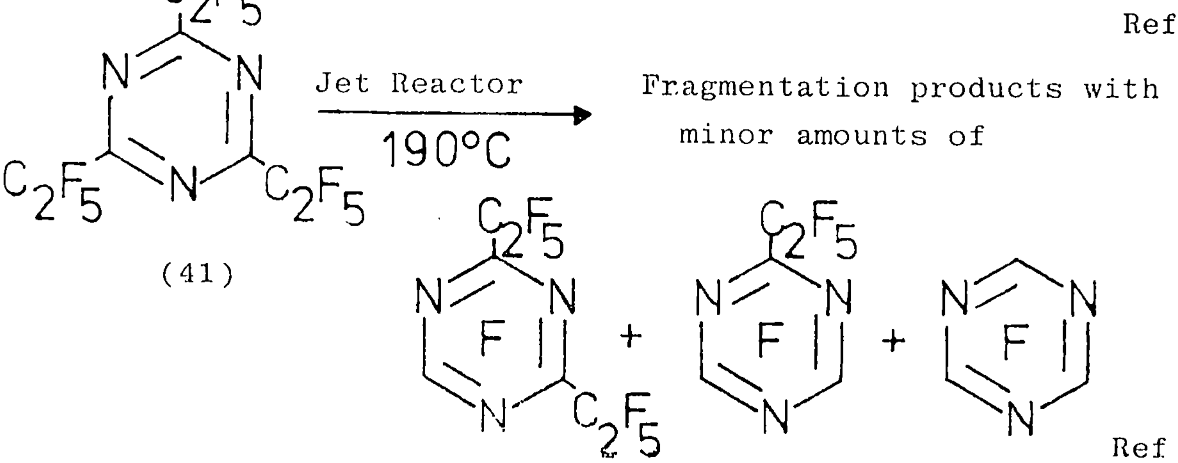
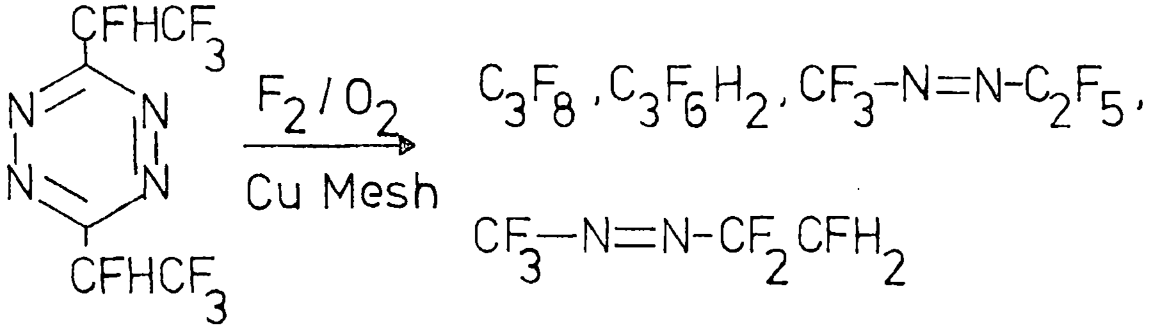


Ref: 45

Ginsburg et al. reported the fluorination of two polyfluoroalkyl-1,2,4,5-tetra-azines (42) and (43).[46] No cyclic addition products were obtained, even at -10°C.



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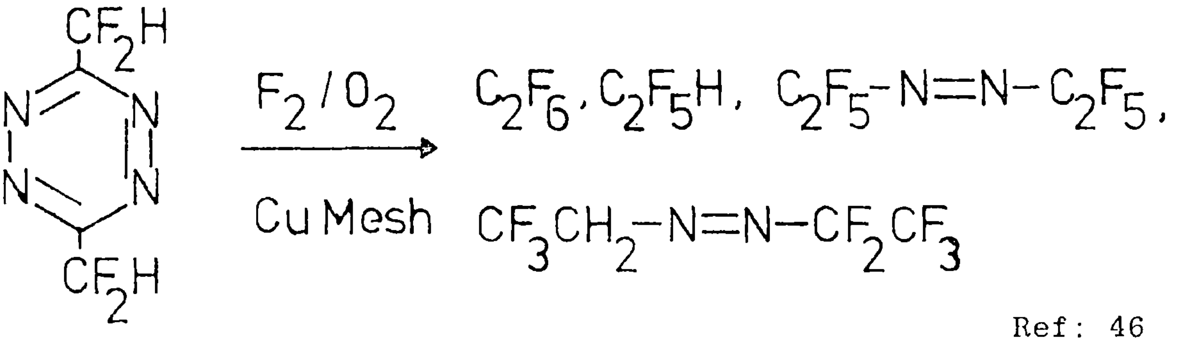


Ref: 46

The solid substrates were mixed with copper mesh which would function as a heat sink.

1.8 Direct Fluorination of Compounds with Functional Groups

As a rule, the presence of a functional group on a molecule increases the tendency towards fragmentation upon direct fluorination and, usually, hetero atoms are oxidised to their highest valency.

1.8A Oxygen containing compounds

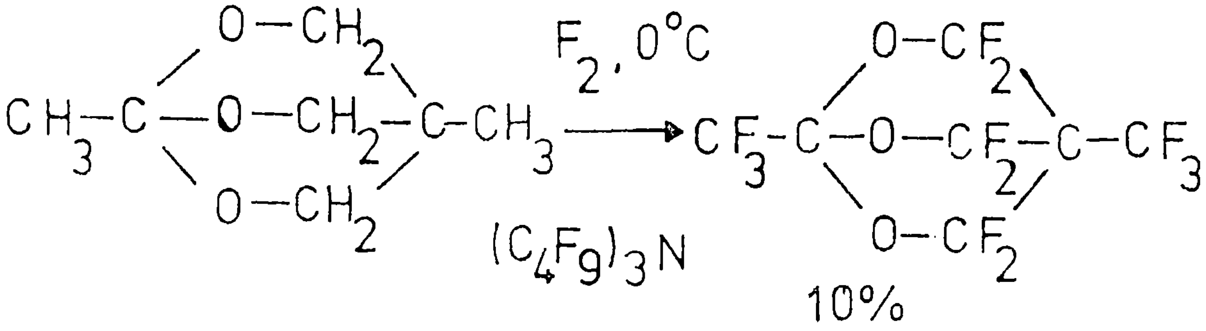
Alcohols are converted to perfluoroalkyl hypofluorites and fragmentation products by direct fluorination, although Cady has obtained useful yields of trifluoromethylhypofluorite (44) by the catalytic fluorination of methanol.[47]

$$\underset{}{CH_3OH} \xrightarrow[\text{Cu/Ag}]{F_2\ 160\text{-}180^\circ C} \underset{(44)}{CF_3OF} \qquad \text{Ref: 47}$$

Perfluoroketones have been obtained in small yields, but the reaction is not a useful preparative method.

$$C_2H_5COCH_3 \xrightarrow{F_2} \underset{15\%}{C_2F_5COCF_3} \qquad \text{Ref: 48}$$

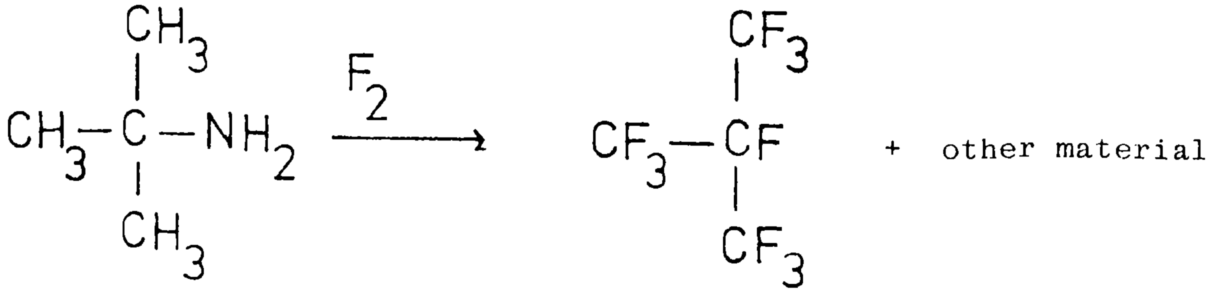
Also, some ether linkages will survive direct fluorination:-



Ref: 49

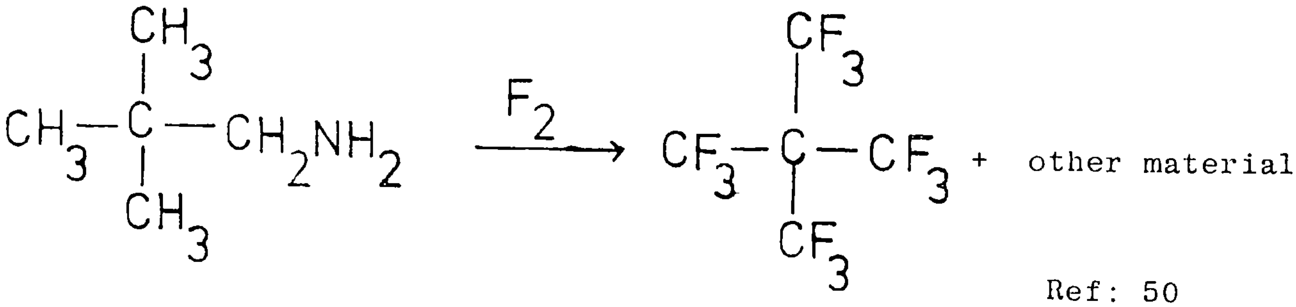
1.8B Nitrogen containing compounds

When nitrogen compounds are directly fluorinated >N-H bonds are attacked, and characteristically, much fragmentation and rearrangement occurs. Lagow has fluorinated pivalonitrile (45) and t-butylamine (46) which resulted in the loss of difluoramino (NF_2.) groups, and good yields of branched fluorocarbons were obtained.[50]



(46)

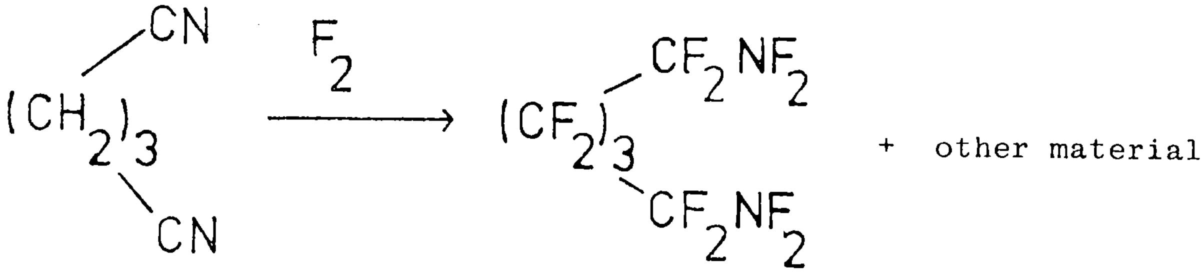
Ref: 50



(45)

Ref: 50

Less branched nitriles e.g. 1,3-dicyanopropane (47) gave reasonable yields of the perfluorinated derivative:-[50]



(47)

Ref: 50

1.8C <u>Sulphur containing compounds</u>

Sulphur is oxidised to the hexavalent state upon direct fluorination.

$$CH_3SH \xrightarrow[200^\circ C]{F_2/N_2} \underset{10\%}{CF_3SF_5}$$

Ref: 51

CHAPTER 2

INDIRECT FLUORINATIONS

2.1 Introduction

The term 'indirect fluorination' was defined at the beginning of Chapter 1, quite simply, as fluorinations achieved with reagents in which the labile fluorine is bonded to a different element. The fluorination of organic compounds may be divided into two categories, the borderlines between which are rather undefined:-

(1) exhaustive fluorinations when all, or nearly all, the hydrogens are substituted and the double bonds saturated;

(2) selective fluorinations when only certain types of hydrogen atoms are attacked or double bonds saturated. Selective fluorinations, typically, concern the addition of only one or two fluorine atoms to the compound and, although the literature on these latter reagents is massive, only a brief mention need be made in the present context.

2.2 Thermodynamics of Indirect Fluorination

The enthalpies of indirect fluorinations are usually lower than those of the corresponding direct fluorinations, a major reason for which is the fact that the labile fluorine in the vast majority of indirect reagents is more strongly bonded than in molecular fluorine. Thus, the enthalpy of the reaction between an organic compound and cobalt III fluoride is said to be about half that of the reaction with molecular fluorine.[52]

In addition to this, indirect fluorinations often involve the reaction of heterogeneous phases which can effectively slow down the process, whereas the reaction between fluorine gas and organic vapours is homogeneous with, therefore, no such restraint. The heterogeneity of the reacting phases formed part of the explanation for the slow, controlled reactions observed between fluorine gas and organic polymers, which were performed by Lagow and Margrave (Section 1.4D).

Hence, characteristically, indirect fluorinations are easier to control and less hazardous than direct fluorinations and polymerisation and fragmentation reactions can, more frequently, be avoided. Limited or selective fluorination, difficult to achieve by direct fluorination, is easily performed with a variety of indirect methods.

2.3 Selective Fluorination Methods

2.3A Introduction

Much effort has been devoted in the past toward solving the difficult problem of synthesising molecules with a small number of fluorine atoms at selected sites. Fresh impetus has been given to this area recently with the discovery of many pharmacologically active, fluorine-containing compounds such as steroids and the anti-tumour agents 5-fluorouracil[53] and 5-trifluoromethyluracil.[54] The established methods and newer methods of less certain value are described briefly in this section. First, reagents in which fluorine is bonded to a metal are described and then reagents in which fluorine is bonded to elements from groups III, IV, and so on, across the periodic table, are mentioned.

2.3B The Alkali Fluorides as Selective Fluorinating Agents

(a) Introduction

The nucleophilic substitution of halogens and, sometimes, good leaving groups such as tosylate,[55] by fluoride ion has been extensively exploited as a method of preparing selectively fluorinated compounds. The method can be used with or without a solvent but, usually, the latter technique is used to perfluorinate the substrate whilst, at best, only poor yields of perfluorinated products can be achieved by the former. Therefore, in spite of the great amount of overlap in their applications, solvent reactions will be described in the present section, whilst reactions without a solvent will be described in section 2.4B as though they were a purely exhaustive technique.

(b) The source of fluoride ion

The commonest source of fluoride ion is a heavy alkali metal fluoride although potassium hydrogen fluoride[56] and the 1:1 adduct of potassium fluoride and sulphur dioxide[57] have also been employed in some instances.

The usual method is to dissolve the chloro compound in a slurry of dry alkali fluoride in a high boiling solvent. The reactivity of the alkali fluorides is usually in the order:-

$$CsF > KF > NaF \sim LiF$$

This has been attributed, at least in the absence of a solvent, to the greater increase in lattice energy on forming the solid alkali metal chloride from the fluoride when M is large, in the process:-[58]

$$-\overset{|}{\underset{|}{C}}-Cl + MF \longrightarrow -\overset{|}{\underset{|}{C}}-F + MCl.$$

Parker stated that 'potassium and caesium fluorides are much more effective than lithium or sodium fluoride in providing nucleophilic fluoride ion in dipolar aprotic solvents'.[59] The lattice energies of the alkali metal halides decrease as the size of the cation increases[60] and presumably this is, in part, responsible for the higher solubilities of the heavier alkali metal halides implied above by Parker.

In most instances, however, the higher cost of caesium fluoride offsets any advantage in reactivity over potassium fluoride which is, hence, the more widely used.

(c) Solvents

The earliest solvents were, usually, glycols which allow a high reaction temperature and they are adequate when only one or two halogens are to be substituted. However, attempts to prepare polyfluorinated compounds from more highly chlorinated substrates led to the discovery that the reactivity of fluoride ion is dramatically increased in aprotic solvents.[61] Fluoride ion is a poor nucleophile in water (and probably, therefore, the other common protic solvents) compared with the other halides, because it is so strongly solvated.[59] For example, the heat of hydration of fluoride ion is 32 K cals (134 K joules) higher than chloride.[60] In aprotic solvents, however, which interact only poorly with anions, the nucleophilicity of fluoride is usually much greater than the other halides.[62,63]

Other desirable characteristics of the solvent were described by Parker and these included that it should have a high dielectric constant and it should solvate the cation in order to allow dissolution of at least traces of the metal fluoride.[59] The reaction temperature is a limiting factor in these reactions and hence it is also desirable that the solvent be high boiling and, of course, of high stability. First row elements such as oxygen and nitrogen act as effective electron donors to alkali metal ions and the most commonly used solvents contain one or other of these hetero atoms. Successful solvents which combine these qualities are listed below:-

Table 2.1 The Common Halogen Exchange Solvents

Ethers	Glymes
Sulphones	Dimethylsulphone(D.M.S.O.)
	Tetrahydrothiophendioxide(sulpholane)
Amides	Dimethylformamide(D.M.F.)
	N-methyl-2-pyrrolidone(N.M.P.)

(d) Reactions

Aliphatic halides may be converted to the corresponding fluoride in reasonable yield:

$$n\text{-}C_7H_{15}Cl \xrightarrow[(CH_2OH)_2]{KF\ 90^{\circ}C\ \ 2\ hr.} \underset{39\%}{n\text{-}C_7H_{15}F}$$

Ref: 64

The reaction proceeds more readily, however, if an activating group such as ester, nitrile, carbonyl or amide is near by:-

$$ClCH_2CONH_2 \xrightarrow[C_2Cl_4]{KF\ 100^{\circ}C} \underset{75\%}{FCH_2CONH_2}$$

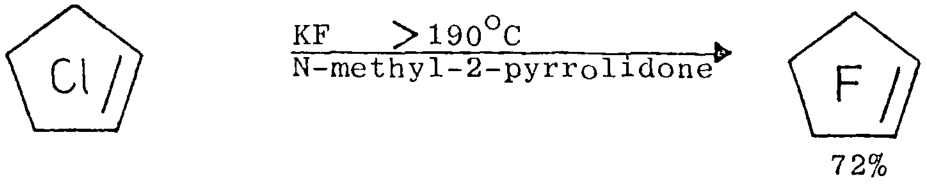
Ref: 65

Aprotic solvents are necessary in the preparation of polyfluorinated alkanes:

$$CCl_3CCl_2CCl_3 \xrightarrow[N\text{-methyl-2-pyrrolidone}]{KF\ 170^{\circ}C} \underset{60\%}{CF_3CCl_2CF_3}$$

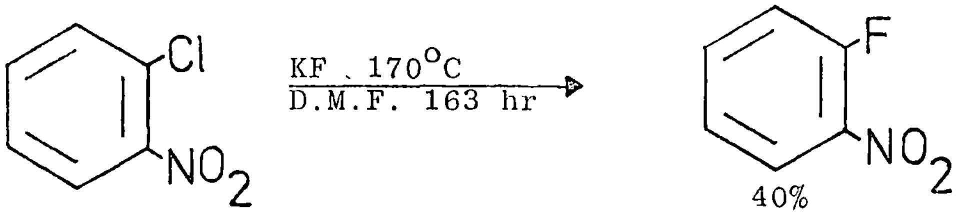
Ref: 61

Olefinic halides have also been reacted and it appears that allylic chlorine is especially reactive, exhaustive fluorination sometimes occurring:



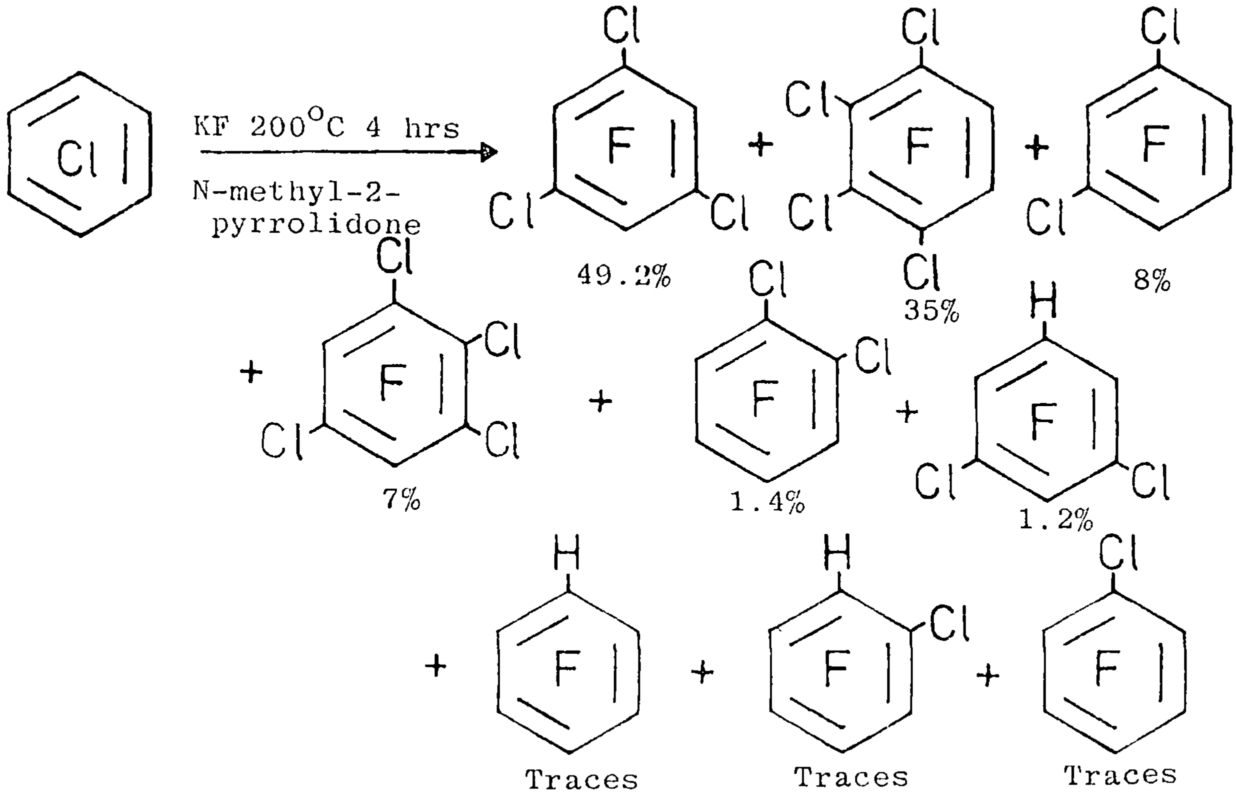
Ref: 61

The preparation of polyfluoro aromatic compounds has attracted considerable attention. Mono chlorides may be reacted in aprotic solvent when an ortho or para electron withdrawing group is present:

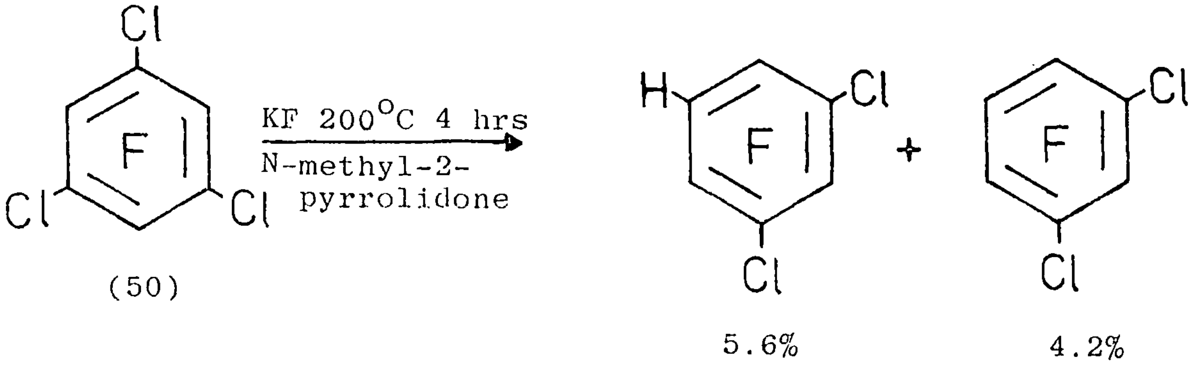


Ref: 66

Polyfluoro aromatic and hetero aromatic compounds have been prepared from highly chlorinated substrates:



Holbrook et al. showed that 1,3,5-trichlorotrifluorobenzene (50) is resistant to further fluorination at temperatures compatible with the use of a solvent and this was thought to reflect the deactivating influence of para fluorines to nucleophilic aromatic substitution.[67] Indeed, recent measurements of substituent rate factors has confirmed the powerful deactivating effect of para fluorine in these reactions.[70] The same argument may be applied to the fluorination of pentachloropyridine. The resistance of (50) to further fluorination was so high that abstraction of protons from the solvent by an unknown mechanism became a competing reaction:



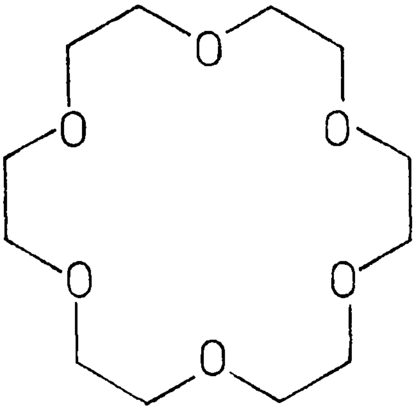
Ref: 67

Another disadvantage of the use of forcing conditions in these reactions is the fact that fluoride ion is a powerful base in aprotic solvents[62] and proton abstraction from the solvent[60] or dehydrohalogenation of the substrate can occur.[71]

(e) Cation complexing reagents

A recent innovation has been the use of cation complexing reagents such as the so-called 'crown ethers', e.g. (51), which, by solvating through a large number of centres, form a stable, bulky cation complex, greatly increasing solubility in organic solvents. For example, a concentration of potassium fluoride in benzene of 5 x 10^{-2}M was observed in the presence of 1.01M

1,4,7,10,13,16-hexaoxacyclooctadecane (51) commonly referred to as 18-crown-6.[71]

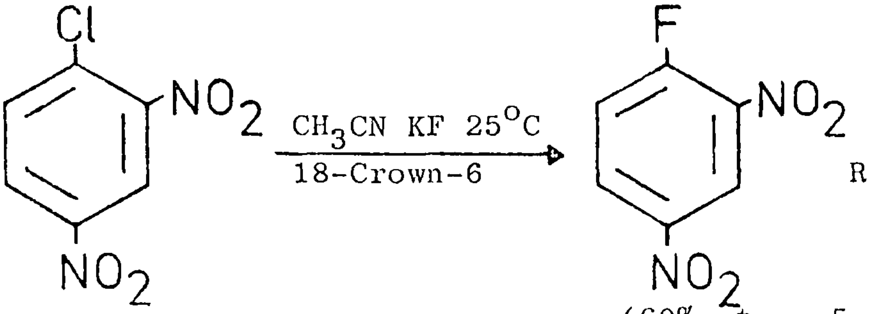


18-Crown-6

(51)

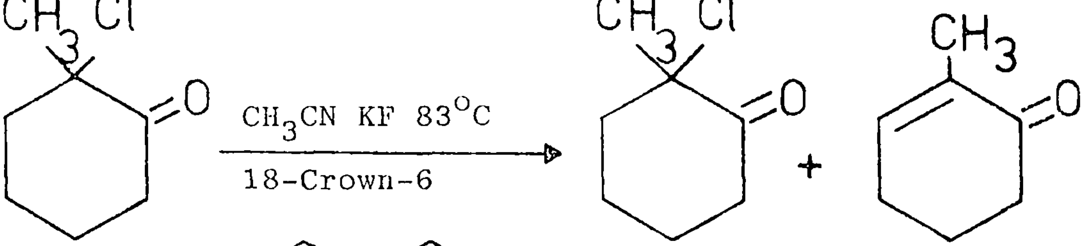
Ref: 71

Fluoride ion is, of course, unsolvated in such a system and the authors referred to it as 'naked fluoride ion'. A series of bromides and chlorides were quantitatively converted at moderate temperature either to fluorides or olefinic products due to dehydrohalogenation as a result of the basicity described above.



Ref: 71

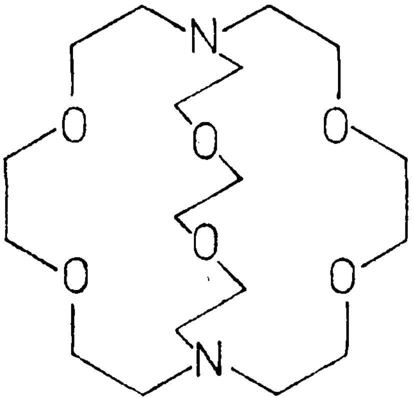
(60%, $t_{\frac{1}{2}}$ = 5 hrs)



31%

65%

Ref: 71



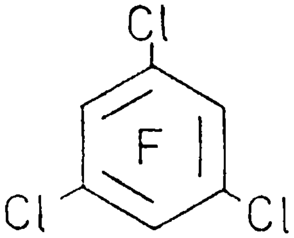
(53)

Ref: 72

The fluorination of pentachloropyridine (52) with the nitrogen containing complexing agent diaza-1,10-hexa-oxa-4,7,13,-16,21,24-bicyclo[8,8,8]hexacosane (53) has been reported,[72] and without a great excess of KF, or a solvent other than molten (52) and at relatively low temperatures, fluorination proceeded as far as dichlorotrifluoropyridine.

(f) Molten salt reactions

Finally, some polyfluoro compounds have been synthesised by passing a polychloro substrate into a melt of an alkali fluoride with another salt.



$$\xrightarrow[780^{\circ}C]{KF:KCl\ =\ 45:55} \underset{11.7\%}{C_6F_6} + \underset{34.6\%}{C_6F_5Cl} + \underset{28.6\%}{C_6Cl_2F_4} + \underset{18.1\%}{C_6Cl_3F_3} + \underset{0.4\%}{C_6Cl_4F_2}$$

Ref: 73

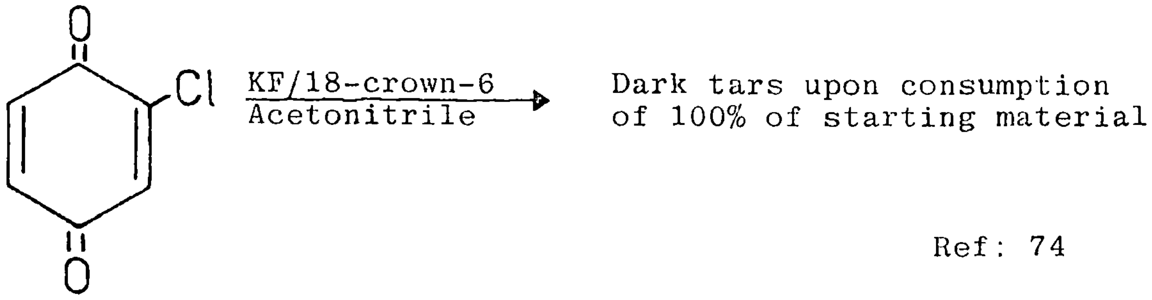
But yields of perfluoro derivatives do not appear to be competitive with the autoclave method (see Section 2.4B) and the technique is, perhaps, less simple to perform than the solvent route to polyfluoro compounds.

2.3C Other Metal Fluorides as Selective Fluorinating Agents

(a) Silver I, Mercury I and Mercury II fluorides

Silver I fluoride, mercury I fluoride and mercury II fluoride were, formerly, widely used in halogen exchange reactions but these reagents have been largely superceded by the alkali fluorides. However silver I fluoride was recently reported to fluorinate a chloroquinone which was found to undergo base catalysed polymerisation with potassium fluoride and 18-crown-

6.[74]



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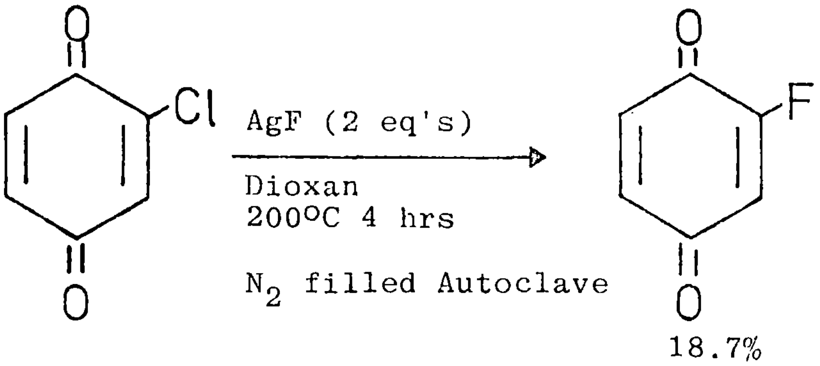

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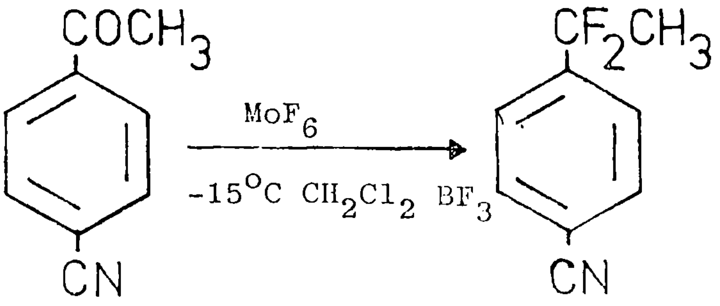
(b) Molybdenum hexafluoride

The use of molybdenum hexafluoride as an alternative to SF_4 (see 2.3F(b)) during the conversion of carbonyl groups to difluoromethylene was said to offer the advantages of being less toxic and easier to handle than SF_4.[75] A wide range of ketones and aldehydes have been reacted with this reagent but, whilst F, Cl, Br, CN, NO_2, COOR, $CONR_2$, $P(O)R_2$ functions do not interfere, complications arise with compounds substituted with OH, NH_2, OR, NR_2 and $>C=C<$, molybdenum containing products resulting in the latter case. BF_3 catalyses the reaction which is usually performed by adding the substrate to a CH_2Cl_2 solution of MoF_6 at -15°C.

$$n\text{-}C_6H_{13}CHO \xrightarrow[CH_2Cl_2,\,BF_3]{MoF_6} \underset{20\%}{n\text{-}C_6H_{13}CHF_2}$$

Ref: 75



42%

Ref: 76

2.3D Reagents in which Fluorine is Bonded to a Group IV Element

(a) 2-chloro-1,1,2-trifluorodiethylamine

This α-fluoroamine sometimes also referred to as F.A.R. (fluoroamine reagent) or the Yarovenko reagent, reacts with a wide variety of hydroxy compounds converting them to fluorides. The reagent has recently been reviewed.[77]

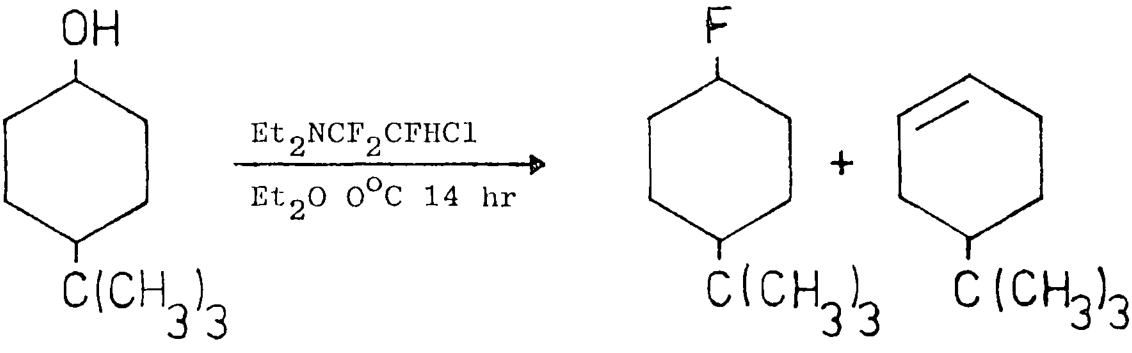
It reacts cleanly with primary and secondary alcohols although cyclic secondary alcohols and tertiary alcohols rarely give useful yields as side reactions predominate. In some ways this reagent complements SF_4 (Section 2.3F(b)) as it will fluorinate the aliphatic alcohols of low acidity which cannot be successfully treated by the latter.

$$CH_3(CH_2)_2CH_2OH \xrightarrow[\substack{\text{No solvent} \\ \text{Exothermic}}]{\substack{Et_2NCF_2CFHCl \\ 0.2\ \text{moles}}} CH_3(CH_2)_2CH_2F$$

67%

Ref: 78

(Et = Ethyl)



9%,cis:trans = 9.1   68%

Ref: 79

Carboxylic acids may also be converted to acid fluorides.

$$\underset{0.2\text{ moles}}{CH_3COOH} \xrightarrow[\text{0.2 moles, No solvent}]{Et_2NCF_2CFHCl} \underset{59\%}{CH_3COF}$$

Ref: 78

2.3E Reagents in which Fluorine is Bonded to a Group V Element

(a) Phosphoranes

Trifluorodiphenylphosphorane[80] and difluorotriphenylphosphorane[81] will convert primary and secondary alcohols to fluorides although the former is the more reactive. Olefins are frequent side-products. Phenyltetrafluorophosphorane is not useful as it gives too many side-products.[82]

$$n\text{-}C_5H_{11}OH \xrightarrow[150\text{-}170^\circ C,\ 5\text{-}7h]{(Ph)_3PF_2} \underset{60.3\%}{n\text{-}C_5H_{11}F}$$

(Ph = Phenyl)

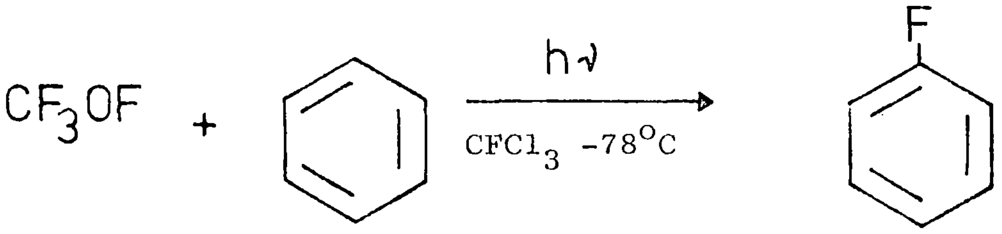
Ref: 80

2.3F Reagents in which Fluorine is Bonded to a Group VI Element

(a) Trifluoromethylhypofluorite - Photofluorination

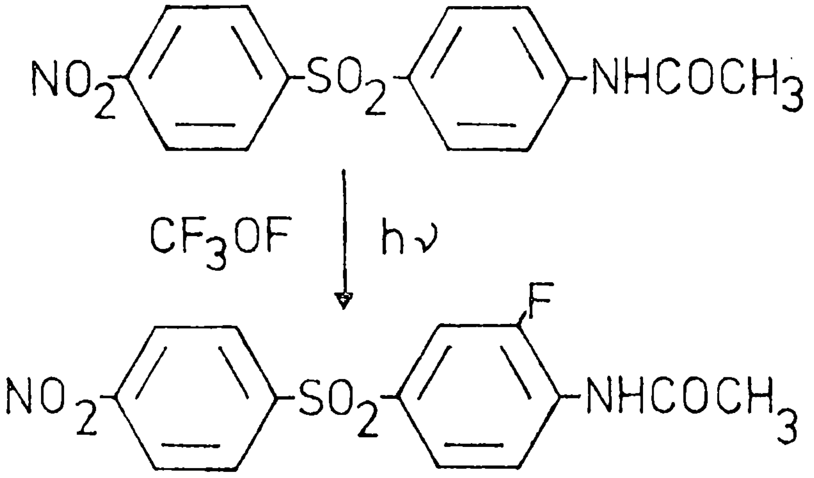
This reagent has been used in two different ways in the synthesis of fluorine containing compounds. The more widely used method has been the electrophilic addition of the reagent to olefins[83] but, as the reaction usually produces compounds containing added oxygen as well as fluorine, it cannot be described as merely a fluorination technique in the strictest sense and hence it will not be described here.

The other method is termed Photofluorination and was developed by Kollonitsch et al.[84] They claimed it to be the first general method for selective substitutive fluorinations and it is based on the reaction between R-H and fluorine atoms generated by the dissociation of trifluoromethylhypofluorite under very high luminous fluxes.



via $$CF_3OF \xrightarrow{h\nu} CF_3O\cdot + F\cdot \quad \text{etc.}$$

Ref: 84



Ref: 85

An advantage of the method is that unlike perchloryl-chloride (Section 2.3G(a)) unactivated hydrogens may be substituted by fluorine[86] sometimes with remarkable selectivity with little risk of explosions.

A good example of selective fluorination is the preparation of the fluoroisoleucine (54) in 39% yield.[86]

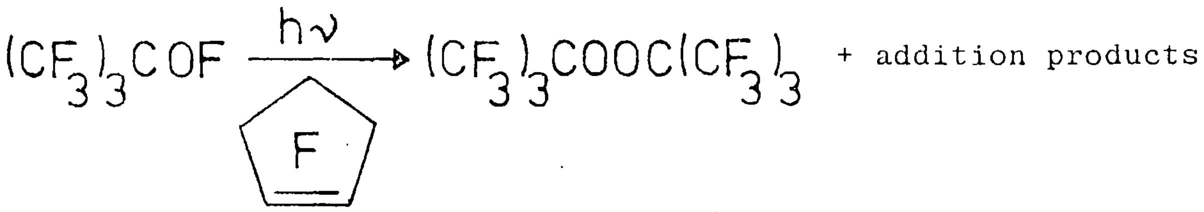
$$CH_3CH_2CH(CH_3)CHNH_3^+COOH \xrightarrow[\text{HF solvent}]{CF_3OF} CH_2FCH_2CH(CH_3)CHNH_3^+COOH$$

39%

(54)

Ref: 174

Evidence for the involvement of fluorine atoms was the observation that the yield of fluorobenzene fell to 17% without irradiation and many side products were produced. Further evidence was the observation that perfluoro-t-butylhypofluorite (55) yielded the peroxide (56) as the major product upon irradiating in the presence of perfluorocycloolefins.[87]



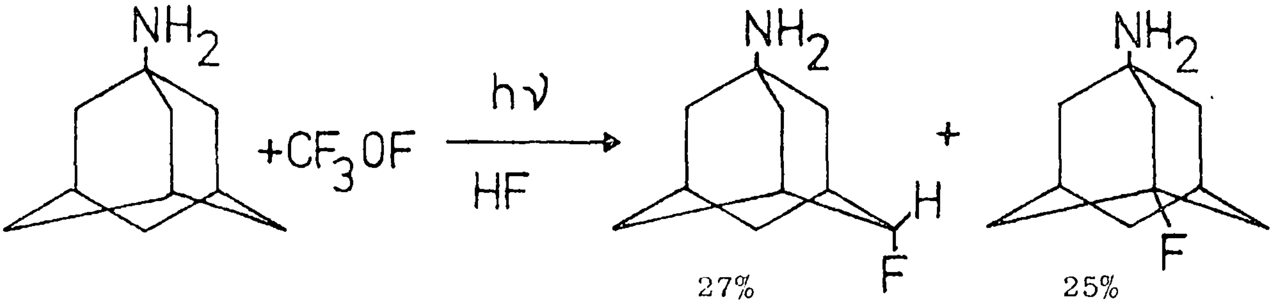
$$(CF_3)_3COF \xrightarrow{h\nu} (CF_3)_3COOC(CF_3)_3 \text{ + addition products}$$

(55) (56) 54%

Ref: 87

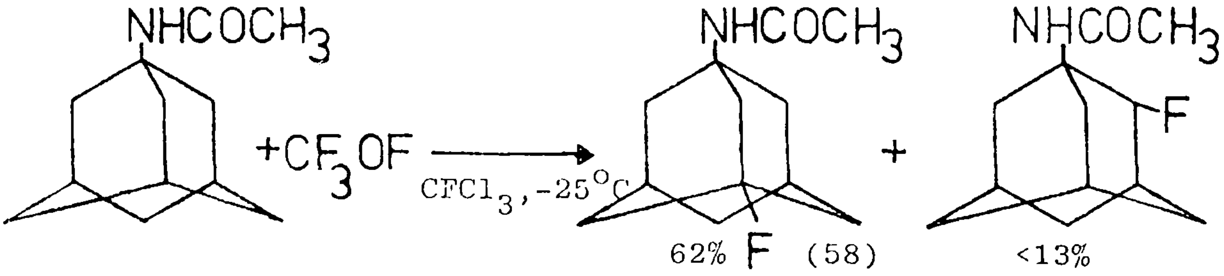
The failure of trifluoromethylhypofluorite (57) itself to produce a dimer was thought to be due to its relatively higher reactivity than the bulkier radical from (55).

Substitution of aliphatic hydrogen atoms has also been achieved,



Ref: 84

but Barton et al. have shown that the hypofluorite (57) can also act as an electrophilic source of fluorine and were able to produce the 1-fluoroadamantane (58) in the presence of radical inhibitors.[88]



Radical inhibitor = m-dinitrobenzene

(0.1 eq.)

Irradiation of the reaction was observed to change the rate but selectivity was reduced indicating the onset of a radical reaction mechanism.

(b) Sulphur tetrafluoride

This reagent will convert a wide variety of carbonyl groups to difluormethylene and some hydroxyl groups to fluorides under mild conditions. Its use as a fluorinating agent has been the subject of a recent review.[89]

The usual procedure is to react the substrate in a stainless steel autoclave containing a solvent and a Lewis acid as a catalyst. Sulphur tetrafluoride is a toxic gas (bp -38°C). Reaction occurs between 50° and 200°C for most carbonyl groups except those highly hindered or deactivated.[2]

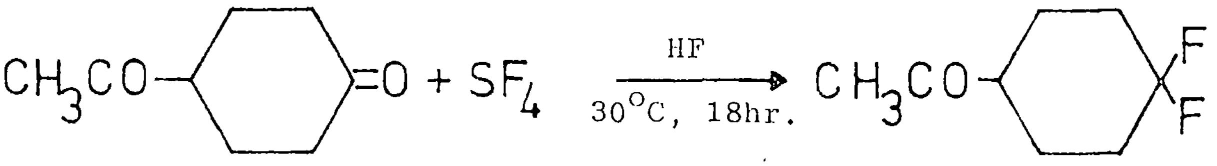
Thus, ketones may be converted to geminal difluorides

$$CH_3COCH_3 \xrightarrow[HF,110^{o}C,16\ hr]{SF_4} CH_3CF_2CH_3$$

60%

Ref: 90

and the selective conversion of activated carbonyl groups in the presence of another carbonyl group is sometimes possible:[91]



57%

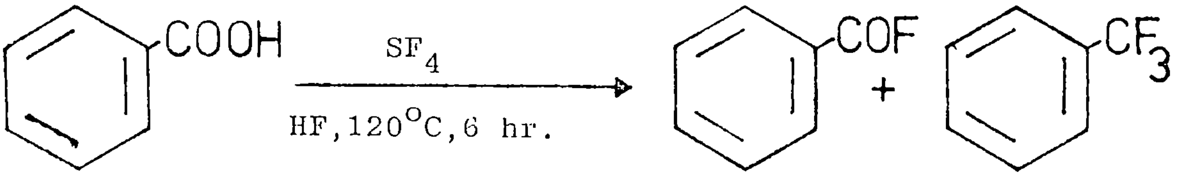
Ref: 91

Yields of monofluorides from aliphatic alcohols are often reduced by side-reactions such as the formation of ethers but may be quite high if the alcohol is activated by an electron-withdrawing substituent. It has been argued that this is because the formation of side products is suppressed rather than because of any higher reactivity of acidic alcohols.[89]

$$\text{n-}C_7F_{15}CH_2OH \xrightarrow[\text{HF},60-80^{\circ}\text{C},8\text{hr}]{SF_4} \text{n-}C_7F_{15}CH_2F$$

54% Ref: 92

Carboxylic acids are first converted to acid fluorides, which may often be isolated, then under vigorous conditions further conversion to trifluoromethyl groups occurs.[93]



41% 22%

Ref: 93

Recently the use of dialkylaminosulphurtrifluoride (D.A.S.T.) reagents has been advocated.[94] It is claimed that DAST's have the advantage of being liquids which are reactive under very mild conditions to give high yields of organofluorides from sensitive alcohols and ketones. Thus alcohols which also bear ester groups or other halogens may be successfully fluorinated with DAST reagents. Carbonium ion rearrangements occur less frequently with DAST's than for example SeF_4.pyridine (see below):

$$(CH_3)_2CHCH_2OH \xrightarrow{(C_2H_5)_2N\ SF_3} (CH_3)_2CHCH_2F + (CH_3)_3CF$$

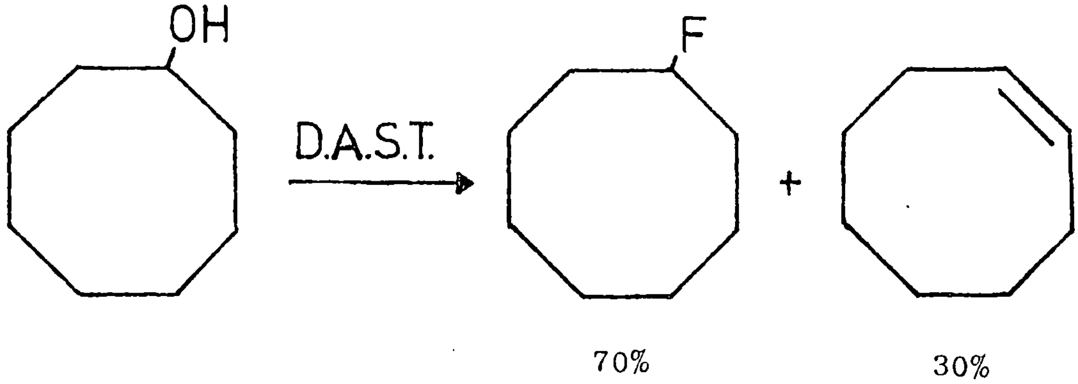
49% 21%

Ref: 94

cf $(CH_3)_2CHCH_2OH \xrightarrow{SeF_4 \bullet C_5H_5N} (CH_3)_3CF$ only
65%

Ref: 94

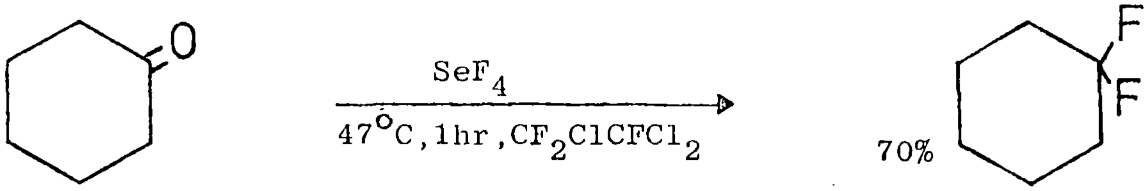
Elimination reactions are less frequent than with the F.A.R. reagent which yields cyclooctene only from cyclooctanol.



Ref: 94

(c) Selenium Tetrafluoride

This reagent reacts with carbonyl and hydroxyl groups and, like D.A.S.T. offers the advantages of being a liquid soluble in halogenated solvents.[96] The use of its complex with pyridine has been reported to circumvent the rearrangement and polymerisation of sensitive arylalkyl and cycloalkyl fluorides by co-produced hydrogen fluoride. Even so, as mentioned earlier, isobutanol rearranged when reacted with the complex.



Ref: 96

$n\text{-}C_5H_{11}OH \xrightarrow{SeF_4 . C_5H_5N} n\text{-}C_5H_{11}F$
60%

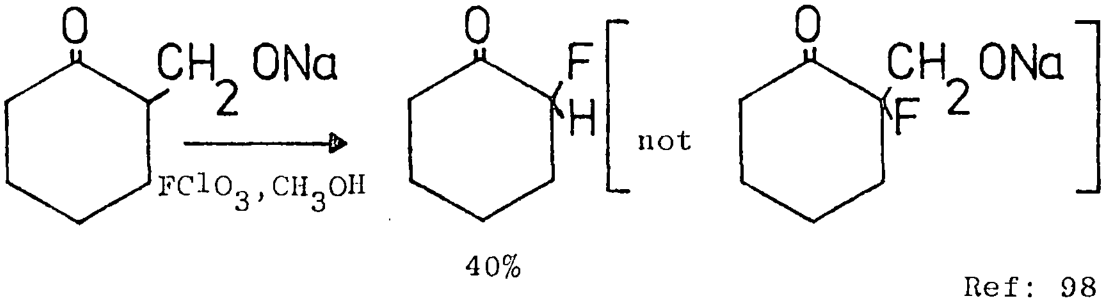
Ref: 96

2.3G Reagents in which Fluorine is Bonded to a Group VII Element

(a) Perchloryl fluoride

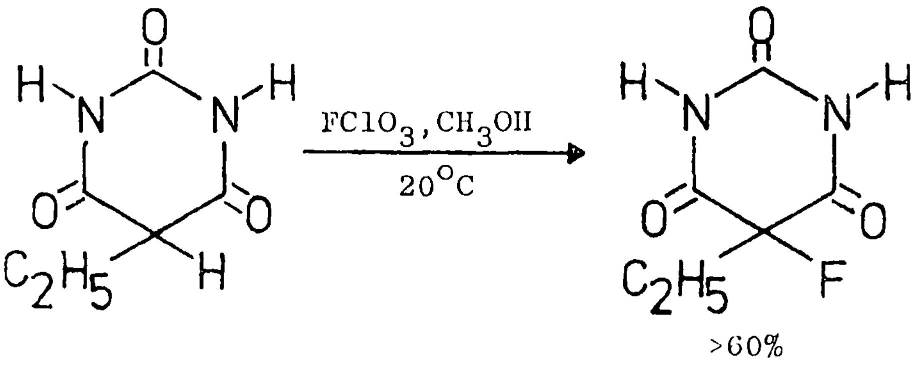
Perchloryl fluoride behaves as a source of 'positive fluorine' and is used to substitute hydrogen atoms in malonic esters and similarly activated compounds.[97]

The reagent is normally bubbled as the vapour (b.p. 46.6°C) through a solution of the substrate in the presence of a base such as an alkali metal, pyridine, or an alcohol. A major disadvantage is the fact that the reagent is a powerful oxidising agent and the risk of explosion is high. Side-reactions can also reduce yields in the case of sensitive substrates, e.g.



Ref: 98

The substrate may be activated by oxygen:



Ref: 99

$$CH_2(CO_2Et)_2 \xrightarrow[\text{Na, Toluene}]{FClO_3} CF_2(CO_2Et)_2 + CFH(CO_2Et)_2$$

10 to 15°C   29%   42%

Ref: 97

Or by other electron withdrawing groups:

$$(CH_3)_2CHNO_2 \xrightarrow[CH_3OH,\ 0^\circ C]{FClO_3} (CH_3)_2CFNO_2$$

32%

Ref: 100

(b) Bromine trifluoride

This reagent will convert carbonyl groups to difluoromethylene and, uniquely, some nitrile groups may be directly converted to trifluoromethyl. The mechanism is thought to be similar to that of SF_4 fluorination.[101]

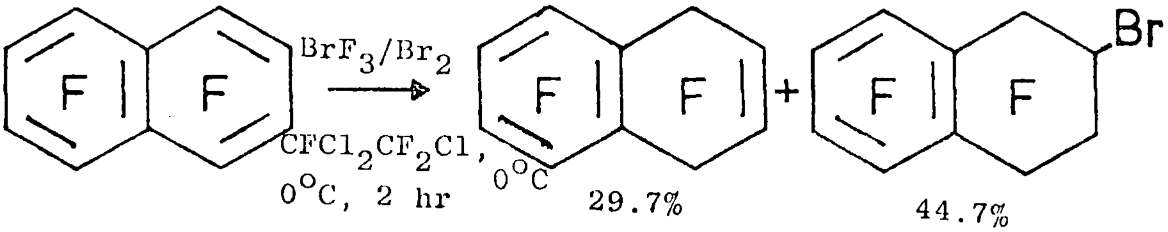
$$CH_3COCH_3 \xrightarrow[HF,\ -15^\circ]{BrF_3} CH_3CF_2CH_3 \quad 92\%$$

Ref: 101

$$CH_3CN \xrightarrow[HF,\ -80^\circ C]{BrF_3} CH_3CF_3 \quad 29\%$$

Ref: 101

The tendency for $\rangle C{-}H$ and $\rangle C{-}C\langle$ bonds to be attacked was thought likely to render the reagent of limited utility.[102] Recently, fluorinations of perfluoroaromatic compounds with mixtures of Br_2 and BrF_3 to give a BrF stoichiometry have been examined.[103]

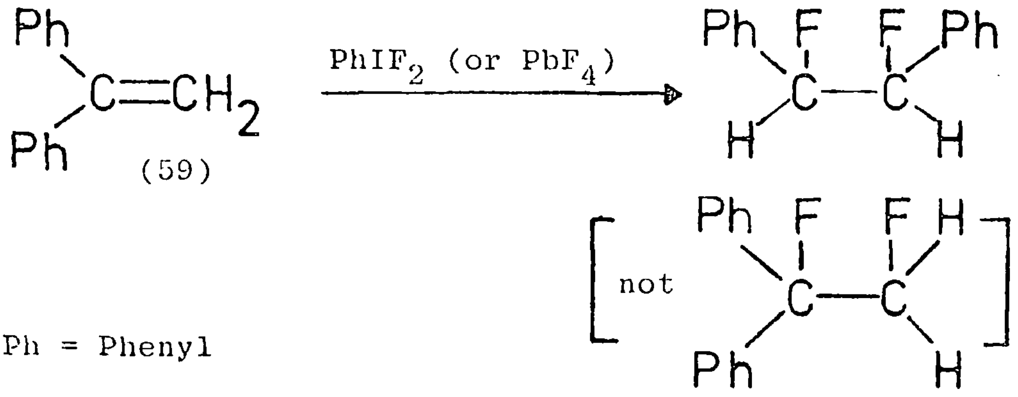


+ $C_{10}F_{14}Br_2$ isomers   Ref: 103

The mechanism in this case was thought to involve radical cationic intermediates as has also been postulated for fluorinations with XeF_2 and CoF_3.

(c) Phenyliododifluoride

Dimroth and Bockemüller[104] first reported the fluorination of the olefin 1,1-diphenylethylene (59) with either phenyliododifluoride or lead IV fluoride but, according to Bornstein et al., who repeated the reaction with lead IV fluoride, assigned an incorrect structure to the product.[105]



Ph = Phenyl

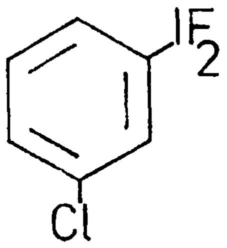
Ref: 105

Recently an easy preparation of phenyliododifluoride has been described[106] and increased interest in the reagent may result from its greater availability.

$$PhI + XeF_2 \xrightarrow[\text{Room temperature}]{HF, CH_2Cl_2} PhIF_2 + Xe \quad 95\%$$

Ref: 106

The m-chloro derivative (60) is reported to have superior stability and results in easier product separations.



(60)

Ref: 106

2.3H Reagents in which Fluorine is Bonded to a Group VIII Element

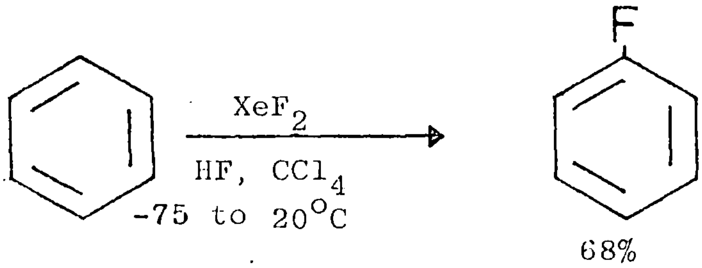
(a) Xenon difluoride

Filler et al. first described the reaction of xenon difluoride with aromatic compounds.[107] Unlike other fluorinating agents, no addition reactions were observed and a wide range of substituted fluorobenzenes were preparable in good yield.

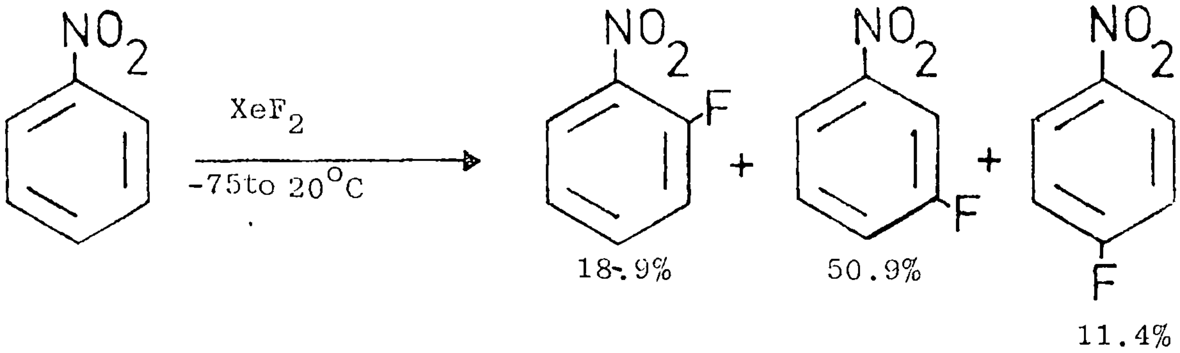
The reaction was performed by pouring or transferring a solution of the substrate into a tube containing crystals of the difluoride at -75°C and carefully allowing it to attain room temperature.

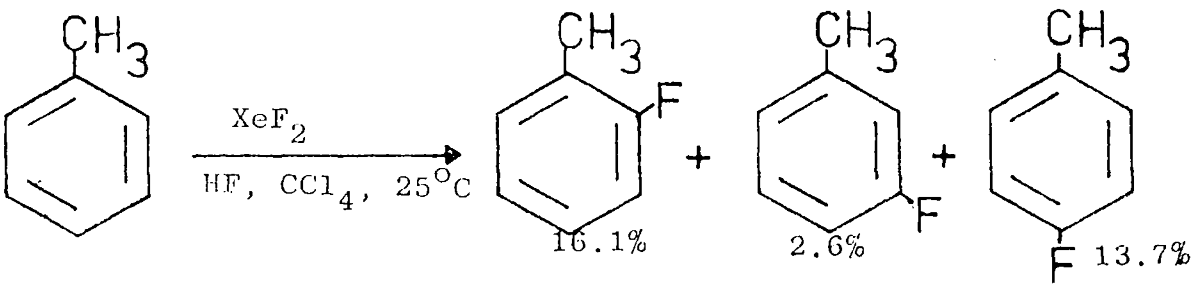
The presence of A.H.F. is necessary to catalyse the reaction. Substituents on the ring may be either electron-donating or electron withdrawing although more catalyst is required in the latter case.

Other functional groups are usually unaffected, although the oxidation of iodides to iododifluorides and the fluorination of substituent alkenyl groups has been reported.[106]



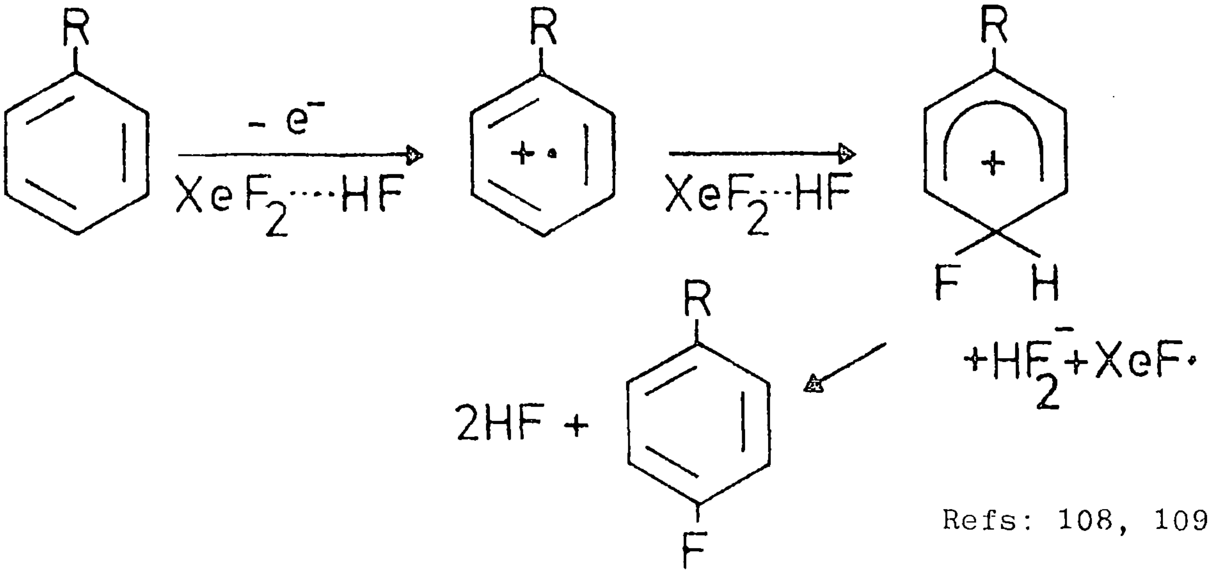
Ref: 107





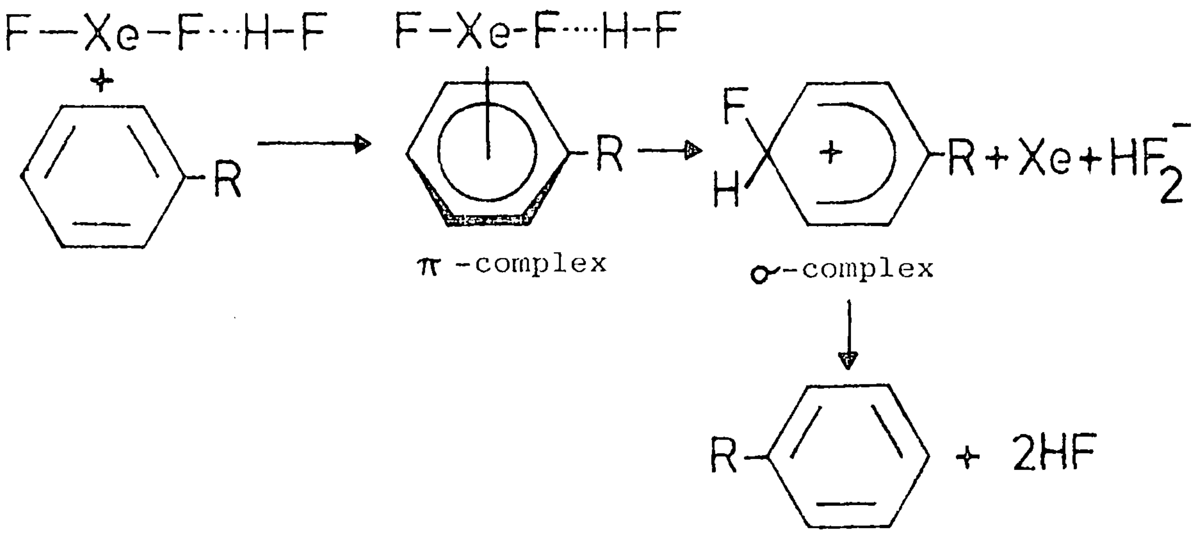
Filler proposed three possible mechanisms[108-109] and it is of interest to describe them briefly as the first one bears a close similarity to the mechanisms proposed for fluorinations by cobalt III fluoride and the other H.V.H.M.F. reagents (as described in Section 2.6F).

In the first mechanism it was envisaged that the xenon difluoride, polarised by co-ordination with HF, oxidises the aromatic starting material to a fully developed radical cation which then abstracts a fluoride ion:



Refs: 108, 109

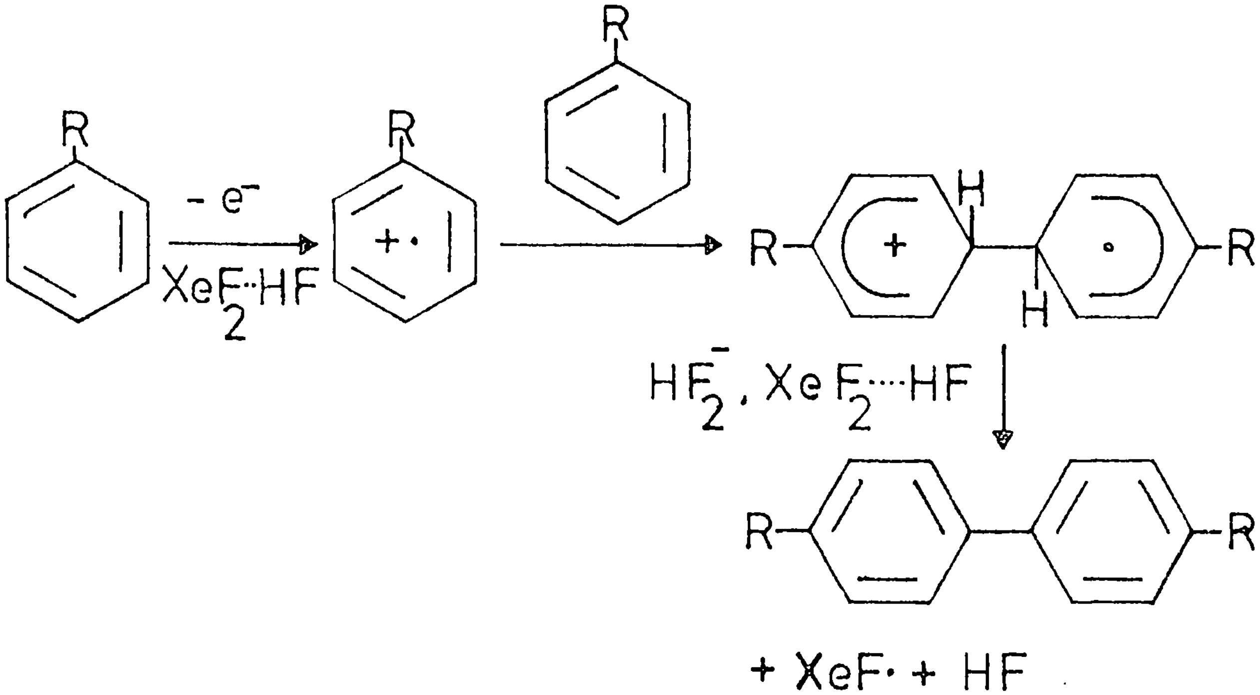
In the second mechanism, reaction occurs via a π-complex which collapses to a cationic σ-complex before a fully radical cation is developed:



Refs: 108,109

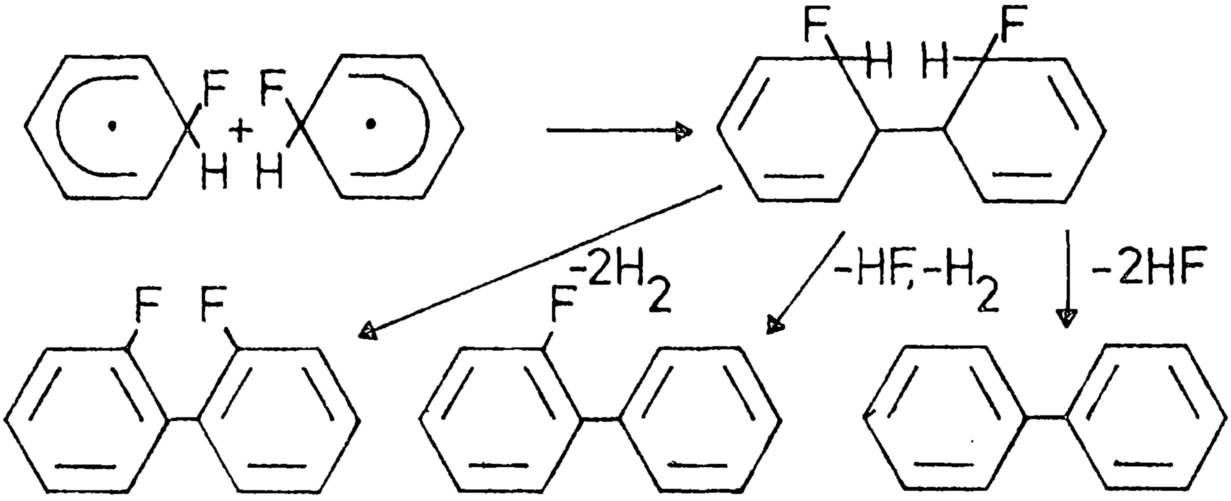
The third mechanism involves an intermediate with a Xe-C$\lessgtr$ - bond and was considered to be the least likely. It is not described further.

Dimerisation to biphenyls is a common side reaction and Filler considered radical cation intermediates to be the most likely for such reactions[109] as, in the products, the ratios of ortho, meta and para isomers were not consistent with reaction between the starting aromatic and either phenyl cations or radicals. The following mechanism was proposed:



Ref: 109

Recently, however, it has been concluded from a study of the reaction between deuterated benzene and XeF_2 that the distribution of deuterium in the dimeric products is more consistent with the reaction between two radicals in a mechanism such as:[110]



Ref: 110

Aryl olefins and acetylenes tend to react at the side chain rather than producing substitution at the aromatic ring:

$$Ph_2C = CHR \xrightarrow[\text{HF or } CF_3COOH \text{ Catalyst}]{XeF_2, CH_2Cl_2} Ph_2CFCFR_2$$

Room temperature 65 — 95%

R = H, Me, F Ref: 111

$$PhC \equiv CR \xrightarrow[HF, CH_2Cl_2]{2XeF_2} PhCF_2CF_2R$$

>50%

R = Ph, CH_3, n-C_3H_7 Ref: 112

Aliphatic olefins may also be fluorinated:

$$CH_3CH = CH_2 \xrightarrow[\text{Room temperature}]{XeF_2 \text{ (or } XeF_4)} CH_3CH_2CHF_2$$

65%

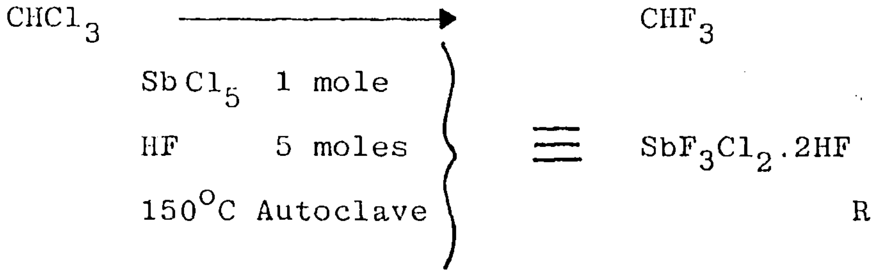
Ref: 113

2.4 Halogen Exchange as an Exhaustive Fluorination Technique

2.4A Reagents based on antimony salts (Swart's reactions)

These reagents are of great importance because of their extensive use in industry in the manufacture of chlorofluorocarbon, refrigerants and aerosol propellants. The reaction of an organic halide with an antimony fluoride is called a Swart's reaction after the chemist who first used the process. Antimony III fluoride, itself, is a very weak fluorinating agent, and will only exchange with particularly activated chlorine atoms, but its action is strongly catalysed by the presence of an antimony V species. Anhydrous hydrogen fluoride is also only a weak halogen exchange reagent, but its activity is catalysed in the same way. It has been suggested that this is because these reactions proceed via cationic intermediates which are stabilised by antimony V salts, the latter being powerful Lewis acids.[60] As an alternative to the simple addition of an antimony V salt, such as the pentachloride, to antimony trifluoride, a powerful fluorinating agent may be formed by oxidising a small proportion of the antimony III, in situ, with either chlorine or bromine.[114]

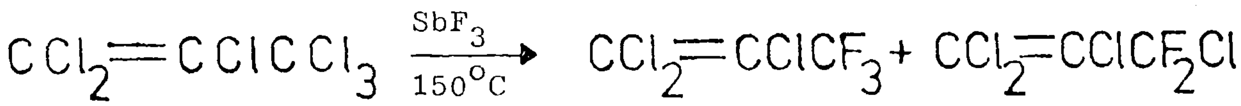
An example of the exchange of unactivated chlorines with an Sb V reagent is:



$$CHCl_3 \longrightarrow CHF_3$$
$$\left.\begin{array}{ll} SbCl_5 & 1\ \text{mole} \\ HF & 5\ \text{moles} \\ 150^{\circ}C & \text{Autoclave} \end{array}\right\} \equiv SbF_3Cl_2.2HF$$

Ref: 114

And exchange of activated chlorines with Sb III alone is illustrated by the reaction of the perchloro-olefin (61)

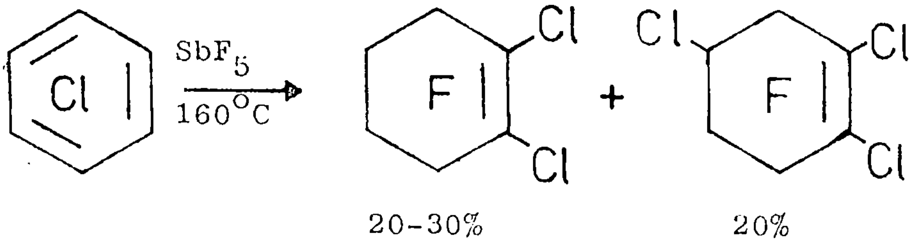


$$CCl_2{=}CClCCl_3 \xrightarrow[150^{\circ}C]{SbF_3} CCl_2{=}CClCF_3 + CCl_2{=}CClCF_2Cl$$

(61) 43% 28%

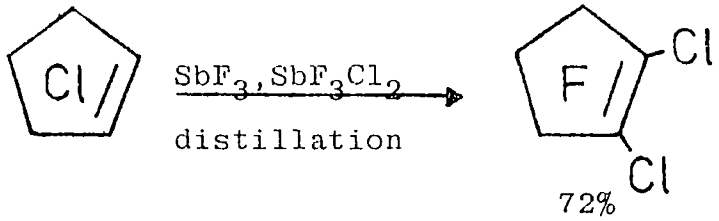
Ref: 60

Additions, as well as substitutions, sometimes occur when chloro-olefins are reacted with reagents containing Sb V and it is possible to prepare semi-saturated cyclic compounds from perchloro-aromatic starting materials.



Ref: 115

But it is very difficult to produce fully saturated compounds by this method, as illustrated by the reaction below:

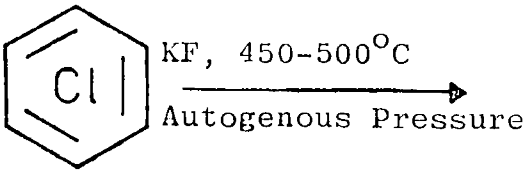


Ref: 116

2.4B Halogen Exchange with Alkali Metal Fluorides as an Exhaustive Technique

In Section 2.3B the reaction of alkali halides with polyhalogenated compounds in the presence of a solvent was described and the difficulties of forcing such systems to produce perfluoro compounds were high-lighted.

Yakobson showed that in the case of hexachlorobenzene (62) these difficulties could be side-stepped by reacting it with an excess of potassium fluoride without a solvent so that very much higher reaction temperatures could be employed.[117]



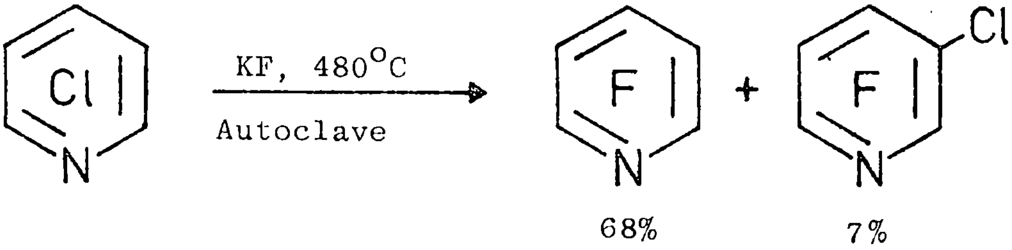
(62)

C_6F_6 + C_6F_5Cl + $C_6F_4Cl_2$
20% 20% 14%

+ $C_6F_3Cl_3$
12%

Ref: 117

The reaction was extended to the perchloro-aza-aromatics by Chambers et al., and, as the perchloro aromatic and hetero-aromatic substrates may be usually prepared in good yield, this method is considered the best available general route to perfluoroaromatic and heteroaromatic compounds.[68,69]



Refs: 68, 69

Products bearing trifluoromethyl groups have been detected in such autoclave reactions and this has been attributed to the formation of difluorocarbene.[118]

2.5 Electrochemical Fluorination

2.5A Introduction

Electrochemical fluorination, pioneered by J.H. Simons[117] et al. during the war, is performed by dissolving the substrate in anhydrous hydrogen fluoride (hereafter referred to as AHF) and passing an electric current through the solution at a voltage below that which generates gaseous fluorine. Organic compounds are extensively fluorinated, with complete, or nearly complete, substitution of hydrogen atoms and saturation of multiple bonds. The method has been the subject of extensive reviews by J. Burdon and J.C. Tatlow,[120] S. Nagase[121] and, more recently, N.L. Weinberg.[122]

It is necessary in the first place that the substrate is soluble in AHF and gives a reasonably conducting solution. Organic compounds containing functional groups usually possess sufficient basicity to interact with AHF and thus fulfil these two requirements. Alkanes and halogenoalkanes do not possess such basicity, however, and, as a result, are only sparingly soluble and difficult to fluorinate. Tatlow quoted an 11% yield of perfluoro-n-octane as the best reported for the conversion of an alkane into its perfluoro analogue although Nagase has since developed a technique of continuous fluorination of gaseous hydrocarbons which has produced tetrafluoromethane (63) in 16.3% yield from methane.[122]

$$n\text{-}C_8H_{18} \xrightarrow[\text{Fluorination}]{\hspace{1em}} \underset{11\%}{n\text{-}C_8F_{18}}$$

Electrochemical Fluorination

Ref: 119

$$CH_4 \xrightarrow[\text{Fluorination}]{\hspace{1em}} \underset{34\%}{CF_4} + \underset{20\%}{CF_3H} + \underset{18\%}{CF_2H_2} + \underset{28\%}{CH_3F}$$

Electrochemical Fluorination

Product Composition

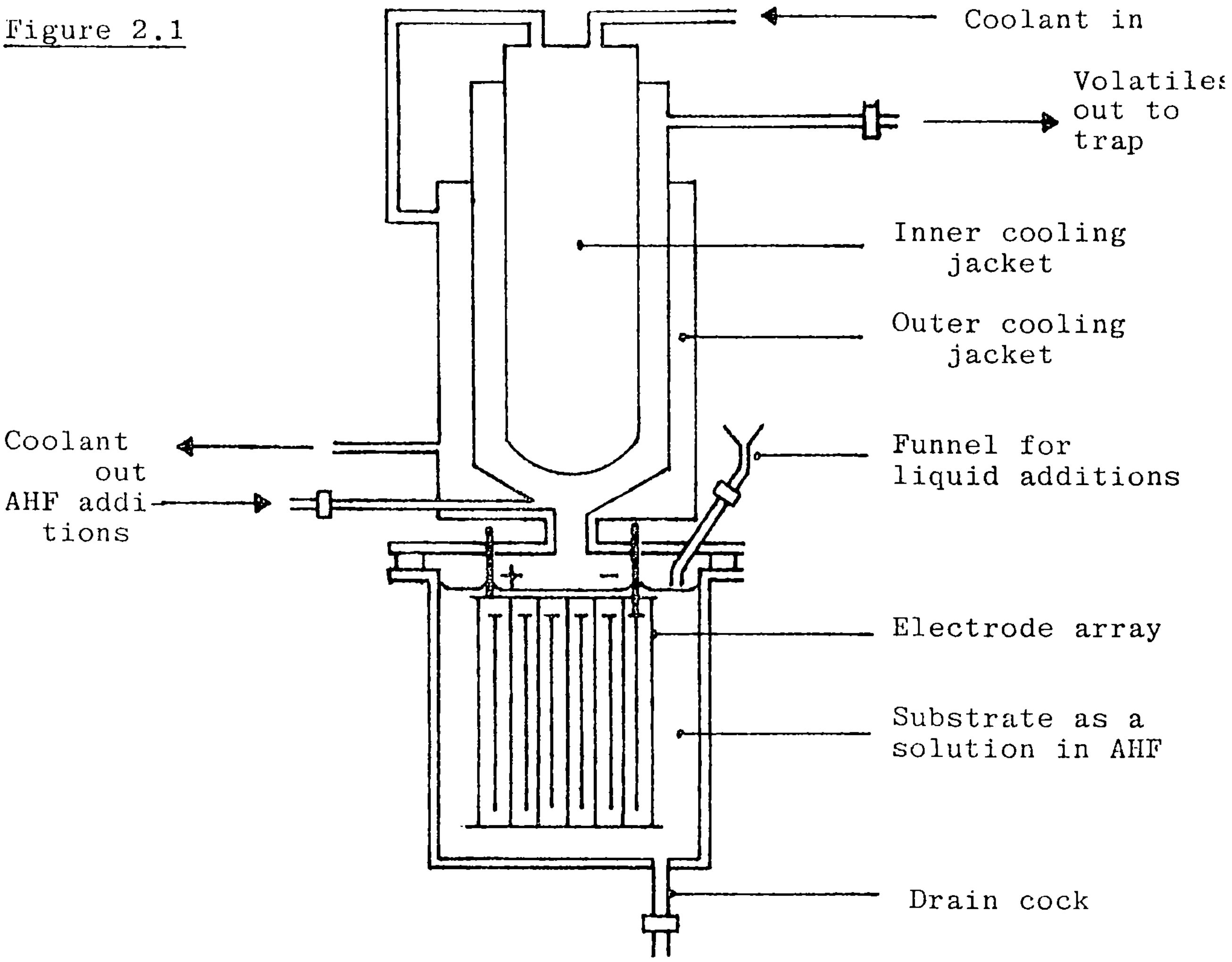
Yield of CF_4 = 16.3%.

Ref: 122

2.5B Apparatus and Techniques

A drawing of an electrochemical fluorination cell is produced below. Such a cell consists of a small tank of Ni, Fe or Cu which contains the solution and an array of interspaced cathode and anode plates as illustrated in Figure 2.1. Diaphragms are unnecessary as the fluorination products are usually inert to cathodic reduction. That the fluorination occurs at the anode plates is evidenced by the adherence of tarry polymeric material formed at their surfaces.[120]

Figure 2.1



The anodes are usually made from either nickel or a nickel based alloy such as monel (66% Ni) although various forms of carbon have also been used. The evidence strongly suggests that different reaction mechanisms are operative for the two types of anode.[122]

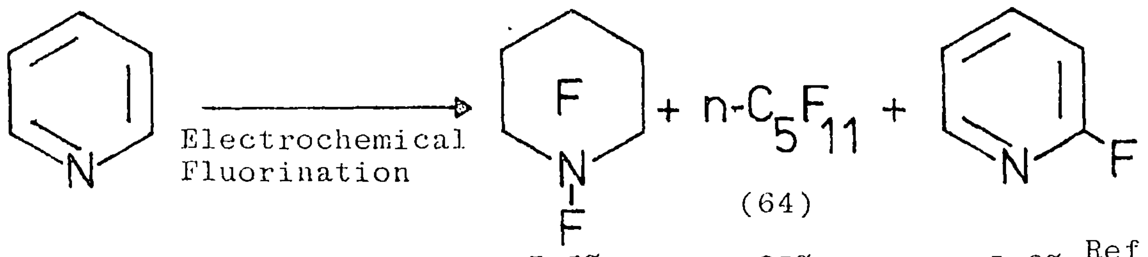
Because of the low boiling point of AHF (19.5°C) and, sometimes, of the substrates and products, cells are equipped with overhead reflux condensors and, if necessary, a cooling coil within the solution itself.

Before commencing a fluorination, it is necessary to eliminate traces of water from the AHF by electrolysis whilst passing dry nitrogen through the system. This is because water, when present during a fluorination, is converted to oxygen difluoride which can cause explosions if concentrated with organic material.

The usual range of cell voltages is from 5 to 7V and, because the solubility and conductivity of products decreases upon fluorination, the progress of a reaction may be followed by the decrease in current with time. Additions of salts such as KF are sometimes made to maintain currents at the end of a reaction or, in the case of poorly conducting initial solutions such as those of alkanes, right from the start.[120,121,122]

2.5C The Fluorination of Hydro-and Halocarbons

Because of the problems already described the electrochemical fluorination of hydro- or halocarbons is not a good route to perfluoroalkanes. In addition, more polar compounds often fragment to produce perfluorocarbons and hence serve as more useful precursors. Thus perfluoropentane (64) may be prepared in better yield from pyridine than from pentane itself.[122,123]



(64)

7.5% 25% 5.3% Ref: 123

Partially fluorinated alkanes give higher yields of the perfluoroalkane, but the problems of solubility and conductance remain:

$$C_6H_{14} \xrightarrow[\text{chemical fluorination}]{\text{Electro-}} C_6F_{14}$$

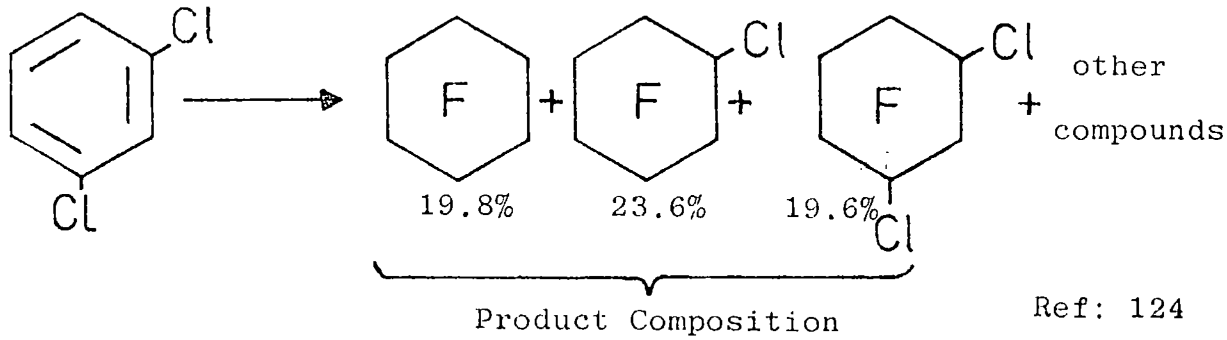
22%

Ref: 122

$$C_6H_{12}F_2 \longrightarrow \underset{63\%}{C_6F_{14}}$$

Ref: 122

The ease with which other halogens are substituted is in the order I>Br>H>Cl, chlorine atoms often remaining in the product.



Ref: 124

Unsaturated sites are preferentially attacked:[125]

$$CHCl = CCl_2 \xrightarrow[\text{Agitated Cell}]{} CHClFCCl_2F + CF_2ClCCl_2F$$

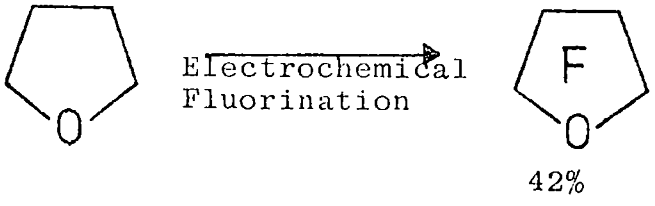
80 : 12

Ref: 125

2.5D The Fluorination of Compounds with Oxygen Functional Groups

Oxygen containing products may be produced in reasonable yield in many cases by electrochemical fluorination in contrast with fluorinations with H.V.H.M.F. reagents (Section 2.6) or fluorine (Chapter 1).

Thus perfluoroethers have been prepared from ethers



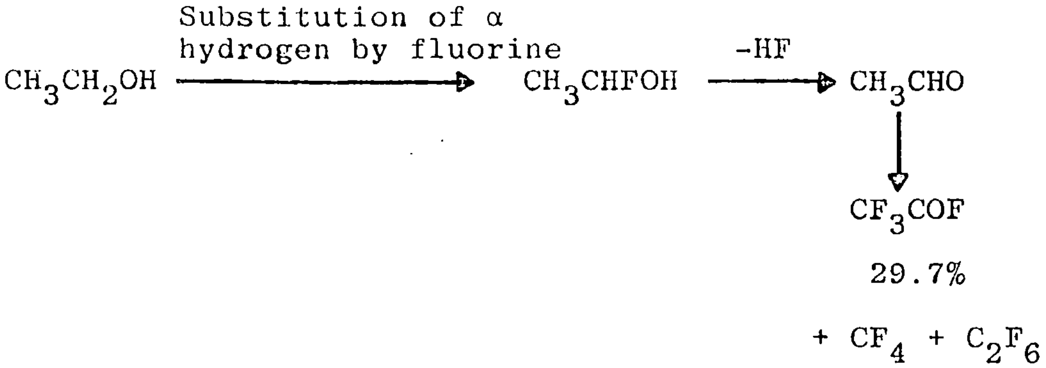
Refs: 126, 127

Perfluorocarboxylic acid fluorides are common side-products.[122]

$$C_4H_9OC_4H_9 \xrightarrow[\text{Fluorination}]{\text{Electrochemical}} \underset{20\%}{n\text{-}C_3F_7COF} + \underset{2.4\%}{C_2F_5COF} + \underset{4.6\%}{CF_3COF}$$

Ref: 122

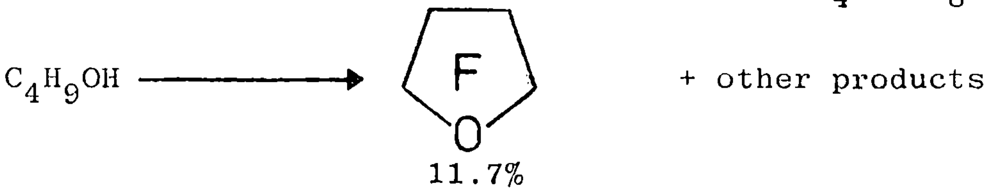
Perfluorocarboxylic acid fluorides are the major products when alcohols, aldehydes and ketones are fluorinated. The similarity in the reactions of these classes of compounds has been accounted for by a mechanism which involves the initial conversion of alcohols into aldehydes under the reaction conditions:



$$CH_3CH_2OH \xrightarrow{\text{Substitution of } \alpha \text{ hydrogen by fluorine}} CH_3CHFOH \xrightarrow{-HF} CH_3CHO \rightarrow \underset{29.7\%}{CF_3COF} + CF_4 + C_2F_6$$

Ref: 122

Recently, however, Nagase has observed the formation of cyclic ethers upon fluorinating primary alcohols from C_4 to C_8.[128]



Ref: 128

$$CH_3COCH_3 \xrightarrow[\text{Electrochemical Fluorination}]{} \underset{59.8\%}{CF_3COF} + CF_4 + CF_3H$$

Ref: 122

$$CH_3COOC_2H_5 \xrightarrow[\text{Fluorination}]{\text{Electrochemical}} \underset{52.3\%}{CF_3COF}$$

Ref: 122

Other carbonyl containing compounds such as acid anhydrides, carboxylic acids and acid halides are thought to react with AHF to produce intermediate acid fluorides which are then converted to perfluoro acid fluorides. Yields may be reduced by side reactions induced by oxygen difluoride and hydroxyl radicals produced from water formed in the initial step.[120,121]

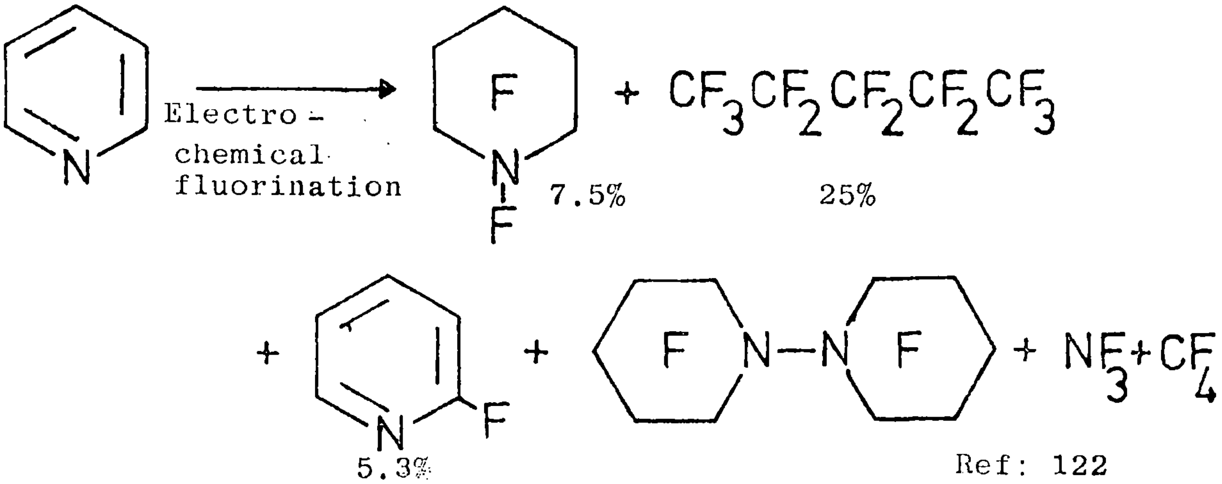
$$CH_3COOH + HF \rightleftharpoons CH_3COF + H_2O$$

$$\begin{array}{c} CH_3COF \\ \downarrow \\ CF_2COF \\ 20\% \end{array}$$

Ref: 120

2.5E Fluorination of Compounds with Nitrogen Functional Groups

Fully fluorinated, nitrogen-containing compounds can usually be produced in better yields than by other fluorination methods. >N-H bonds are initially converted to >N-F bonds although loss of nitrogen as NF_3 or dimerisation may be subsequent reactions.



Ref: 122

2.5F The Mechanisms of Electrochemical Fluorination

Fluorination with nickel anodes is typified by an induction period before the onset of fluorination and, in contrast to fluorinations with elemental fluorine, the production of perfluoro-compounds in relatively high yield. These observations argue against mechanisms involving the in situ generation of fluorine or organic radical cations, at the nickel anode and the induction period suggests that the fluorinating agent is a high valency nickel compound formed on the anode surface. However it has been argued that nickel III fluoride itself is unstable with respect to loss of fluorine and a complex nickel III or nickel IV species is preferred.[129]

$$Ni + 2F^- \longrightarrow NiF_2 + 2e^-$$

$$NiF_2 + 2F^- \longrightarrow NiF_4 + 2e^-$$

$$NiF_4 + 2F^- \longrightarrow NiF_6^{2-}$$

$$NiF_6^{2-} + \text{substrate} \longrightarrow \text{products} + NiF_2$$

Ref: 129

It has also been suggested that the substrate itself may complex with the high valency nickel species followed by a collapse of this species to products.[130]

$$RH \longrightarrow (RH)_2NiF_6 \longrightarrow \text{Products}$$
$$\text{or } (RH)_3NiF_6$$

Ref: 130

However, fluorination at carbon anodes probably proceeds via the generation of fluorine as there is no induction period and the electrode potentials are sufficiently high.[131]

There is no induction period when platinum anodes are employed either, but the reactions proceed at potentials which will generate radical cations but not fluorine. Therefore the fluorinations are thought to result from the reaction between the organic radical cation and fluoride ion.[132]

2.6 Fluorinations with Cobalt III Fluoride and Other High Valency Heavy Metal Fluorides

2.6A Introduction

Cobalt III fluoride, either as itself or in the form of a complex such as potassium tetrafluorocobalt III and, to a lesser extent, other high valency metal fluorides or fluoro complexes such as those of silver II, manganese III, cerium IV, lead IV and nickel IV, have been used extensively for the preparation of saturated perfluoro analogues of organic compounds. Throughout this chapter these reagents will be referred to as H.V.H.M.F. reagents. Their reactions bear some similarity to electrochemical fluorination in that extensive substitution of hydrogen and saturation of multiple bonds occurs but, unlike electrochemical fluorinations, functional groups are not usually retained. The method does possess the advantage, however, of being a simpler and easier procedure to perform than electrochemical fluorination whilst sharing with the latter the advantage that fragmentations are much lower than those of the more exothermic direct fluorination techniques.[52]

This group of reagents is also characterised by the fact that reduction of the metal to a lower, more stable, oxidation state occurs upon reaction although it has been pointed out that the Swart's reagent, antimony V fluoride, also possesses some of these characteristics[60] and hence a rigid classification is not possible.

2.6B Experimental Techniques for Fluorinations with Cobalt III Fluoride and other H.V.H.M.F. Reagents

Fluorinations with cobalt III fluoride and similar reagents are now usually performed by passing the substrate as a vapour over a heated bed of the reagent in the form of a finely divided powder.[52] Some reactions have been reported in which the substrate is reacted with a stirred slurry of cobalt III fluoride powder in a relatively inert solvent, such as Freon 113, but this method has not been used very frequently in recent years[133].

The earliest vapour phase reactors were simply externally heated copper tubes which contained a carpet of the reagent,[133] but the performance of such reactors was improved in terms of yields and reproducibility of results when co-axial paddles to continuously expose a fresh reagent surface, were introduced. The history and development of cobalt III fluoride reactors has been described in detail by Stacey and Tatlow in their comprehensive review of H.V.H.M.F. reagents.[133]

Figure 8.1 (Chapter 8) describes a typical, modern, stirred reactor. It consists of a nickel barrel containing the reagent which is stirred by a co-axial paddle turned by an external motor. The barrel is surrounded by a lagged electrical heater capable of raising the reactor to 300°C and above and the exit chimney is guarded by a baffle system to reduce losses of cobalt salts in the purging gas stream. The apparatus is sealed by lead gaskets and P.T.F.E. glands.

Such reactors are charged with a suitable cobalt II salt such as the chloride or fluoride and cobalt III fluoride is generated in situ by passing fluorine through the reactor whilst maintaining a temperature of about 300°C. The interior surfaces of the reactor are passivated by the fluorine. After passing a calculated excess of fluorine, all the reagent is converted to cobalt III fluoride and the reactor is ready for use.

The reactor is then adjusted to the desired reaction temperature whilst purging with a dry, inert gas to expel any remaining fluorine. The organic substrate is introduced, either by vapourising it in the gas stream, or by dropping the liquid directly into the reactor entrance. Products are purged from the reactor by the gas and collected in traps. Hydrocarbons produce hydrogen fluoride as a co-product but, as perfluorocarbons are immiscible with hydrogen fluoride, separation is achieved by simply draining off the lower layer.

It is usual to regenerate the reagent after exhausting about 25% of the cobalt III and this is done by passing an excess of fluorine over the spent reagent at about 300°C, as in the start-up procedure. Residual polymeric products and tarry contaminants are combusted by this and the regenerated reagent is essentially pure.

The tetrafluorocobaltate III reagents are utilised in the same manner and are generated by fluorinating the alkali metal trifluorocobaltate II.[134]

$$KCoF_3 \xrightarrow[\Delta]{F_2} KCoF_4$$ Ref: 134

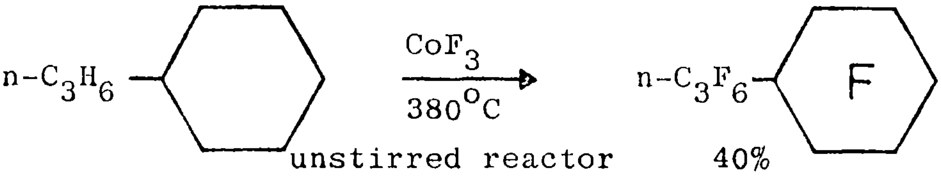
2.6C The Fluorination of Alkanes by H.V.H.M.F. Reagents

Alkanes may usually be converted to the corresponding perfluoroalkane in high yield (50-75%) when a stirred reactor is used.[52] Many of the earliest fluorinations were performed in less efficient unstirred reactors but yields in many cases were reasonable in spite of this.

$$n\text{-}C_7H_{16} \xrightarrow[175\ -\ 300^{\circ}C]{CoF_3} n\text{-}C_7F_{16}$$

stirred reactor 69%

Ref: 135



Ref: 134

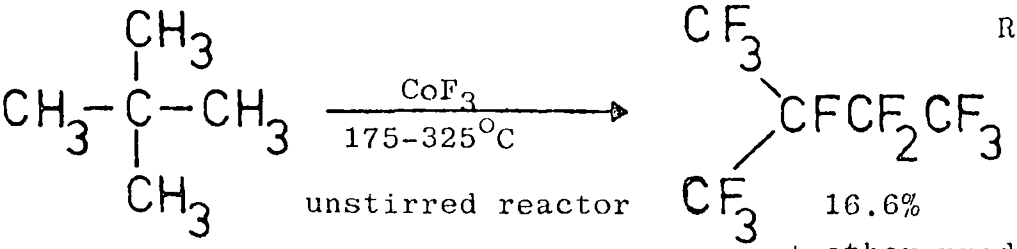
With higher molecular weight alkanes the yield of products in which hydrogen is retained increases unless higher reaction temperatures or longer exposures to the reagent are employed which, concomitantly, increases the number of fragmentation side-products. Thus cetane, when fluorinated under conditions sufficiently vigorous to remove all hydrogen, produced some perfluorooctane as a side product.[136]

$$n\text{-}C_{16}H_{34} \xrightarrow[\text{unstirred reactor}]{CoF_3,\ 400^{\circ}C} n\text{-}C_{16}F_{34} + \text{some } C_8F_{18}$$

Ref: 136

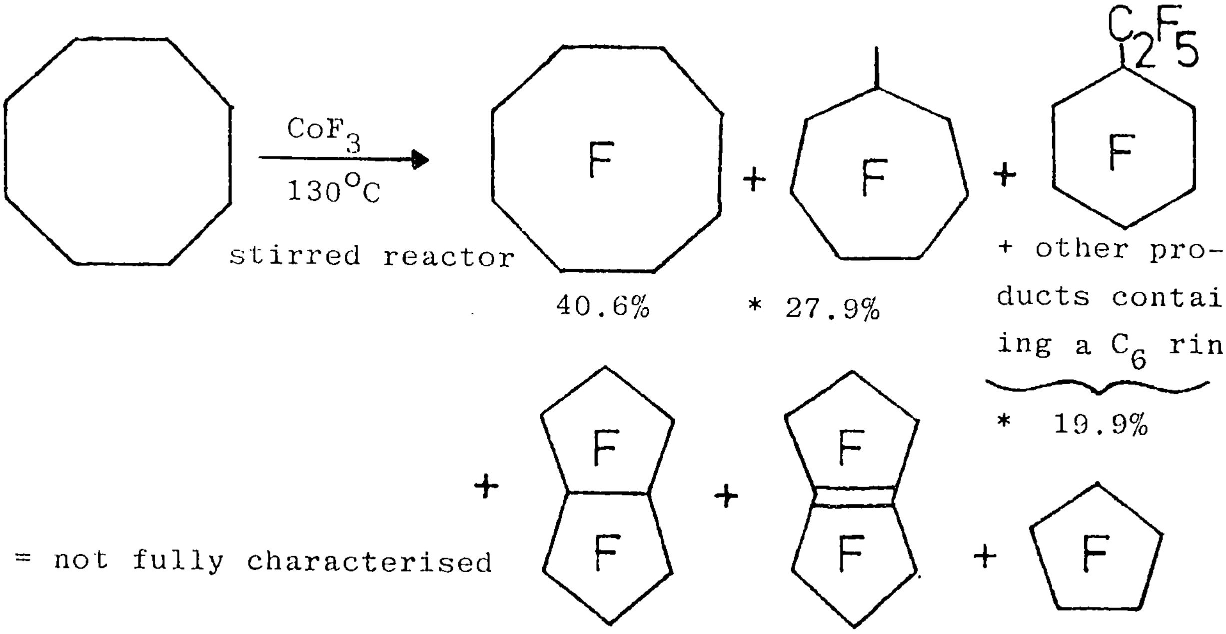
Branched hydrocarbons are also prone to fragmentation and yields are not, usually, as high as for straight chain alkanes of the same molecular weight. In the product from neo-pentane, no perfluoro(neo-pentane) was detected.[137]

Ref: 137



+ other products

Re-arrangements have also been reported in the fluorinations of bridged ring hydrocarbons and monocycloalkanes with more than six carbon atoms.

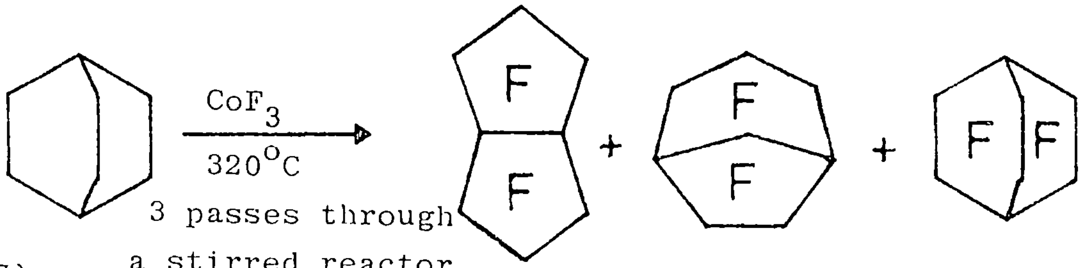


40.6% * 27.9% + other products containing a C_6 ring * 19.9%

* = not fully characterised

7.3% * 3.9% * 0.4%

Ref: ~~136~~ 138

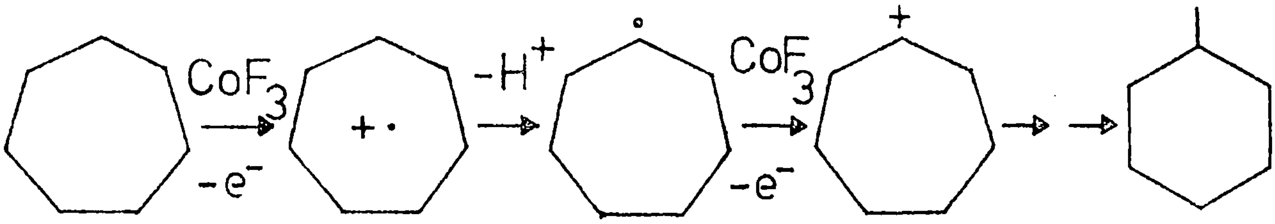


(67) (64) (65) (66)

(64):(65):(66) = 63:29:8

Ref: 139

These latter reactions were thought to result from intramolecular re-arrangements of the proposed intermediate carbocations generated by the cobalt III fluoride acting as either a strong Lewis acid or an oxidising agent (see Section 2.6F). Thus in the fluorination of cycloheptane (68) the following process was envisaged:-



(68)

Ref: 138

The carbocation undergoes a standard re-arrangement to produce the methylcyclohexane skeleton, fluorinated derivatives of which are observed.[138] Evidence for the intermediacy of cationic species in the fluorination of bicyclo[2.2.2.]octane (67) was that similar proportions of bicyclo[3.3.0]-and bicyclo[3.2.1]-octanes to those produced by fluorination were produced by equilibration with aluminium bromide.[139]

The partial fluorination of ethane[140] and 2-methylpropane[141] with both cobalt III fluoride and, in the case of ethane, the milder potassium tetrafluorocobaltate III, at low temperatures, has been studied in some detail. Whilst the proportions of products from ethane were similar to that predicted for the random addition of fluorine, it was noted that products from 2-methylpropane in which the tertiary hydrogen is substituted were 10 times commoner than if due to random substitution. This was taken as further evidence for the intermediacy of either radicals or carbocations in the reaction between alkanes and cobalt III fluorides.

2.6D The Fluorination of Alkenes

The addition of fluorine to olefins, using cobalt III fluoride, occurs even more readily than the substitution of hydrogen atoms as evidenced by the high yields, under mild conditions, of 1,2-difluoroethane from ethylene reported by Burdon et al.[140]

$$CH_2 = CH_2 \xrightarrow[200^{\circ}C]{KCoF_4} CH_2FCH_2F + \text{other products}$$

(67% of product, 93.4% conversion)

Ref: 140

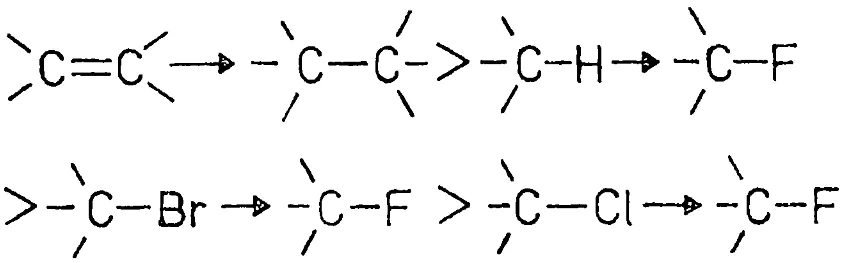
Under more forcing conditions, perfluoro compounds are produced in high yield.

Addition occurs before substitution in halo-alkenes as well as hydrocarbon systems, as demonstrated by Rausch et al.[142] who obtained 1,2-difluoro derivatives of a wide variety of olefins using cobalt III fluoride at low temperatures and with short contact times.

$$CHCl = CCl_2 \xrightarrow[\substack{0.5\text{ g olefin min.}^{-1} \\ 500\text{ mls. }N_2\text{ min.}^{-1}}]{CoF_3,\ 18\text{-}32^{\circ}C} \underset{31\%}{CHClFCFCl_2} + \underset{4\%}{CHClFCF_2Cl}$$

Ref: 142

The results for olefins containing hydrogen, chlorine and bromine were in accord with earlier observations cited by Rausch et al. that the processes below occur in the following order of ease:-



Ref: 142

1,1-dichloroethylene gave rise to products in which the chlorine atoms had migrated which was thought to be consistent with its lack of stability.

$$CH_2 = CCl_2 \xrightarrow[20\text{-}50^{o}C]{CoF_3} \underset{2\%}{CHClFCClF_2} + \underset{11\%}{CHClFCCl_2F}$$

1 g. substrate min.$^{-1}$

800 mls. N_2 min.$^{-1}$

$$+ \underset{4\%}{CCl_2FCCl_2F} + \underset{2\%}{CHCl_2CCl_2F}$$

Ref: 142

More recently, high yields of the addition product have been obtained on fluorinating 1,2-bis(perfluoroalkyl)ethylenes.[143]

$$\underset{\text{(both isomers)}}{CF_3CF_2CF_2CH{=}CHCF_2CF_2CF_3} \xrightarrow[210\text{-}220^{o}C]{CoF_3} \underset{24.9\%}{CF_3CF_2CF_2CHFCHFCF_2CF_2CF_3}$$

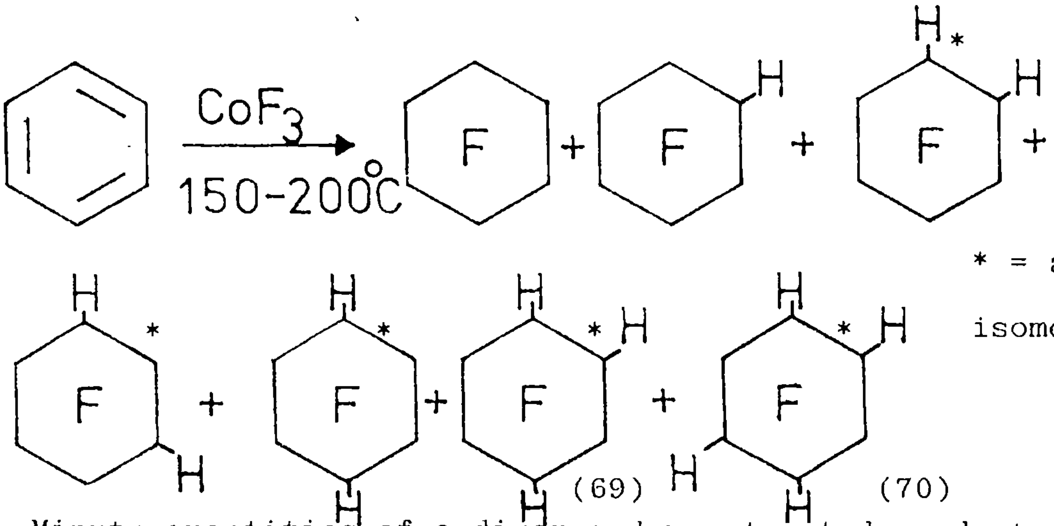
+ other products

Ref: 143

Cleavage can occur at the double bond during exhaustive fluorinations. Thus Haszeldine and Smith noted perfluorononane amongst the side-products of their unstirred fluorination of 1-decene.[144] Possible mechanisms of the fluorination of olefins are discussed later in Section 2.6F.

2.6E The Fluorination of Aromatic Compounds

Stacey, Tatlow and co-workers have studied the partial fluorination of benzene and other aromatic hydrocarbons in some detail.[52] With cobalt III fluoride at temperatures between 150 and 200^{o}C the major products were polyfluorocyclohexanes of formula $C_6H_nF_{12-n}$ (where n = 1 to 4). All possible isomers of $C_6H_nF_{12-n}$ were produced for n = 0, 1 and 2 but, interestingly, for n = 3 and 4, only isomers of the 1,2,4-trihydro (69) and 1,2,4,5 tetrahydro (70) compounds were produced.

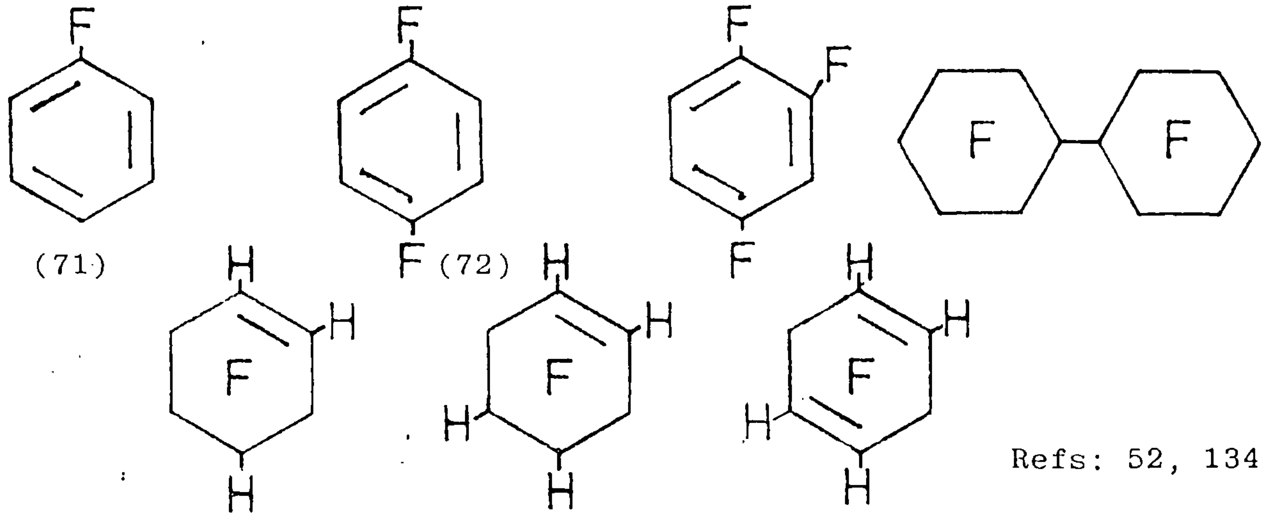


(69) (70)

* = all possible isomers produced

Minute quantities of a dimer and unsaturated products, including some aromatics, were also isolated and they are presented below.

Minor Products of the Mild CoF_3 Fluorination of Benzene



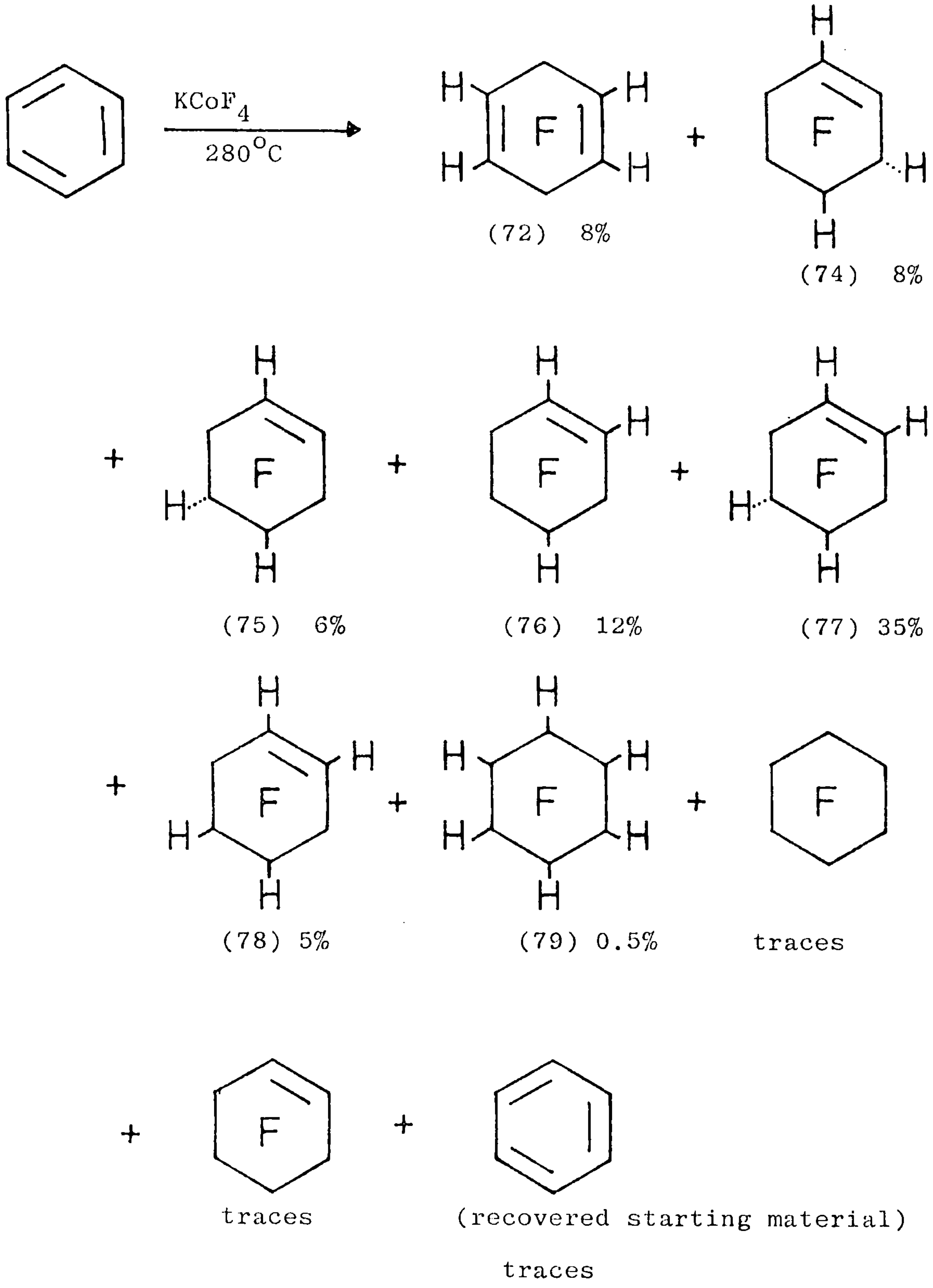
(71) (72)

Refs: 52, 134

Fluorobenzene (71) and p-difluorobenzene (72) gave almost identical fluorination products, suggesting them to be intermediates for the other products.

Unsaturated products were obtained in high yield when benzene was fluorinated with the milder reagent potassium tetrafluorocobaltate III [134] (see Figure 2.3).

Figure 2.3

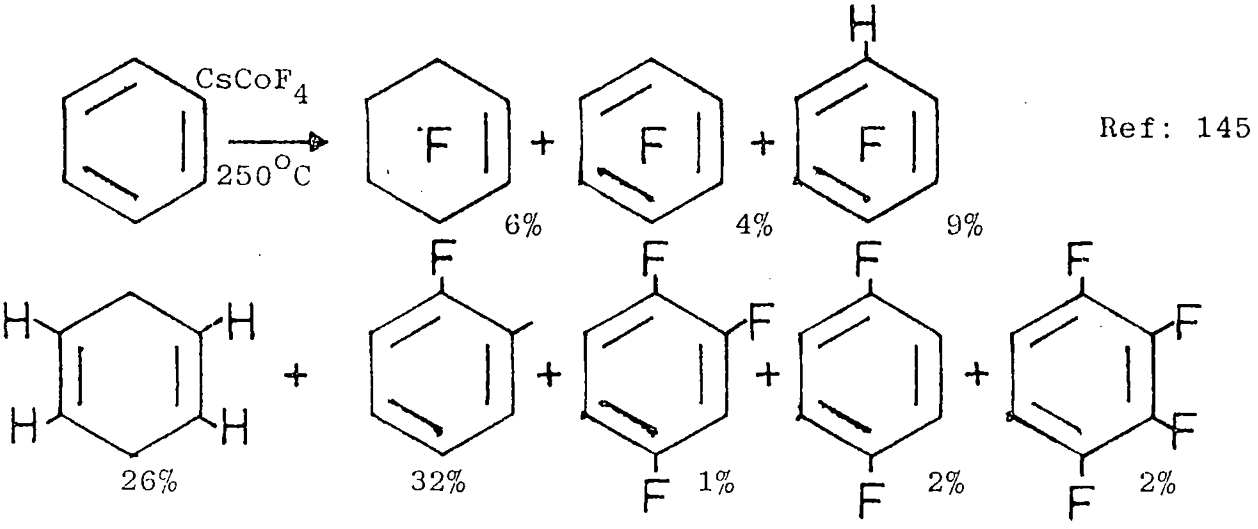


Ref: 134

Once again, an almost identical product was obtained when fluorobenzene (71) and p-difluorobenzene (72) were fluorinated with potassium tetrafluorocobaltate (III) under similar conditions.[134]

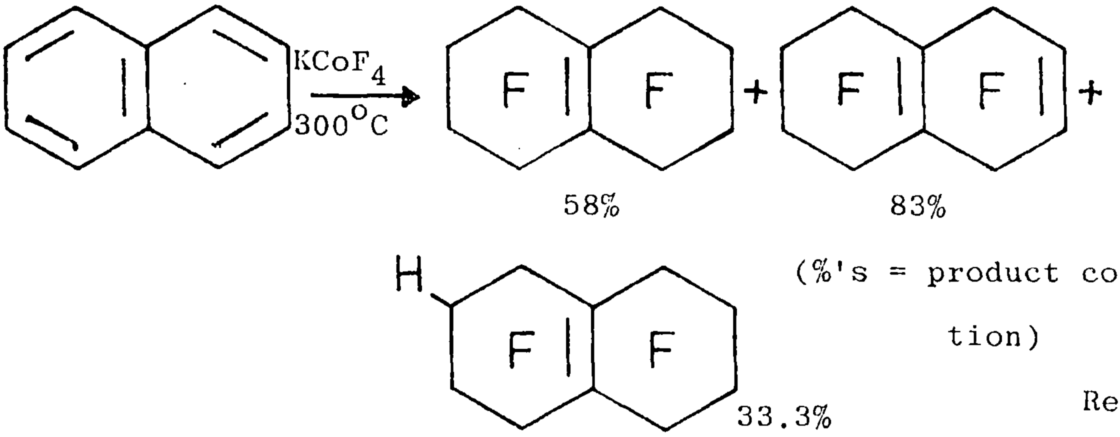
These results were in accord with the earlier postulate that (73) to (79) inclusive are all intermediates in the formation of the higher fluorination products when benzene is fluorinated by the cobalt III containing, and other, high valency heavy metal fluoride reagents.[134] The formation of these intermediates has been explained by a proposed mechanism for cobalt III containing, and other, high valency heavy metal fluoride reagents which will be described in Section 2.6F.

Benzene has also been reacted with other alkali metal tetrafluorocobaltates.[145] The lithium salt was observed to give higher yields of the proposed intermediate 3,3,6,6,tetrafluorocyclohexa-1,4-diene than the potassium salt, whilst sodium and rubidium were very similar. More interesting, however, were the small yields of perfluorobenzene and other fluorobenzenes obtained when the caesium salt was employed.



Ref: 145

Perfluoro olefins were the major products when fused ring aromatics such as naphthalene[146] and anthracene[147] were fluorinated with potassium and caesium tetrafluorocobaltates. The scarcity of hydrogen containing products was thought to indicate perfluoroaromatic compounds to be important intermediates.

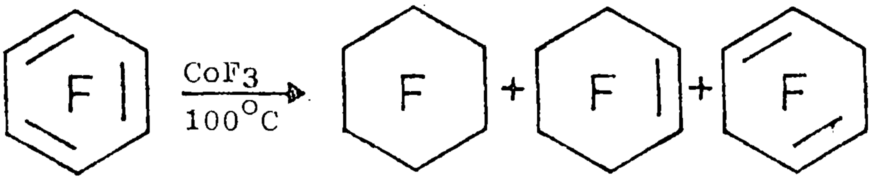


58% 83% 33.3%

(%'s = product composition)

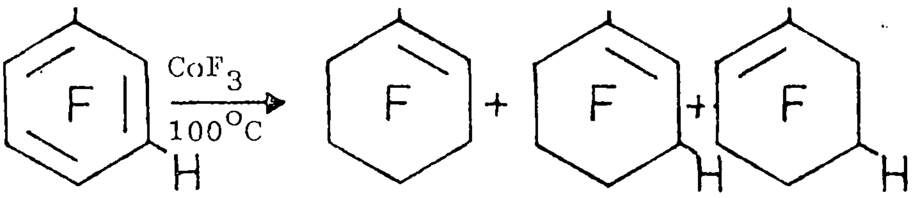
Ref: 146

The fluorination of a long series of polyfluoro-aromatic compounds has been reported.[148] Interestingly, unsaturated products accounted for the bulk of the product, at reaction temperatures between 80°C and 160°C, except when at least two hydrogens were present on the aromatic ring.



8% 90% 2%

(%'s = product composition) Ref: 148

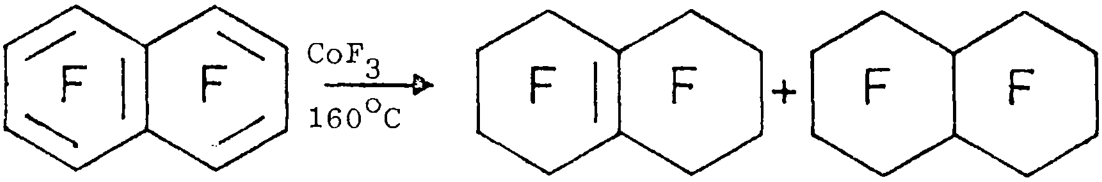


5% 17% 15%

+ saturated compounds 62%

(%'s = product composition) Ref: 148

(80) is obtained as almost the only product when (81) is fluorinated which is consistent with the latter being an important intermediate in the fluorination of napthalene.



(81)

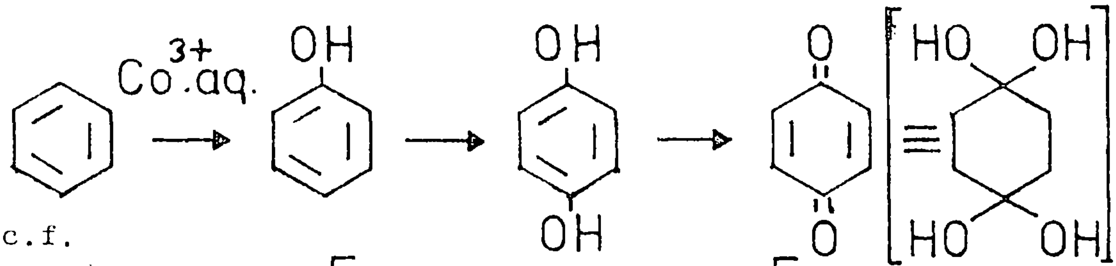
(80) (both isomers)

98% 2%

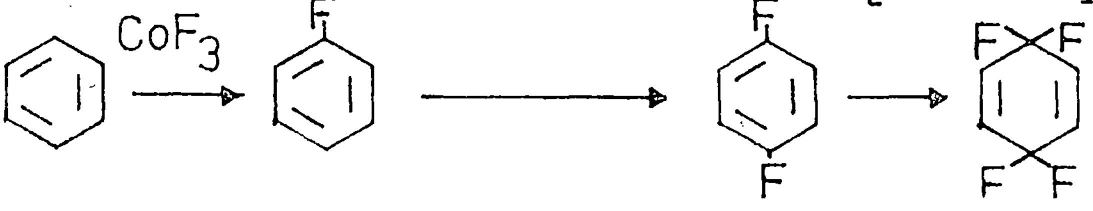
(%'s = product composition) Ref: 148

2.6F The Mechanism of the Reaction between H.V.H.M.F. Reagents and Unsaturated and Homoaromatic Compounds

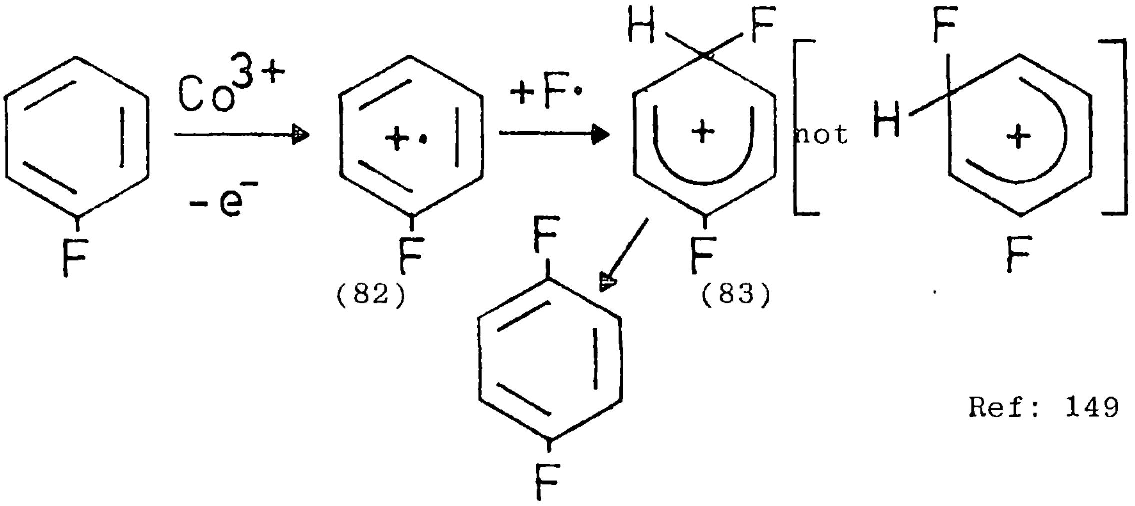
Although the main reaction pathways of the fluorination of many aromatic compounds by H.V.H.M.F. reagents had already been elucidated to varying degrees of certainty, it was not until 1972 that the first detailed reaction mechanisms were proposed.[149] The indicated intermediates during the fluorination of benzene and other aromatic compounds were all substituted as would have been the case for an electrophilic mechanism. Thus, for example, para, rather than meta, difluorobenzene was isolated from the products of the fluorination of benzene. Many similar examples were noted. It was further noted that cobalt III produced strikingly analogous substitution patterns when used as an oxidising agent in aqueous media:-



c.f. Ref: 149



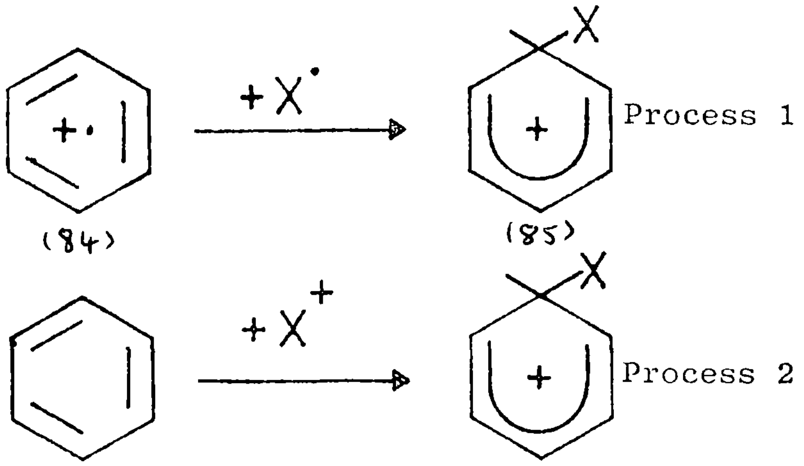
Thus, it was postulated that oxidation of the aromatic substrate is the first step during fluorination to yield a radical cation such as (82). Abstraction of a fluorine atom then leads to a species very similar to a Wheland cationic intermediate (83).



Ref: 149

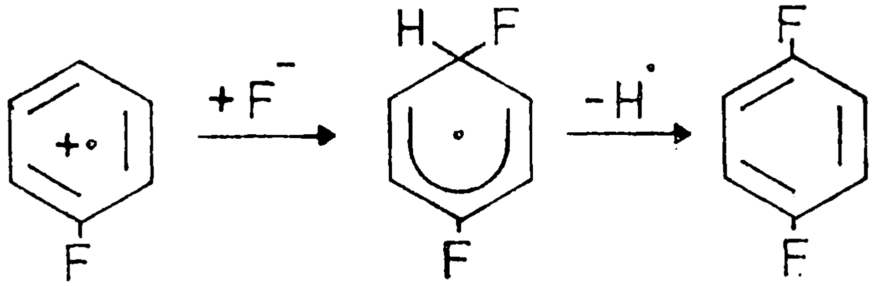
If the reaction was controlled by the stabilities of such cations then, it was argued, the observed reaction pathways would be favoured.

The authors qualified their proposed mechanism, however, by pointing out that the stability of a radical cation such as (84) is much closer to that of the intermediate cation (85) than is that of a neutral aromatic molecule.



Ref: 149

Therefore the transition state may not be very similar to the cation in process 1, unlike process 2, and the substitution could be controlled by initial rather than final state effects. A result of this is that quenching by fluoride ions to yield radical intermediates such as (86) must be considered an alternative possibility, as the isomer distribution could be



(87) (86)

controlled by the distribution of charge in species (87) rather than by the relative stabilities of radicals such as (86). Whilst the latter effect would be expected to give a random distribution, control by the distribution of charge in (87) could lead to the observed isomer ratios and the authors cited electrochemical cyanations which give isomer ratios similar to those predicted for electrophilic aromatic substitutions although no cyanide radicals are present to quench the initial radical cations.[150]

A third possibility mentioned was that quenching by fluorine atoms occurs but that the observed isomer ratios are a result of the distribution of electron spin on the radical cation.

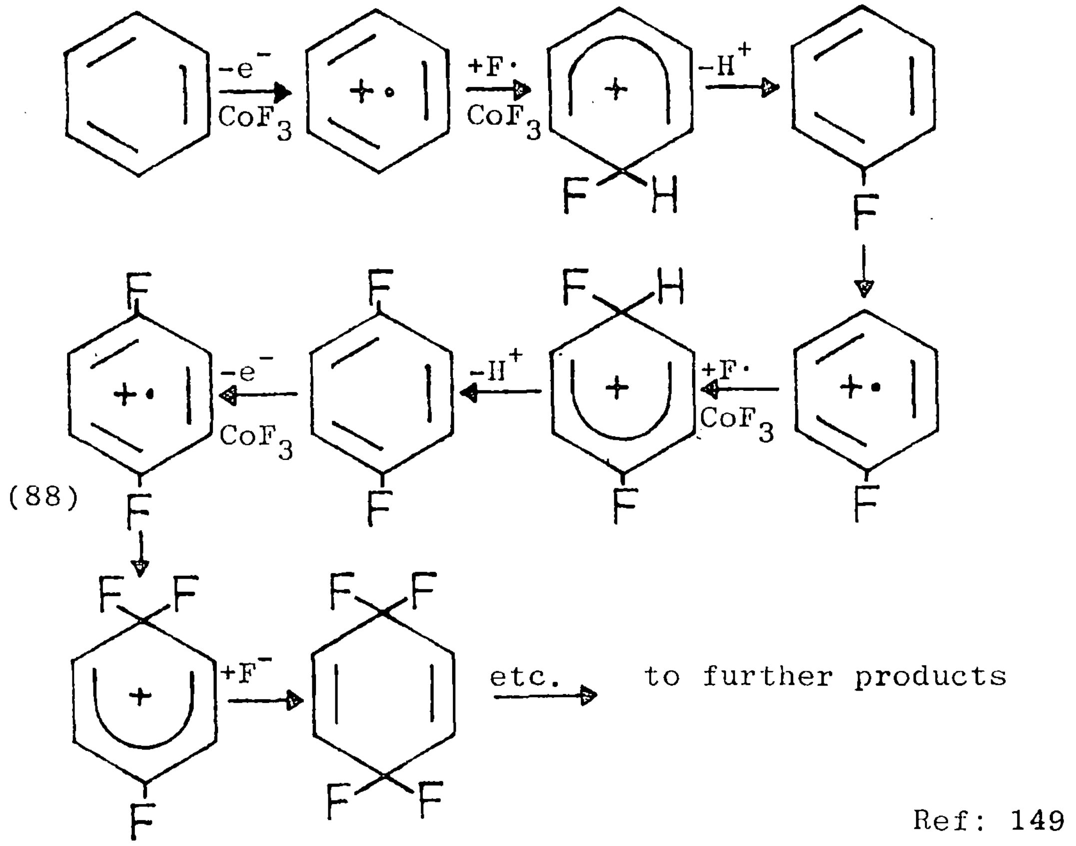
Whatever the subsequent fate of the radical cation, several convincing, additional items of evidence for the oxidation process were cited. Amongst these were:-

(a) The fluorinating power of the H.V.H.M.F. reagents apparently declines with the oxidation potential of the metal in the order:-

$$Ag^{2+} > Co^{3+} > Mn^{3+} > Ce^{4+}$$

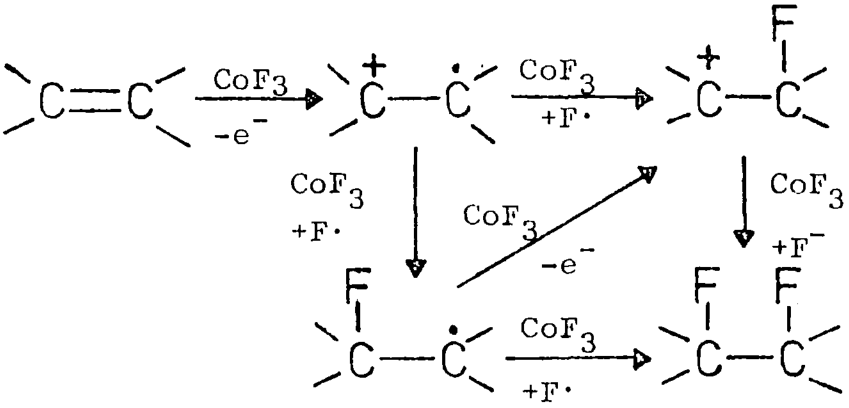
(b) When benzene is fluorinated with the strong reagent CoF_3, saturated products predominate whilst weaker MnF_3 produces polyfluorocyclohexenes and CeF_4 produces polyfluorocyclohexenes, -dienes and-aromatics, i.e. the ionisation potential of the substrate appears to determine its reactivity.

The fluorination of benzene was therefore described by the following mechanism, assuming cationic intermediates as a working hypothesis:-[149]



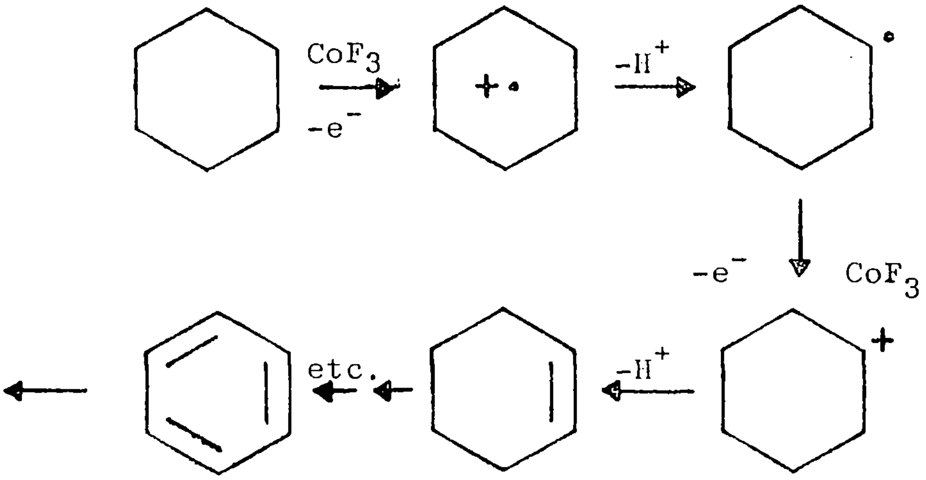
Cerium IV fluoride gives a higher proportion of aromatic products than cobalt III fluoride and tetrafluorobenzenes were detected amongst them which indicates that addition of fluorine at C-H rather than C-F in species (88) is a competing side reaction.

The further reaction of the diene would account for all the monoenes and saturated compounds produced from benzene. A similar mechanism was proposed for the saturation of olefins although, again, it is not certain whether radical or cationic intermediates were produced.[140]



Ref: 140

The mechanism was also adapted to unsaturated hydrocarbons where oxidation to a radical cation was followed by loss of a proton. This process could proceed as far as aromatisation with some alicyclic compounds and evidence cited for such was the similarity between the fluorination products of naphthalene and tetralin.[149]



Ref: 151

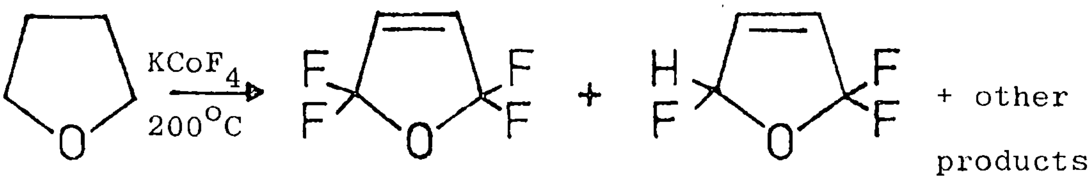
2.6G The Fluorination of Heterocyclic Compounds by H.V.H.M.F. Reagents

(a) Early Work

Early attempts to fluorinate heterocyclic compounds with cobalt III fluoride were very discouraging. Thus, Haszeldine reported only very low yields (0.2%) of perfluoropiperidine when he attempted the fluorination of pyridine.[152] It was thought that much material was lost due to the formation of involatile hydrofluorides within the reactor. 2-methylindole[153] and thioaromatic heterocycles[153,154], by contrast, were polymerised by the hydrogen fluoride by-product.

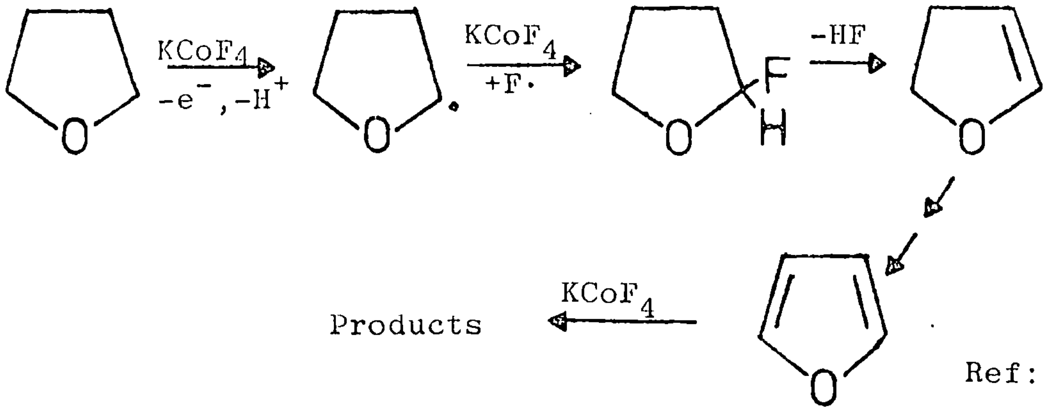
(b) Oxygen Heterocycles

When tetrahydrofuran was fluorinated with cobalt III fluoride, however, no problems associated with reactions with hydrogen fluoride were encountered,[155] Under mild conditions (100-110°C) the major products were polyfluorotetrahydrofurans, with minor polyfluoropropanes and polyfluorocarboxylic acids representing products due to ring fission. When the milder reagent potassium tetrafluorocobaltate (III) was used, however, unsaturated products accounted for 87% of the product.



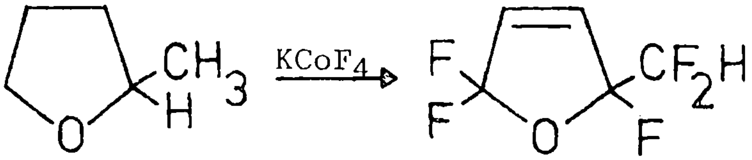
(90) (91) 26% (92) 61% Ref: 155

Therefore, a reaction mechanism was proposed which involved the initial oxidative aromatisation of (90) to furan, via additions of fluorine and eliminations of hydrogen fluoride, in a manner reminiscent of the aromatisation processes supposed to occur during the fluorination of alicyclic compounds mentioned in Section 2.6F.



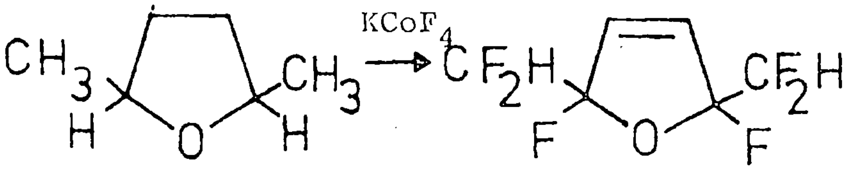
Ref: 155

The subsequent reaction of the aromatic intermediate was originally suggested to occur via successive 2,5 additions of fluorine followed by 2,5 elimination of hydrogen fluoride, but this mechanism was, later, less favoured than one involving the intermediacy of radical cations[156]. An aromatisation process and a subsequent radical cation process was also suggested to account for the simple products from mono and dimethyl derivatives of tetrahydrofuran (93) and (94).[156]



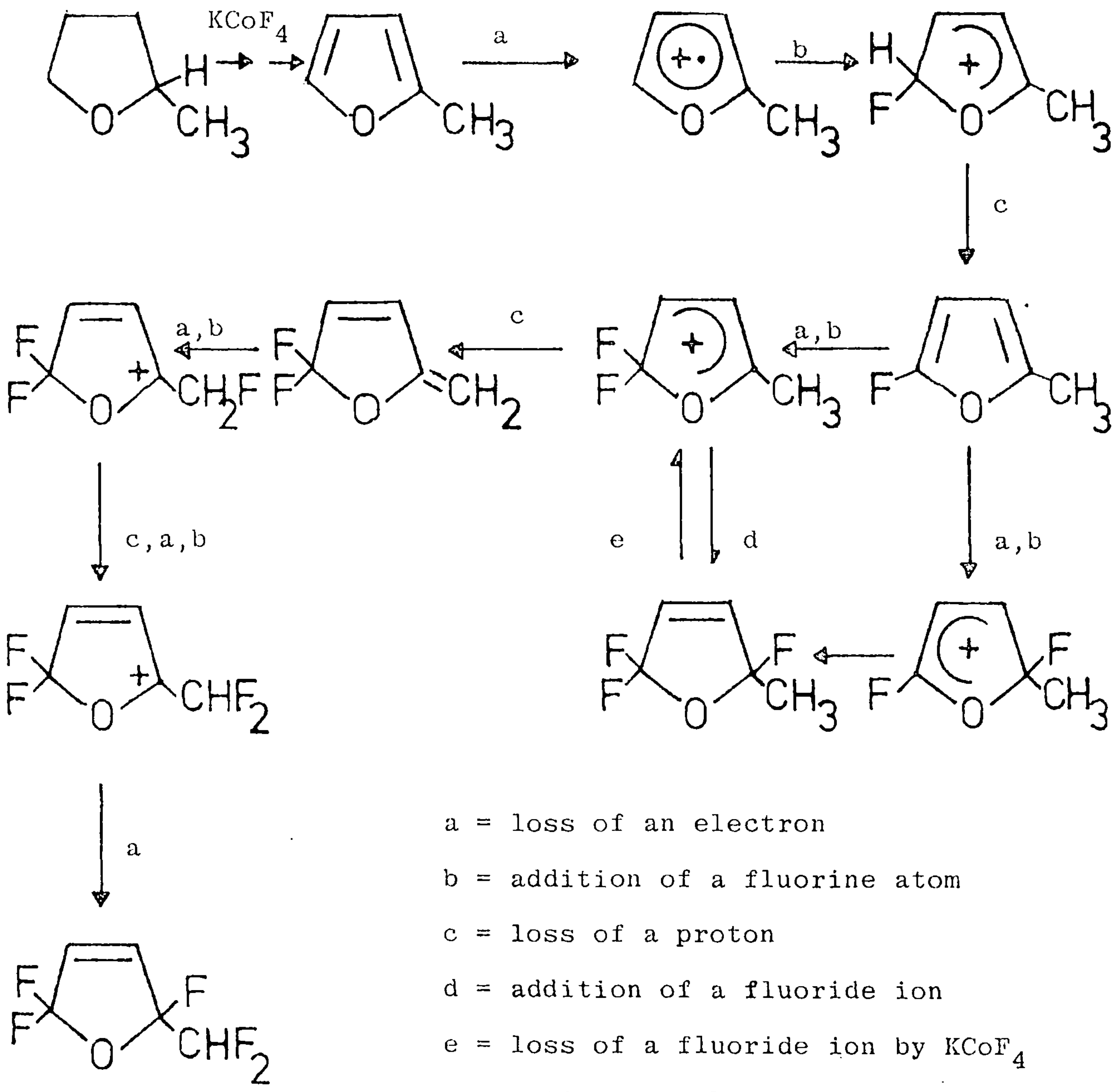
(93) 85%

Ref: 156



(94)

Ref: 156



a = loss of an electron

b = addition of a fluorine atom

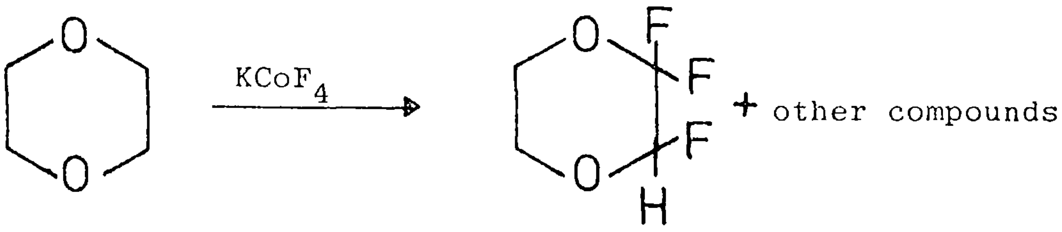
c = loss of a proton

d = addition of a fluoride ion

e = loss of a fluoride ion by $KCoF_4$
acting as a Lewis acid

Ref: 156

The exclusive formation of difluoromethyl groups was considered to reflect the low acidity, i.e. reluctance to lose a proton, of such groups. 1,4-dioxan yielded 1,1,2-trifluorodioxan as the major product when fluorinated with potassium tetrafluorocobaltate (111).[157]

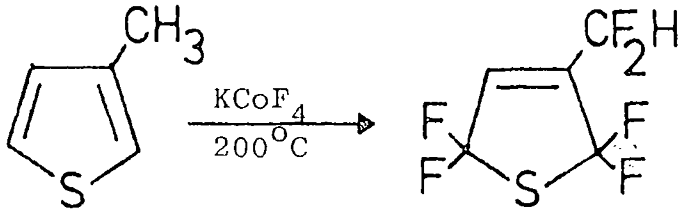


65% of product Ref: 157

Although no unsaturated products were detected, olefins were suspected intermediates, it being impossible to form aromatic intermediates. The ionisation potential of intermediate olefins, with hetero atoms next to each carbon, would be low, it was argued, and hence the formation of radical cations and resultant saturation would take place easily as is consistent with the lack of unsaturated products.

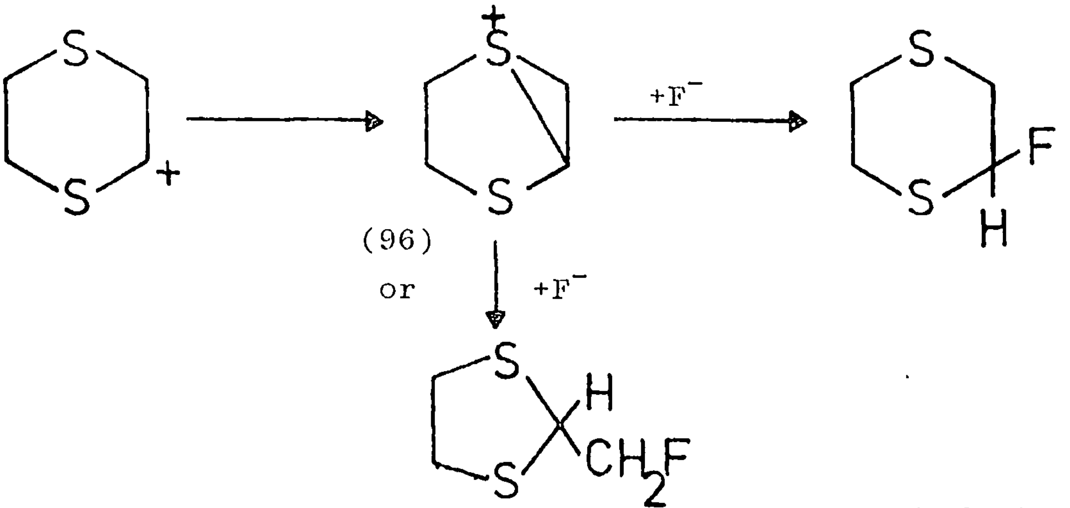
(c) Sulphur heterocycles

Certain sulphur heterocycles have also been fluorinated successfully. The productsfrom thiophen and tetrahydrothiophen were closely analogous to those of the tetrahydrofurans, consisting mainly of polyfluorothiolans and -3-thiolens[156]. Also analogously, a simple product was obtained when the -3-methyl derivative of tetrahydrothiophen (95) was fluorinated.[15]



87% Ref: 159

The reaction of 1,4-dithian differed from that of 1,4-dioxan, however, in that compounds resulting from a ring contraction reaction accounted for most (56%) of the product. This was thought to result from the stabilisation of intermediate carbocations by sulphur as in (96) although, it was added, considerable bond strain would be involved.[160]



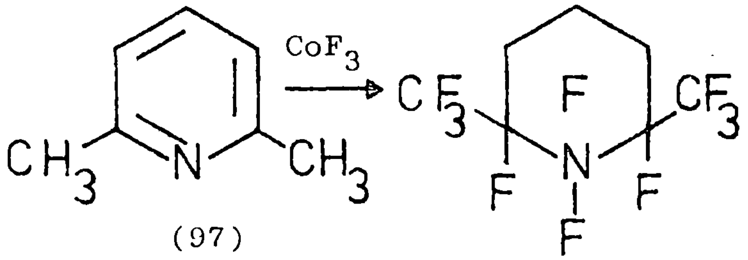
(96)

or

Ref: 160

(d) Nitrogen heterocycles

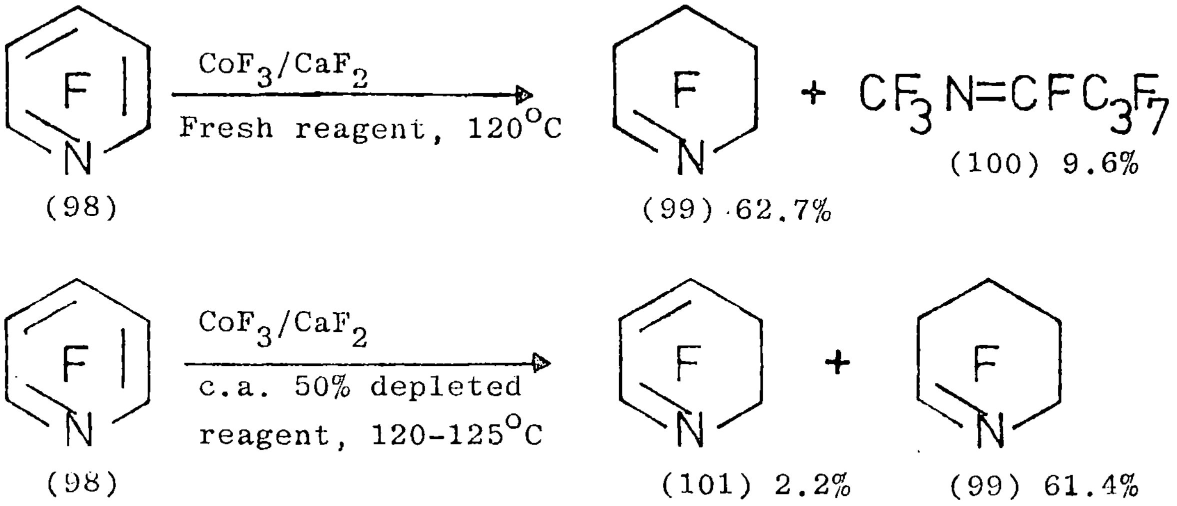
2,6-dimethylpyridine (97) was reported to yield the corresponding piperidine (97a) in 5% yield when reacted with cobalt III fluoride,[161] but reaction of pyridine and 4-methylpyridine with potassium tetrafluorocobaltate (III) yielded complex mixtures of ring opened or ring contracted products only.[149]



(97)

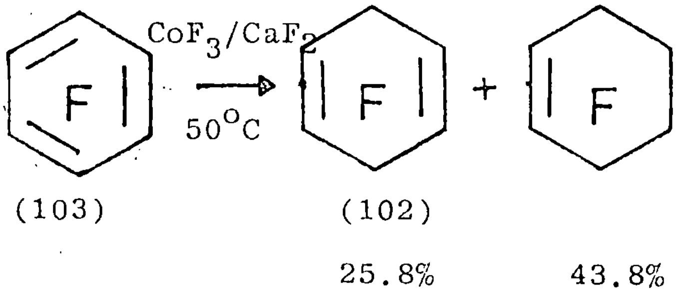
(97a) 5% Ref: 161

Ring retained products were reported in high yield, however, when a series of perfluoro- and fluorochloro- nitrogen heterocycles were fluorinated by a mixture of cobalt III fluoride and calcium fluoride.[163] Pentafluoropyridine (98) reacted to give perfluoro-1-azacyclohex-1-ene (99) and a ring opened product (100) at 120°C, but under milder conditions a 1,3-diene (101) was also isolated.



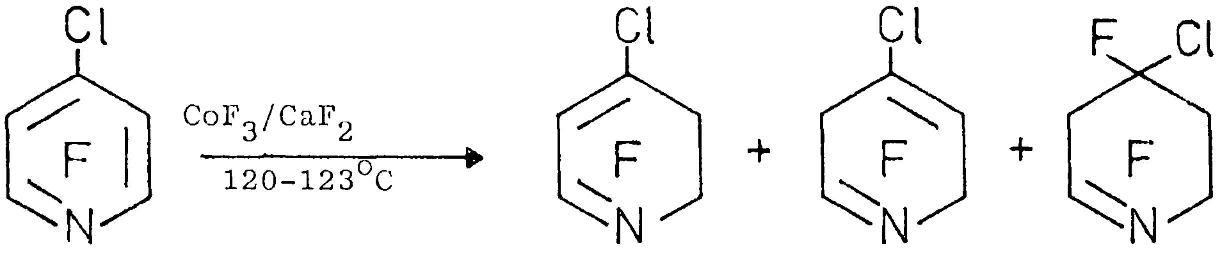
Ref: 163

This was compared with the reaction of hexafluorobenzene (103) with the same reagent which gave good yields (25.8%) of a 1,4-diene (102) but no -1,3-diene. An earlier fluorination of hexafluorobenzene was performed under conditions too vigorous for the optimum yield of dienes.[148]

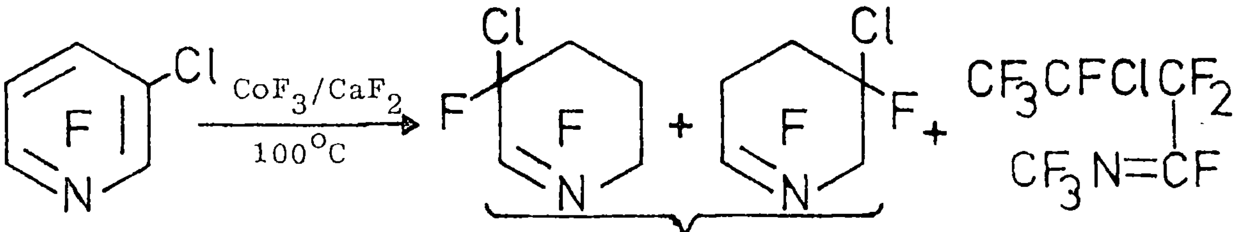


Ref: 163

-3- and -4-chlorotetrafluoropyridines yielded -1,3-dienes in higher yield than -1,4-dienes and it was noted that, under comparable conditions, the presence of a chlorine atom at C-4 on the pyridine lead to increased amounts of dienes in the products. Thus high proportions of dienes were obtained from the -4-chloro (104) and -3,4-dichloro derivative whereas -1-enes and ring opened aza-olefins were the preferred products of the -3-chloro (105) and -3,5-dichloro derivatives.



(104) 45% 2.3% 12.1%



(105)

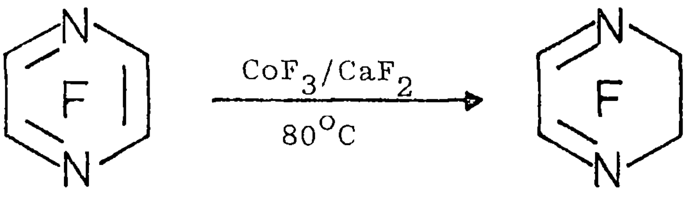
inseparable mixture, 35%

30.6%

Ref: 163

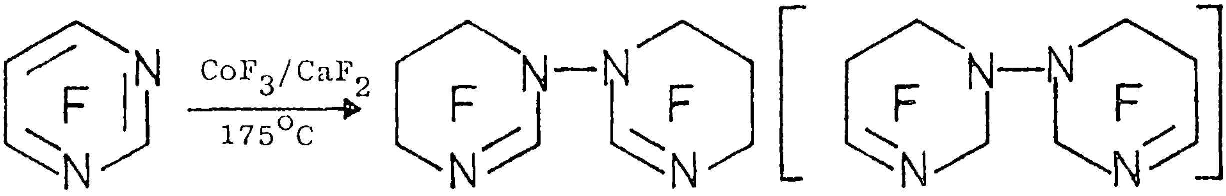
A >C=N- bond was present in all products detected.

Two perfluorodiazines were also fluorinated. Tetrafluoropyrazine (106) gave a -1,3-diene (107) but, interestingly, tetrafluoropyrimidine (108) gave a dimer, either (109) or (109a) as the major product.



(106) (107)

28.8% (46.2% conversion)



(108) (109) (109a)

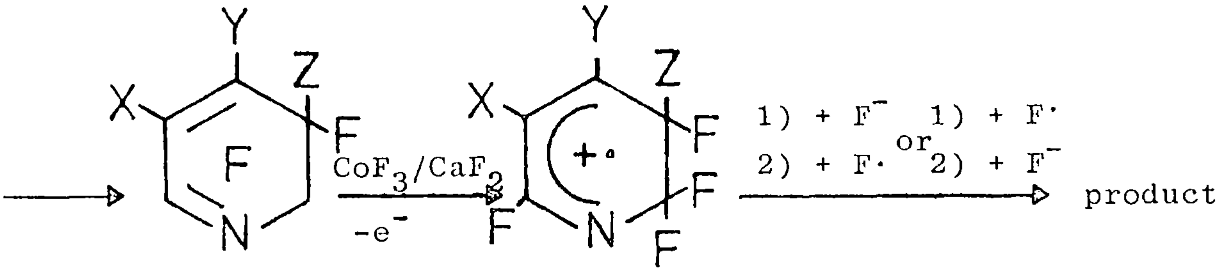
14% (73.5% conversion)

Ref: 163

The formation of dimer (109) was considered compelling evidence for the intermediacy of radicals in these reactions and mechanisms were proposed in which initial radical cations reacted by the addition of fluoride ions, rather than fluorine atoms, to yield radical, rather than cationic, intermediates. Calculations of the spin and charge density distributions of the various possible intermediate species were also performed and these indicated that, if it is assumed that these initial state factors control the reaction pathway rather than the relative stabilities of possible resultant cations or radicals, then:-

(a) given the above assumption, the model predicted the preferred formation of a-1,4-diene from perfluorobenzene and a -1,3-diene from perfluoropyridine, in accord with experimental fact, only if reaction is via radical intermediates.

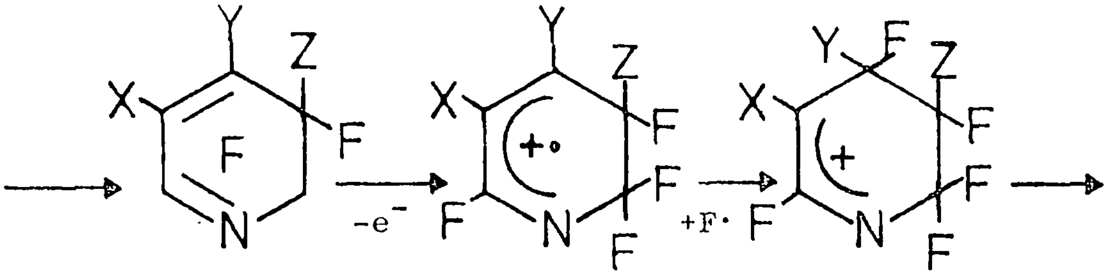
(b) when the reaction of the observed dienes to mono-enes was considered, it was assumed that the nearly complete absence of dienes from the pyridines without chlorine at C-4 was due to a higher susceptibility of such dienes to further fluorination. The same reaction sequence as for the aromatic starting materials was proposed.



(110)

(X, Y and Z = Cl or F)

The stabilities of the various possible cations produced from species (110) by adding a fluorine atom, (calculated from bond energy data), indicated that if the reaction is controlled by cation stabilities then addition is most likely at C-4 for all the chlorofluorodienes to give a species such as (111)

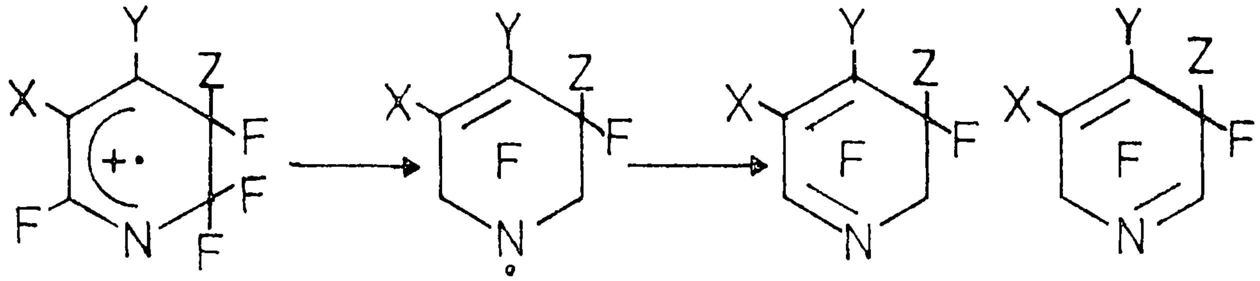


(113) (112) (111)

(X, Y and Z = Cl or F) Ref: 163

but the stabilities of the possible isomers of (111), relative to each other, seemed to indicate those with chlorine at C-4 to be the most stable, implying dienes with chlorine at C-4 to be the most reactive, in apparent contradiction with experimental evidence. The calculated spin densities of the various isomers of (112) uniformly indicated that, if the site of fluorine atom addition were controlled by the spin densities, then attack at nitrogen was preferred whilst addition to C-2, C-3 or C-4 seemed of nearly equal probability for all isomers. It was therefore concluded that the addition of a fluorine atom to radical dienes did not lead to a clear-cut picture of the relative reactivities of the possible -1,3-dienes (113).

In contrast, the calculated charge densities of the radical dienes were in the order C-2 > C-4 > C-3 > N for all the isomers. If the radical dienes react by the addition of a fluoride ion at a site determined by the distribution of charge density, addition at C-2 was indicated. It was argued, however, that this would be more likely to be followed by the elimination of a fluorine atom than the formation of an >N-F bond, hence regenerating either a -1,3- or -1,4-diene.



(114) (X, Y and Z = Cl or F)

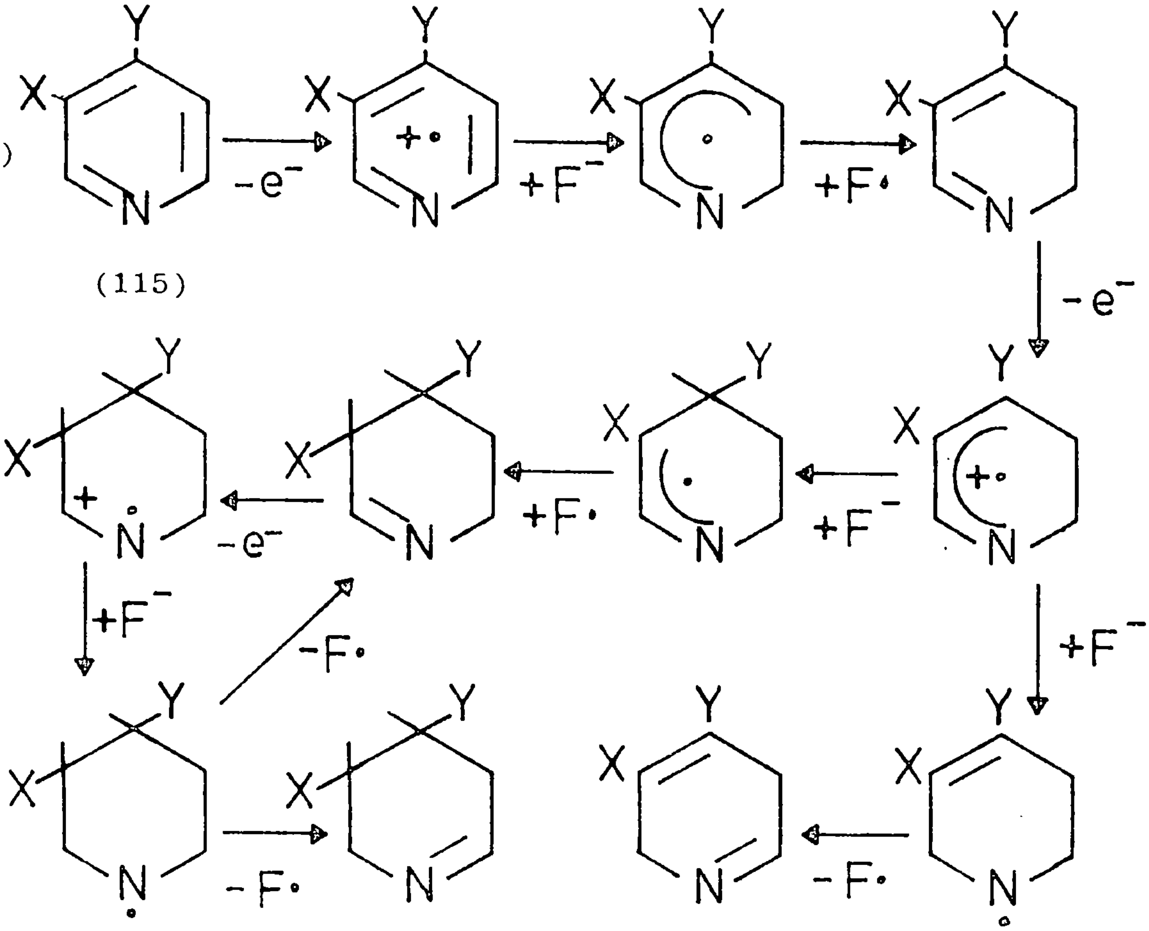
Therefore the production of mono-enes would have to proceed by attack of fluoride ion at C-4 in the radical cations (114), and the charge densities at the C-4's were indicated to be significantly lower when they bore a chlorine rather than a fluorine atom.

It was concluded, therefore, that the apparent deactivating effect of chlorine at C-4 in the -1,3-dienes was, also, best understood if the reaction proceeded via radical intermediates.

(c) Finally, it was argued that the only radical intermediate combining a sufficiently high unpaired spin density at a site of high steric accessibility is produced from tetrafluoropyrimidine resulting in the only observed dimerisation amongst all the compounds fluorinated.

On the basis of these experimental observations and calculations the following detailed reaction mechanisms were proposed:-

(1)



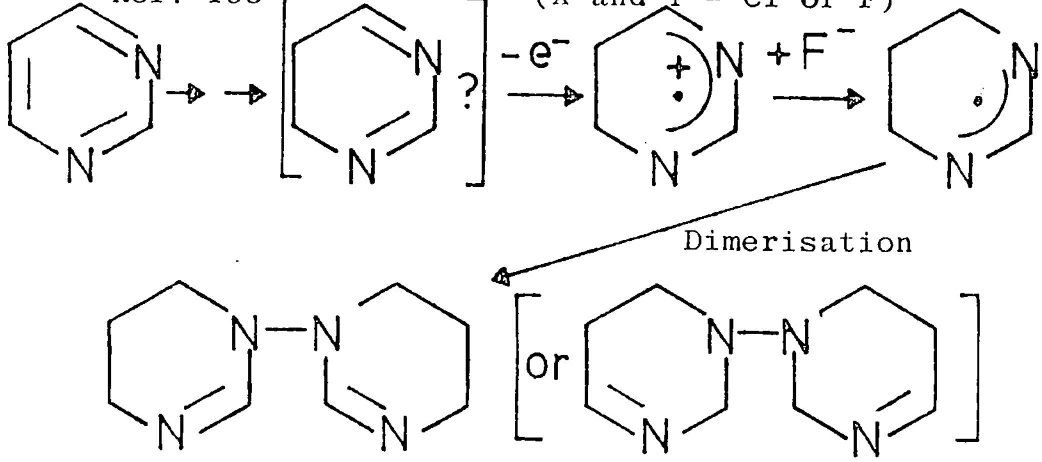
(115)

(117) N.B. All unmarked bonds are to fluorine

Ref: 163

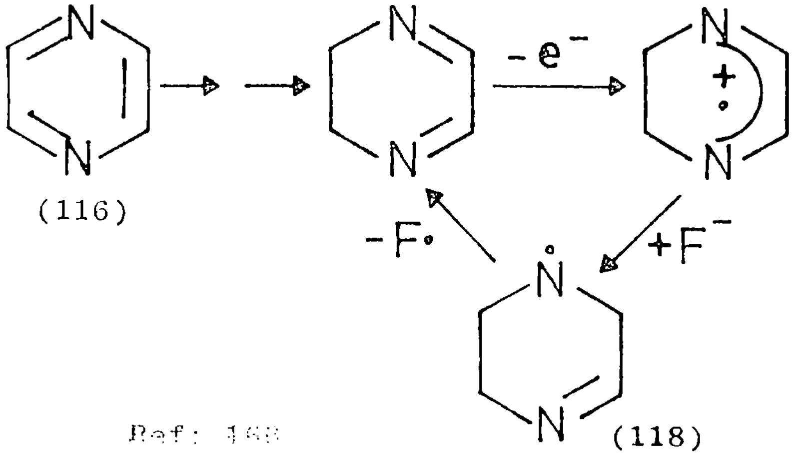
(X and Y = Cl or F)

(2)



Ref: 163

(3)



(116)

(118)

Ref: 168

Both the pyridines (115) and the pyrazine (116) eventually produce a localised nitrogen radical ((117) and (118) respectively) which would be susceptible to elimination, rather than addition, of a fluorine atom and therefore act as barriers to further reaction.

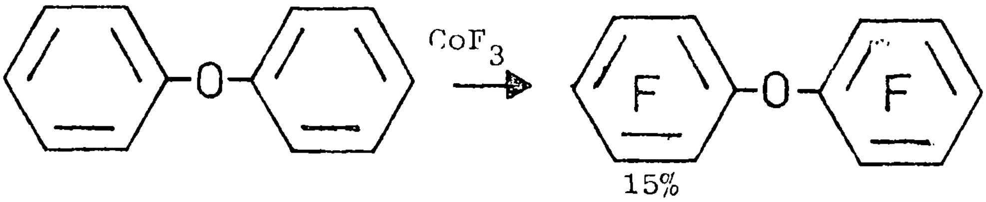
2.6H The Fluorination of Compounds Containing Functional Groups by H.V.H.M.F. Reagents

(a) Introduction

Functional groups do not tend to survive the H.V.H.M.F. process and the usual fate for hetero atoms in functional groups is fission from the rest of the molecule to appear in a small fragment and in the highest possible oxidation state. Some notable exceptions are described, briefly, below:-

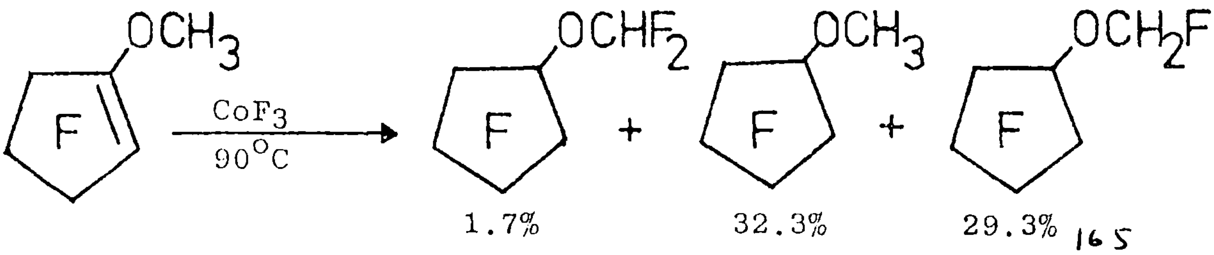
(b) Oxygen compounds

Some perfluoro and polyfluoro ethers have been isolated in the products from the fluorination of ethers with cobalt III fluoride,



Ref: 133

but usually yields are lower than in the example given. Highly fluorinated substituents have an apparently stabilising influence on the ether linkage however, and good yields of polyfluoro ethers were reported from alkoxypolyfluoroalkenes.



Ref: ~~152~~ 165

Ketones are reported to yield acyl fluorides with potassium tetrafluorocobaltate (111) but carbonyl difluoride is the major oxygen containing product with cobalt III fluoride.

$$C_2H_5COC_2H_5 \xrightarrow[100^{\circ}C]{CoF_3} COF_2 + \text{polyfluoroethanes}$$

Ref: ~~151~~ 164

$$C_2H_5COC_2H_5 \xrightarrow[150^{\circ}C]{KCoF_4} \underset{9.3\%}{CF_3CH_3} + \underset{28\%}{CF_3CFH_2} + \underset{12.1\%}{CH_3CHFCOF^*}$$

$$+\underset{30\%}{CH_3CF_2COF^*} \quad (\% = \text{composition of product})$$

Ref: ~~153~~ 166

(* isolated by hydrolysis and esterification)

The successful conversion of a series of esters to acyl fluorides with potassium tetrafluorocobaltate (111) has also been reported.

$$C_2H_5COOCH_3 \xrightarrow[350^{\circ}C,\ N_2]{KCoF_4} CH_3CF_2COF^* + CH_2FCF_2COF^*$$

$$+ CH_2CHFCOF^* + \text{cleaved products}$$

(* isolated by hydrolysis and esterification) Ref: ~~154~~ 167

(c) Nitrogen compounds

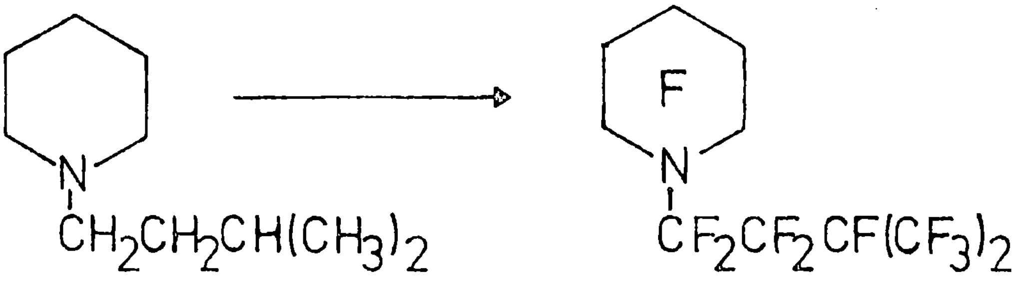
Amines may be perfluorinated but yields are usually low, possibly as a result of salt formation with HF in the initial stages of the reaction, as well as fragmentation.[52]

$$(CH_3)_3N \xrightarrow[130\text{-}220^{\circ}C]{CoF_3} (CF_3)_3NF$$

40-70% of product

Ref: ~~155~~ 168

A reasonable yield of uncleaved product was obtained from the bulky amine N-isoamylpiperidine (119).[156]



(119)

10%

Ref: ~~156~~ 169

(d) Sulphur compounds

Compounds retaining carbon-sulphur bonds have been obtained in some cases although the production of sulphur hexafluoride is the usual result when an organic sulphide is fluorinated.

$$CH_3SH \xrightarrow[200\text{-}275^{\circ}C]{CoF_3} CF_3SF_5$$

40%

Ref: ~~158~~ 170

CHAPTER 3

THE FLUORINATION OF PERFLUOROALKYL-AZABENZENES WITH COBALT III FLUORIDE/CALCIUM FLUORIDE

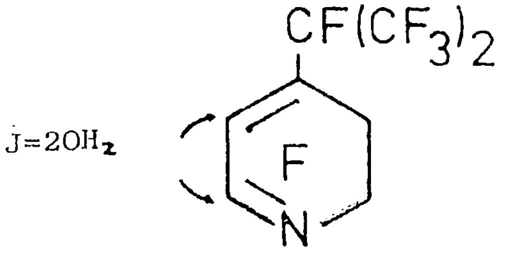
3.1 Introduction

In this chapter the fluorination of a series of perfluoro-aza-aromatic compounds is described. The fluorinations were achieved by reacting the substrate vapour with a heated mixture of cobalt III fluoride and calcium fluoride (50:50 w/w) in a conventional stirred reactor. Full details of the reactor and the experimental method are given in Chapter 8. In general, highly specific reactions occurred by the discreet addition of two or four fluorine atoms to the aromatic nucleus and high yields of the resultant perfluoro semi-saturated systems were obtained.

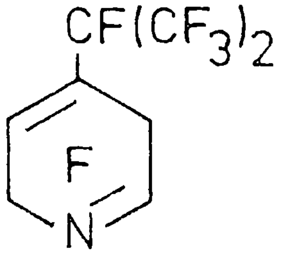
3.2 The Fluorination of Perfluoro-4-isopropylpyridine (120)

Perfluoro-4-isopropylpyridine (120) was reacted with the CoF_3/CaF_2 mixture at 118°C, to give a product consisting of, apart from recovered starting material, two major components and a complicated mixture of minor components.

The first component (60% yield) was identified as perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) by its parent ion at m/e = 357, and by its ^{19}F n.m.r. spectrum. Six chemically shifted absorptions were observed, integrating in the ratio 6:2:2:1:1:1. Two simple structures, (121) and the corresponding -1,4-diene (122), are consistent with these data.



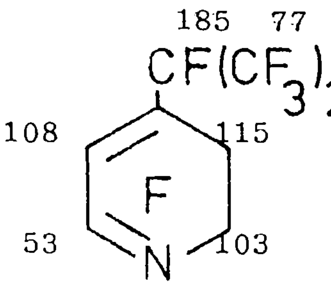
(121)



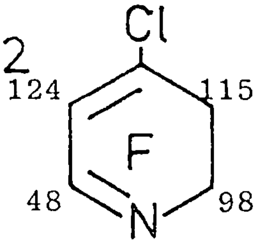
(122)

(122) was eliminated because strong coupling (J = 20 Hz) was observed between the signal due to the imino (-CF=N-) fluorine, readily identified by its extremely low field resonance at 52.55 p.p.m., and the olefinic (-CF=C$<$) fluorine. Comparison of the observed chemical shifts with those published for the model compounds below, provided additional confirmation of the structure:-

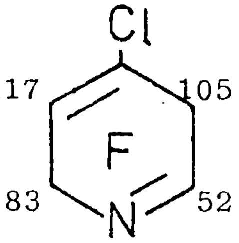
^{19}F n.m.r. shifts (p.p.m.)



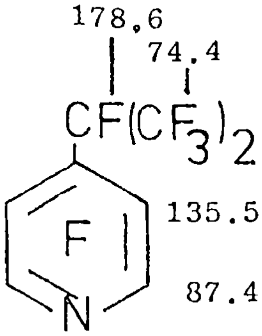
(121)



(123) Ref:163



(124) Ref:163

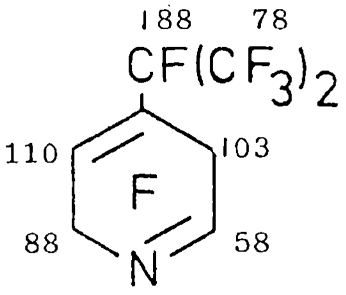


(124a) Ref: 173

I.r. absorptions at 1775 cm^{-1} and 1687 cm^{-1} were consistent with the presence of two double bonds.

The second component (18% yield) was identified as perfluoro-4-isopropyl-1-azacyclohexa-1,4-diene (122) by its parent ion at m/e = 357 and by its ^{19}F n.m.r. spectrum which also gave six signals in the ratio 6:2:2:1:1:1. The presence of an imino (-CF=N-) fluorine was deduced, as before, from the presence of a signal at very low field which integrated to 1. Absorptions at 1742 cm^{-1} and 1767 cm^{-1} in the i.r. spectrum were additional evidence for the imino and, at least, one other double bond. Coupling of the imino fluorine to a -CF$_2$- group to produce a triplet (J = 26 Hz) and the absence of any coupling to the olefinic (-C=CF) fluorine and comparison of its chemical shifts with the models (123) (124) and (124a) given earlier, confirmed the structure.

^{19}F n.m.r. shifts p.p.m.

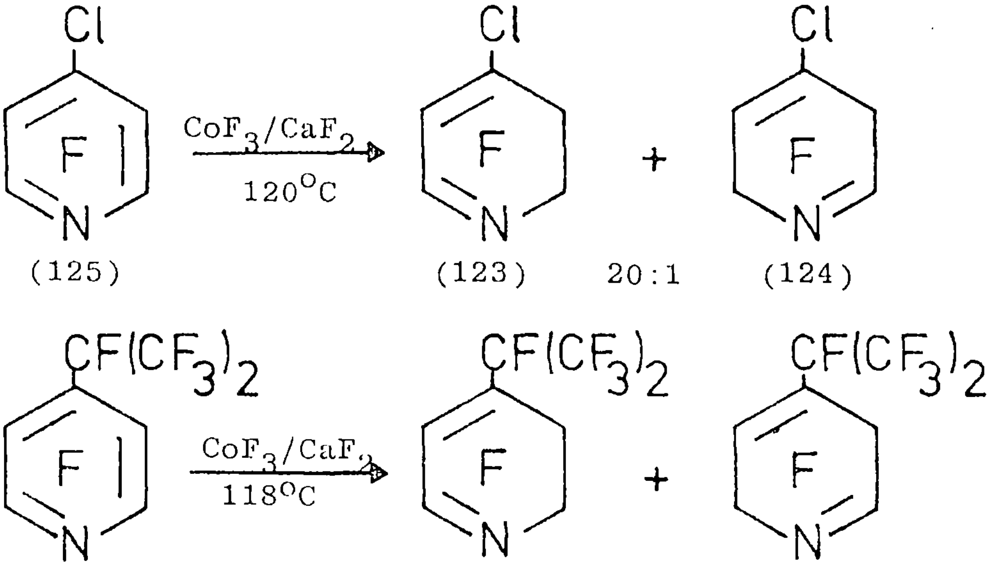


(122)

The remainder of the product (~20%) was shown by m.s./g.l.c. to consist of a complicated mixture of components of higher molecular weight than the dienes (121) and (122) and also fragmentation products. No individual component was present in high yield and so no further compounds were isolated and identified.

The behaviour of (120) upon fluorination with CoF_3/CaF_2 is, therefore, very similar to that of 4-chlorotetrafluoropyridine (125) with two slight differences. Firstly, the production of -1,4-dienes is more favourable in the reaction with (120) than with (125).

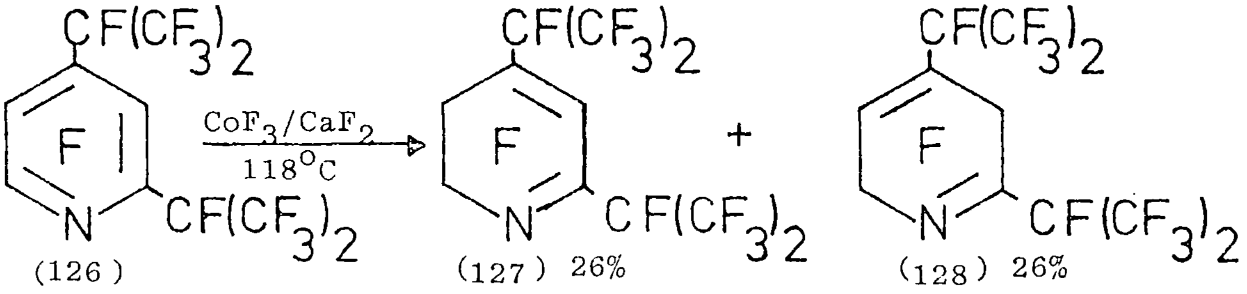
Ratio of -1,3- over -1,4-dienes



Secondly, the perfluoroisopropyl system(120) seems to be less reactive than the chloro-system (125) under comparable conditions. (120)was only about 90% converted to new products, whereas no starting material was reported in the product from (125).

3.3 The Fluorination of Perfluoro-2,4-di-isopropylpyridine (126)

When perfluoro-2,4-di-isopropylpyridine (126) was fluorinated under similar conditions to (120) the product consisted of, apart from recovered starting material,(7%), an inseparable mixture of perfluoro-2,4-di-isopropyl-1-azacyclohexa-1,3-diene (127) and perfluoro-2,4-di-isopropyl-1-azacyclohexa-1,4-diene (128) and unidentified material.



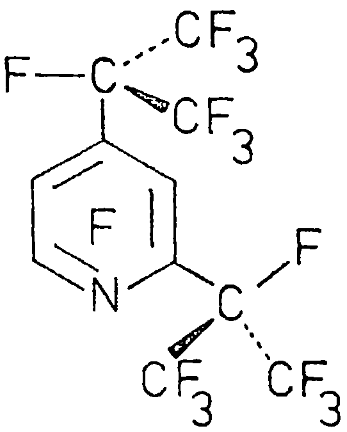
(126) (127) 26% (128) 26%

+ other products

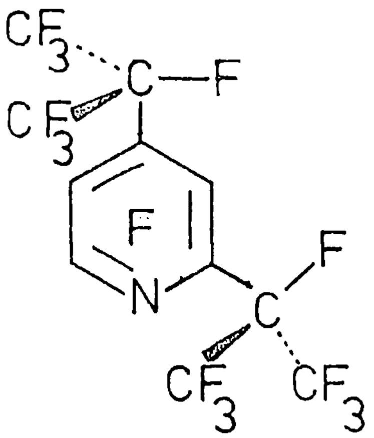
The dienes were readily characterised as the mixture which gave a parent ion at m/e = 507 in the mass spectrum. Elemental analysis was consistent with a mixture of isomers of $C_{11}NF_{19}$. Four separate signals in the region 75 to 78 p.p.m. of a ^{19}F n.m.r. spectrum, each integrating to 6, were indicative of 4 perfluoroisopropyl ($(CF_3)_2CF-$) groups. The absence of signals in the low field region of the spectrum (i.e. below 75 p.p.m.) indicated the absence of imino fluorines (-CF=N-). This evidence, alone, is sufficient to eliminate all structures other than the -1,3-diene (127) and the -1,4-diene (128).

It was not until the ^{19}F n.m.r. spectrum had been further analysed, however, that it was possible to confirm that both the -1,3-diene and the -1,4-diene were present in the mixture as the data presented, so far, does not eliminate the possibility that the species in the mixture were in fact two rotational isomers, of only one of the above structures.

Rotational isomerism, caused by the hindered rotation of substituent perfluoroisopropyl groups, has been observed in other six-membered rings. The rotamers (126a) and (126b) of perfluoro-2,4-di-isopropylpyridine, itself, have sufficient life-times at -40°C to be clearly resolved in its ^{19}F n.m.r. spectrum,[171]



(126a)

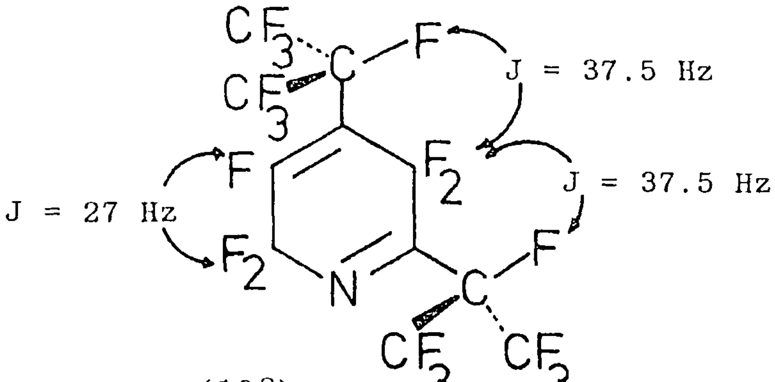


(126b) Ref: 171

whilst those of the more hindered system perfluoro(tetra-isopropylpyrimidine) are clearly observed in the ^{19}F n.m.r. spectrum at temperatures higher than +35°C.[172]

The presence of the -1,4-diene was established because one of the difluoromethylene ($-CF_2-$) signals, identifiable as such by its integration and mid-field position (98.17 p.p.m.), was coupled to two tertiary ($\geq$C-F) fluorines, identifiable, in their turn, by their high-field positions ($>$170 p.p.m.) and integration. Thus, both tertiary fluorines were triplets (both

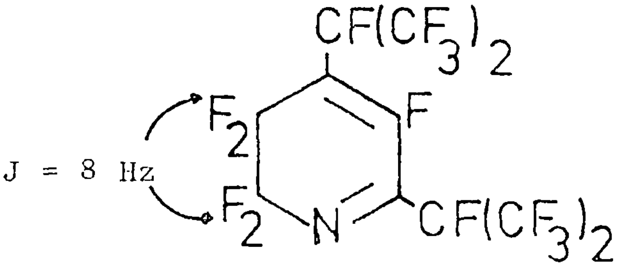
J's = 37.5 Hz) and the difluoromethylene signal was a doublet of doublets (both J's = 37.5 Hz) in the form of an apparent triplet. Only (128) would give rise to such coupling:-



(128)

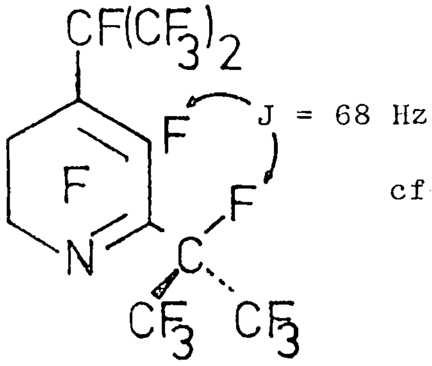
The strength of the coupling between this difluoromethylene group and the tertiary fluorines (J = 37.5 Hz), compared with its lack of observable coupling to the trifluoromethyl ($-CF_3$) fluorines (J < 3 Hz) suggests that the perfluoroisopropyl groups are in fixed or nearly fixed orientations at 40°C. In keeping with the proposed structure, the other difluoromethylene group gave rise to a sharp doublet (J = 27 Hz) because it was coupled to the olefinic fluorine only. The olefinic fluorine itself was not fully resolved, but it was broad and complex, as would be expected if the adjacent perfluoroisopropyl group ($(CF_3)_2CF-$) was oriented with its trifluoromethyl groups inclined toward it.

The two remaining difluoromethylene signals could therefore be assigned to the other isomer. That it is a -1,3-diene was immediately apparent because one of the difluoromethylene signals was a triplet (J = 8 Hz), indicating the only nearby fluorines to be on the other difluoromethylene.



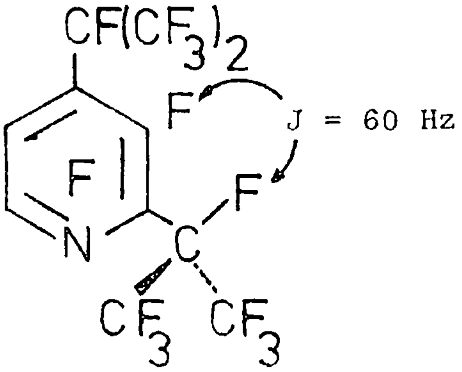
(127)

The perfluoroisopropyl group at C-2 in (127) was in fixed orientation as evidenced by the very strong coupling between its tertiary fluorine and the olefinic (CF=C) fluorine at C-3:-



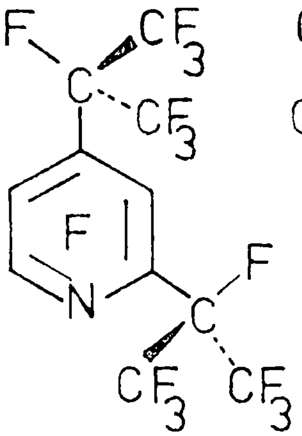
(127)

cf.

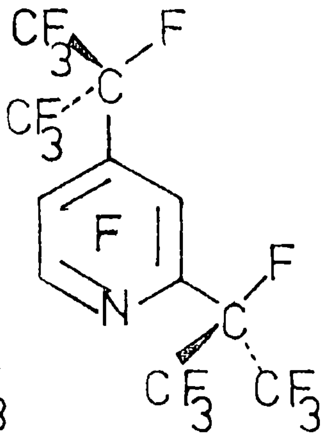


(126) Ref: 171

The perfluoroisopropyl group at C-4 appeared to be rotating, however, as the tertiary fluorine of the C-4 perfluoroisopropyl group, the difluoromethylene (CF_2) group at C-5 and the olefinic fluorine (CF=C) at C-3, were all broad, semi-resolved multiplets. This is consistent with the behaviour of the parent compound (126) which, it was observed, gave rotamers where the perfluoroisopropyl group at C-4 was fixed in two orientations, whereas that at C-2 adopted only one orientation.[171]

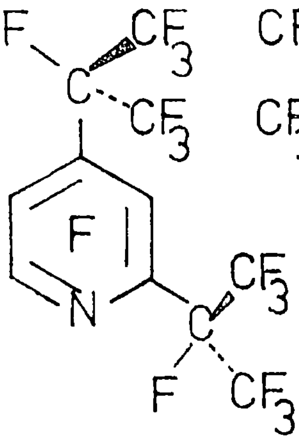


(126a)

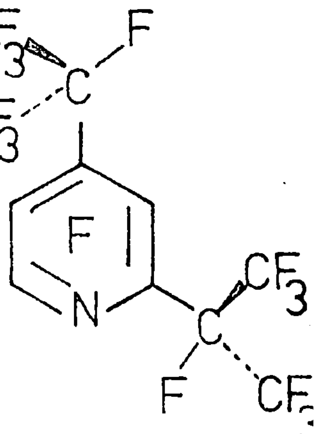


, (126b)

cf.



(126c)

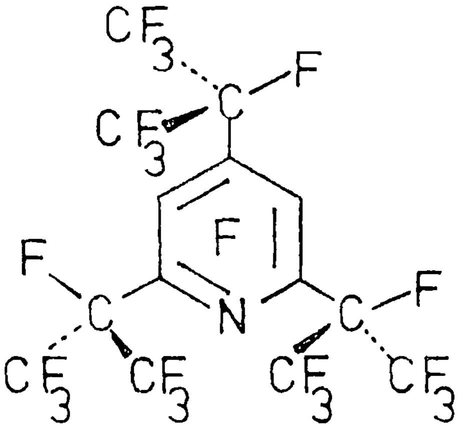


, (126d)

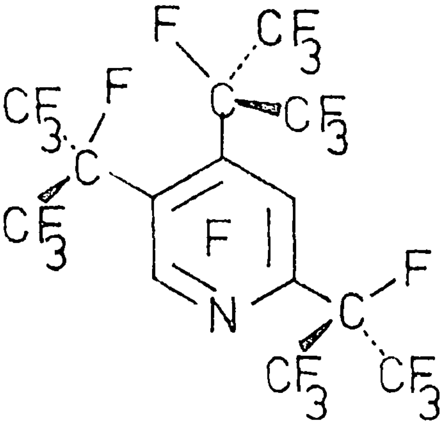
Observed Rotamers

Not observed

Perfluoro-2,4,6-tri-isopropylpyridine (130) and perfluoro-2,4,5-tri-isopropylpyridine (131) also oriented their perfluoroisopropyl groups at C-2 and C-5 with the trifluoromethyl groups towards nitrogen.[171]



(130)



(131)

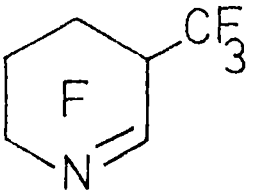
Ref: 171

Therefore this behaviour of C-2 and C-5 perfluoroisopropyl groups appears to be fairly general and presumably results because, although in some of the examples quoted (e.g. perfluoro-2,4-di-isopropylpyridine) the perfluoroisopropyl group at C-4 appears to be the most hindered, the least hindered conformation of the C-2 perfluoroisopropyl group is so stable that only one fluorine on C-3 is sufficient to prevent rotation even at relatively high temperatures.

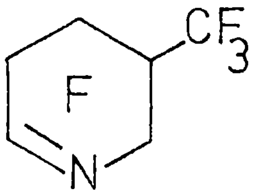
3.4 The Fluorination of a Mixture of Perfluoro-3- (134) and -4-methylpyridine (133)

Perfluoromethylpyridines were prepared by heating tetrafluoropyridine and polytetrafluoroethylene chips at 550°C in an autoclave under autogenous pressure.[174] The product, a mixture of perfluoro-3- (134) and -4-methylpyridine (133) in the molar ratio 9:1, was not separable and, therefore, the two isomers were reacted with cobalt III fluoride at 120°C as the mixture.

Unreacted starting material accounted for most (55%) of the product, but two new compounds were also produced. The first of these (37% of the mixture) gave a parent ion at m/e = 295 and its ^{19}F n.m.r. spectrum consisted of six signals, integrating in the ratio 1:1:2:2:2:3. One of the signals, integrating to 1, resonated at low field (41.0 p.p.m.) indicating the presence of an imino fluorine (FC=N-). Therefore the compound was identified as either perfluoro-3- (135) or perfluoro-5-methyl-1-azacyclohex-1-ene (136)



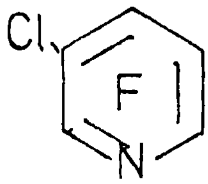
(135)



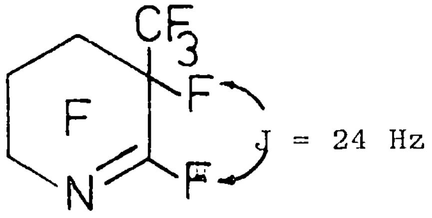
(136)

The other signals were consistent with both structures, with a signal at high field (177.4 p.p.m.) attributable to a tertiary fluorine, a signal which integrated to three, resonating at 72.23 p.p.m., indicating the presence of a trifluoromethyl group ($-CF_3$) and three other signals exhibiting the AB structure and mid-field positions typical of ring difluoromethylene ($-CF_2-$) groups.

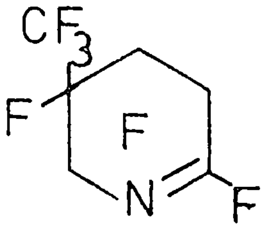
The signal due to the tertiary ($\geq$C-F) fluorine was a poorly resolved doublet (J = 24 Hz) and the only other signal which was broad enough to accommodate a reciprocal doublet of J = 24 Hz, although not resolved, was that of the imino (-CF=N-) fluorine atom. On the basis of this evidence, the data appears to favour the -3-methyl- structure (135) over structure (136).



(137)



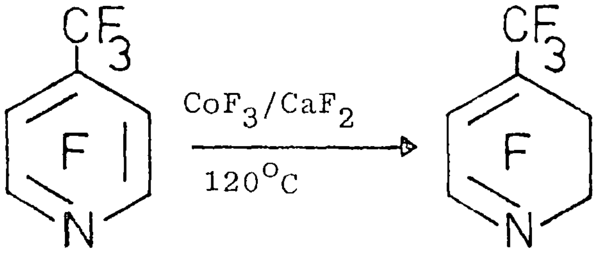
(135)



(136)

The fact that only one mono-ene is produced from (134) contrasts with the behaviour of the chloro compound (137) which was reported to yield both the -3-chloro- and -5-chloro- mono-enes in a 1:1 ratio.[163] This difference is not understood at present.

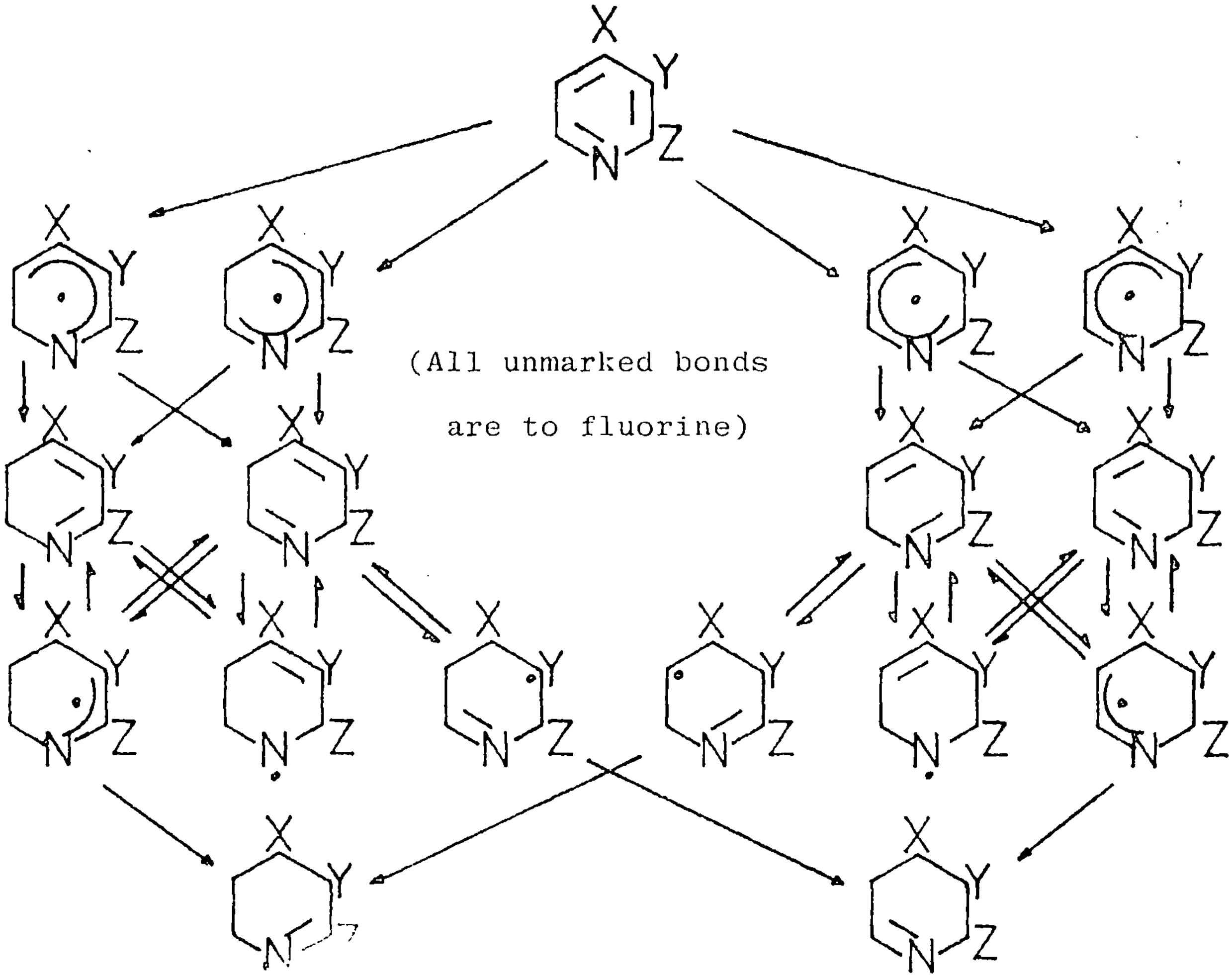
The second new product of the fluorination (7.1% of the mixture) was a diene as evidenced by its parent ion at m/e $\doteq$ 257 and by its i.r. spectrum, which gave two absorptions at 1745 cm^{-1} and 1756 cm^{-1} respectively. There were no high-field resonances in the ^{19}F n.m.r. spectrum, which indicated the absence of tertiary fluorines, and, therefore, the trifluoromethyl group is situated on an unsaturated carbon. A signal identifiable as that of the imino fluorine (FC=N-) atom by its characteristically low field shift (52.26 p.p.m.) was a doublet (J = 18.5 Hz) coupled to the olefinic fluorine ($>$C=$\overset{|}{C}$-F) atom identifiable in its turn by its mid-field shift (114.83 p.p.m.) and its integration. Therefore the olefinic fluorine atom is on C-3, adjacent to the imino fluorine atom and the trifluoromethyl group is on C-4 and the compound is identified as perfluoro-4-methyl-1-azacyclohexa-1,3-diene (140), and is a product of the fluorination of the perfluoro-4-methylpyridine (133) which was present in the starting material. All other observed couplings were consistent with the assigned structure.



(133) (140)

3.5 Mechanism of the Fluorination of Perfluoroalkylpyridines

The perfluoroalkylpyridines react with CoF_3/CaF_2 in a manner very similar to the chlorofluoropyridines and hence it is thought that the same type of mechanism that was proposed for the latter[163] is applicable to the former, i.e.



Where $X = CF_3$, $Y = F$, $Z = F$

or $X = F$, $Y = CF_3$, $Z = F$

or $X = (CF_3)_2CF$, $Y = F$, $Z = F$

or $X = (CF_3)_2CF$, $Y = F$, $Z = (CF_3)_2CF$

N.B. The radical forming steps in the above scheme represent two discrete stages:-

$$M \xrightarrow[CoF_3/CaF_2]{-e^-} M^{+\bullet} \xrightarrow[CoF_3/CaF_2]{+F^-} [M\text{-}F]^{\circ}$$

The radical quenching steps occur by the addition of fluorine atoms in the case of forward reactions and loss of fluorine atoms in the case of retro-reactions. Several aspects of the reaction are discussed below in the light of the proposed mechanism:-

3.5A Observed Isomers

In the products from both the perfluoroalkyl- and the chlorofluoropyridines only what are thought to be, the most stable of the many possible isomeric dienes and mono-enes were observed hence many equilibration pathways have been included in the proposed mechanism to account for this.

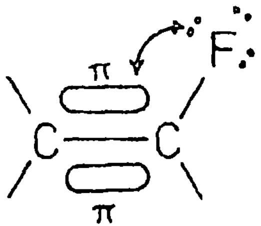
In the case of the -1,3- and -1,4-dienes, (121) and (122), it has been shown (see Section 5.6C) by equilibration of pure samples of each with fluoride ion that they are produced in a ratio which is close to that for thermodynamic equilibrium.

Also, relatively unstable compounds containing the weak nitrogen to fluorine ($\supset$N-F) bond were not observed in these reactions.

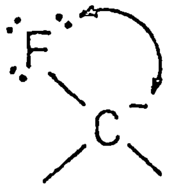
$\rangle$N-F, bond energy = 65 K.cals.mole^{-1} (272 K.joules.mole^{-1})
Ref: 175

$\rangle\overset{|}{C}$-F, bond energy = 116 K.cals.mole^{-1} (485 K.joules.mole^{-1})
Ref: 175

Similarly, the only isomers of the many possible dienes and mono-enes that were produced from either the perfluoroalkyl or the chlorofluoropyridines were those which contained the minimum number of fluorines bonded to unsaturated carbon atoms. The destabilising effect of fluorine at unsaturated sites is now well established[60], and has been interpreted in two ways. Firstly, it has been suggested that the carbon-fluorine bond energy decreases when the carbon changes its hybridisation from sp^3 to sp^2 and hence becomes more electronegative. The alternative explanation is that a strong repulsive interaction occurs between the lone pairs of the fluorine atom and the electrons of the double bond in a manner similar to the destabilising effect of fluorine atoms on a carbanionic centre.[60] It is not proposed to discuss the merits of each theory here as in either case the effect is the same.

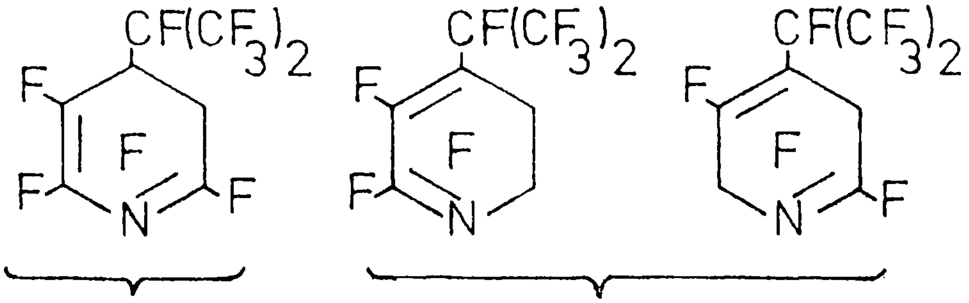


Repulsive interaction between lone pair and pi electrons.



Repulsive interaction between anionic centre and lone pair electrons.

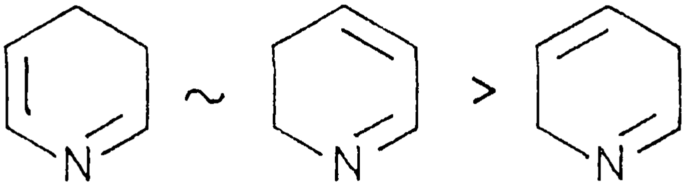
This would explain the absence of -1,5-dienes in the reaction products which, it can be seen by inspection, always have more fluorines bonded to unsaturated carbon than the observed -1,3- and -1,4-dienes.



Not observed, 3 interactions; Both produced, 2 interactions.

An additional, or alternative, argument might be that perfluoroisopropyl substituents are sufficiently bulky to sterically hinder the addition of a fluorine species to the carbon to which they are bonded.

M.O. calculations were claimed to indicate the following order of stability in the analogous hydrogen systems below:-[176]

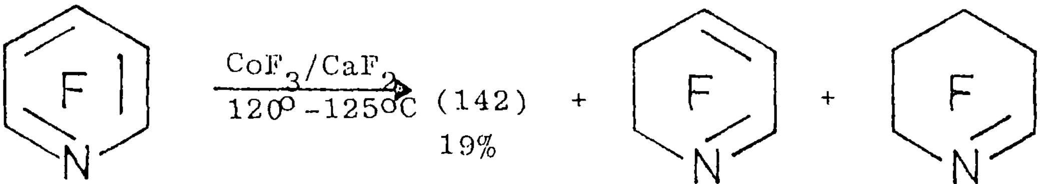


Ref: 176

Thermodynamic stability.

Hence in the absence of the electronic effects or the steric effects it would be reasonable to expect -1,5-dienes to have been formed.

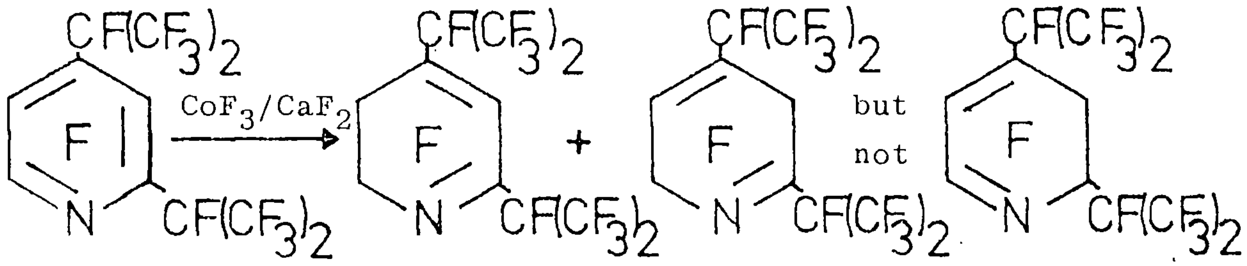
As a consequence of these arguments pentafluoropyridine (142) itself ought to have yielded a -1,5- as well as a -1,3-diene, when it was fluorinated under mild conditions.[163] However, the yield of diene was so low that it may not be significant that no -1,5-diene was detected.



(142) (Reagent depleted by 50%) (143), 2% (144), 50%

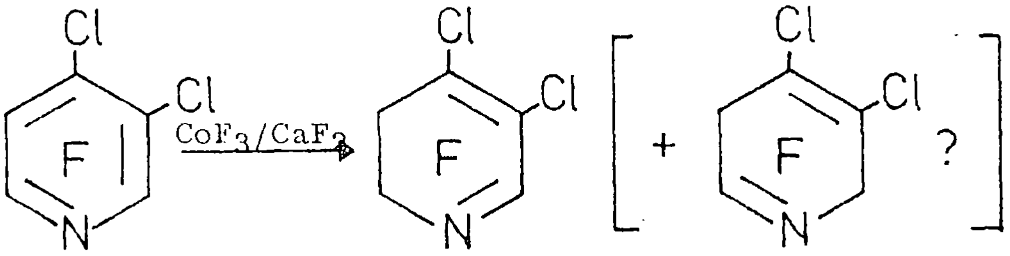
Ref: 163

The same arguments may be used to explain why a -4,6-diene is not produced from the pyridine (126):-



(126) (127) (128) (145)

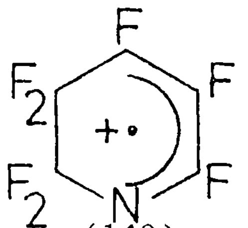
The unidentified diene material produced in the fluorination of (146) can only be the -1,4-diene (148) if these arguments may be extrapolated to that case.[163]



(146) (147) (148)

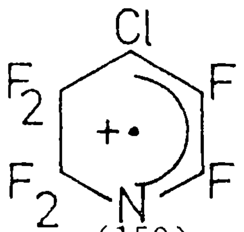
3.5B The Effect of Perfluoroisopropyl Groups on the Reactivity of the Dienes

In the chlorofluoropyridines, it was noted that a chlorine, as compared with a fluorine, substituent at C-4 resulted in the recovery of dienes, rather than mono-enes, under comparable conditions. It was proposed that this could be explained in terms of the calculated effect on the charge density at C-4 in the intermediate species (149) when the substituent was changed from fluorine to chlorine.[163]



(149)

Calculated charge at C-4 = 0.24;



(150)

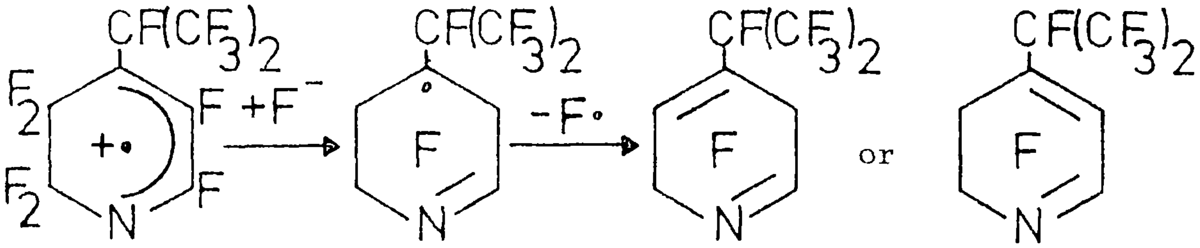
Ref: 163

Calculated charge at C-4 = 0.07.

In fact the calculations indicated that, in all the chlorofluoropyridines fluorinated, the cyclohexadienyl radical cations had highest charge densities at C-2, but it was argued that the attack of a fluoride ion at C-2 would only be followed by the elimination of a fluorine atom to re-generate a diene. Therefore reaction can only proceed via the attack of a fluoride ion at C-4.

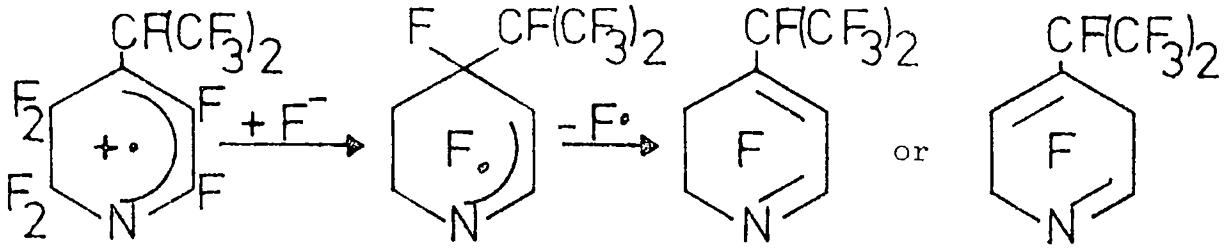
It is not worthwhile trying to predict by inspection the change in charge and spin distributions on substituting the fluorine on C-4 by a perfluoroalkyl group in species (149) save to note that if the drop in charge density at C-4 on substitution by chlorine results from the lower inductive effect of the chlorine atom, then a similar effect would be expected if a perfluoro alkyl group was the new substituent.

In addition to the electronic effects, it could also be argued that substitution of C-4 by a perfluoroalkyl group will inhibit the formation of mono-enes as a result of two steric effects. The first is that addition of a fluoride ion is actually hindered, so that addition occurs at C-3 followed by loss of a fluorine atom:-



Short lived radical

Or alternatively, attack does occur at C-4 but that elimination of the newly created tertiary fluorine at C-4 in species (151) becomes a favourable process:-



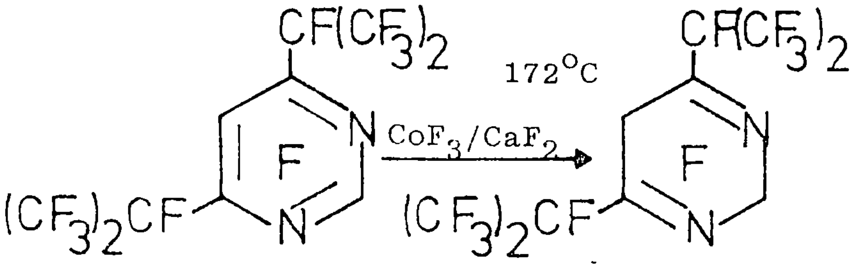
(151)

3.5C Ratio of -1,3- to -1,4-dienes

As was remarked upon earlier, when discussing the fluorination of perfluoro-4-isopropylpyridine (Section 3.2), the production of -1,4-dienes seems to be more favourable in the perfluoroisopropylpyridines than in the chlorofluoropyridines. For -2,4-di-isopropylpyridine, the -1,4- to -1,3- diene ratio is as high as 1:1. Whilst it is thought that this reflects an increase in the thermodynamic stability of the perfluoroisopropyl-1,4-dienes compared to the respective -1,3-dienes, the reasons are not immediately apparent.

3.6 The Fluorination of Perfluoro-4,6-di-isopropylpyrimidine (152) with CoF_3/CaF_2

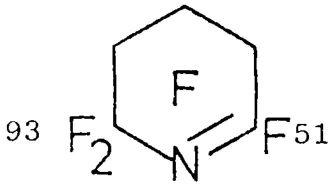
The pyrimidine (152), when reacted with CoF_3/CaF_2, gave only one new product, in significant yield, which was shown to be perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153).



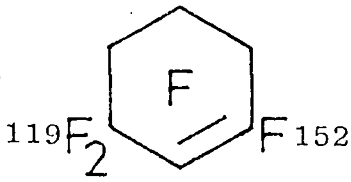
(152) (153) 83%

The parent ion in the mass spectrum of the product was at m/e = 490 and a peak at 295 was interpreted as due to loss of C_3F_7CN (see Section 3.14). Elemental analysis indicated the empirical formula $C_{10}N_2F_{18}$. Two bands, one at 1700 cm^{-1}, the other at 1732 cm^{-1}, in the i.r. spectrum indicated the presence of at least two double bonds, whilst the ^{19}F n.m.r. spectrum consisted of only four signals integrating in the ratio 6:1:1:1. Therefore the two isopropyl groups are equivalent and the molecule has retained the high symmetry of the starting material. The chemical shifts of the trifluoromethyl ($-CF_3$) groups and the tertiary fluorine atoms fall into typical ranges at 78 and 185 p.p.m. respectively. One signal, identifiable as due to a difluoromethylene ($>CF_2$) group by its integration, had a very low field chemical shift (74 p.p.m.). It was assigned as the C-2 signal on the ring because it was not coupled to any other resonances whereas the other difluoromethylene ($>CF_2$) signal was coupled to both the tertiary fluorine atom and the trifluoromethyl groups. The lack of coupling of the C-2 difluoromethylene group is a reflection of the isolation of its position from the other fluorine nuclei.

The chemical shift of the C-2 difluoromethylene group is very low compared with the range of values associated with difluoromethylene groups bonded to carbon atoms which is from 136 p.p.m. down to 82 p.p.m. (Figures adapted from data in Ref. 177) and this may be attributed to the combined downfield effects of two adjacent nitrogen atoms. Such effects can be very large and they are well established. The model compounds below illustrate this point:



cf.



^{19}F n.m.r. shifts in p.p.m. Ref: 163

3.7 The Fluorination of Perfluoro-4-isopropylpyrimidine (154)

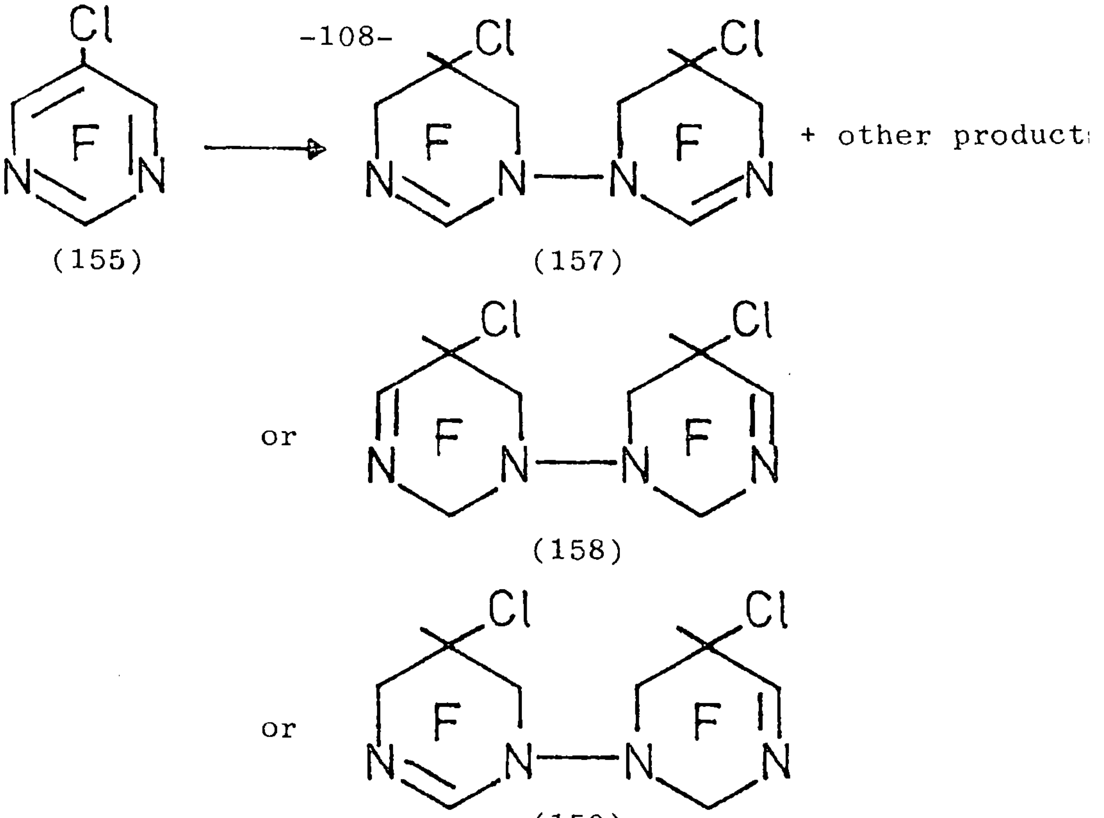
It was thought that a dimeric product might result from the fluorination of perfluoro-4-isopropylpyrimidine as one of the nitrogens is unhindered. Such a result would provide further evidence for the intermediacy of radicals during the fluorination of organic compounds with cobalt III fluoride.

However, the results of several fluorinations disappointingly indicated that any dimer, if formed as an intermediate, is extremely susceptible to ring opening and fragmentation as, at a temperature comparable to that at which the di-alkyl pyrimidine was fluorinated, 90% of the recovered product consisted of gaseous fragmentation products. On lowering the reaction temperature the proportion of starting material in the product increased without the appearance of significant amounts of unfragmented material as indicated by combined mass spectroscopy/g.l.c. on the non-gaseous products.

3.8 The Fluorination of Perfluoro-5-chloropyrimidine (155)

The pyrimidine (155) behaved in a similar manner to perfluoropyrimidine (156) when it was fluorinated, in that dimeric products were produced. At 178°C dimeric products comprised about 20% of the total product by weight, the remainder consisting of starting material (10%) and a complex mixture of volatile fragmentation products.

The species present in the mixture were identified as either the -2-enyl dimer (157), the -3-enyl dimer (158) or the unsymmetrical dimer (159). The data were insufficient to determine whether all three or only two of these compounds were present. It is even possible as argued later that only one of these species is present



Thus, the mixture was indicated to contain isomers of $C_8N_4F_{10}Cl_2$ by elemental analysis and mass spectroscopy which gave a parent ion at m/e = 450. The intensity ratio P:P+2:P+4 = 100:66:11 which also confirmed the presence of two chlorines in the empirical formula.

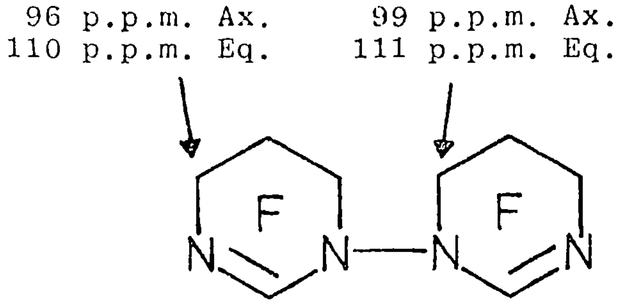
A strong absorption at 1749 cm^{-1} in the i.r. spectrum was assigned to imine (C=N-) stretching. The fact that only one band was present suggests that the species present in the mixture are structurally similar to each other.

The ^{19}F n.m.r. spectrum suggested the presence of more than one species but was complex and contained many broad, overlapping signals so that a detailed analysis was not possible. No simplification of the spectrum occurred on heating to 80°C. The signals fell into three distinct groups defined by their chemical shifts, however, as indicated in Table 3.1 below.

Table 3.1 ^{19}F n.m.r. spectrum of dimeric products

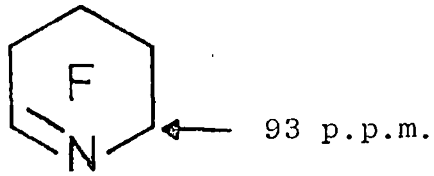
Group	Chemical Shifts p.p.m. ($CFCl_3$)	Integration
1	60.59 → 62.00	1
2	82.34 → 112.02	4
3	137.62 → 141.65	1

The signals in group 1 have the low field chemical shifts typical of imino fluorine atoms ($\rangle$CF=N-), those in group 3 have mid-field shifts attributable to chlorofluoromethylene (-CFCl-) signals (Banks gives a range of 111 to 148 p.p.m. for CFX where X = halogen^{177}) whilst the signals in group 2 may be assigned to difluoromethylene ($\rangle CF_2$) groups in the situation ($-CF_2-N=C\langle$) or, possibly, ($\rangle N-CF_2-N=$) by comparison with the models (160), (161) and (152) below.

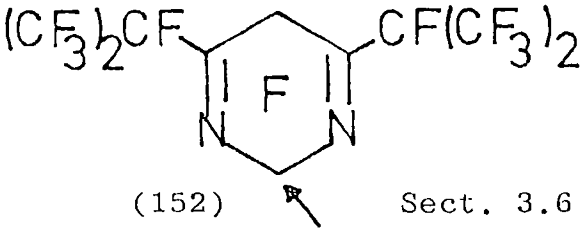


(160) Ref: 163

^{19}F n.m.r. shifts (w.r.t. $CFCl_3$)



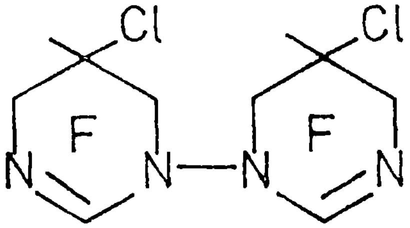
(161) Ref: 163



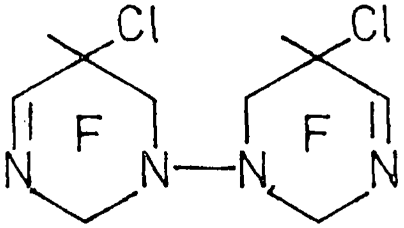
(152) Sect. 3.6

74.3 p.p.m.

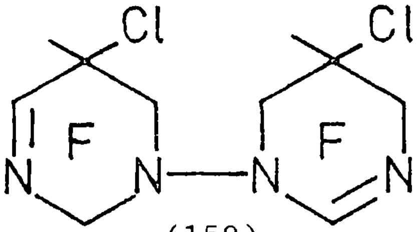
Therefore, according to the data presented so far, the dimers may be a mixture of any of the compounds (157), (158) or even (159) below:



(157)



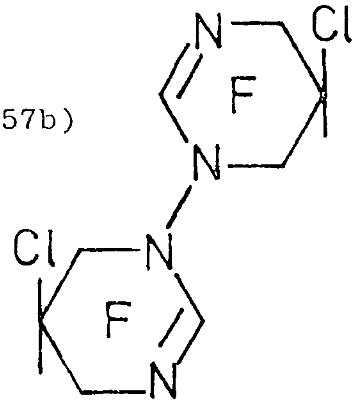
(158)



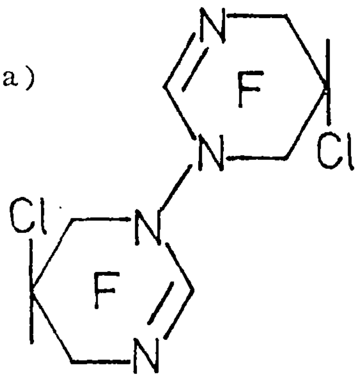
(159)

The situation is further complicated when it is realised that all three structures (157), (158) and (159) can exist as either cis or trans isomers such as (157a) and (157b) for (157) below:

(157b)



(157a)

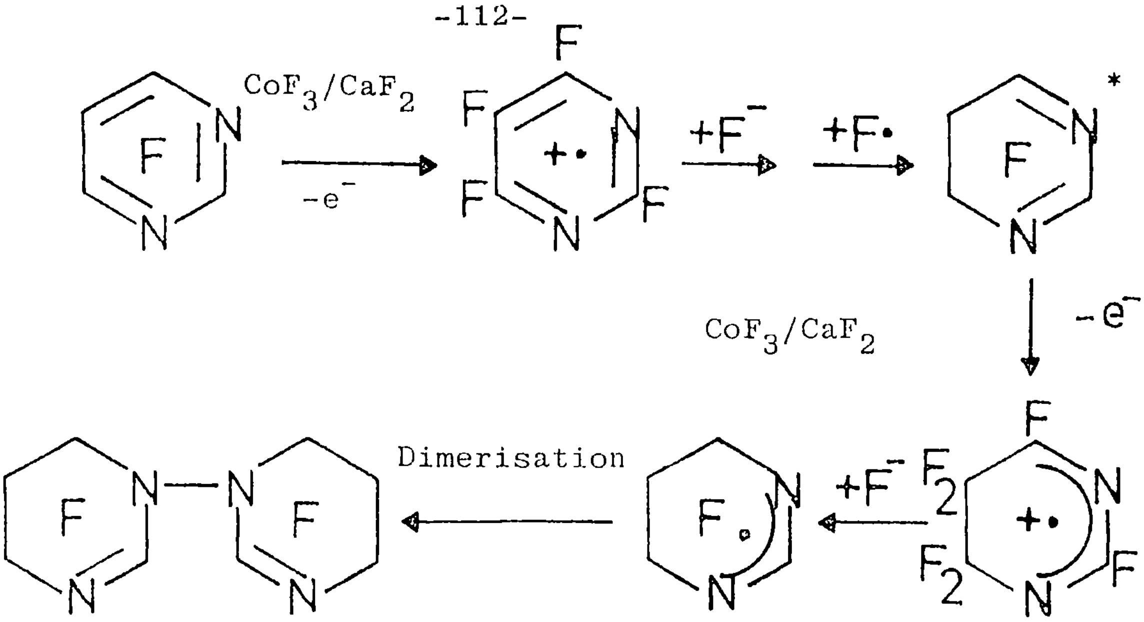


It was apparent from the ^{19}F n.m.r. spectrum that a minimum of three different signals were present in group 3 (see Table 3.1) in approximately equal intensities.

Therefore, at least three different species are present in the mixture. As (157), (158) and (159) each have only cis and trans isomers this could indicate that at least one compound containing a -3-enyl bond, either (158) or (159), has been produced in contrast to the reaction of tetrafluoropyrimidine. Alternatively, however, because the chlorine substituents in (157), (158) and (159) are meta to nitrogen atoms, then the 1,3 interactions which normally destabilise 6-membered ring conformers with axial chlorine atoms will be absent and, hence, nearly equal populations of axially and equatorially substituted conformers of (157), (158) and (159) may be possible. Therefore it is even possible that only one of the compounds (157), (158),and (159) need be present to give rise to the observed spectrum.

3.9 Mechanisms for the Fluorination of Substituted Fluoro-pyrimidines

Chambers et al. argued that the dimeric product formed when tetrafluoropyrimidine (156) was fluorinated could be accounted for within the framework of their general mechanism for CoF_3/CaF_2 fluorinations.[163] The proposed steps were:-

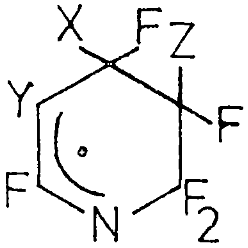


(162)

* = unobserved

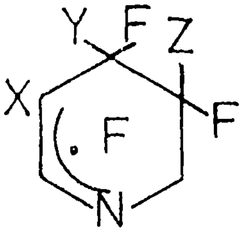
Ref: 163

Although radical intermediates were also proposed for the pyridine and pyrazine systems they fluorinated, no other dimerisation reactions were detected. The explanation for this was that only the allylic radical intermediates such as (162) or, in the case of the pyridines (163) contained sites of

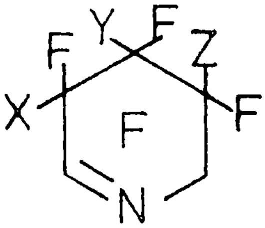


(163)

high enough spin density for coupling reactions whilst at the same time having sufficient lifetimes to collide with an identical species. In spite of this, the pyridine intermediates (163) still do not couple, it was proposed, because the spin density is concentrated at C-3 and the approach of two such species through their C-3's would be sterically hindered. There would not be any great steric interference for the corresponding approach of intermediates (162). Further to these arguments, it may be added that, whilst the addition of the much more numerous and sterically small fluorine atoms to the pyridine species (163) at C-3 leads to a stable cyclic aza-alkene (164),

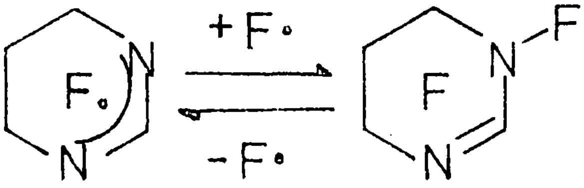


(163)



(164)

the addition of a fluorine atom to the pyrimidine radical (162) results in an entirely different situation:-

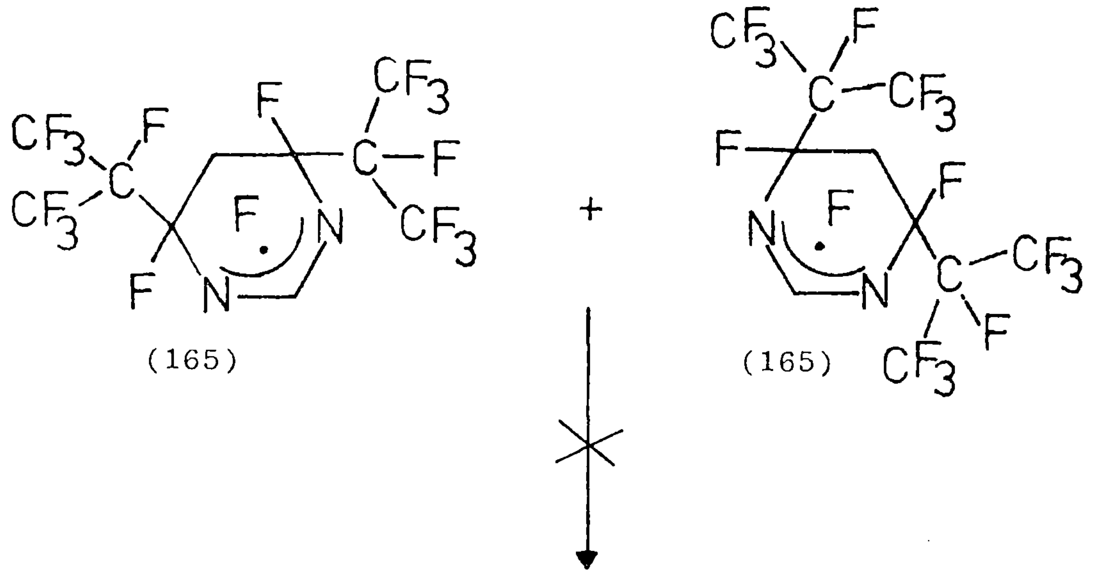


(162)

Thus, addition to the nitrogens, the most likely event on the basis of spin density distribution, leads to the formation of an unstable compound with fluorine bonded to nitrogen and a retro reaction would be very favourable. Addition to C-2 is clearly impossible. Therefore tetrafluoropyrimidine may be regarded as a special case where there is no real alternative to dimerisation.

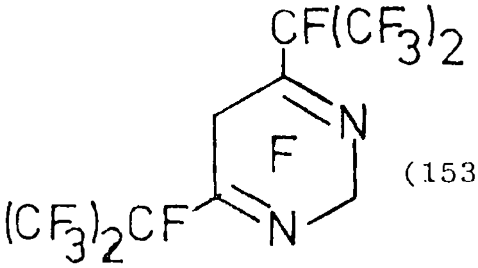
The same mechanism may be proposed for 5-chlorotrifluoropyrimidine which also produces a dimeric product.

The failure of perfluoro-4,6-di-isopropylpyrimidine (152) to do likewise is easily accommodated within the framework of this mechanism, for two different reasons. The first is that the approach of two allylic radicals species such as (165) would be subject to considerable steric hindrance in most, if not all, orientations due to the interaction of the two perfluoroisopropyl groups.



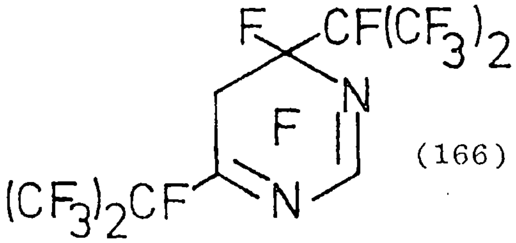
(165) (165)

Secondly, it is considered unlikely that an allylic species such as (165) can be formed in any case, as its precursor, the -2,6-diene (166), is arguably much less stable than the observed -3,6-diene (153) and would hence either not be formed or would quickly isomerise to the -3,6-diene, if, as is proposed, these fluorinations are under thermodynamic rather than kinetic control.



(153)

Observed diene

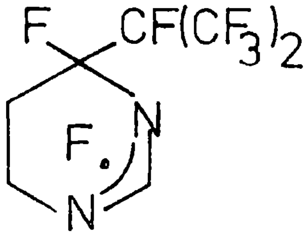


(166)

Hypothetical diene

Thus, using the arguments already established in the discussion concerning the pyridine systems, (166) will be the less stable diene because it has more than the minimum number of fluorines bonded to unsaturated carbon. In addition, the structure has a perfluoroisopropyl group bonded to a saturated carbon atom which would be sterically unfavourable. These arguments are supported by the experimental observation described in Section 5.6D that (153) does not produce any other isomers after prolonged stirring in the presence of caesium fluoride. By contrast, however, none of these considerations affect the 5-chloropyrimidine (155) which produces dimeric products in reasonable yield.

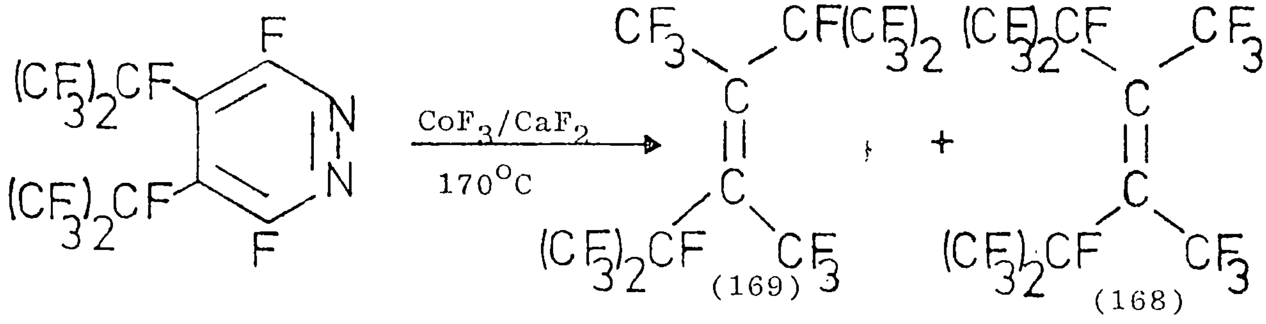
The failure of the mono substituted pyrimidine (154) to produce dimeric products is not fully understood but it is noteworthy that only one in four collisions will present an unhindered nitrogen on one species (166a) to an unhindered nitrogen on another species (166a).



(166a)

3.10 The Fluorination of Perfluoro-4,5-di-isopropylpyridazine (167)

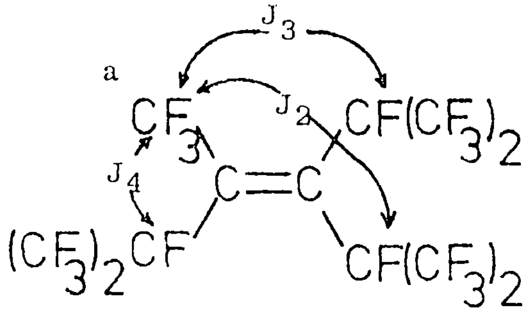
Upon fluorination at 170°C, the pyridazine (167) gave four products. The two most abundant products were inseparable by either distillation or g.l.c. and were identified as the mixture. These latter were the cis and trans isomers of perfluoro-2,3,4,5-tetramethylhex-3-ene (168) and (169) respectively, and were obtained in a combined yield of 53%. The two other products were identified, in order of abundance, as the already known perfluoro-2,3-dimethylpentane[179] (170) and the new compound perfluoro-2,3,4,5-tetramethylhexane (171).



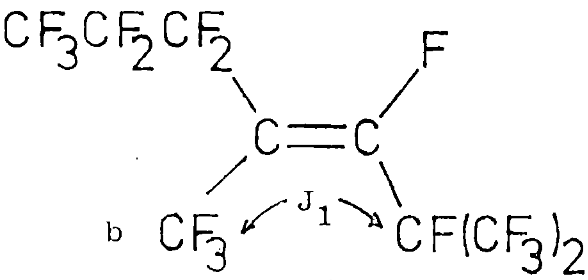
+ $CF(CF_3)_2CF(CF_3)CF_2CF_3$ + $CF(CF_3)_2CF(CF_3)CF(CF_3)CF(CF_3)_2$

(170) 12% (171) 9%

The mixture of (168) and (169) gave a P-F ion at m/e = 481 in its mass spectrum (see Section 3.13 for further comment) which, together with its analyses, gave an empirical formula of $C_{10}F_{20}$. The absence of absorption above 1400 cm^{-1} in the i.r. is consistent with either a ring structure or a highly symmetrical olefin. The ^{19}F n.m.r. spectrum contained two broad overlapping signals integrating together as 12 with chemical shifts at 72 p.p.m. typical for trifluoromethyl groups (CF_3) bonded to saturated carbon atoms.[177] Two signals at high field (159 and 161 p.p.m.) each integrated to 1 and were assigned to tertiary fluorine (-$\overset{|}{\underset{|}{C}}$-F) atoms.[177] The only remaining signals were in mid-field and consisted of a broad singlet (58 p.p.m.) overlapping a doublet (57 p.p.m. J = 50 Hz). The two signals gave a total integration of 6 and were identified therefore as due to two trifluoromethyl groups (-CF_3). By comparison with the models below, their shifts are seen to be typical of trifluoromethyl groups bonded to unsaturated carbon (CF_3-C=C). These data easily eliminate structures other than (168) and (169).



(172)



(173)

Chemical shifts of CF_3 groups bonded to unsaturated carbon

p.p.m. w.r.t. $CFCl_3$.

a = 52.6

b = 51.0

Ref: 199

Coupling constants (Hz)

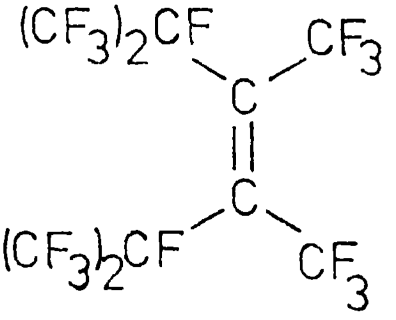
$J_1 = 45$

$J_2 = 0$

$J_3 = 68$

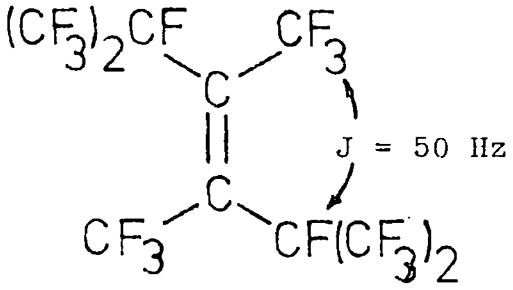
$J_4 = 0$

The large doublet splitting (J = 50 Hz) of one of these latter trifluoromethyl groups was caused by coupling to one of the tertiary fluorines at 161 p.p.m. as evidenced by its quartet structure (J = 50 Hz). Consideration of the coupling constants in the model compounds (172) and (173) indicated that these signals belong to the trans isomer (169). The tertiary fluorines were not overlapped and integration gave the cis to trans isomer ratio as 36:64.



(168)

36:64



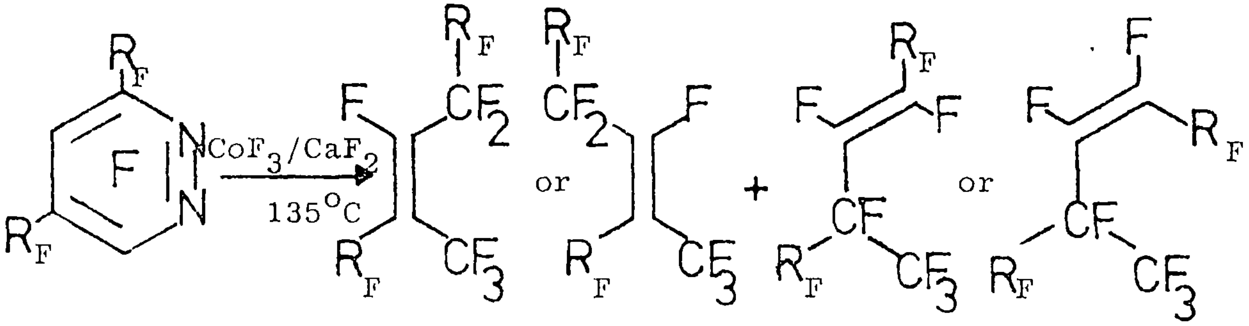
(169)

The third most abundant product was readily identified as perfluoro-2,3-dimethylpentane (170) by its P-F ion at m/e = 369 and elemental analysis which established its identity as a perfluoroheptane. Its ^{19}F n.m.r. spectrum contained six signals, two of which overlapped. Their integrations were 9 (two signals overlapping):3:2:1:1. The signals integrating to 1 were both attributable to tertiary fluorine atoms ($\rangle$C-F) by their high field shifts at 178 and 182 p.p.m. These data alone are sufficient to establish the identity of the third product. The remaining signals in the ^{19}F n.m.r. spectrum had chemical shifts consistent with the assigned structure and the i.r. spectrum did not contain any absorptions at higher wavenumber than 1343 cm^{-1}. An i.r. spectrum of what was claimed to be perfluoro-2,3-dimethylpentane was published in 1948[179] but it differed markedly from that observed in the present work in that it contained many absorptions not present in the i.r. spectrum of the present sample. Therefore it seems likely that the material described in 1948 was not pure and it is believed that the data published in the present work represent the first accurate characterisation of perfluoro-2,3-dimethylpentane (170)

The fourth product was easily identified as perfluoro-2,3,4,5-tetramethylhexane (171) by its P-F ion at m/e = 519 and elemental analysis which established its identity as a perfluorodecane ($C_{10}F_{22}$). Its ^{19}F n.m.r. spectrum was simple, consisting of four signals in the ratio 12:6:2:2, the signals integrating to 6 and 3 identified by their chemical shifts (69 and 72 p.p.m. respectively), as trifluoromethyl groups bonded to saturated carbon atoms ($CF_3-C\overset{/}{\underset{\backslash}{-}}$) and the remaining signals were identified by their high field shifts (166 and 170 p.p.m.) as due to tertiary fluorine atoms ($\overset{\backslash}{\underset{/}{-}}CF$). No coupling was resolved. Finally, the i.r. spectrum was devoid of bands at higher wavenumber than 1326 cm^{-1}.

3.11 The Fluorination of Perfluoro-3,5-di-isopropylpyridazine (174)

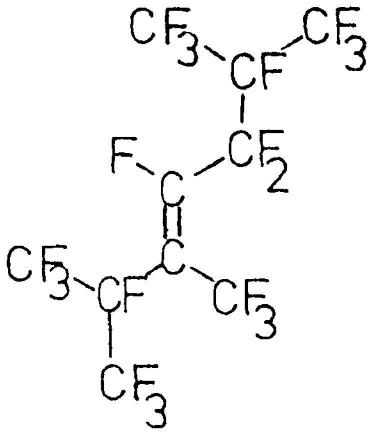
The -3,5-substituted pyridazine (174) was reacted with CoF_3/CaF_2 to give a product which was resolved into two components by available g.l.c. columns. However i.r. and ^{19}F spectroscopy indicated both components to consist of more than one compound. In each case the most abundant compound was estimated by ^{19}F n.m.r. spectroscopy to comprise over 85% of the respective mixtures and, although careful peak chopping, in a further attempt to isolate the major compounds by g.l.c., did not lead to further purification, it was possible to identify the two major compounds as either cis or trans perfluoro-2,3,6-trimethylhept-3-ene (175) or (176) and either cis or trans perfluoro-2,5,6-tri; methylhept-3-ene (177) and (178)



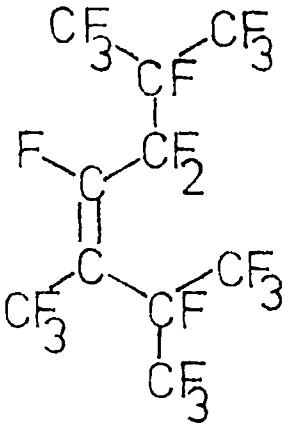
(176) (175) (178) (177)

$R_F = CF(CF_3)_2$

The first component was indicated by a very weak parent ion at m/e = 500 and strong P-F ion at m/e = 481 and elemental analysis to be a mixture of isomers of $C_{10}F_{20}$. The i.r. spectrum contained a strong band at 1671 cm^{-1} with a weaker one at 1714 cm^{-1} indicating the major and at least one other compound in the mixture to be perfluorodecenes. Signals due to the major compound in the ^{19}F spectrum were clearly distinguishable. They integrated in the ratio 6:6:3:2:1:1:1. The presence of two non-equivalent perfluoroisopropyl groups was deduced from the shifts of the two signals of integration 6 (76 and 77 p.p.m.) and two high field signals (181 and 185 p.p.m.) integrating to 1. The signal integrating to 3 had a typical trifluoromethyl group shift of 62 p.p.m. (Banks gives a range from 47 to 90 p.p.m. for $-CF_3$ in saturated or unsaturated fluorocarbons).[177] The signal integrating to 1 was identified as due to a fluorine atom bonded to unsaturated carbon (-CF=C) as its chemical shift was too low (89.11 p.p.m.) for it to be assigned as a tertiary fluorine atom (>C-F) which are reported not to resonate below 140 p.p.m.[177] The signal integrating to 2 had a shift (107 p.p.m.) typical for a difluoromethylene (-CF_2-) group in a fluorocarbon. Only the cis or trans isomers of perfluoro-2,3,6-trifluorohept-3-ene (175) or (176) could accommodate the data given.



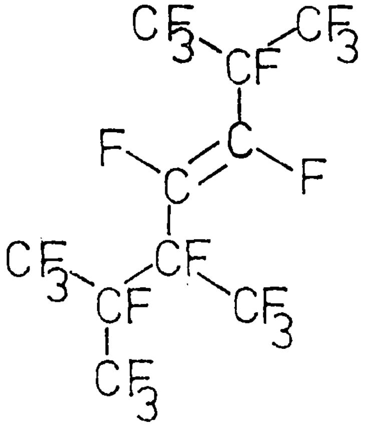
(176)



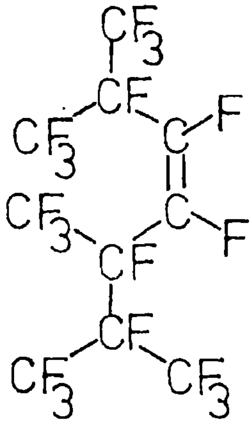
(175)

The ^{19}F n.m.r. spectrum was insufficiently resolved to distinguish between (175) and (176) by analysing the coupling constants.

In a similar manner, the most abundant compound in the second component was identified as a perfluorodecene also, namely either cis or trans perfluoro-2,5,6-trimethylhepta-3-ene (177) or (178).



(178)



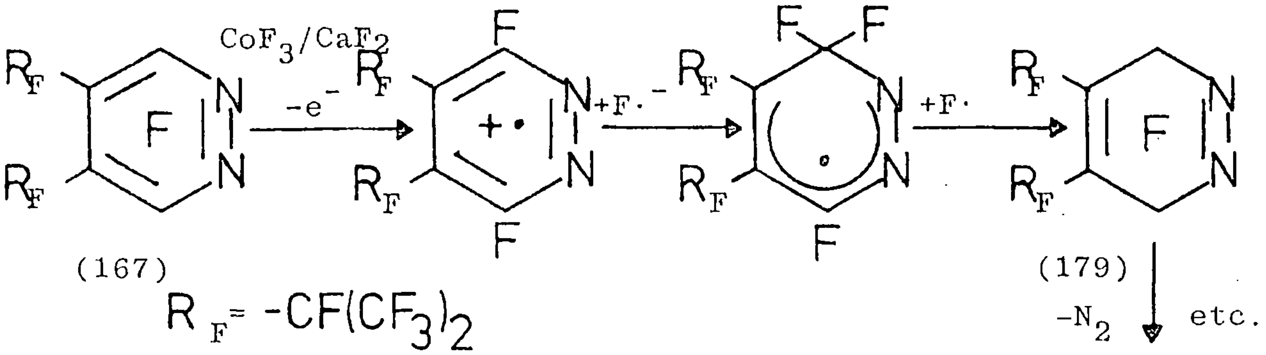
(177)

As with the earlier mixture, the mass spectrum of the second g.l.c. component gave a very weak signal at m/e = 500 (P) and a strong signal at m/e = 481 (P-F). A band at 1719 cm^{-1} and a weaker one at 1740 cm^{-1} were taken as evidence that the mixture contained a perfluorodecene ($C_{10}F_{20}$) as the major compound with minor amounts of at least one other perfluorodecene. Elemental analysis was in agreement with this. Once again, signals in the ^{19}F n.m.r. spectrum due to the major compound in the mixture were clearly distinguishable from the much weaker signals of the unknown compound. The major compound gave signals in the ratio 9:6:1:1:1:1:1. Of the signals integrating to 1, three were assigned as due to tertiary fluorine atoms ($-\overset{\backslash}{\underset{/}{C}}-F$) because of their high field shifts (194, 201 and 207 p.p.m.) and two were thought to be bonded to unsaturated carbon atoms (-CF=C), because of their mid-field shifts (126 and 129 p.p.m.). This identifies the compound as perfluoro-2,5,6-trimethylhept-3-ene, (177) or (178), but all the signals were broad envelopes except for one of the tertiary fluorine atoms which was a multiplet and hence because of the lack of data on the coupling between signals it was not possible to deduce whether it was the cis or trans isomer.

By comparison with the fluorination of the -4,5-di-isopropylpyridazine (167) (see Section 3.10) where cis trans isomerisation was found to occur during the fluorination, it would be surprising if the same did not apply during the fluorination of the -3,5-isomer (174) and it is possible that the inseparable minor co-products detected with the major products are the respective cis or trans isomers.

3.12 Proposed Reaction Mechanisms for the Fluorination of Pyridazines

The intermediacy of the unobserved -1,4-diene (179) is proposed during the fluorination of the -4,5-pyridazine (167). Such an intermediate would reflect the behaviour of the previous aza-aromatics in that it does not contain destabilising nitrogen to fluorine bonds or fluorines bonded to an unsaturated carbon atom.

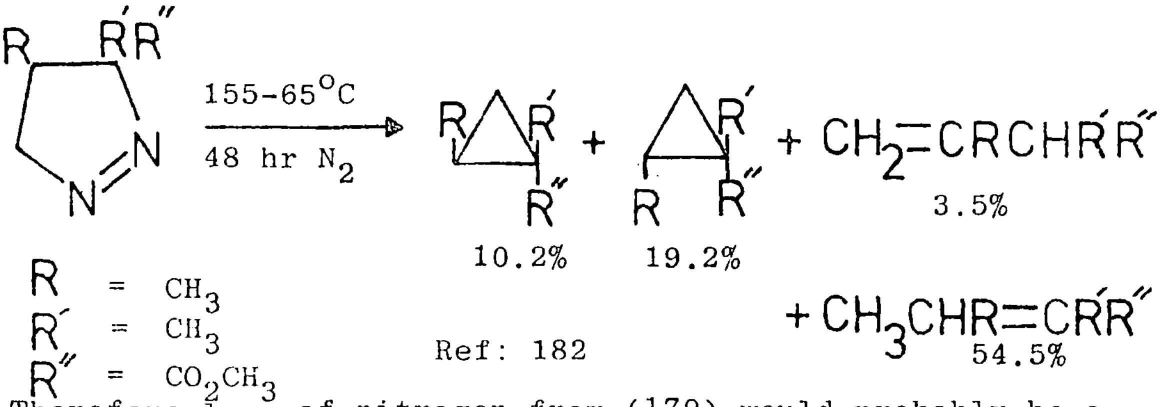


(167)

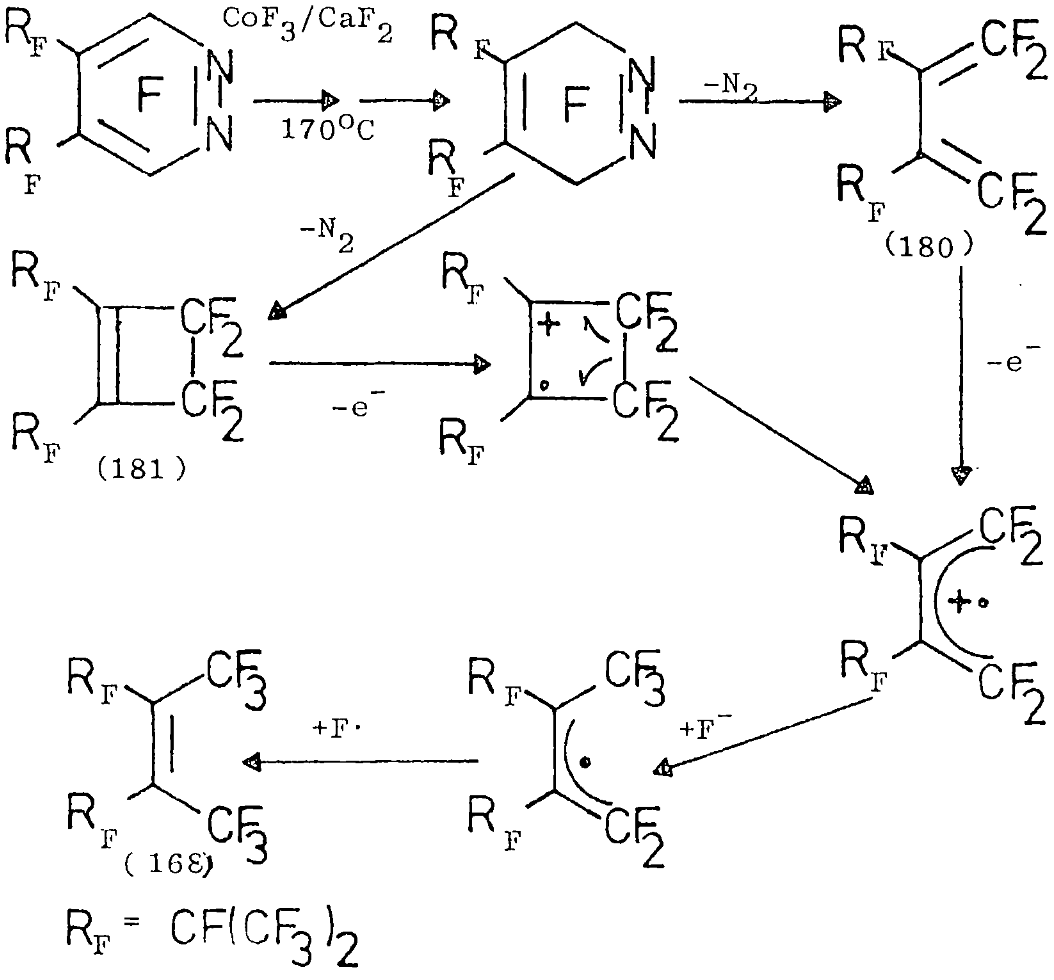
(179)

$R_F = -CF(CF_3)_2$

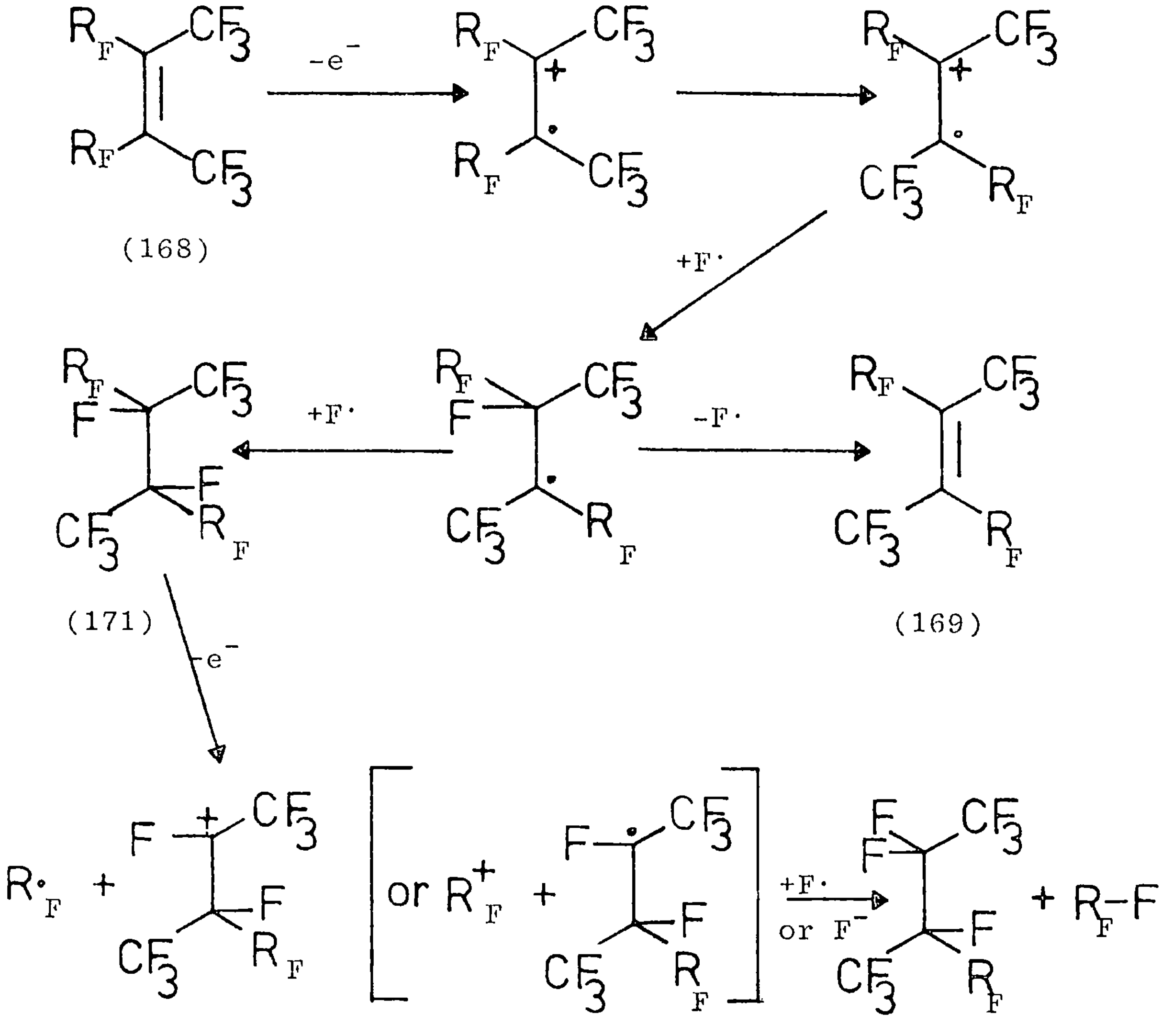
Thermal loss of nitrogen from a -1,2-diazacyclohexa-1,4-diene usually occurs via a concerted mechanism rather than a biradical mechanism, according to Brown,[181] and losses of N_2 from diaza compounds can lead to either ring opened or cyclic products[182,183]



Therefore loss of nitrogen from (179) would probably be a concerted reaction but it is not clear whether a diene (180) or cyclobutene (181) would result. Either (180) or (181) would be highly activated to further fluorination, (180) as a result of the destabilising interaction between four fluorine atoms and the π bonds or (181) as a result of ring strain.



The isomerisation of the cis olefin (168), saturation and fragmentation to the other products could then occur via processes such as:-

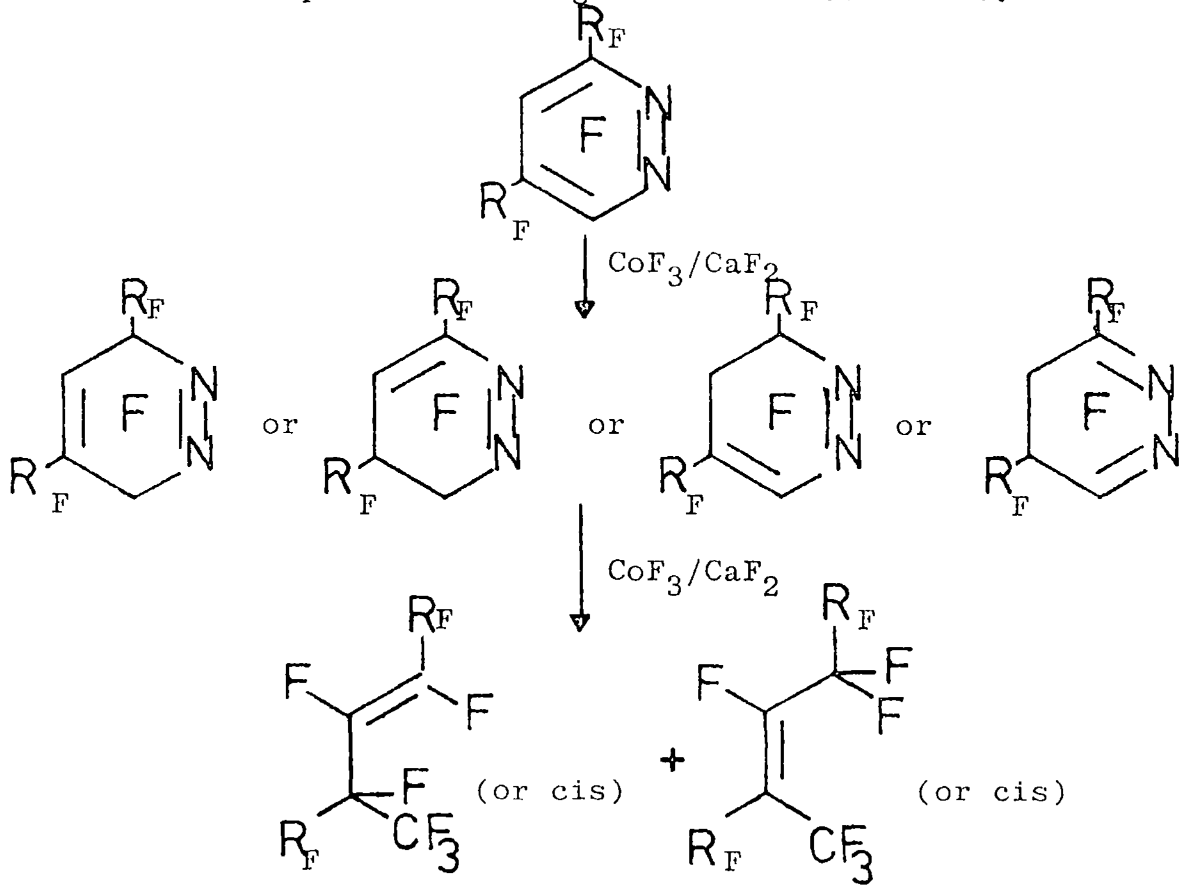


(168) (171) (169) (170)

$R_F = CF(CF_3)_2$

Alternatively, the trans olefin (169) might arise directly from the unobserved diene (180) if the latter is free to rotate into a trans configuration and has time to do so.

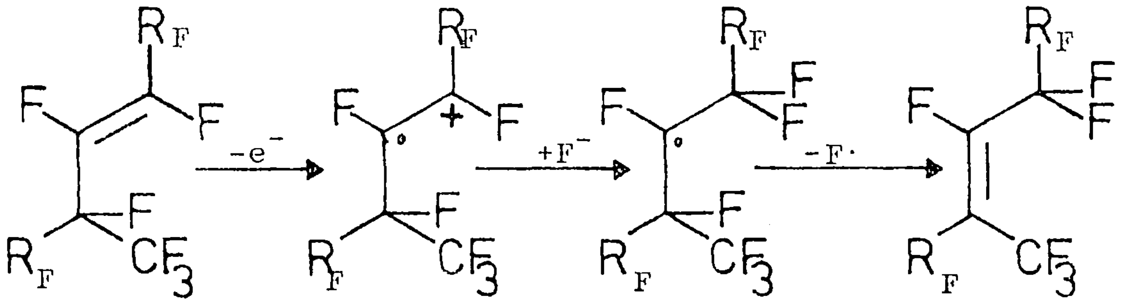
Much less can be said about the fluorination of the -3,5- substituted pyridazine (174) as there are four possible diene intermediates which are equally likely using the usual criteria of thermodynamic stability, and all of which could lead to the observed products through feasible mechanisms.



(178) (176)

$R = CF(CF_3)_2$

The proportion of (176) in the product appeared to increase with increasing reaction temperature. Thus the ratio of (176) to (178) at 132°C was 1:1 going up to 2:1 at 158°C. Therefore (178) might be the precursor of (176) by a process such as:-



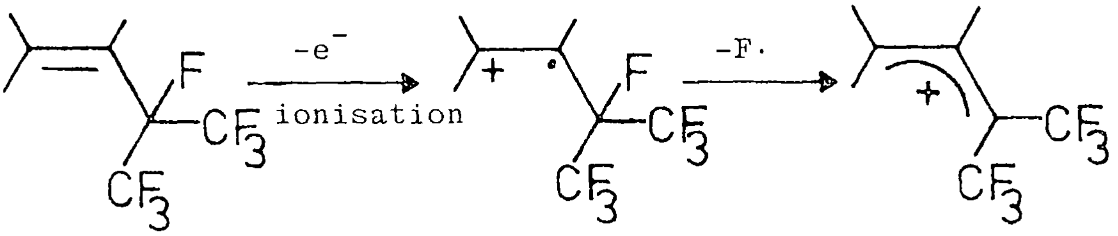
(178) (176)

$R_F = CF(CF_3)_2$

3.13 Parent Ion Intensities of the Pyridazine Fluorination Products

It was noted that the perfluorodecane and -decene products from the pyridazine fluorinations gave parent ions in their mass spectra of either very low or zero intensity at 14eV. The spectrum of the mixture of the cis and trans perfluorodecenes (168) and (169) was also recorded at 3eV but a parent ion was still not observable.

In the case of the decenes it is thought that this is a result of the ease with which a fluorine atom can be lost upon ionisation in the spectrometer as a result of the following process:-

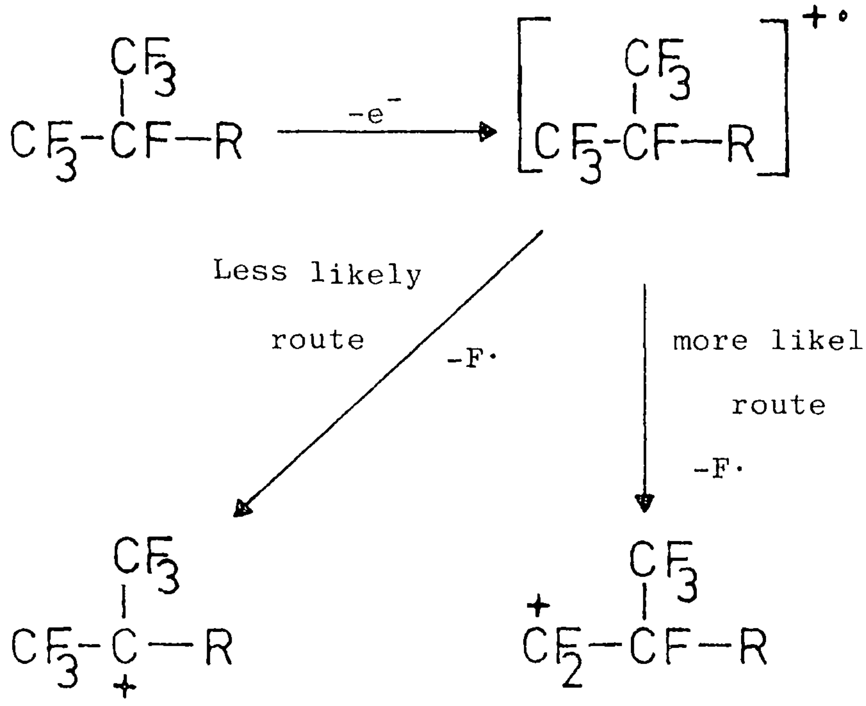


(182) (183)

Formation of P-F ion in mass spectra of perfluorodecenes

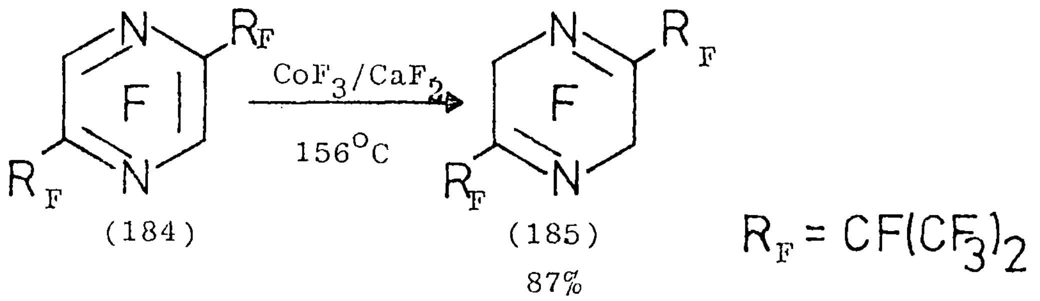
This is reasonable as the process leads from a localised radical cation such as (182) via the loss of a tertiary fluorine atom to the allylically stabilised cation (183).

In the case of the perfluorodecanes it is not possible to predict which bond will lose an electron the most easily upon ionisation as there are no π electrons available and hence it is less easy to understand why these compounds, too, appear to lose fluorine atoms readily upon ionisation. However, it can at least be said that the loss of a tertiary fluorine atom from the radical cation would not be expected this time as the resultant tertiary carbocation would be highly destabilised by electron withdrawing perfluoroalkyl groups and a process leading to a primary carbocation, such as the one below, would be preferable:-



3.14 The Fluorination of Perfluoro-2,5-di-isopropylpyrazine (184)

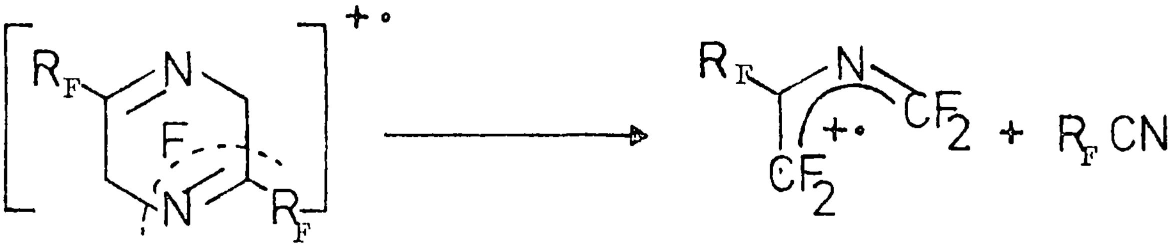
The pyrazine (184) reacted with CoF_3/CaF_2 at 156°C to give a new product which was identified as perfluoro-2,5-di-isopropyl-1,4-diazacyclohexa-1,4-diene (185).



A weak parent ion at m/e = 490 and elemental analyses established $C_{10}N_2F_{18}$ as the empirical formula. Bands at 1709 and 1721 cm^{-1} in the i.r. indicated at least two double bonds and the simplicity of the ^{19}F n.m.r. spectrum which contained only three chemically shifted bands integrating in the ratio 12:4:2

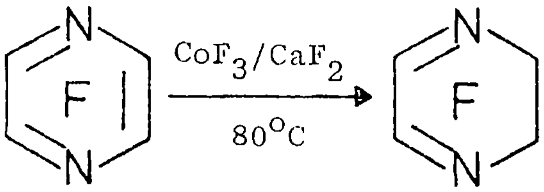
was sufficient data to rule out all structures other than (185). Chemical shifts and observed couplings were consistent with structure (185).

A prominant feature in the mass spectrum of (185) at 14eV was a peak at m/e = 295. This is readily interpreted as resulting from the loss of perfluoroisopropylnitrile from the parent ion. A similar feature was observed in the spectrum of the pyrimidine product (153) which has a closely similar structure to (185).

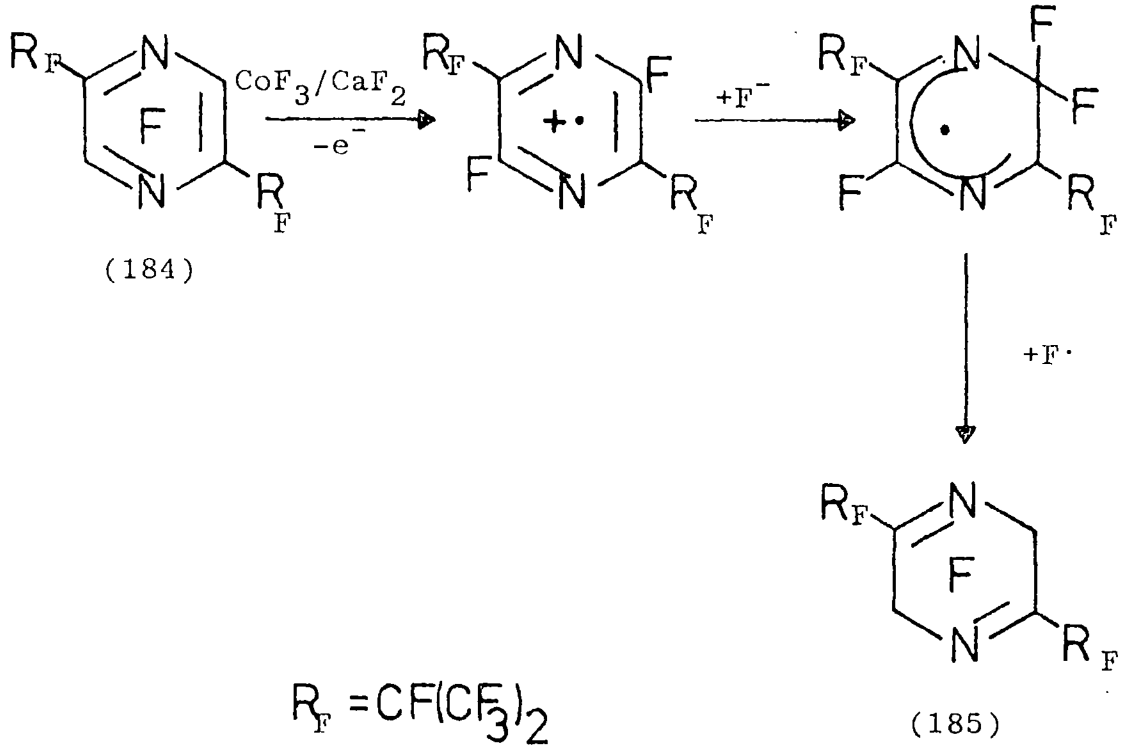


$R_F = CF(CF_3)_2$

The product from the -2,5-di-substituted pyrazine (184) contrasts with that from tetrafluoropyrazine itself which was reported to yield a conjugated diene rather than a -1,4-diene.[163] The effect of substituents in the 2 and 5 positions provides further evidence that products which minimise the number of fluorines directly bonded to saturated carbon are preferred in these reactions.



(186) (187) Ref: 163



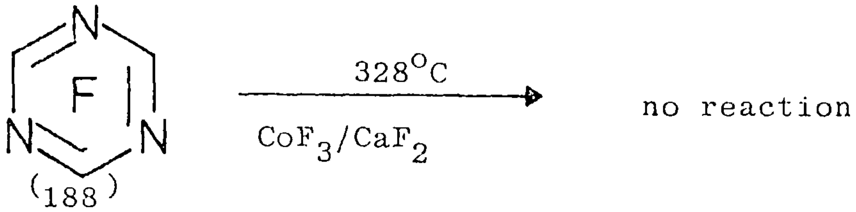
(184)

(185)

$R_F = CF(CF_3)_2$

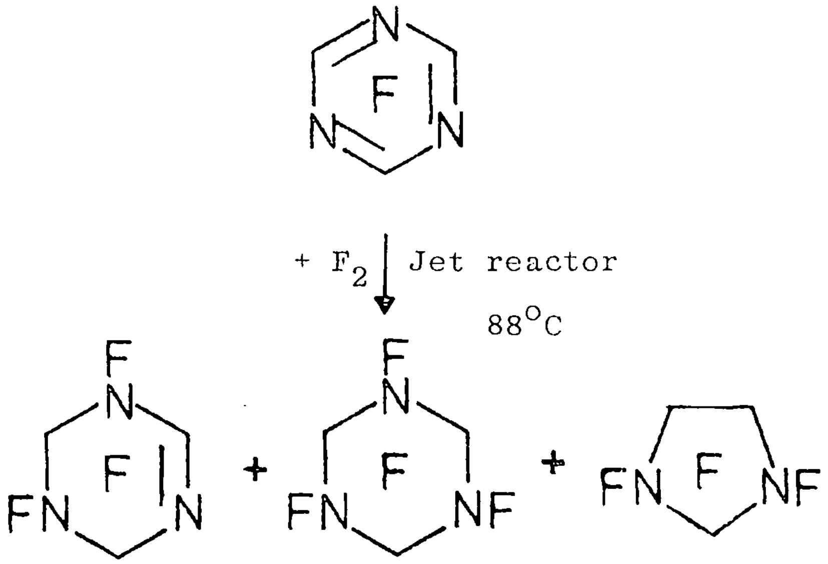
3.15 Attempted Fluorination of Cyanuric Fluoride (188)

Attempts to fluorinate the triazine system, cyanuric fluoride with silver II fluoride were reported to be unsuccessful, even in an autoclave at 150°C for 10 hrs.[44] Not surprisingly, therefore, when a sample of cyanuric fluoride was passed through the CoF_3/CaF_2 reactor almost total recovery of starting material was made, even at reaction temperatures as high as 328°C.



(188)

In contrast, Bigelow found that smooth reaction occurred when he reacted cyanuric fluoride with fluorine directly in his jet reactor at the mild temperature of 88°C.[43]



Ref: 43

This provides further evidence that the first stage in the mechanism of cobalt III fluoride fluorination is oxidation of the substrate as it is reasonable to suppose that as ring carbon atoms are replaced by more electro negative nitrogen in a perfluoro-arene, the ionisation potential will increase. Also underlined is the fact that cobalt III fluoride does not behave as simply a donor of fluorine atoms.

CHAPTER 4

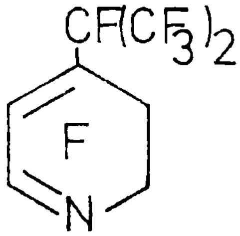
THE DIRECT FLUORINATION OF SOME PERFLUOROAZABENZENES

4.1 Introduction

In this chapter the reactions between elemental fluorine diluted with nitrogen and some perfluoro-azabenzenes are described. The compounds were fluorinated by passing the fluorine/nitrogen mixture through externally cooled, dilute solutions of the starting materials in Freon 113 (the Du Pont trade name for 1,1,2-trifluorotrichloroethane) which functioned as an efficient and inert heat sink. The fluorination apparatus and precautions taken to eliminate oxygen containing species contaminating the fluorine are fully described in the experimental Chapter 8 (Section 8.15).

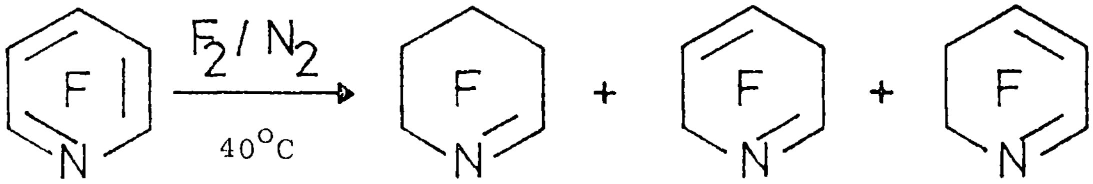
4.2 The Attempted Direct Fluorination of Perfluoro-4-isopropylpyridine (189)

Upon passing two moles of fluorine (diluted two-fold in nitrogen) per mole of -pyridine (189) through a solution of the latter in Freon 113 at a temperature of -20°C only traces of new products were formed, one of which (1% by g.l.c.) had identical retention times to the -1,3-diene (121) on a series of columns. The other (2%) had lower retention times on all columns. No further attempts to verify the identity of these products were made.



(121)

This result contrasts with the reported reaction of pentafluoropyridine (190), itself, with fluorine,[184] published since the completion of this work, which gave high yields of perfluoro-1-azacyclohex-1-ene (191), the -1,3- and -1,4-dienes (192) and (193) and dimeric and oligomeric material. However the latter reaction was performed without a solvent and at higher temperatures (40 and 100°C). Indeed, it was noted that little reaction appeared to occur below 40°C in the case of pentafluoropyridine.[192]



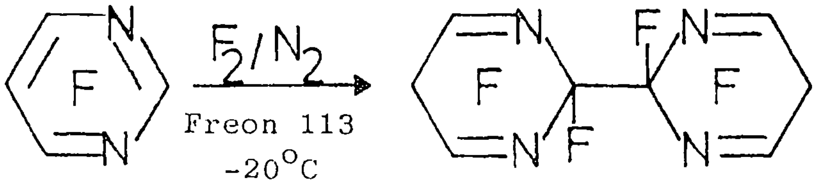
(190) (191) 5% (192) 20% (193) 8%

+ oligomeric material

Ref: 192

4.3 The Direct Fluorination of Tetrafluoropyrimidine (194)

Tetrafluoropyrimidine (194) was dissolved in Freon 113 and, after cooling to -20°C, was then treated with fluorine diluted with twice its volume of nitrogen. After removing the solvent by distillation, only one product, apart from recovered starting material (194), was detected by g.l.c. It was purified by sublimation onto a cold finger and was identified as the dimer perfluoro-2,2'-bi-1,3-diazacyclohexa-3,6-dienyl (195)

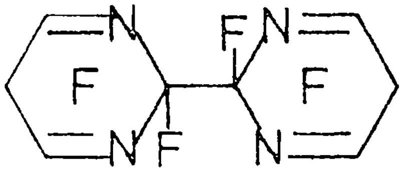


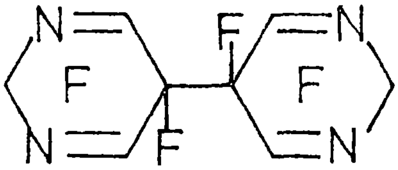
(194) (195) 24.9%

+ recovered starting material (194) 42%

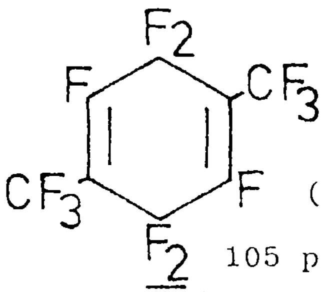
The structure of the product (195) was deduced from its mass spectrum, elemental analysis and its ^{19}F n.m.r. spectrum.

Thus, a parent ion at m/e = 342 in the mass spectrum and elemental analysis indicated an empirical formula of $C_8N_4F_{10}$. The ^{19}F n.m.r. spectrum of (190) was very simple, containing only three groups of signals integrating in the ratio 1:2:2. A satisfactory i.r. spectrum was not obtained because the material hydrolysed rapidly. Only the structures (195) and (196) have sufficient symmetry to accommodate the data so far:


(195)

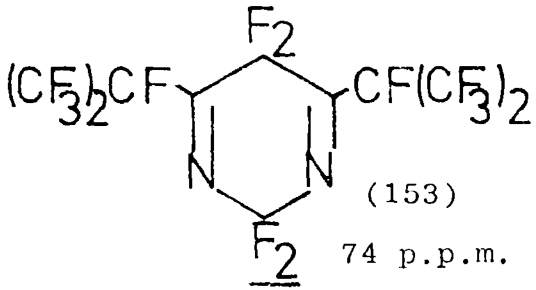

(196)

The -5,5'- dimer (196) was eliminated as a possibility, however, as the chemical shifts of the difluoromethylene ($>CF_2$) group signals (120.9 and 121.2 p.p.m.) were in a region typical for a difluoromethylene group bonded to two sp^2 hybridised carbon atoms, but well above the region for difluoromethylene bonded to nitrogen atoms, as the models (197) and (153), below, illustrate:


(197)

105 p.p.m.

Adapted from data in Ref: 148,


(153)

74 p.p.m.

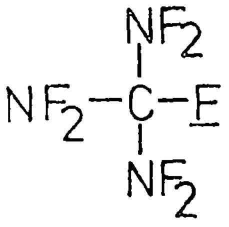
Ref: Section 3.6

The difluoromethylene group signals were identified as such because, as already implied, they exhibited what was interpreted as an AB pattern although, as might be expected, the difference in the chemical shifts of the individual fluorine atoms within the difluoromethylene group was very small (0.3 p.p.m. or 18 Hz) and therefore the outer lines of the AB system were too weak to be observed. In spite of this, the signal is readily proven to be an AB system for two reasons;

(a) The signal at 120.9 p.p.m. consisted of a triplet (J = 24 Hz) of doublets (J = 6 Hz) whereas that at 121.2 p.p.m. was a triplet (J = 24 Hz) of multiplets too narrow to contain a doublet with J = 6 Hz.

(b) None of the other signals was broad enough to contain a triplet with J = 18 Hz and hence the 18 Hz shift between the inner AB lines cannot be alternatively interpreted as a coupling constant and, in any case, it is hard to envisage how the -2,2'- dimer (195) could give rise to such a doublet.

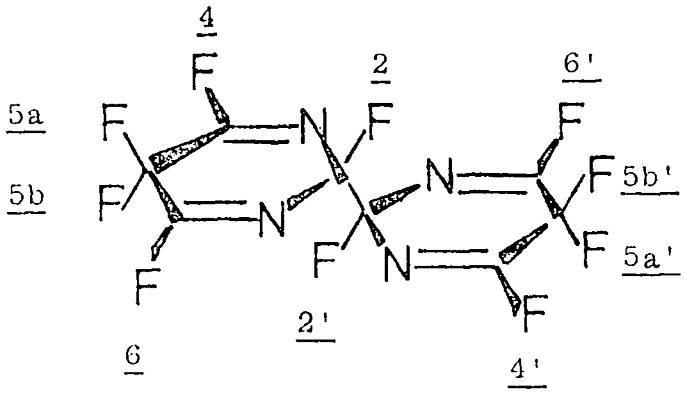
The remaining signals in the ^{19}F n.m.r. spectrum were consistent with the assigned structure and consisted of a signal at 60 p.p.m., integrating to 2 and assigned to the imino (>CF=N-) fluorine atoms and a signal at 118 p.p.m. assigned to the tertiary ($\geqslant$C-F) fluorine atoms. The chemical shift of the latter is very low compared to the shifts of tertiary fluorines on carbon atoms bonded to three sp^3 hybridised carbon, atoms. the lower limit on the range of chemical shifts for which is 151 p.p.m., adapted from figures given by Banks.[177] However, as the model (198), below indicates, substitution of the sp^3 carbon atoms by three nitrogen atoms reduces the chemical shift of a tertiary fluorine atom to 139 p.p.m. and it seems reasonable, therefore, to suppose that two substituent nitrogen atoms would be sufficient to reduce the shift of a tertiary fluorine atom to 118 p.p.m..



$NF_2-\overset{NF_2}{\underset{NF_2}{C}}-F$ 139 p.p.m.

(198) Ref: 185

The observed couplings were also consistent with the -2,2'- dimer (195)



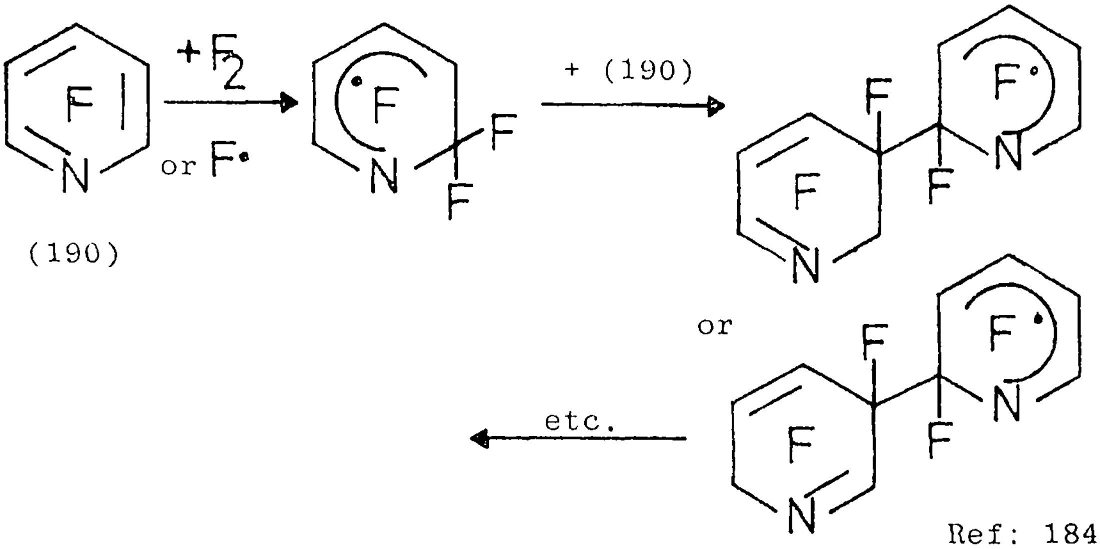
(195)

J4.5a= 24 Hz

J4.5b= 24 Hz

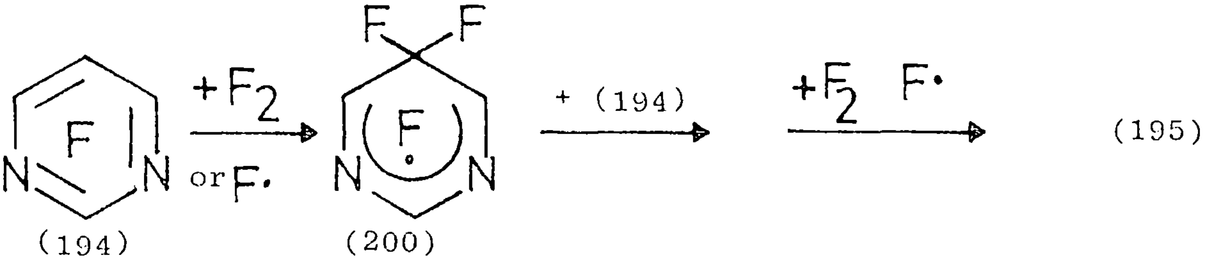
J2.5a= 6 Hz? (not confirmed because the signal of 2 was not resolved).

The mechanism by which the -2,2'- dimer (195) is formed is not clear but the following points may be noted. First, Hotchkiss et al. proposed mechanisms for the dimerisation of both hexafluorobenzene (199)[186] and pentafluoropyridine (190)[184] which involved the addition of a fluorine atom, by either F_2 or F•, to the initial aromatic species, followed by attack by the resultant intermediate radical also on the initial aromatic species e.g.



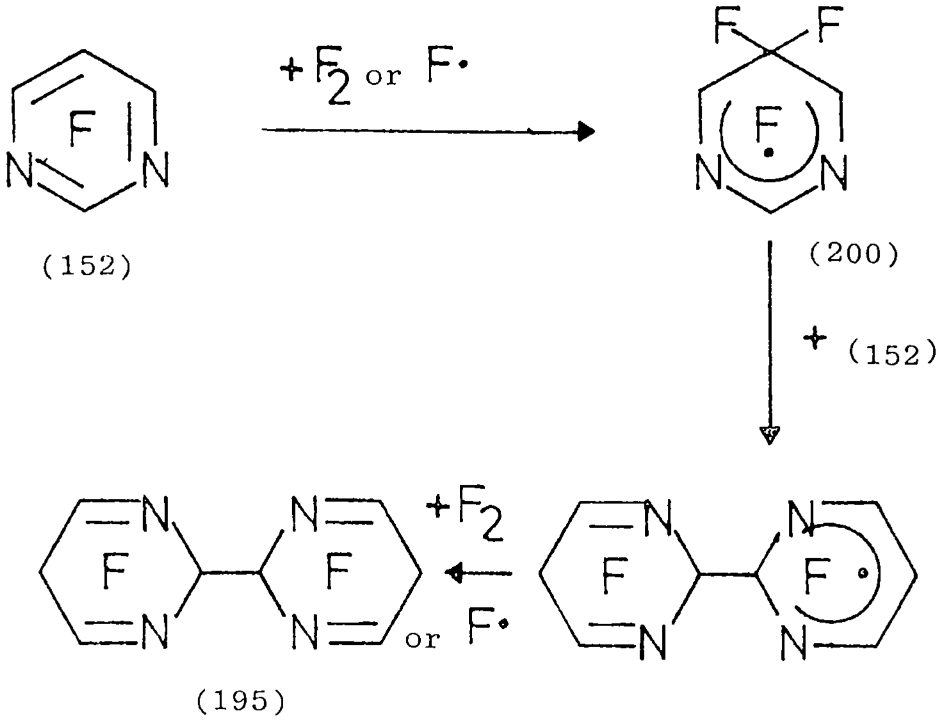
Ref: 184

It seems reasonable to assume that this is also how dimer (195) is formed, as the alternative would be the reaction of two intermediate radicals of structure (200).



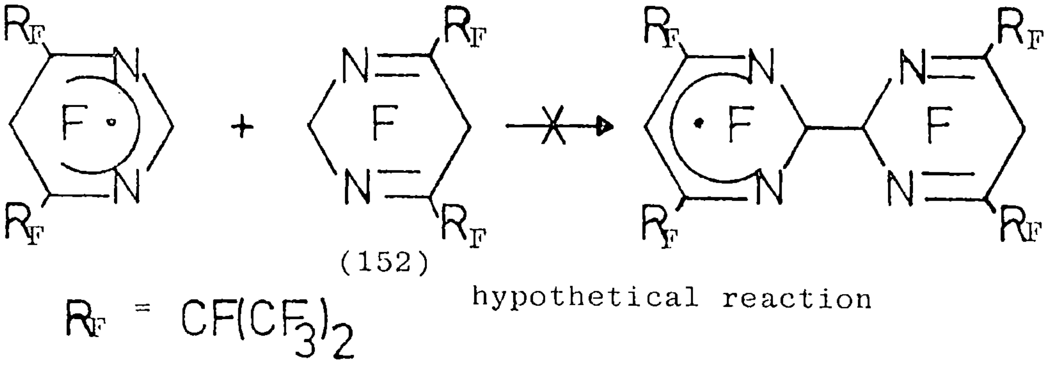
However such an event seems highly unlikely as radical (200) if sufficiently stable to build up the necessary concentrations for reaction with other radicals of the same structure, would also have time to react with fluorine, but no such products have been observed.

Nevertheless, to form the -2,2'- dimer (195) by reaction of the intermediate (200) raises the problem that intermediate (200) apparently attacks a different site on the tetrafluoropyrimidine to that attacked by fluorine or a fluorine atom. A possible explanation might be that, unlike the small fluorine atom or molecule, the radical (200) is large and prefers to attack tetrafluoropyrimidine at C-2 which is flanked by two nitrogen atoms and is therefore of slightly higher steric accessibility compared with C-4.



4.4 The Attempted Fluorination of Perfluoro-4,6-di-isopropylpyrimidine (152)

After passing three moles of fluorine (diluted two-fold by nitrogen) per mole of the -pyrimidine (152) into a dilute solution of the latter in Freon 113 at -10^{o}C, no reaction was detected. In view of the ready reaction of tetrafluoropyrimidine, this is a surprising result as the substituent perfluoroalkyl groups in the pyrimidine (152) are too remote to interfere with a coupling reaction such as:



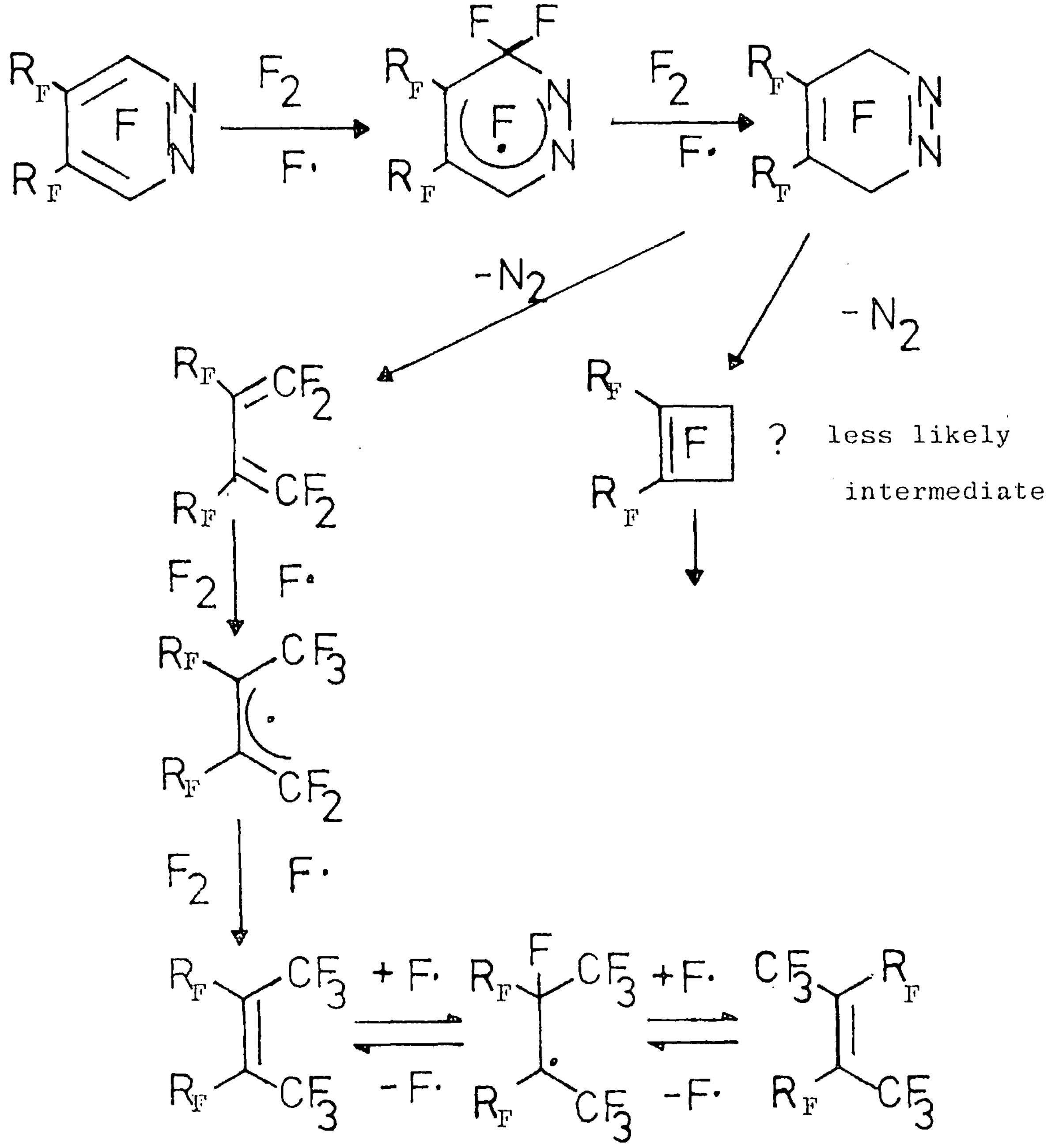
hypothetical reaction

Hotchkiss et al. thought that the lower reactivity of pentafluoropyridine towards elemental fluorine, compared with hexafluorobenzene, might, amongst other reasons, be due to the deactivating influence of the ring nitrogen.[184] The substituent perfluoroisopropyl groups on the -pyrimidine (152) would be similarly deactivating and this may explain its low reactivity, as well, but it must be noted, in contradiction to this, that perfluoro-4,5-di-isopropylpyridazine (167) which also bears two ring nitrogens and two substituent perfluoroisopropyl groups reacts quite readily under comparable conditions as described in Section 4.5. Therefore the situation remains unclear.

4.5 The Direct Fluorination of Perfluoro-4,5-di-isopropylpyridazine (167)

The -pyridazine (167) behaved in a similar manner when treated with gaseous fluorine as it did when fluorinated with cobalt III fluoride (Section 3.10). Thus, after passing an excess of fluorine (13 moles per mole of (167)) through a solution of the -pyridazine (167) in Freon 113 at -5^{o}C, apart from traces of less volatile material, the only product detected was an inseparable mixture of cis- and trans-perfluoro-2,3,4,5-tetramethyl-hex-3-enes (168) and (169) in approximately the same ratio (1:1.8) as they are produced in the cobalt III fluoride reaction. The yield of the -3-enes (168) and (169) was also similar at 57% combined. The olefins (168) and (169) were identified by comparison of their spectra with those of material produced by the reaction with cobalt III fluoride.

The following mechanism is proposed for this reaction:



$R_F = CF(CF_3)_2$

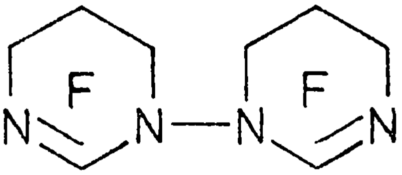
The intermediacy of the cyclobutene is less likely in this case as the route to the observed products is more straightforward from a diene intermediate

CHAPTER 5

THE REACTION OF PERFLUORO-CYCLIC-IMINES WITH NUCLEOPHILIC REAGENTS

5.1 Introduction

The preparation of a series of new perfluoro-cyclic-imines was described in Chapter 3. When compared with the work which has been done on the isoelectronic perfluoro-olefins, comparatively little is known of the chemistry of this class of compounds although work by several authors has already shown that perfluoro-imines are susceptible to attack by nucleophilic reagents in a manner analogous to the reactions of perfluoro-olefins.[184] In this chapter the reactions of some of the new perfluoro-cyclic-imines and the previously known perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)[163] with a series of nucleophiles are described.



(160)

The dimer (160) is prepared by the cobalt III fluoride fluorination of tetrafluoropyrimidine as described in Section 2.6G(d) and the slight doubts about its structure expressed by the original authors have now been removed by an experiment described in Section 5.7A.

The order in which the reactions are described is determined by the nature of the particular nucleophile. Thus a reaction with perfluoroisopropyl carbanion is described first as its nucleophilic centre is a carbon atom. Then reactions with nucleophiles based on oxygen, moving to the right across the periodic table, are described and then, finally, reactions with halide ions are described. Any reactions performed on products isolated from the nucleophilic reaction are dealt with immediately after describing their preparation.

5.2 Perfluoroisopropyl Carbanion as a Nucleophile

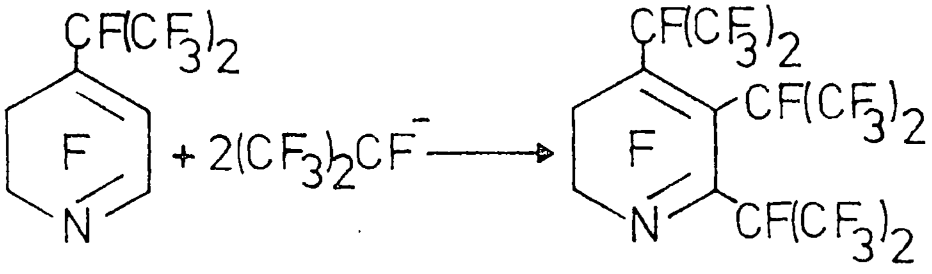
5 2A Reaction with perfluoro-4-isopropylcyclohexa-1,3-diene (121)

The -1,3-diene (121) was reacted with the perfluoroisopropyl carbanion (187), generated in situ by the dissolution of hexafluoropropene (190) in a slurry of dry caesium fluoride and tetrahydrothiophen dioxide as a solvent. Nucleophilic aromatic substitutions with perfluoroisopropyl carbanion, using similar techniques, are well known.[185]

Upon distilling the products, a mixture of oligomers of hexafluoropropene and one new product was obtained. The new product was separated from the oligomers by further distillation. It was identified as the disubstituted product perfluoro-2,3,4-tri-isopropyl-1-azacyclohexa-1,3-diene (201).

$$CF_3CF{=}CF_2 + F^- \rightleftharpoons (CF_3)_2CF^-$$

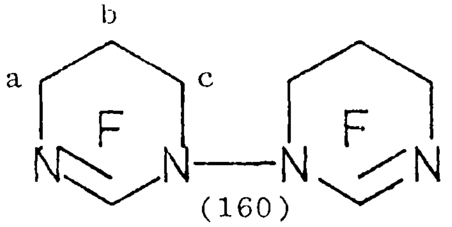
(190) (187)



(121) (201)

Thus, a parent ion at m/e = 657 confirmed the new product to have formed by the substitution of two fluorine atoms for perfluoroisopropyl ($(CF_3)_2CF-$) groups. The ^{19}F n.m.r. spectrum revealed three signals in the high field region above 150 p.p.m., each integrating to one, which were evidence of the presence of three tertiary ($\geq$CF) fluorine atoms. A complicated group of signals between 66 p.p.m. and 76 p.p.m., integrated to 18 and was therefore assigned to the trifluoromethyl groups of three non-equivalent heptafluoroisopropyl groups. The only other groups of signals in the spectrum were two occurring in mid-field, both integrating to 2. Both signals exhibited an AB splitting pattern and were assigned to ring difluoromethylene ($>CF_2$) groups.

The chemical shifts of the fluorine atoms in one of the AB systems were at the downfield part of the usual range of shifts for difluoromethylene ($>CF_2$) signals, at 107 p.p.m. and 116 p.p.m., by comparison with the models (160) and (161) below, this was taken as evidence that one of the difluoromethylene groups was bonded to the nitrogen atom:



(160)

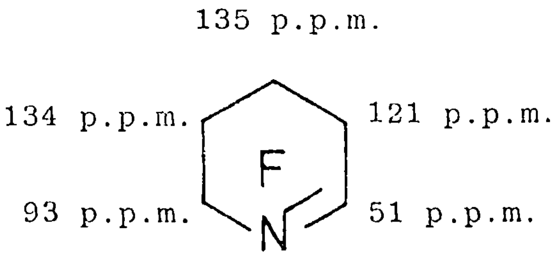
a = 96 p.p.m. (Ax.)
101 p.p.m. (Eq.)

b = 134 p.p.m. (Ax.)
141 p.p.m. (Eq.)

c = 99 p.p.m. (Ax.)
111 p.p.m. (Eq.)

Ax = axial

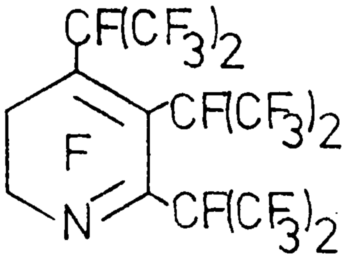
Eq = equatorial



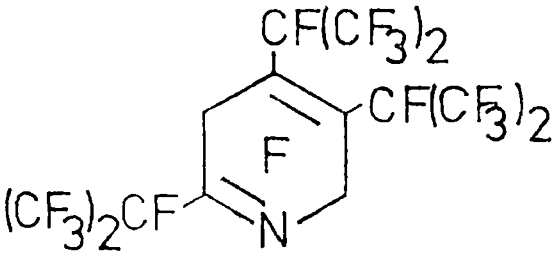
(161)

Ref: 163

Two structures, (201) and (202), were considered possible on the basis of the data so far. (202) could have formed as a result of fluoride ion rearrangements.

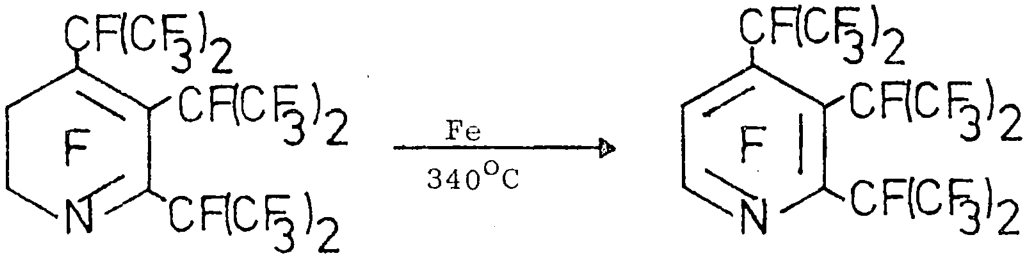


(201)



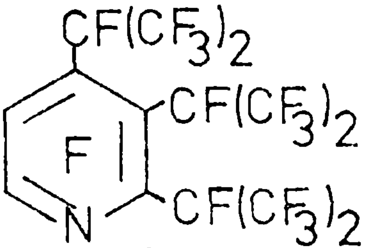
(202)

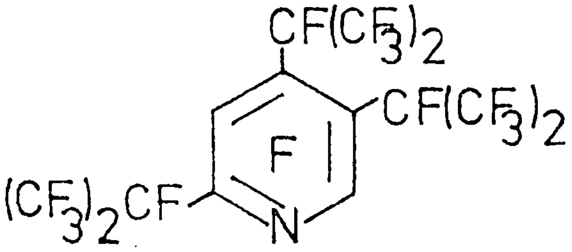
Final confirmation that the product was the -1,2,3-tri-iso-propyl-isomer (201) was only possible after the product had been defluorinated to a pyridine identified as perfluoro-2,3,4-tri-isopropylpyridine (203).



(201) (203)

Thus, by passing the new diene in a stream of nitrogen over heated iron filings in a silica tube at 340^{o}C, a crystalline product was isolated. The new product gave a parent ion at m/e = 619. Its ^{19}F n.m.r. spectrum consisted of a complicated band of signals between 69 and 73 p.p.m. integrating to 18 and three signals at highfield each integrating to 1 which were assigned as the signals of three substituent non-equivalent perfluoroisopropyl groups. The only remaining signals in the spectrum were two at mid-field, each integrating to 1, identifying them as bonded to the ring carbons of a pyridine. This confirms the formation of a pyridine from the diene. The possible pyridines from the dienes (201) and (202) are (203) and (204).


(203)

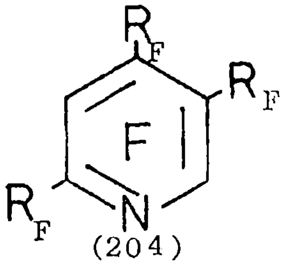

(204)

The -2,4,5-isomer (204) is known[185] and was immediately eliminated because the ^{19}F n.m.r. and i.r. spectra of an authentic sample were different from those of the new pyridine. This, therefore, confirmed the new pyridine as the -2,3,4-isomer (203) and the initial diene as the -2,3,4-isomer (201).

The ^{19}F n.m.r. spectrum of the diene (201) was insufficiently resolved to allow any firm conclusions about the stereochemistry of the substituent alkyl groups. Changes took place in the spectrum on heating to 161°C (16 degrees below the b. pt.) but they have not been interpreted as the resolution concomitantly became much worse.

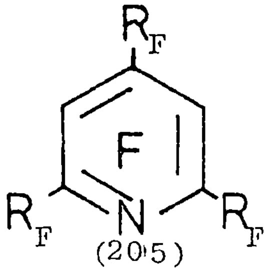
The i.r. spectrum of the new diene (201) contained only one strong band in the double bond region (1400 to 1800 cm^{-1}) at 1,657 cm^{-1}. This is not considered inconsistent with the proposed structure as, although both the double bonds in (201) are assymetric, the assymetry of the olefin ($>C=C<$) bond is much less pronounced than that of the imine ($>C=N-$) bond and hence the i.r. absorption band of the former would be expected to be much weaker than that of the latter.[186] Therefore, the band at 1,657 cm^{-1} is assigned to the imine ($>C=N-$) bond. In addition, it is possible that the band is due to two coinciding resonances.

The pyridine (203) contained bands at 1,448 (shoulder), 1,471, 1,580 (shoulder) and 1,587 cm^{-1} at wavelengths typical of fluoroaromatic compounds as the following models indicate:



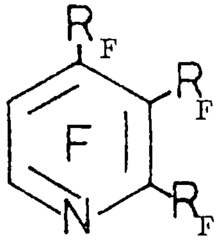
(204)

λ_{max} = 1,562 and 1,600 cm^{-1} Ref: 185



(205)

λ_{max} = 1,453 and 1,587 cm^{-1} Ref: 185

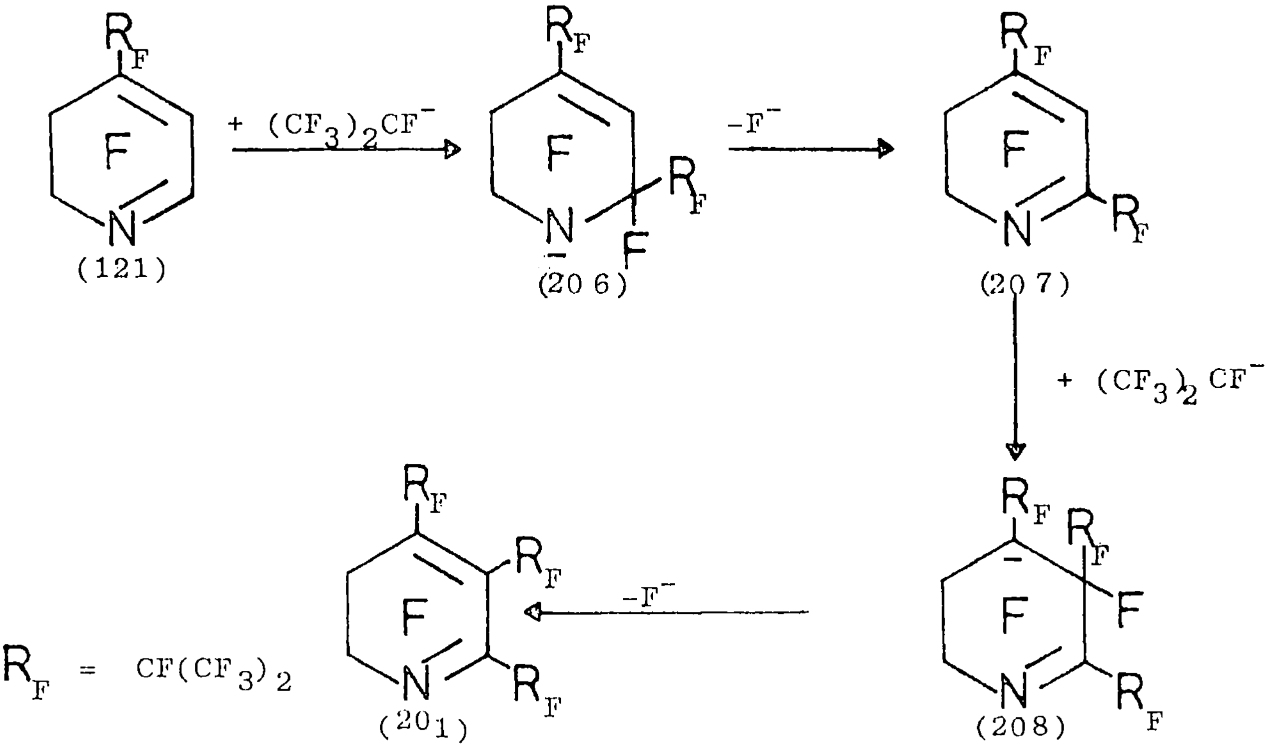


(203)

λ_{max} = 1,471 and 1,587 cm^{-1}

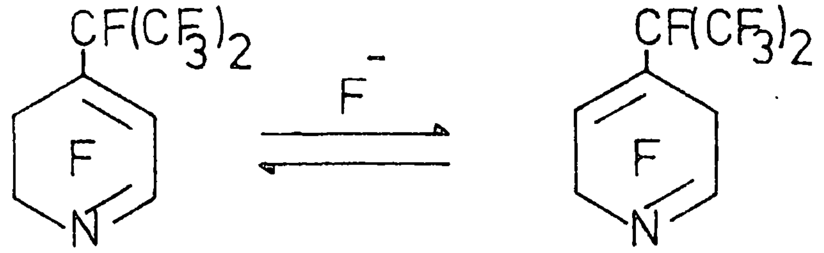
$R_F = CF(CF_3)_2$

The following mechanism is proposed to account for the formation of diene (201).



The initial attack at C-2 in the mechanism is consistent with the observations that other nucleophiles attack diene (121) at C-2 to give isolable mono substituted products (see Sections 5.3C and 5.4B).

As is described in Section 5.6C, the -1,3-diene (121) is equilibrated by fluoride ion, in the absence of hexafluoropropene, to produce a small proportion of the -1,4-diene (122).

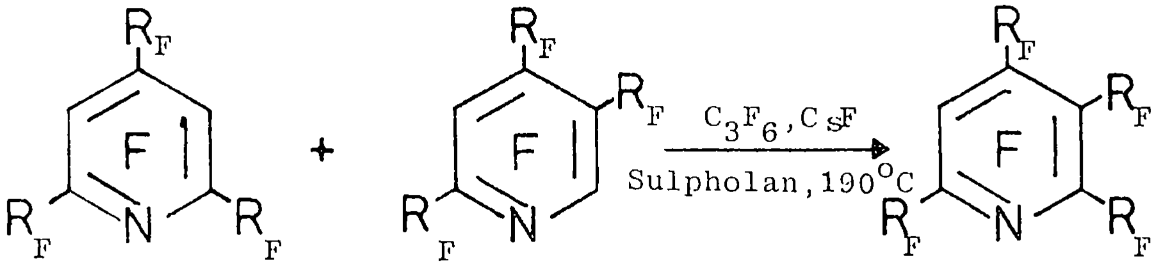


(121) (122)

Therefore it must be concluded that, as in the presence of hexafluoropropene there are apparently no products derived from the -1,4-diene (122), then either (121) reacts to form the dialkyl diene intermediate (207) more quickly than it reacts with fluoride ion or that, in the presence of hexafluoropropene, the concentration of free fluoride ion is negligible as a result of the following equilibrium,

$$C_3F_6 + F^- \rightleftharpoons C_3F_7^-$$

Once formed, the dialkyl diene (207) would not be expected to be susceptible to rearrangement to a -1,4-diene as such a process would involve the elimination of a secondary rather than a hindered tertiary fluorine from the anion (208) and it would also increase the number of fluorines on unsaturated carbon atoms. Nevertheless, it is interesting that the further substitution of the dialkyl diene (207) occurs with such apparent ease as it was reported that forcing conditions were required to insert a perfluoroisopropyl group into a similar position in the perfluorotri-isopropylpyridines (203) and (204):



(204) (203) (209)

>2%

Ref: 185

The authors thought that steric hindrance was the major reason for the reluctance of these pyridines to react, and, indeed, as the mixture contained a high proportion of the symmetrical pyridine (204) which, because it does not bear a fluorine atom para to the site of attack, would otherwise be supposed to be susceptible to further substitution,[187] this is quite reasonable.

In contrast with the pyridines (203) and (204), however, the dialkyldiene intermediate (207) and the trialkyldiene product (201) do not necessarily have planar rings and the steric crowding may therefore be correspondingly less severe.

5.3 Reactions with Methanol

5.3A Introduction

Several reactions between perfluoro-imines and methanol have already been reported and it is clear that imines with fluorine atoms bonded directly to the unsaturated carbon are highly reactive. In fact, perfluoro-2-azapropene (210) reacts so vigorously that all its fluorine atoms are removed.[191]

$$CF_3\text{-}N{=}CF_2 + CH_3OH \longrightarrow HF + NH_3 + (CH_3O)_2CO + CH_3OCH_3$$

Ref: 191

Two alternative mechanisms were proposed. The first involves a series of additions of methanol across the double bond followed by HF elmination,

$$\begin{tikzcd}
\underset{(210)}{CF_3\text{-}N{=}CF_2} \arrow[rr, "+\,CH_3OH"] & & CF_3\text{-}NH\text{-}CF_2OCH_3 \arrow[d, "-HF"'] \\
(CH_3O)_3C\text{-}NH\text{-}C(CH_3O)_3 \arrow[d, "CH_3OH"] & & CF_2{=}N\text{-}CF_2OCH_3 \arrow[ll, "\substack{i)\ +\,CH_3OH\\ ii)\ -\,HF}", "\text{Several times}"'] \\
C(OCH_3)_4 + NH_3 \arrow[r, "HF"] & (CH_3O)_2CO + CH_3OCH_3 &
\end{tikzcd}$$

Ref: 191

(The author considers the following elimination step to be the more likely however on the grounds that it minimises the number of fluorines bonded to unsaturated carbon,

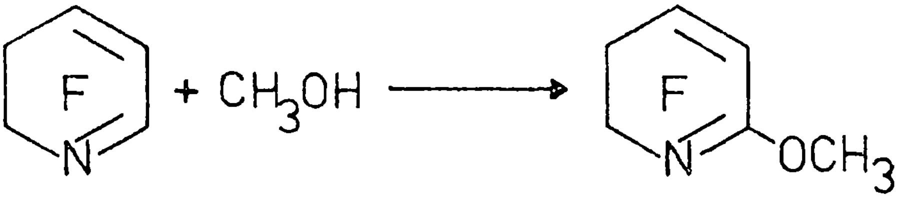
$$CF_3\text{-}NH\text{-}CF_2OCH_3 \xrightarrow{-HF} CF_3\text{-}N{=}CFOCH_3 \xrightarrow{etc.}\ )$$

The alternative mechanism involved the following initial steps:

$$\begin{tikzcd}
CF_3N{=}CF_2 \arrow[r, "+CH_3OH"] & , \arrow[r, "+CH_3OH"] & CF_3NH_2 + CH_3OCH_3 + COF_2 \arrow[d, "CH_3OH"] \\
 & & \text{Products}
\end{tikzcd}$$

Ref: 191

The reaction of the cyclic aza-1,3-diene (193), however, was more controlled and good yields of the simple mono substituted product (211) were reported,[192]

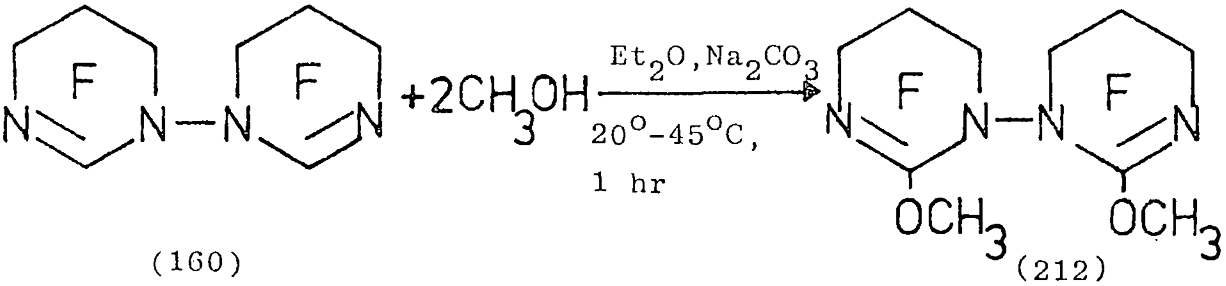


(193) (211)

Ref: 192

5.3B The Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Methanol

The imine dimer (160), when reacted with twice the stoichiometric amount of methanol, as a solution in diethyl ether, gave the -2,2'-dimethoxy derivative (212) in 38% yield.



(160) (212)

38%

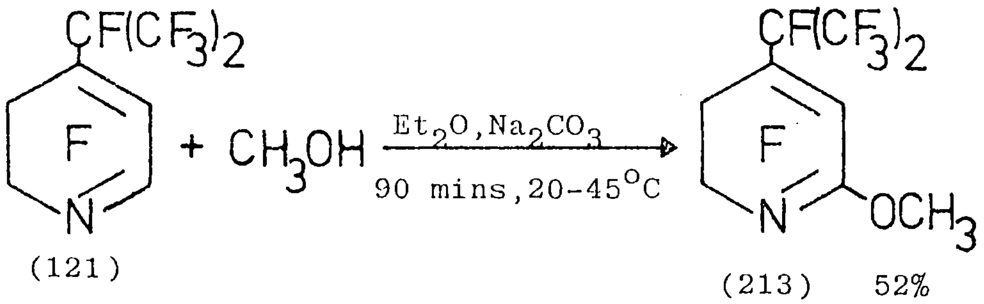
The dimethoxy derivative (212) was identified by its parent ion at m/e = 442 and by its ^{19}F and ^{1}H n.m.r. spectra. Thus, its ^{19}F spectrum consisted simply of three AB patterns, two of which overlapped at low field (92.4 and 95.3, 97.9 and 111.2 p.p.m.) identifying them as due to difluoromethylene groups next to nitrogen and the third was to higher field (135.7 and 138.1 p.p.m.) in a region typical of difluoromethylene bonded to carbon.

The ^{1}H n.m.r. spectrum contained a broad singlet only (at 3.12 p.p.m.) and the i.r. spectrum contained a weak band at 2,979

cm^{-1} assigned to the aliphatic $\geq$C-H bond in the methoxy groups and an intense absorption at 1,675 cm^{-1} was assigned to the imino ($>$C=N-) bond.

5.3C The Reation of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) with Methanol

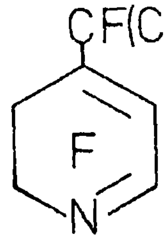
The -1-aza-1,3-diene (121) reacted with methanol in 1:1 stoichiometric amounts under the same conditions as the dimer (160) to give the -2-methoxy derivative (213) in good yield (52%) and traces of two unidentified products. The -2-methoxy derivative (213) was identified as such because its mass spectrum gave a parent ion at m/e = 369 whilst its ^1H n.m.r. spectrum consisted of a broad singlet only (3.13 p.p.m.) and the ^{19}F spectrum was similar to that of the starting diene (121) except that there was no signal in the low field region attributable to an imino fluorine (-CF=N). A weak band at 2,960 cm^{-1} in the i.r. was assigned to $\geq$C-H stretches in the methoxy substituent group and an intense band at 1,661 cm^{-1} with a shoulder at 1,680 cm^{-1} was assigned to the olefin and imine bonds.



(121)

(213) 52%

Upon reacting (121) with methoxide ion in molar ratio 1:4, at room temperature, a complicated mixture of polysubstituted products was obtained. The mixture was investigated by mass spectroscopy/g.l.c. which indicated the following degrees of substitution



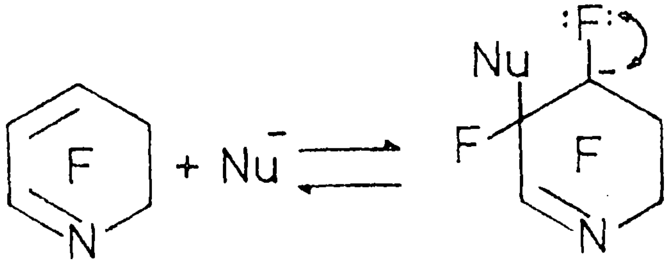
$$+ CH_3ONa \xrightarrow[CH_3OH]{20^{o}C,\ 18\ hr}$$

	Proportion of product estimated from g.l.c.
$C_8NF_{12}OCH_3$	8%
+ $C_8NF_{11}(OCH_3)_2$	11%
+ $C_8NF_{11}(OCH_3)_2$	22%
+ $C_8NF_{10}(OCH_3)_3$	20%
+ $C_8NF_{10}(OCH_3)_3$	16%
+ $C_8NF_9(OCH_3)_4$	23%

None of the isomers were isolated in a pure state upon attempting a separation by g.l.c.

The isolation of the monomethoxy derivative (213) of diene (121) confirms the higher reactivity of the imino fluorine at C-2 compared with the vinylic fluorine at C-3 in (121).

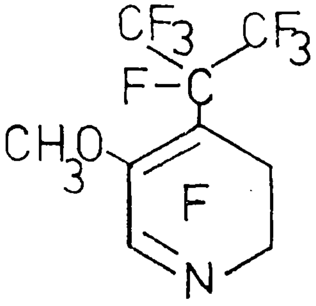
Whilst the low reactivity of C-3 to nucleophiles of the unsubstituted -1,3-diene (193) could be explained by the necessity for an unfavourable intermediate carbanion which would be destabilised by the electron pair repulsions of the fluorine bonded to the charged carbon atom thus:-



(193) (214)

when C-4 bears a perfluoroisopropyl group the equivalent anion would no longer be subject to such destabilisation. Therefore the absence of a -3-methoxy derivative such as (215) in the reaction of the -4-perfluoroisopropyl-1,3-diene (121) may rather be because the intermediate anion for a C-3 attack would be sterically destabilised by the perfluoro-isopropyl

Hypothetical product
from C-3 substitution



(215)

An alternative explanation which seems equally plausible is based on the observation that the unsubstituted -1,3-diene (193), itself, is also reported to react exclusively at C-2[192] although reaction at C-4 might have been predicted by analogy with the behaviour of pentafluoropyridine, and other aza-aromatics, which are usually most reactive at positions para to nitrogen.[190] Therefore, it might be that, in the -1-aza-1,3-diene systems, attack occurs preferentially at C-2 because, in the initial state, this site is highly polarised by the electronegative nitrogen. It is not possible to distinguish these possibilities for the -4-perfluoroisopropyl compound on the basis of the available evidence.

5.3D The Reaction of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153) with Methanol

The -1,3-diaza-3,6-diene (153) was recovered unchanged after refluxing it for an hour in ether with methanol in 1:1 stoichiometry. However, when reacted with sodium methoxide in 1:1 stoichiometry in methanol for 20 hrs a complicated mixture of at least eight products was obtained. The steric problems of attacking an imino group substituted by perfluoroisopropyl would be great but, if achieved, rearrangements to render further sites available could well occur.

5.4 Reactions with Phenol

5.4A Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Phenol

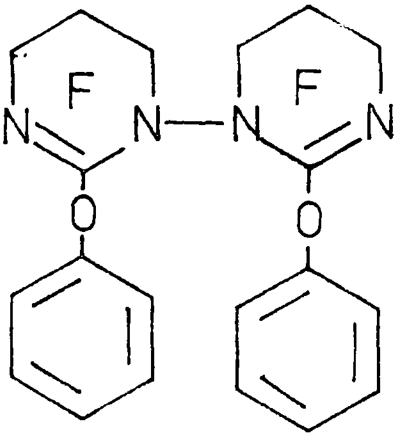
The di-imine (160) was reacted with phenol in 1:2 stoichiometry in ether in the presence of triethylamine. The product was a high melting solid for which no suitable solvent for n.m.r. spectroscopy could be found. A parent peak at m/e = 566 was consistent with the formation of a diphenoxy derivative. The i.r. spectrum contained weak bands at 3070 and 3098 cm^{-1} attributable to phenolic $\gtrdot$C-H stretches, a strong broad band at 1705 cm^{-1} attributable to $>$C=N- stretching and sharp bands at 1590 cm^{-1} and 1603 cm^{-1} attributable to phenolic $>$C=C$<$ stretches.

On the basis of this evidence the product was thought likely to be the diphenoxy compound (216).

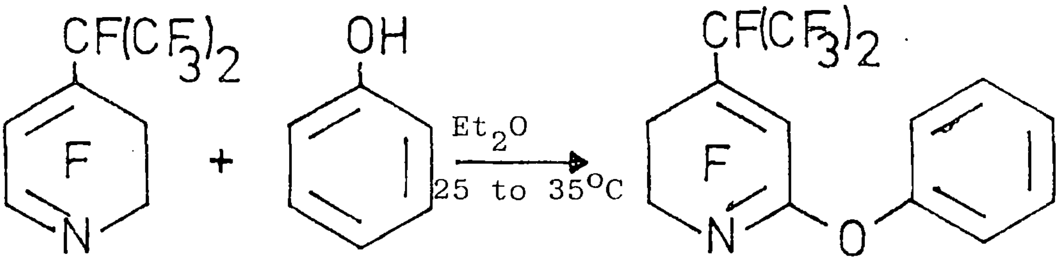
5.4B The Reaction of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) with Phenol

The product from the reaction between the aza-diene (121) and phenol in 1:1 stoichiometry was identified as the -2-phenoxy derivative (217), confirmed by a parent ion at m/e = 431 in its mass spectrum and ^{1}H and ^{19}F n.m.r. spectra. Thus, the ^{19}F n.m.r. spectrum was similar to that of the starting aza-diene (121) except for the absence of a low-field signal attributable to an imino fluorine (-FC=N-) whilst an envelope of unresolved signals at 7.11 p.p.m. (from T.M.S.) in the aromatic region of the ^{1}H n.m.r. was attributed to the phenolic protons.

The reactions of the imines with phenol are hence very similar to the reactions with methanol and similar mechanisms are thought to apply.



(216)

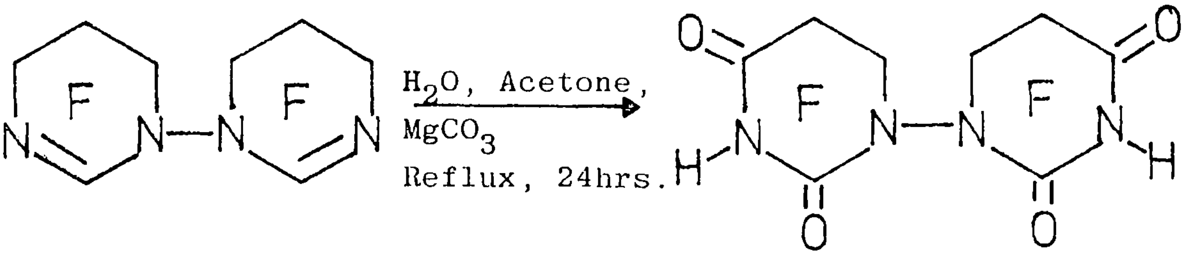


(121) (217)

5.5 Hydrolyses

5.5A The Hydrolysis of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)

Upon refluxing the dimer (160) with an excess of water in acetone for 24 hours a single product was obtained in high yield which was found to be the tetraketo derivative (218).



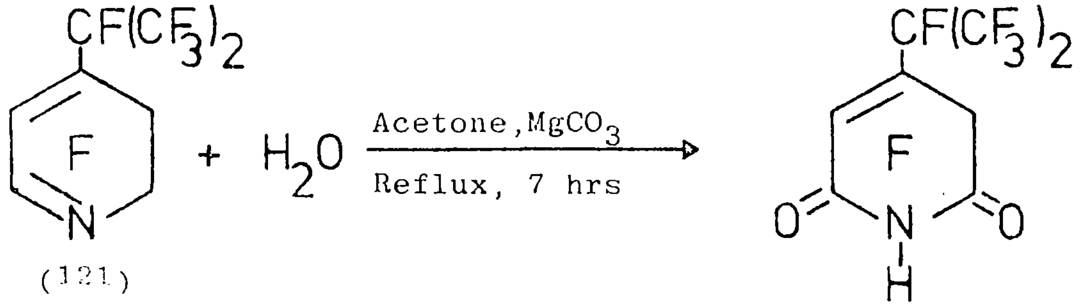
The tetraketone (218) was identified as such by its ^{19}F n.m.r. spectrum which consisted, simply, of two AB patterns, one of which was to lowfield in a region typical of a CF_2 group next to nitrogen (98.72 and 105.41 p.p.m.) whilst the other was to higher field in a region typical of a $>CF_2$ bonded to carbon atoms only (120.71 and 130.07 p.p.m.).

The mass spectrum gave a parent ion at m/e = 370 which together with the data from elemental analysis, confirmed the empirical formula $C_8N_4O_4F_8H_2$. Peaks due to the successive loss of two HF molecules from the parent ion were present at m/e = 350 and 330 and a peak at m/e = 328 was interpreted as due to the loss of a hydrogen isocyanate (HNCO) molecule from the parent ion.

A multiple band peaking at 3143 and 3239 cm^{-1} in the i.r. spectrum was typical of the $>$N-H stretches of a lactam associated in the solid state and a very strong multiple band with peaks at 1740 and 1795 cm^{-1} was assigned to the $>$C=O absorptions. These latter were at shorter wavelengths than is typical for a lactam but it is known that electron withdrawing groups on the adjacent nitrogen, in this case a difluoromethylene group for one carbonyl group and a carbonyl group for the other, cause shifts to shorter wavelengths.[193]

5.5B <u>The Hydrolysis of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (^{121}) and -1,4-diene (^{122})</u>

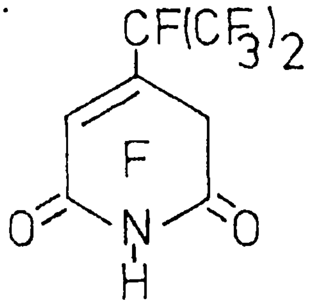
The diene (121) was hydrolysed with excess water in acetone under similar conditions to those of the dimer (^{160}). The product, obtained in reasonable yield, was identified as the amido compound (219).



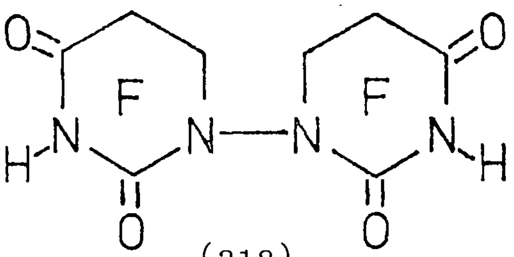
(121)

(219) 46%

Thus, the ^{19}F n.m.r. spectrum contained, apart from signals readily identifiable as those due to a perfluoroisopropyl group by integration and chemical shifts (75.5 and 185.5 p.p.m.), two sets of signals integrating to 2 and 1 respectively. Both signals were at midfield (93.7 and 100.4 p.p.m.) and were identified as due to a ring difluoromethylene group ($>CF_2$) and a vinylic fluorine atom ($F-\overset{|}{C}=C<$). Strong coupling between the difluoromethylene group and the tertiary fluorine of the perfluoroisopropyl group confirmed the proximity of the former to C-4 whilst the high field chemical shift of the vinylic fluorine confirmed that it was not adjacent to nitrogen. The mass spectrum did not give a discernible parent ion, however, and the highest m/e value was at 314, interpreted as due to the P-F ion. Elemental analysis confirmed the empirical formula as $C_8NO_2HF_{10}$. A prominent peak at m/e 290 was interpreted as due to a loss of a hydrogen isocyanate fragment (P-HNCO). The same fragmentation process was noted, earlier, in the mass spectrum of the amido compound (218) derived from the dimer (160) and this reflects the structural similarities between the pyridine product (219) and the dimer product (218).

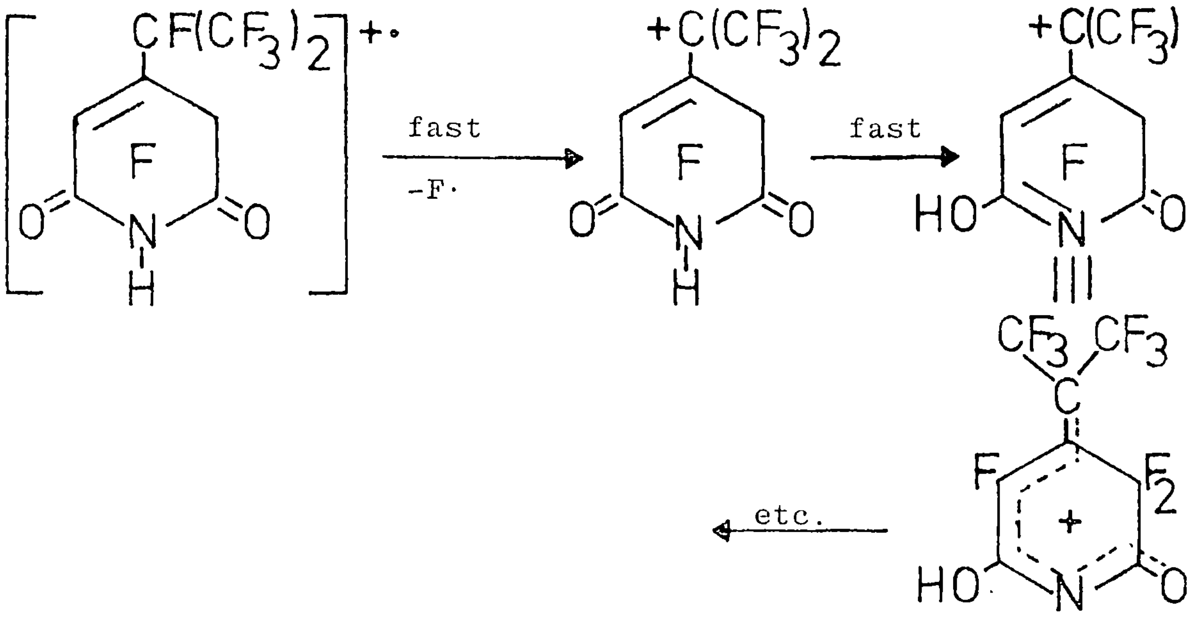


(219)



(218)

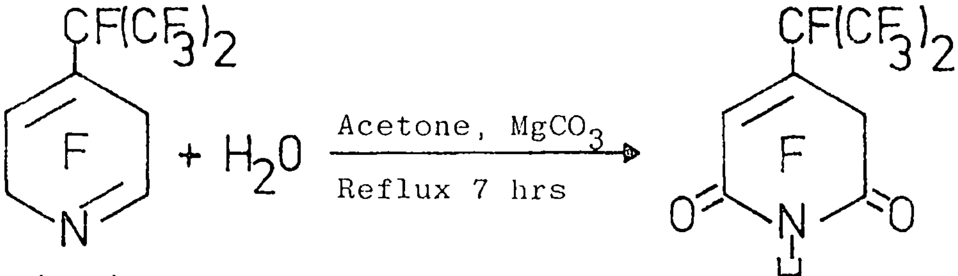
The lack of an observable parent ion peak in the mass spectrum of amide (219) is thought to reflect the ease with which the parent ion would lose the tertiary fluorine atom ($\geqslant CF$) in the substituent perfluoroisopropyl group to form a highly delocalised cationic species (220). The similarity of the structures of the amides (218) and (219) was also reflected in



(220)

some features of their i.r. spectra. Thus (219) also displayed a multiple band of $>$N-H stretches (at 3118 and 3212 cm^{-1}) and of carbonyl stretches (at 1735 and 1778 cm^{-1}) but, by contrast with (218), the olefinic bond in (219) gave rise to an additional band in the double bond region at 1685 cm^{-1}.

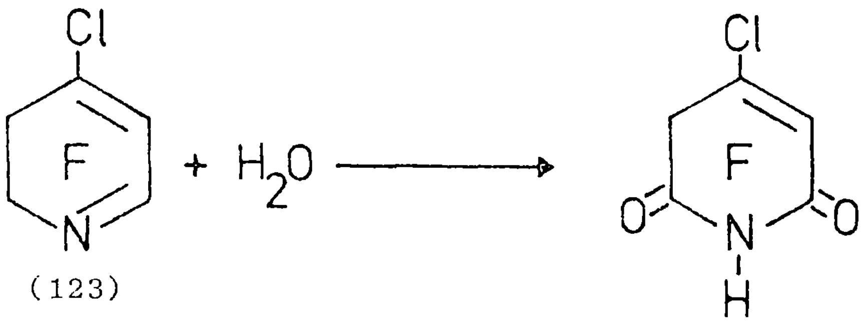
The -1,4-diene (122) when reacted under the same conditions was also converted to the amide (219).



(122)

(219) 32%

The -4-chloro-diene (123) was also reported to hydrolyse to an amide.[192]

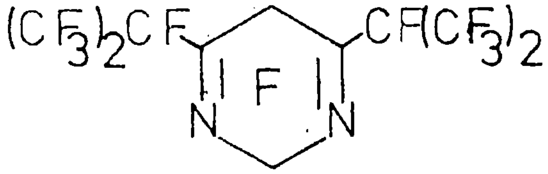


(123)

Ref: 192

5.5C Attempted Hydrolysis of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153)

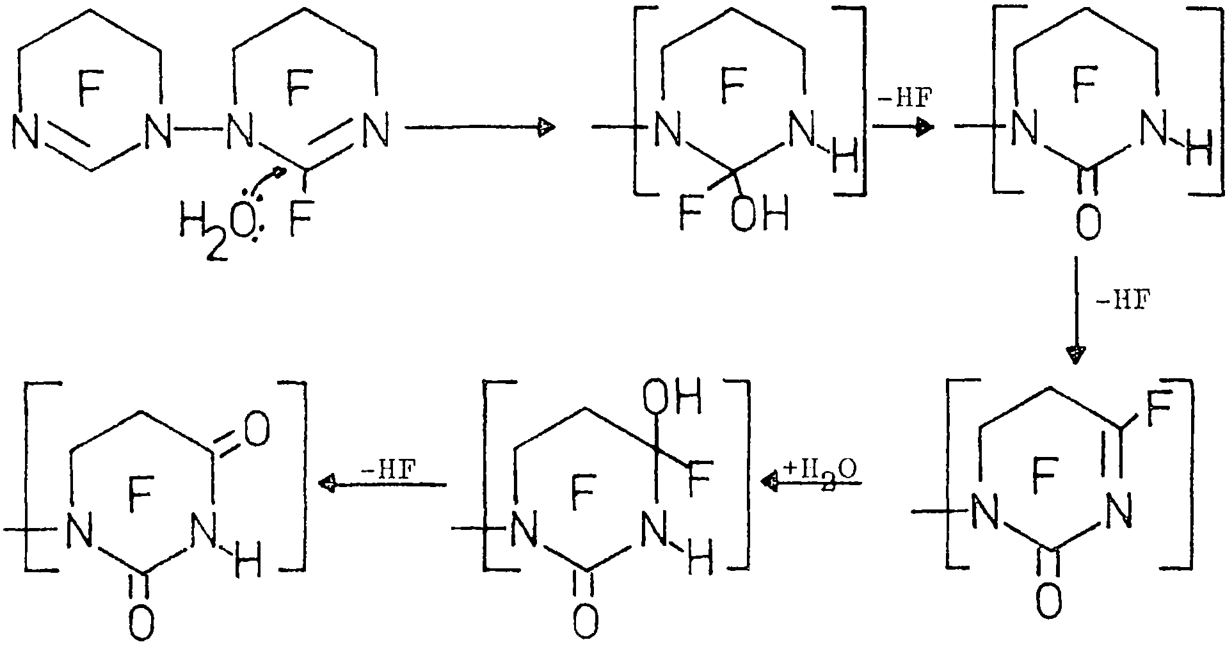
The diene (153) appeared inert to reaction with water under conditions similar to those in which the imines (160), (121) and (122) were converted to amides.



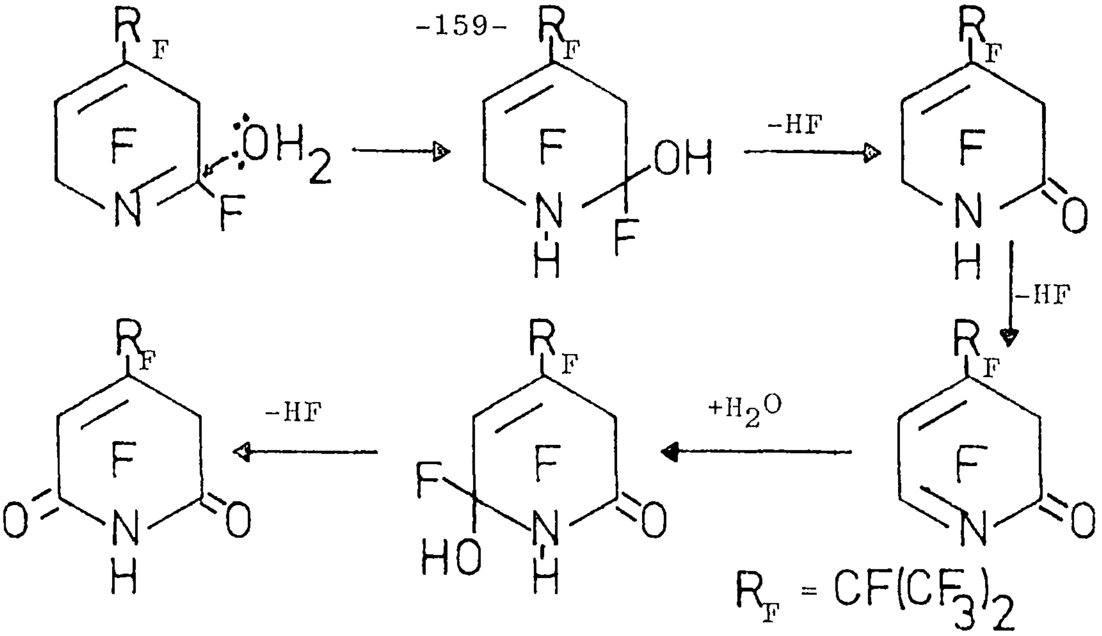
(153)

5.5D Possible Mechanism for the Hydrolyses

The hydrolyses are thought to proceed via a series of additions of water followed by the elimination of HF as in:-



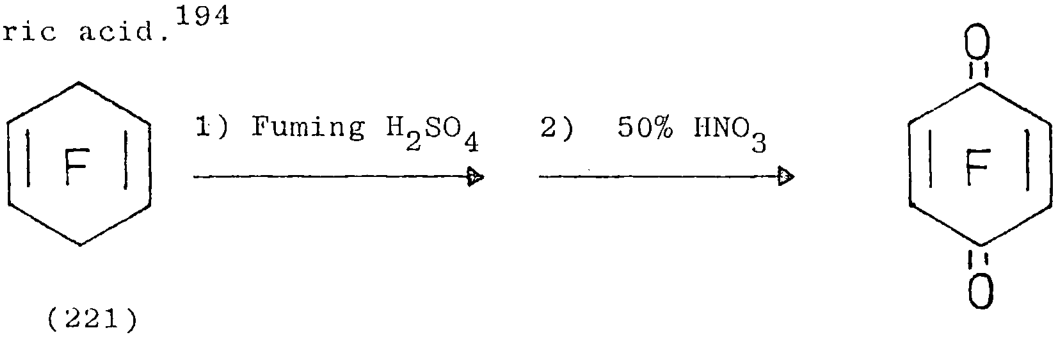
In the dienes (121) and (122), the imino fluorine is, once more, seen to be more labile than the olefinic fluorine atom and, again, it seems most likely that this is because the nitrogen atom activates C-2 to attack by polarisation.



A similar mechanism is proposed for the -1,3-diene (121). The failure of the dialkyl diene (153) to react is presumably a result of unfavourable steric interactions between the substituent perfluoroisopropyl group and the incoming nucleophile.

5.5E Attempted Hydrolysis of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153) in Sulphuric Acid

It was reported that the difluoromethylene groups of the -1,4-diene (221) may be hydrolysed to carbonyl by hydrolysis in fuming sulphuric acid followed by oxidation of the residue in nitric acid.[194]



(221)

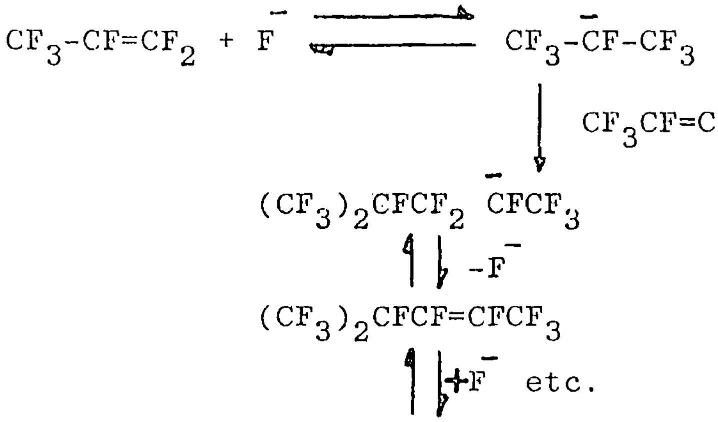
Ref: 194

The -3,6-diene (153) has an analogous structure to the -1,4-diene (221) but upon subjecting a sample to prolonged heating and shaking with fuming sulphuric acid at 145°C for 17 hrs the starting material was recovered unchanged. It is not known whether this is because the -3,6-diene (153) is not reactive towards sulphuric acid or whether the immisibility of the reactants was responsible for the lack of reaction.

5.6 Reactions with Fluoride Ion

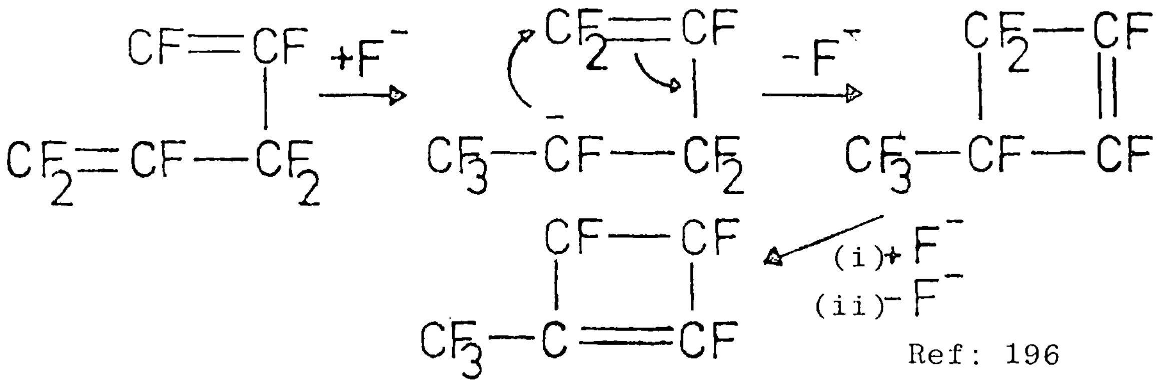
5.6A Introduction

As described in Chapter 2 (Section 2.3B) fluoride ion, when not solvated, behaves as a powerful nucleophile and it will add to an olefin or an imine to generate a carbanion. An example is the oligomerisation of hexafluoropropene.[195]



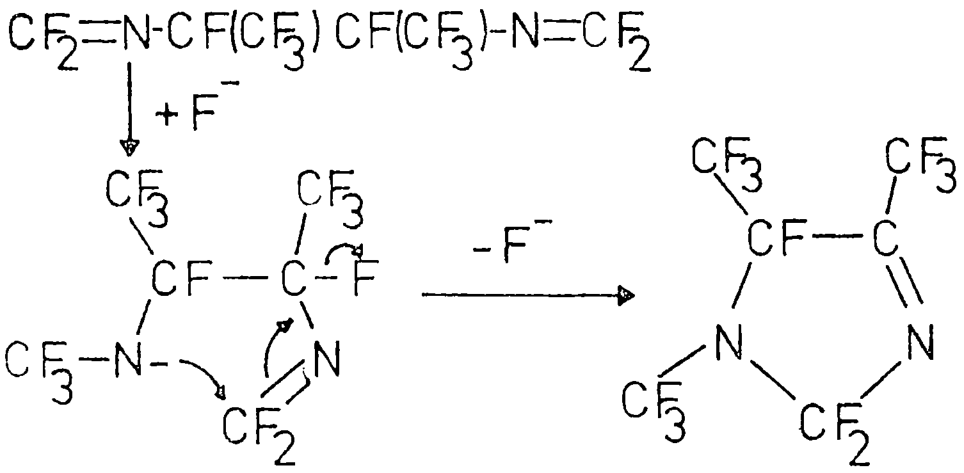
Ref: 195

In the absence of a trapping agent and when oligomerisation is less favourable, rearrangements often occur and perfluoro-olefins are converted into thermodynamically more stable isomers.[196]



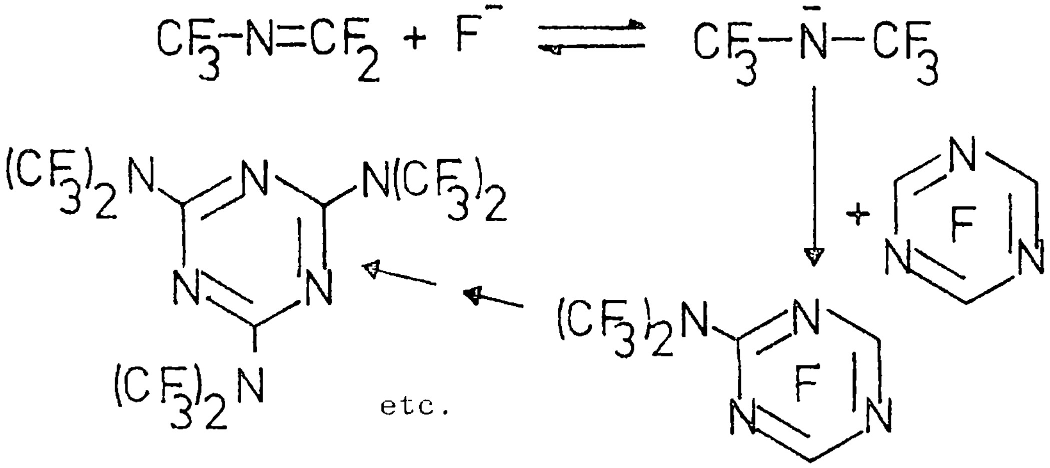
Ref: 196

Similar fluoride ion induced reactions have been observed with imines. The negative charge resides on the nitrogen in the resultant anionic intermediate. An example of a fluoride ion induced rearrangement of a perfluoroimine is:-



Ref: 197

The intermediate anion may be trapped by a suitable trapping agent such as a perfluoro-aromatic compound activated to nucleophilic substitution. Cyanuric fluoride is a highly suitable reagent in that respect.[198]

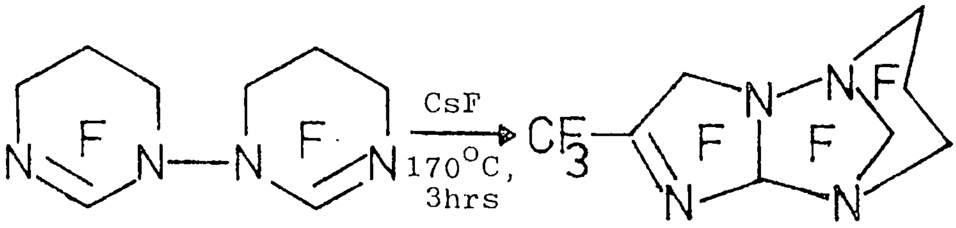


Ref: 198

5.6B Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Fluoride Ion

The dimer (160) was reacted with caesium fluoride to give, apart from recovered starting material, one of two isolated products, or a mixture of the two, depending on the conditions. Only one of the two new products was identified.

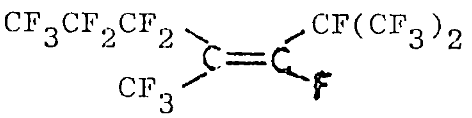
Thus, when the dimer (160) was heated with caesium fluoride, in the absence of a solvent, the product consisted of recovered (160) and a new compound (222) which has been tentatively identified as perfluoro-4-methyl-1,2,5,7-tetra-azatricyclo-[5.3.1.0^{2,6}]undec-4-ene (222).



(160) (222)

A parent ion at m/e = 418 and elemental analysis confirmed the product (222) to be an isomer of the starting material (160). The ^{19}F n.m.r. spectrum contained five sets of signals attributable to difluoromethylene ($>CF_2$) groups by their integrations and mid-field shifts. In addition, four out of these five sets of signals exhibited AB splitting patterns. The only signals not attributable to difluoromethylene groups were a singlet integrating to 3 at 58.6 p.p.m. and a signal, hidden under one line of one of the AB patterns, integrating to 1 at 106.3 p.p.m.

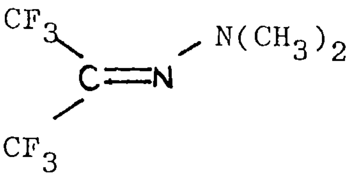
The signal at 58.6 p.p.m. indicates the presence of a trifluoromethyl ($-CF_3$) group on the molecule which in turn indicates a ring contraction to have occurred during the formation of the product. The absence of other signals in the low-field region below 80 p.p.m. indicates the absence of imino fluorine atoms ($-CF=N-$). The shift of the trifluoromethyl signal (58.6 p.p.m.) is typical for a trifluoromethyl group bonded to an unsaturated carbon, as the following models indicate:



56 p.p.m.

Ref: 199

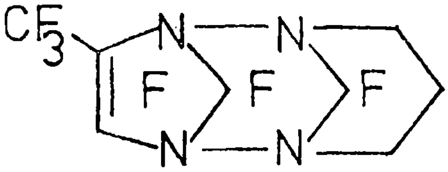
52 p.p.m.



63.7 p.p.m.

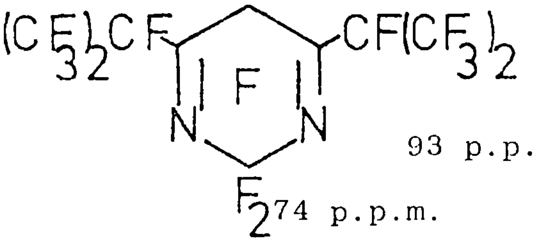
Ref: 200

A strong absorption at 1740 cm^{-1} in the i.r. spectrum confirmed the presence of an unsaturated bond. To accommodate these data, the trifluoromethyl group ($-CF_3$) must be situated either on a carbon doubly bonded to nitrogen ($CF_3C=N-$), as in the preferred structure (222), or on a carbon doubly bonded to carbon ($CF_3-C=C\langle$). The latter situation would imply the presence of four bridgehead nitrogen atoms in structures such as (223), but it is difficult to see how such compounds could have formed from the starting material (160).

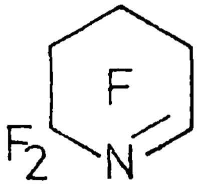


(223)

The experimental data does not appear to be consistent with such structures, either, as only one of the difluoromethylene ($\rangle CF_2$) groups resonates at sufficiently lowfield, with lines at 88.3 and 98.6 p.p.m., to have two adjacent nitrogen atoms, as the models below indicate:

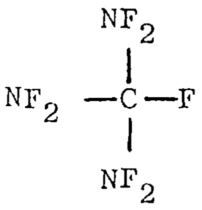


Ref: Section 3.7



Ref: 163

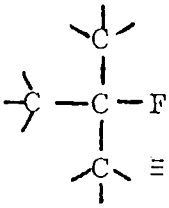
The signal at 106.3 p.p.m., integrating to 1, could be interpreted as due to a fluorine atom bonded to unsaturated carbon ($-CF=C\langle$) as in the less favoured structure such as (223) but it is argued on the basis of the model compound (198) that the deshielding influence of three adjacent nitrogen atoms might well be sufficient to reduce the chemical shift from the high field position usually observed when tertiary fluorines are adjacent to carbon atoms only, as in (224), and structure (222) remains preferred.



139 p.p.m.

(198)

Ref: 185



F 70 to 120 p.p.m. w.r.t CF_3COOH

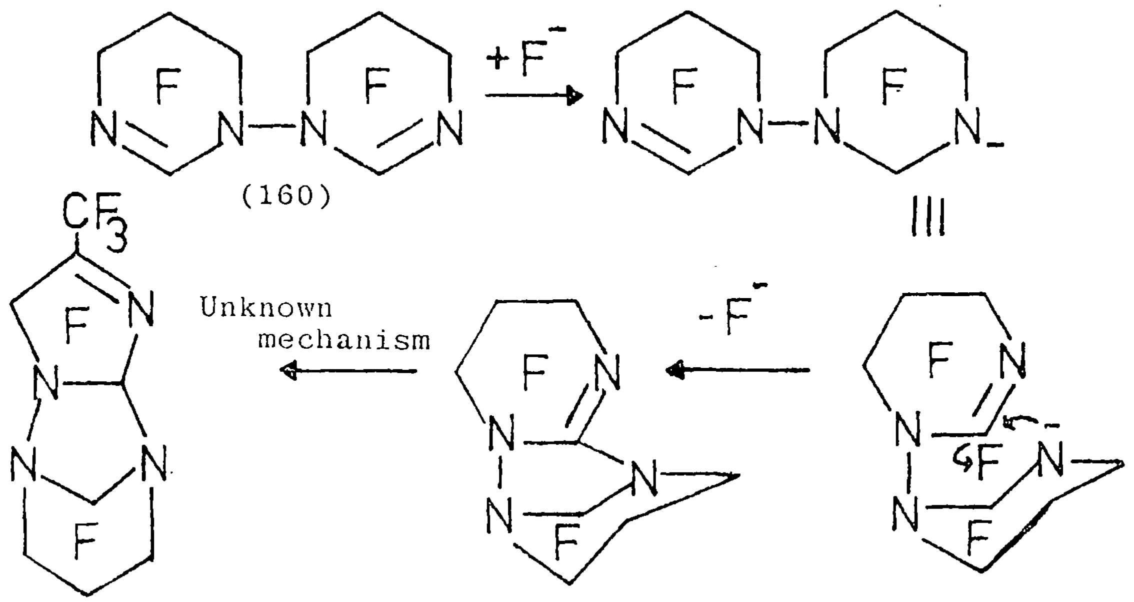
≡148 to 198 p.p.m. w.r.t $CFCl_3$

(224)

Ref: 177

When the dimer (160) is heated with caesium fluoride in the presence of sulpholan as a solvent, at 140°C for 2 hrs, a new product, (225) which was not identified, is obtained as well as (222). With the same solvent at 180°C for 3 hrs the new compound (225) is the only volatile product apart from gaseous fragmentation products.

The formation of (222) is only partially understood. Intra-molecular reaction to form a tricyclic system could easily occur via the following nucleophilic mechanism:



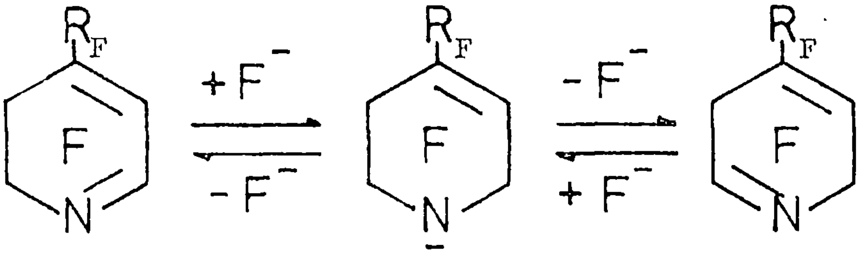
(160)

(222)

The ring contraction reaction, however, is not understood at present.

5.6C The Reaction of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) and -1,4-diene (122) with Fluoride Ion

As already referred to in Section 2.5A, when either the -1,3- or the -1,4-dienes (121) or (122) are heated with caesium fluoride, in the presence of a solvent, a mixture of both in molar ratio 7:3 is obtained.



$R_F = CF(CF_3)_2$

By analogy with the behaviour of other nucleophiles it is assumed that C-2 is the site of addition.

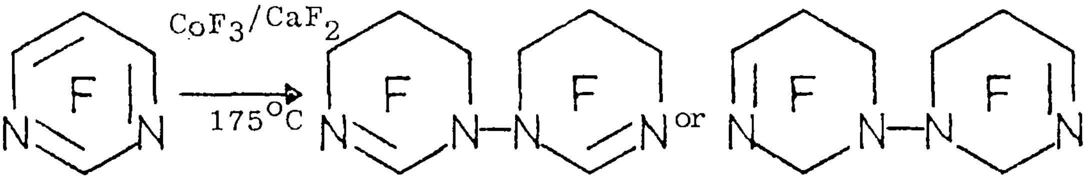
5.6D The Attempted Reaction of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153) with Fluoride Ion

Upon stirring the diene (153) with caesium fluoride in tetraglyme at 50°C for 15 hrs, no new products could be detected. It is unlikely that fluoride ion addition does not take place under these conditions and hence it is concluded that diene (153) is more stable than its possible isomers. This conclusion was used to interpret the mechanism of its formation from the pyrimidine (152) in Section 3.10.

5.7 Reactions with Chloride Ion and Reactions of Chloride Ion Derivatives

5.7A Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Chloride Ion

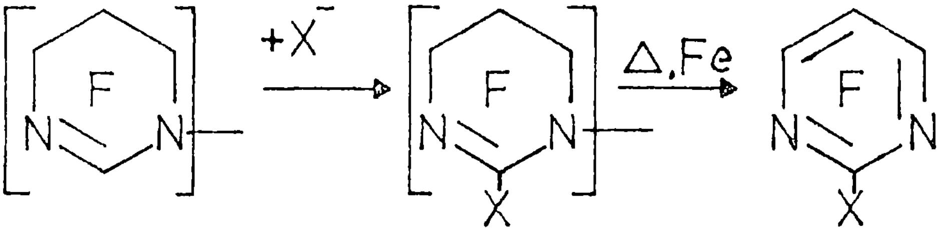
When the fluorination of tetrafluoropyrimidine (156) with cobalt III fluoride was reported, the authors were not prepared to completely dismiss the possibility of the alternative structure (226) for the dimeric product although the ^{19}F n.m.r. evidence strongly favoured (153).[163]



(156) (153) (226)

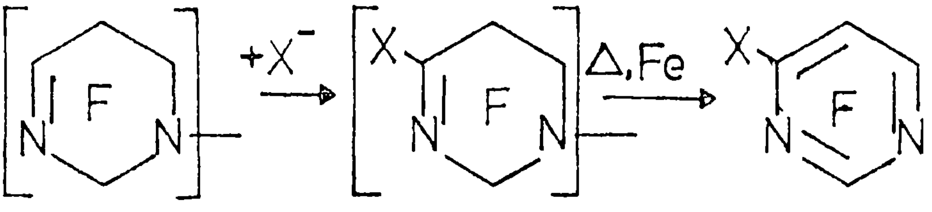
Ref: 163

In view of the proven susceptibility of the imino fluorine (-CF=N-) in the dimer to nucleophilic substitution and the ease with which the dimer may be defluorinated to regenerate a pyrimidine (described in Section 7.3) it was anticipated that an unambiguous proof of structure (153) might be obtained by the following series of reactions:



(227)

Nucleophilic substitution, Defluorination



(228)

X^- = nucleophile

Thus the symmetrical pyrimidine (227) would be readily distinguished from (228) by ^{19}F n.m.r. spectroscopy.

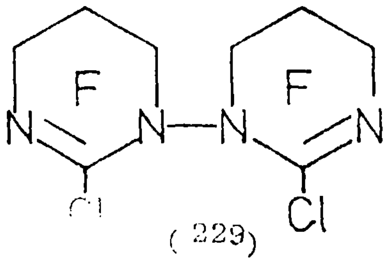
Chloride ion was the chosen nucleophile on the grounds that a chlorine atom would be less thermally labile at the necessary defluorination temperature than other possible substituents.

Lithium chloride was chosen as the source of chloride ion because, as was discussed in Section 2.3B (a), although when M is a large cation such as K^+ or Cs^+, the equilibrium below tends to the left, a reduction in the ionic radius of M reverses the equilibrium to the right:

$$R - F + MCl \rightleftharpoons R - Cl + MF$$

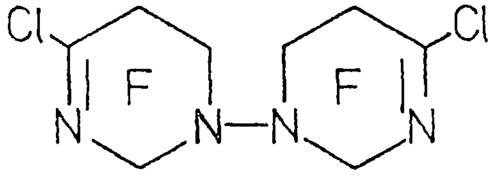
This has been attributed to the higher lattice energy of lithium fluoride compared with the chloride.

Thus, upon stirring the dimer (160) with a slurry of lithium chloride in sulpholan at 112°C for 12 hrs, a dichloro derivative was obtained in 68% yield. The product was identified as a dichloro derivative by its mass spectrum which gave a parent ion at m/e = 450 with a P:P+2:P+4 intensity ratio of 100:66:11. The ^{19}F n.m.r. spectrum contained three AB systems, one to high field (131.76 and 141.43 p.p.m.) and two overlapping at low field (91.05 and 129.98, 93.02 and 102.76 p.p.m.) suggesting the presence of two non-equivalent difluoromethylene groups next to nitrogens and one difluoromethylene in a position isolated from nitrogen as in structure (229) rather than (230). The absence of any other signals confirmed that the imino fluorines (-C$\underline{F}$=N-) in the starting material had been substituted.



(229)

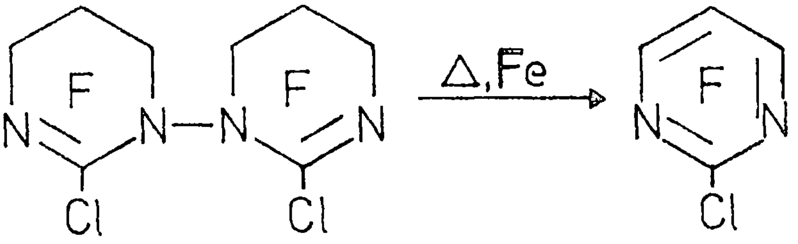
or



(230)

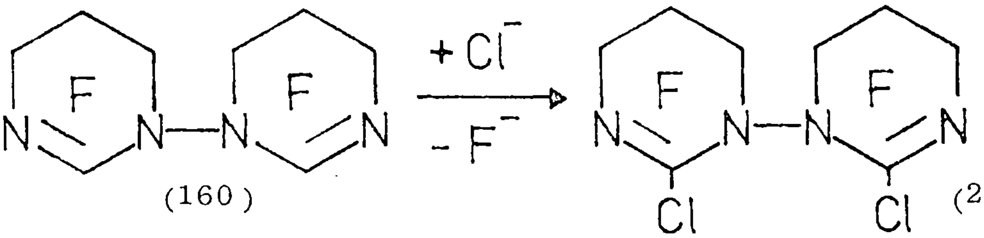
G.l.c./mass spectroscopy of the crude product prior to the isolation of the dichloro compound by recrystallisation indicated, in addition to the dichloro compound, the presence of a monochloro derivative (7% of the product), a trichloro derivative (8% of the product) and traces of a tetrachloro derivative.

The dichloro derivative (229) or (230) was then defluorinated by passing it, as the vapour in a stream of nitrogen, over heated iron filings. The product contained only one major component which, after isolation by g.l.c., was identified as 2-chlorotetrafluoropyrimidine (228) by its parent ion at m/e = 168, with P:P+2 = 100:33 indicating one chlorine, and the ^{19}F n.m.r. spectrum which contained only two signals in the intensity ratio 1:2. The more intense signal was a doublet at low field in a typical (-CF=N-) region and the other signal was coupled to it as a triplet to higher field.



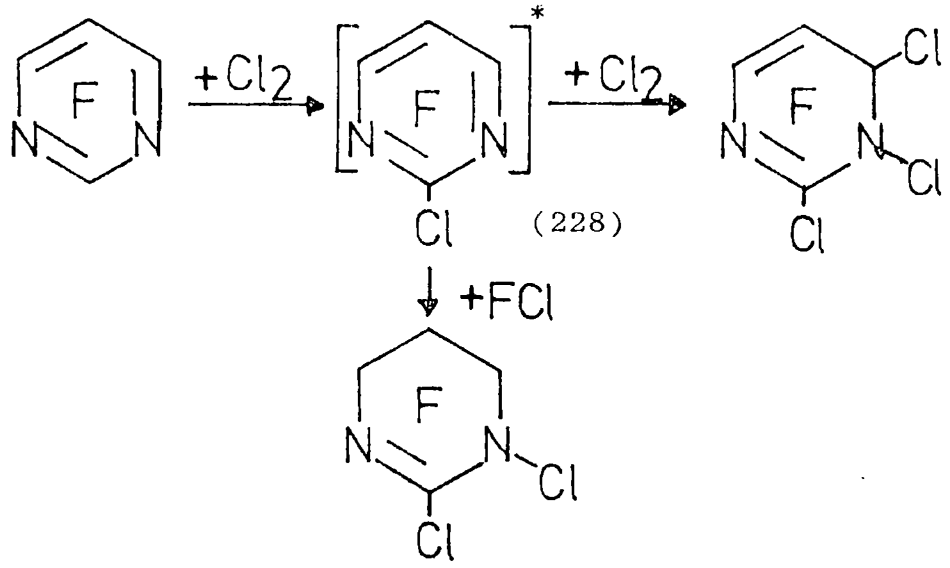
(229) (228) 59%

Therefore the structure of the original dimer can be confirmed as (160) and its dichloro derivative as (229).



(160) (229)

The pyrimidine (228) was proposed as an intermediate in the reaction between tetrafluoropyrimidine and chlorine.[201]



* = not isolated

Ref: 201

CHAPTER 6

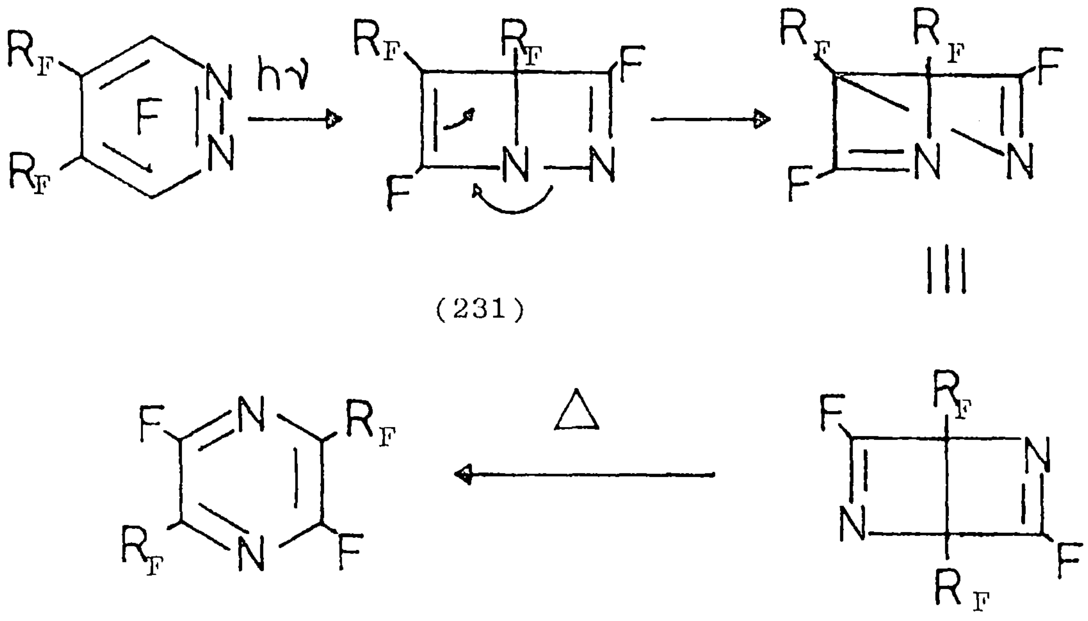
THE PHOTOLYSIS OF SOME PERFLUORO-AZADIENES AND -IMINES

6.1 Introduction

In this chapter the results of a series of photolyses of some of the new perfluoro-azadienes and -imines, whose syntheses were described in Chapter 3, are discussed. These reactions were performed in co-operation with R. Middleton.

The photolytic rearrangement of perfluoropolyalkylpyridines and -pyridazines has been studied in detail recently,$^{202-205}$ and, by trapping and identifying the intermediates of some unambiguously labelled systems, Chambers et al. have elucidated the reaction pathways of some of these reactions and have been able, in some cases, to propose detailed mechanisms.

The reactions were found to proceed via Dewar benzene intermediates, such as (231) or (232), and prismanes such as (233):

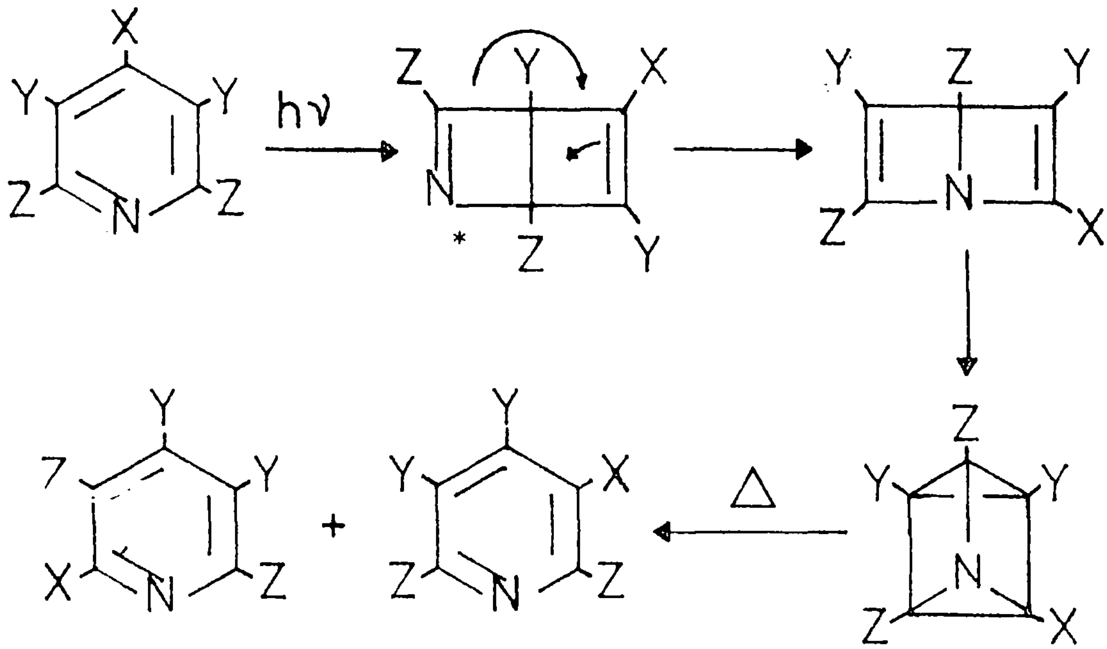


(231)

(232)

$R_F = CF(CF_3)_2$

Ref: 203, 205

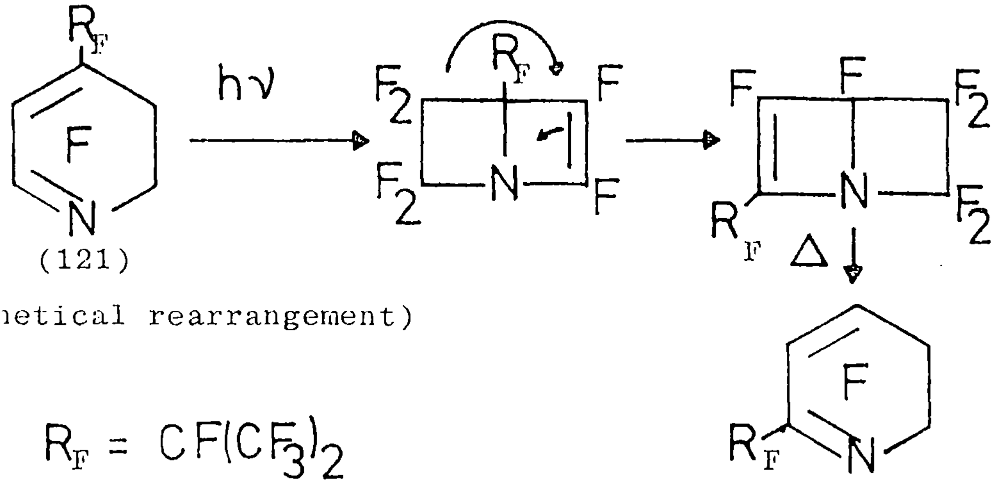


(233)

X = C_2F_5 * not isolated
Y = CF_3
Z = $CF(CF_3)_2$

Ref: 205

The formation of para-bonded intermediates analogous to the Dewar benzenes and subsequent rearrangement of azadienes, such as (121), seemed possible therefore, although of course, the formation of analogues of prismane intermediates is impossible.



(121)

(hypothetical rearrangement)

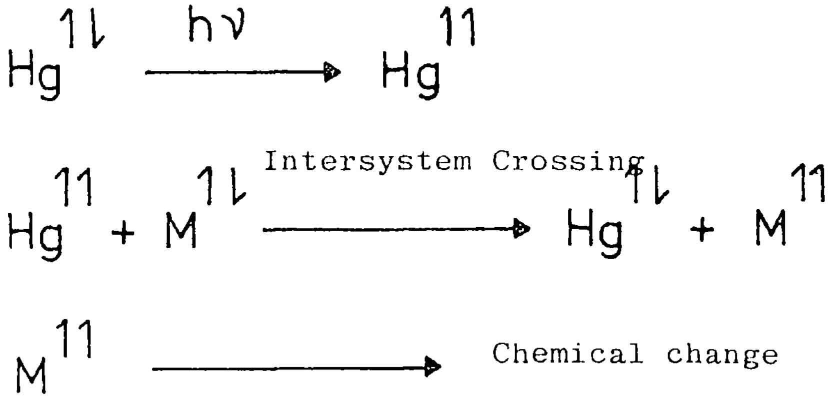
$R_F = CF(CF_3)_2$

However, in no case was this process observed in practice and quite different behaviour was encountered, as is described below.

The photolyses were performed by irradiating silica tubes into which small amounts of substrate had been sealed in vacuo. The silica is transparent to the mercury emission at 253.7 nm but in several cases where the substrate contained only one double bond, or was an unconjugated diene, its absorption maximum was at much shorter wavelength than 253.7 nm and it was necessary to include traces of mercury vapour in the reaction vessels in order to sensitise the substrate to the radiation.

Mercury sensitisation is a well established technique in photochemistry[206] and is based on the principle that molecules whose absorption is very weak at a particular wavelength may still be caused to absorb energy indirectly from excited mercury triplet states.

Thus energy is initially absorbed by mercury vapour with the formation of excited mercury triplet states and is then transferred from the mercury triplet to the ground state of the organic substrate by intersystem crossing. This generates excited triplet states of the organic substrate which may then proceed to further reaction.



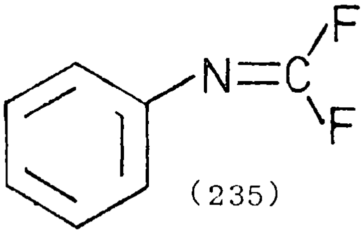
M = Organic molecule

The behaviour of -1-aza-1,3-dienes is described firstly, followed by -diaza- analogues of -1,4-dienes and, finally, the behaviour of perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160), in a sense a -1,5-diene, and the imine perfluoro-1-azacyclohex-1-ene (161) is described.

6.2 The Photolysis of Perfluoro-4-isopropyl-1-azacylclohexa-1, 3-diene (^{121})

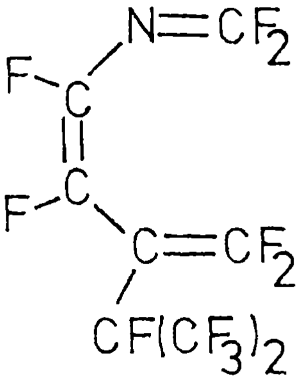
The -1,3-diene (121) gave a broad absorption in the ultra-violet with a maximum at 228 nm ($\epsilon = 5.77 \times 10^3$) with sufficient absorption at 253.7 nm for reaction to be possible without the need for a sensitiser (see Section 6.1).

Upon irradiation in the vapour phase, (121) reacted to give two new products and traces of other material. The major product (70% of the mixture) was identified as perfluoro-6-methyl-5-methylene-2-azahepta-1,3-diene (234) by its parent ion at m/e = 357 in the mass spectrum, which indicated it to be an isomer of the starting material, and by ^{19}F n.m.r. and i.r. spectroscopy. Thus, apart from signals in the ^{19}F n.m.r. spectrum readily identifiable as due to the perfluoroisopropyl group there were six other signals, all integrating to 1. Two were at very low field (32.9 and 51.2 p.p.m.) and were broad and they indicate the presence of a difluoroimine group ($-N=CF_2$). Fluorine atoms in similar sites on the model compound (235) were reported to resonate at 50.4 p.p.m. and 58.2 p.p.m. and were also broad.

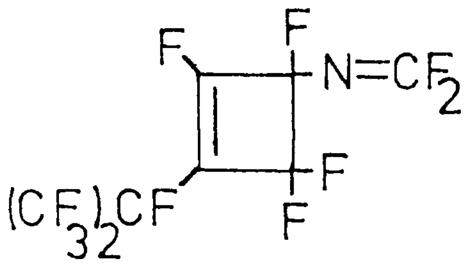


(235) Ref: 207

The remaining signals resonated in mid-field (96.1, 113.8, 114.3 and 136.7 p.p.m.) and can therefore be attributed to fluorine atoms at olefinic sites as is consistent with the assigned structure. The possibility of an alternative structure namely the cyclobutene (236), was also considered. The evidence presented so far does not eliminate the cyclobutene as the non-equivalent geminal fluorine atoms and, plausibly, the tertiary fluorine atom, under the downfield influence of an adjacent nitrogen atom, might also resonate at mid-field.



(234)



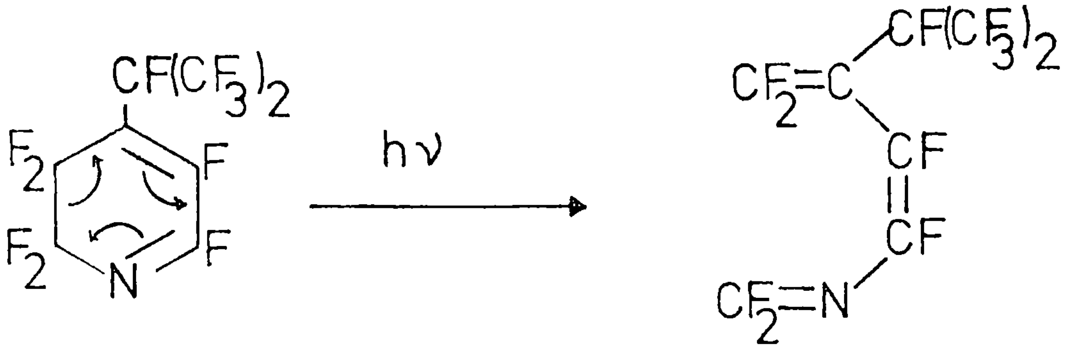
(235)

Structure (235) was discounted however on the basis of i.r. evidence which gave three absorptions in the $>C=C<$ and $>C=N-$ stretching region at 1680, 1767 and 1775 cm^{-1}.

Triene (234) was found to be the cis isomer because the fluorine atoms on C-3 and C-4 were coupled to each other with a coupling constant of 19 Hz, typical for cis olefins but well below the range of values for trans olefins (Banks gives a range of 0 to 58 Hz for cis coupling and 105 to 148 Hz for trans coupling).[177]

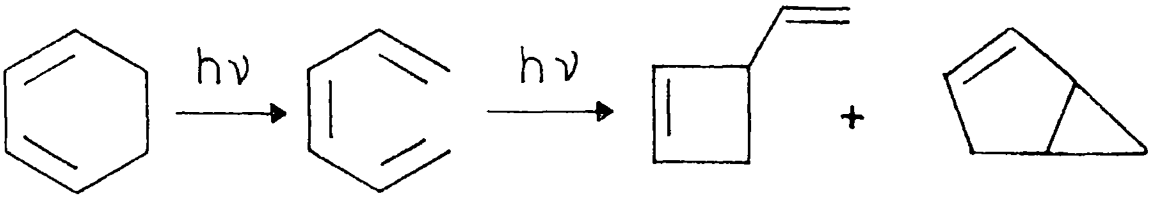
The minor product was not isolated in a sufficiently pure state to be identified.

The formation of triene (234) is thought to result from a concerted electrocyclic ring opening mechanism which is consistent with its retention of configuration:



(121) (234)

A similar reaction was noted when cyclohexa-1,3-diene (237) was irradiated, a triene (238) being first formed.[208]



(237) (238) (239) (240)

Ref: 208

Upon further irradiation a compound (239) equivalent to (236) was formed.

6.3 Attempted Photolysis of Perfluoro-2,3,4-tri-isopropyl-1-azacyclohexa-1,3-diene (201)

By contrast with the -4- substituted -1,3-diene (121), the -2,3,4- trisubstituted -1,3-diene (201) failed to react even after irradiating under the same conditions as for (121) for 203 hrs. Its u.v. spectrum indicated λ_{max} at 231 nm ($\varepsilon = 3.9 \times 10^3$) and at the exciting wavelength, 253.7 nm, ε was approximately 1.3×10^3 and therefore the molecule was sufficiently absorbing for reaction to occur.

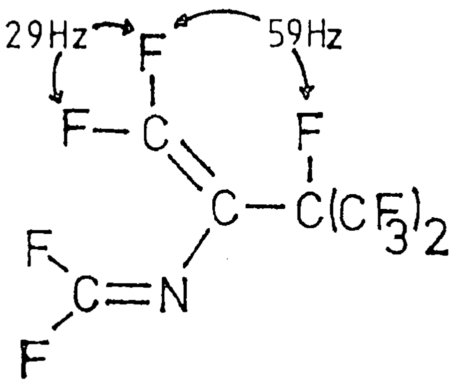
This may be understood if it is assumed that, as is apparently the case with (201), any reaction would take place by an electrocyclic triene formation. As was postulated in Section 5.2, the diene ring is probably deformed out of plane to relieve the steric interactions between the substituent perfluoroisopropyl group. It seems likely that the formation of a triene would proceed through a planar transition state and in the case of (201) this would be sterically destabilised.

6.4 The Photolysis of Perfluoro-2,5-di-isopropyl-1,4-diazacyclohexa-1,4-diene (185)

The u.v. spectrum of the unconjugated diene (185), did not contain any significant absorptions above 215 nm and therefore, it was irradiated in the presence of mercury vapour (see Section 6.1) to give, apart from recovered starting material (6% of the product), two other components.

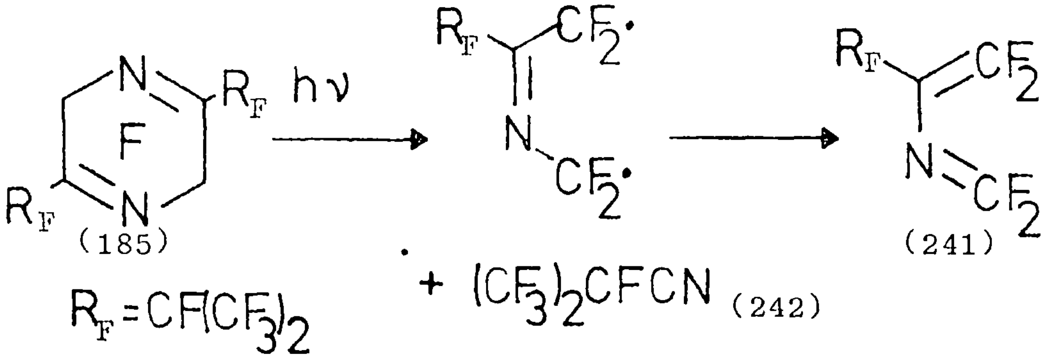
One (37% of the product) was identified as perfluoroisobutyronitrile by comparison of its i.r. and mass spectra with those of an authentic sample.[203]

The other component (57% of the product) was new and has been characterised as perfluoro-4-methyl-3-methylene-2-azapent-1-ene (241). Its mass spectrum contained a parent ion at m/e = 295 with λ_{max} at 1,805 and 1,732 cm^{-1} in the i.r. indicating the presence of a $>C=C<$ and $>C=N-$ bond. Its ^{19}F n.m.r. spectrum consisted of six chemically shifted signals integrating in the ratio 6:1:1:1:1:1. The signals at 78.9 p.p.m. (integrating to 6) and at 187 p.p.m. (integrating to 1) were readily identifiable as belonging to a perfluoroisopropyl group. Two of the other signals were broad and at very low field (42.6 and 55.9 p.p.m.) and were therefore, also by comparison with (235), the model employed in Section 6.2, identifiable as due to the fluorine atoms of a difluoroimine group ($-N=CF_2$). The two remaining signals had chemical shifts typical of fluorine atoms bonded to unsaturated carbon atoms (83.1 and 93.0 p.p.m.). The observed coupling was consistent with the assigned structure:



(241)

The ring fission of (185) is considered unlikely to be a concerted process as the Woodward-Hoffman rules for the conservation of orbital symmetry indicate that a photochemical retro-$2\pi + 4\pi$ reaction is a disallowed process.[208] Therefore a process involving radical intermediates is suspected.
One such process would be:



(185) (241)

$+ (CF_3)_2CFCN$ (242)

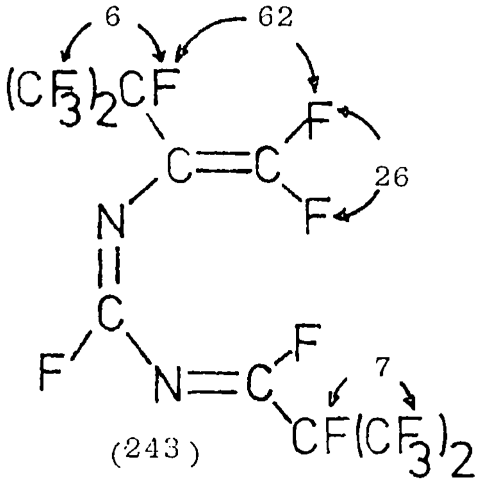
$R_F = CF(CF_3)_2$

6.5 Photolysis of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153)

The unconjugated -3,6-diene (153) reacted when irradiated at 253.7 nm in the vapour phase, in the presence of mercury vapour as a sensitiser, to give, apart from recovered starting material, three main products and traces of other material.

The first two were identified from their i.r. and mass spectra as (241) and (242), respectively, which were also produced when (185) was irradiated as described earlier. The third component was starting material.

The fourth component (48% of the mixture) was shown by mass spectroscopy to be an isomer of the starting material. Signals in the ^{19}F n.m.r. spectrum at 76.6 and 77.9 p.p.m. both integrating to 6, and, upfield, at 182.2 p.p.m. and 185.9. p.p.m., both integrating to 1, were attributed to 2 non-equivalent perfluoroisopropyl groups. There were four other signals, two integrating to 1 and two integrating to 2. Two of these had chemical shifts at 77.7 and 91.3 p.p.m. respectively, both typical of olefinic ($>C=CF$) fluorines and the other two were to low field, 41.8 p.p.m. and were assigned as accidentally equivalent fluorine atoms in a difluoroimine group ($-N=CF_2$). The coupling constants confirmed the structure:

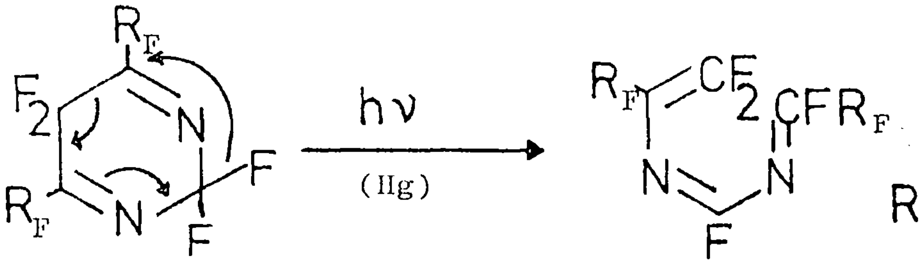


(243)

Coupling constants in Hz

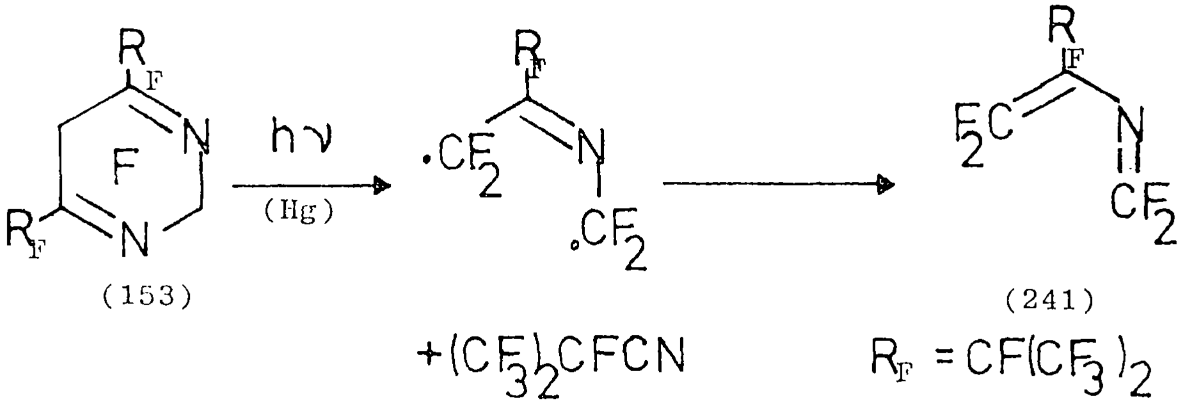
The i.r. spectrum gave three absorptions at λ_{max} = 1678, 1731 and 1799 cm^{-1} consistent with the presence of three double bonds.

The formation of (243) involves a 1,3 migration of fluorine which could be part of a ring opening process such as:-



$R_F = CF(CF_3)_2$

(241) and (242) are formed in a competing reaction which has a similar mechanism to the reaction of (185) which gives rise to the same products:



(153)

(241)

$R_F = CF(CF_3)_2$

(242)

6.6 Attempted Photolysis of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) and Perfluoro-1-azacyclohex-1-ene (191)

The photolyses described so far have apparently involved mechanisms in which two double bonds are simultaneously involved. Therefore it was of interest to see if any reaction would ensue upon irradiating compounds with only one double bond as in the case of (191) or a diene whose double bonds were so remote from each other than reactions simultaneously involving both of them would be unlikely, as in the case of (160).

Naturally, because isolated imine bonds do not absorb significantly at 253.7 nm, mercury vapour was included in the reaction vessels as a sensitiser. However in neither case, even after prolonged periods of irradiation, was any reaction detected.

CHAPTER 7

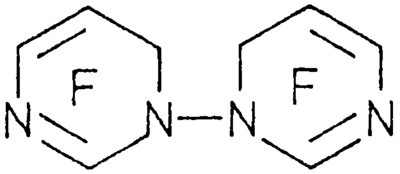
SOME MISCELLANEOUS REACTIONS OF PERFLUORO-CYCLIC-IMINES

7.1 Introduction

Most of the reactions performed on the fluorination products described in Chapter 3 were either reactions with nucleophilic reagents (Chapter 5) or photolyses (Chapter 7). However a few reactions do not fit accurately into these categories and they are described in this chapter.

7.2 The Defluorination of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)

Maslakiewicz noted tetrafluoropyrimidine (155) amongst the products derived by pyrolysing the dimer (160) on passing it through a heated silica tube containing glass wool.[210] It was of interest therefore to see if improved yields of (155) and, more interestingly, other defluorination products, such as the hypothetical dimeric tetraene (244), could be produced under more efficient conditions, by passing the substrate over iron filings rather than glass wool.



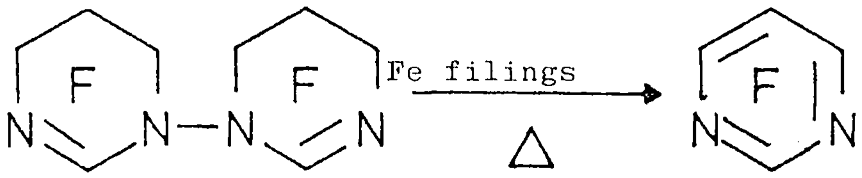
(244)

In the event, defluorination to tetrafluoropyrimidine was shown to occur with high efficiency but upon lowering the reaction temperature increased amounts of starting material were recovered without the appearance of intermediate defluorination products,

Table 7.1 The Defluorination of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)

		Product Composition %		Actual Yields %	
Run	Temp. °C	Starting Material (160)	Tetrafluoropyrimidine (155)	Starting Material (160)	Tetrafluoropyrimidine (155)
1	345	5	75	1.4	28.0
2	257	70	15	35.5	10.5

such as (244), in isolable amounts. The results of two typical experiments are tabulated in Table 7.1.



(160) (155)

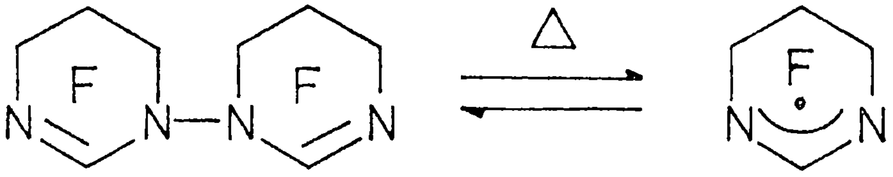
The materials described in Table 7.1 are the products remaining liquid at room temperature, most of the starting material which is unaccounted for having been converted to gaseous fragmentation products.

The -2,2'-dichloro derivative of (160) was similarly converted to the corresponding pyrimidine as was described in Section 5.7.

7.3 Attempted Radical Dissociation of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)

7.3A Attempted Reaction with Mercury

It seemed possible that the -1,1'- bond of the dimer (160) might be easily cleaved, upon heating, to generate allylically stabilised radicals in a hypothetical scheme such as:



(160) (162)

Indeed it has been argued that the radical species (162) must be relatively stable for dimer (160) to be produced, upon fluorinating tetrafluoropyrimidine, at all.[163]

Therefore an attempt was made to trap any radicals produced on heating (160) with mercury metal. Mercury has previously been shown to form fairly stable covalent compounds containing mercury-nitrogen bonds.[211] However on heating dimer (160) and mercury in Carius tubes at a series of temperatures (Table 7.2) no covalent mercury compounds were formed.

Table 7.2 Attempted Reaction Between Mercury and Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)

Run	Temp. °C	Time hrs	(160) recovered %	Mercury recovered %
1	240	59	96	100
2	400	5.75	~1	100

The unaccounted for starting material in Run 2 was converted to a complicated mixture of mainly gaseous fragmentation products.

7.4B Attempted Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Nitric Oxide

Arguably, the dimer (160) might react more readily with nitric oxide than mercury as the former is a stable free radical. However, as with mercury, nitric oxide failed to react with the dimer under a variety of conditions (Table 7.3).

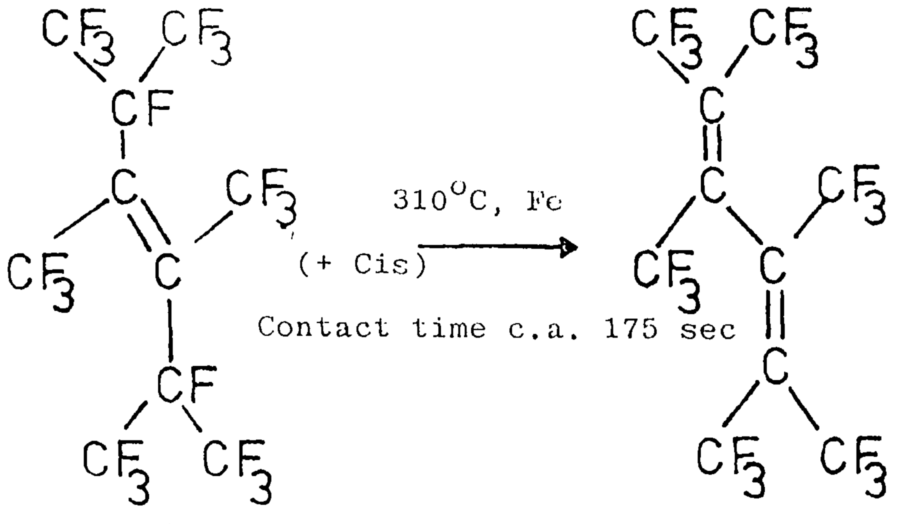
Table 7.3 Attempted Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Nitric Oxide

Run	Temp. °C	Time hrs	Recovered (160) %	Recovered NO %
1	180	12	>95	30
2	345	16	>90	40

7.4 The Defluorination of a Mixture of Cis- and Trans-Isomers of Perfluoro-2,3,4,5-tetramethylhex-3-ene (168) and (169)

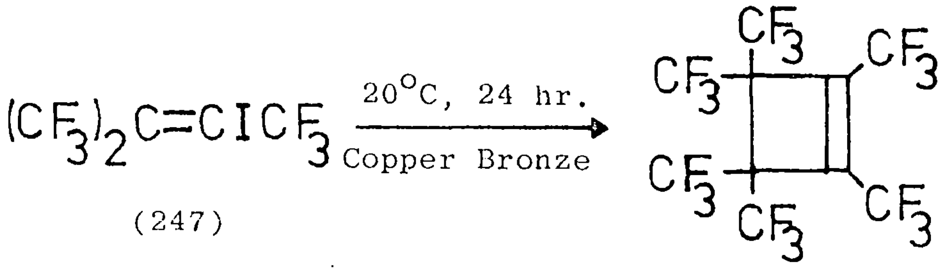
The preparation of an inseparable mixture of (168) and (169), in the ratio 7:3, from the fluorination of the disubstituted pyridazine (167) was described in Section 3.10. Further confirmation of the assignment of the structure of these two compounds has been obtained by defluorinating the mixture over heated iron filings to give a product containing only two major components. One (15% of the product from g.l.c.) was not isolated in a sufficiently pure state for identification but gave a parent ion by g.l.c. mass spectroscopy at m/e = 462 indicating it to have formed from the starting material by the loss of two fluorine atoms.

The other component (70% of the product) was obtained, by careful peak chopping during preparative g.l.c., as a fraction indicated by ^{19}F n.m.r. to be 90% pure and was identified as perfluoro-2,3,4,5-tetramethylhexa-2,4-diene (245). Thus it contained two broad signals at 78.3 and 79.9 p.p.m. integrating in the ratio 1:2. A product reported by Evans et al.[209] had been identified as either the -2,4-diene (245) or perfluoro-2,3-dimethylcyclobut-2-ene (246) but the ^{19}F n.m.r. spectrum of their compound is different to that of the present compound in that although they, also, observed two broad signals in the ratio 1:2 the reported chemical shifts were 95.2 p.p.m. (adapted from +18.7 p.p.m. w.r.t. CF_3COOH) and 93.7 p.p.m. (adapted from +17.2 p.p.m. w.r.t. CF_3COOH), respectively. Thus the compound described by Evans et al. has its most intense signal at lower field than the other signal whilst for the defluorination product the reverse is true. Further, in the case of the defluorination product the signal of integration 2, although not resolved, was distinctly assymetric and was therefore due to two different signals overlapping, consistent with the 2,4-diene (245) but not with the cyclobutene (246). Integration ruled out the possibility that the assymetry is due to an impurity. The chemical shifts are typical of trifluoromethyl ($-CF_3$) groups.^{177} The mass spectrum gave a parent ion at m/e = 462 and the i.r. spectrum gave a band at 1652 cm^{-1}, assigned to the ($>C=C<$) stretches.



(169)

(245)



(247)

(246)

Ref: 209

It is, therefore, concluded that the compound observed by Evans et al. was the cyclobutene (246). The synthesis of (246) was achieved by reaction of hexafluoro-2-iodo-3-trifluoromethylbut-2-ene (247) with copper bronze.

CHAPTER 8

DESCRIPTION OF INSTRUMENTS AND EXPERIMENTAL FOR CHAPTERS 3 and 4

8.1 Instrumentation

In this section the instruments employed in separations and structure determinations in the work described in this thesis are briefly described.

8.1A Gas-liquid Chromatography

Analytical chromatograms were obtained on either a Pye 'Series 104' Instrument using a flame ionisation detector or a Griffin and George Gas Density Balance.

Preparative separations were performed using either a Perkin Elmer model F21 preparative scale instrument or an Aerograph 'Autoprep' instrument.

Most of the work was performed with one of two types of column. The first contained a non-polar stationary phase, silicone elastomer and the second a polar stationary phase di-isodecylphthalate. 'Chromosorb P' (80-100 mesh) was the supporting material in both cases.

8.1B Distillations

Some separations were achieved using a Fischer Spaltrohr-Column FB-MMS200 microstill with a concentric tube column of extremely low hold up.

8.1C Infra-Red Spectrometry

I.r. spectra were obtained on a Perkin Elmer 157 instrument with a range from 250 to 4000 cm^{-1}. Samples were variously examined as either liquid films, vapours or KBr discs as stated in the spectra presented in Appendix 2.

8.1D Ultra-Violet Spectrometry

U.v. spectra were obtained using a Unicam S.P. 800 instrument as dilute solutions in spectrograde cyclohexane. The examined range was from 200 to 450 nm.

8.1E Nuclear Magnetic Resonance Spectroscopy

^{1}H and ^{19}F n.m.r. spectra were obtained using a Varian A56/60D instrument operating at 56.4 MHz for fluorine nuclei and 60 MHz for protons. In some cases a Bruker HX90E instrument was also used, as its higher operating frequency (84.67 MHz for ^{19}F) gave a usefully higher resolution.

Samples were run either neat or in solution and chemical shifts, quoted in p.p.m., were measured, unless stated otherwise, against external $CFCl_3$.

8.1F Mass Spectrometry

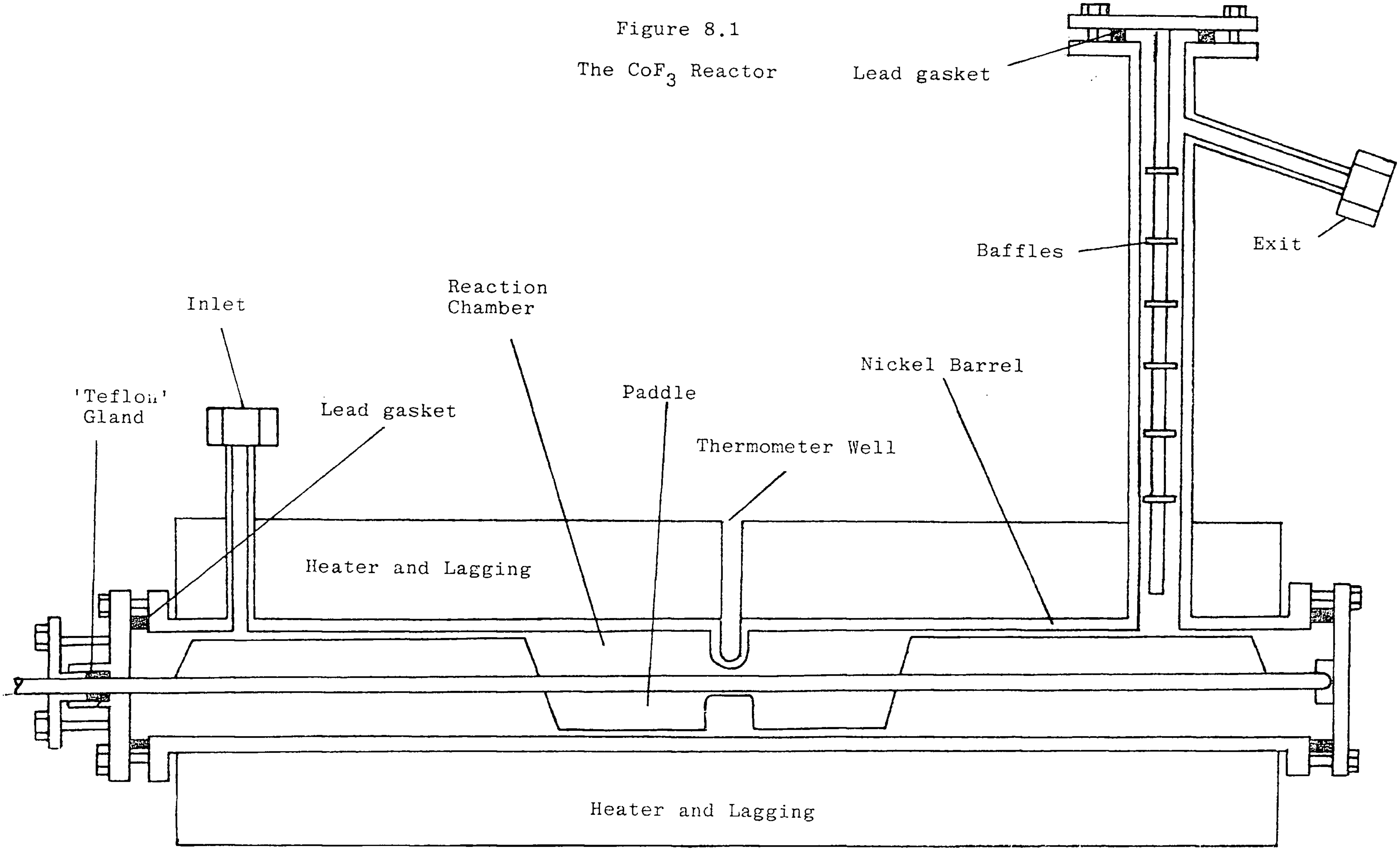
Mass spectra were obtained using an A.E.I., M.S.9 instrument operating, unless stated otherwise, at 70 eV. Difficult spectra were counted with the aid of added perfluorokerozene. G.l.c./mass spectroscopy was performed on a Vacuum Generator Micromass 12B instrument operating at 2.7 kV, coupled to a Pye Series 104 chromatograph. Heptacosafluoro-tri-n-butylamine, instead of perfluorokerozene, was used as a reference compound for counting purposes.

8.2 The Cobalt III Fluoride Reactor

The CoF_3 reactor is illustrated in diagram 8.1. The reagent consisted of 300g of a 50:50 (w/w) mixture of cobalt III

Figure 8.1

The CoF_3 Reactor



fluoride and calcium fluoride. The constructional materials are indicated in the diagram. During a run the paddles were rotated at a rate of about 4 r.p.m. The paddles were arranged as illustrated so that the reagent stayed near the middle of the reaction rather than drifting to one end.

8.3 The Fluorine Gas Generator

The fluorine used to regenerate the CoF_3/CaF_2 reagent and for the direct fluorinations described in Chapter 4 was generated by an I.C.I. 10 amp fluorine cell. This generator electrolyses an electrolyte of approximate composition KF.2HF, maintained as a liquid at 85°C. It produces 6.5 g (0.17 moles) of fluorine per hour at 10 amps. The fluorine was transferred to the reactor through passivated copper pipes (8 mm o.d.) under the autogenous pressure of the generator (which is fitted with a safety lute containing a head of approximately 5 cm of fluorolube (a grade of perfluorokerozene) in case of blockages developing downline.

8.4 Experimental Procedure for Cobalt III Fluoride Fluorinations

The same general procedure was employed for all the cobalt III fluoride reactions described in Chapter 3. The reagent was regenerated no earlier than 24 hrs prior to use by passing fluorine gas through the reactor whilst the latter was maintained at a temperature above 300°C. The fluorine was generated at 10 amps and was passed through the reactor for 90 mins. so that the reagent was exposed to approximately 9.5 g of fluorine. The reagent contained 150 g of cobalt III fluoride when fully regenerated which is equivalent to 24.6 g of theoretically available fluorine and the amount of substrate fluorinated before regenerating afresh was limited so that the reagent was unlikely to lose more than 25% of the theoretically available fluorine.

After regenerating the reagent, the reactor was purged with dry nitrogen to expel residual elemental fluorine whilst the reactor temperature was adjusted to that desired for the reaction.

Substrates were then introduced into the reactor whilst the nitrogen purge was maintained in order to carry the substrate to the reagent and to purge the resultant products from the reactor. Liquid substrates were dropped directly into the reactor at a slow rate by using a modified burette as a dropping funnel. The burette was, of course, equipped with a rubber tube to equalise the carrier gas pressure either side of the tap. It was attached to the reactor by a standard olive and union nut.

All the solid compounds fluorinated were sufficiently volatile to be passed into the reactor by vaporising them in a heated glass tube through which the carrier gas was conducted.

Products were collected by trapping them from the effluent gases at either liquid air or cardice temperatures.

8.5 The Reaction of Perfluoro-4-isopropylpyridine (120) with Cobalt III Fluoride/Calcium Fluoride

To the CoF_3/CaF_2 reactor, at an initial temperature of 118°C, was added (120) (9.6 g., 30.1 m.moles). The addition took 90 mins., after which the reactor temperature had risen to 122°C. The nitrogen flow was 300 $mls.min^{-1}$. The product (9.2 g) was collected over a period of 8 hrs and was found, by g.l.c. analysis (G.D.B., silicone elastomer, 78°C), to consist of three major components in the ratio 9.7%, 64% and 19% in order of decreasing retention times and a complicated mixture of more volatile minor components. Separation of the major components was achieved by preparative scale g.l.c. (F21, di-isodecylphthalate, 60°C).

The first component (1.8 g) was identified as starting material (120) by comparison of spectra. The second component was identified as perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) (4.9 g). [Found: F, 68.8%; M, 357, $C_8F_{13}N$ requires F, 69.27%; M, 357]; b.pt. 112-113°C uncorr., i.r. spectrum No. 1, ^{19}F n.m.r. spectrum No. 1, u.v. spectrum No. 1.

The third component (1.5 g) was identified as perfluoro-4-isopropyl-1-azacyclohexa-1,4-diene (122) (1.5 g.). [Found: F, 68.9%, M, 357, $C_8F_{13}N$ requires, F, 69.17%; M, 357]; b.pt. 103-104°C uncorr.; i.r. spectrum No. 2, ^{19}F n.m.r. spectrum No. 2

8.6 The Fluorination of Perfluoro-2,4-di-isopropylpyridine (126) with Cobalt III Fluoride/Calcium Fluoride

The pyridine (126), (5.5 g, 11.7 m. moles) was dripped, as the liquid, into the reactor (initial temperature 118°C, nitrogen flow 100 $mls.min^{-1}$), the addition taking 25 mins. The product was collected in the usual manner by trapping at liquid air temperature. The receiving trap was removed after purging the reactor for 16 hours. A colourless liquid product (4.5 g) was collected. Analysis by g.l.c. (G.D.B. silicone elastomer, 20°C) revealed three major components, 7%, 52% and 26% of the product, respectively, in order of decreasing retention times.

A separation of the mixture was achieved by careful preparative g.l.c. (Aerograph, silicone elastomer, 20°C).

The first component (0.3 g) was identified as starting material by comparison of spectra.

The second component (0.5 g) was not identified and was thought to be a mixture of more than one compound. The highest m/e in its mass spectrum was at 545.

The third component was identified as a 50:50 mixture of perfluoro-2,4-di-isopropyl-1-azacyclohexa-1,3-diene (127) and perfluoro-2,4-di-isopropyl-1-azacyclohexa-1,4-diene (128) (2.1 g). [Found: C, 25.8%; N, 2.7%; F, 71.5%; M, 507, $C_{11}NF_{19}$ requires C, 26.05%; N, 2.76%; F, 71.18:, M, 507]. i.r. spectrum No. 3, ^{19}F n.m.r. spectrum No. 3.

8.7 The Fluorination of Perfluoro-3-methylpyridine (134) with Cobalt III Fluoride/Calcium Fluoride

A sample of (134), also containing perfluoro-4-methylpyridine (133) (10% w/w) from which it could not be separated, (8.6 g, 39.3 m.moles of mixture) was dripped into the reactor in the usual manner. The initial reactor temperature was 116°C rising to 127°C after addition of the substrate, which took an hour. The nitrogen flow was 100 mls.min^{-1}, and the product, a liquid (8.8 g), was collected by trapping at liquid air temperatures. Analysis by g.l.c. (G.D.B., silicone elastomer, 78°C) of the product revealed three components. The mixture was separated by distillation at atmospheric pressure using the concentric tube microdistillation apparatus. The first component (45% of the product) was collected between 61.5°C and 62.5°C. It was identified as either perfluoro-3-methyl-1-azacyclyhex-1-ene- or perfluoro-5-methyl-1-azacyclohex-1-ene, (135) or (136) (3.4 g). [Found: C, 24.6%; N, 5.2% F, 71.2%; M, 295, C_6NF_{11} requires C, 24.42%; N, 4.75%; F, 70.83%, M, 295]. ^{19}F n.m.r. spectrum No. 4. A satisfactory i.r. spectrum was not obtained owing to hydroly; sis.

The second component (8% of the product) was collected as an impure fraction between 62°C and 79°C, which was then purified by preparative g.l.c. (Autoprep., silicone elastomer, 25°C). It was identified as perfluoro-4-methyl-1-azacyclohexa-1,3-diene (140) (0.4 g). [Found: C, 27.6%; N, 5.6%; F, 66.5%; M, 257, C_6NF_9 requires C, 28.03%; N, 5.45%; F, 66.52%, M, 257]. i.r. spectrum No. 4, ^{19}F n.m.r. spectrum No. 5.

The third component (47% of the product) was identified as unreacted starting material by comparison of its g.l.c. retention time and i.r. spectrum. Its n.m.r. spectrum indicated the proportion of (133) in this recovered starting material to have been reduced by about half.

8.8 The Fluorination of Perfluoro-4,6-di-isopropylpyrimidine (152) with Cobalt III Fluoride/Calcium Fluoride

The pyrimidine (152), (10.4 g, 23 m.moles) was added to the reactor by the usual method for a liquid. The reactor was at an initial temperature of 172°C and the nitrogen flow was 200 mls min^{-1}. The addition took one hour during which the air temperature rose to 176°C. The product (9.8 g) was collected by trapping at liquid air temperature and appeared to have finished purging from the apparatus after 7 hrs. It was analysed by g.l.c. (G.D.B., silicone elastomer, 78°C) and consisted of one major component with traces of both more and less volatile products.

The major component was isolated by distillation (concentric tube column) as a fraction b.p. 126-127°C. It was identified as perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153) (8.5 g). [Found: F, 70.1%; M, 490, $C_{10}N_2F_{18}$ requires F, 69.78%; M, 490]. i.r. spectrum No. 5 ^{19}F n.m.r. spectrum No. 6. A small fraction (0.8 g) boiling below 126°C was collected which contained an unidentified product. The pot residue (0.4 g) was found by g.l.c. and ^{19}F n.m.r. spectroscopy to consist of (152) with traces of (153).

8.9 The Fluorination of Perfluoro-4-isopropylpyrimidine (154) with Cobalt III Fluoride/Calcium Fluoride

8.9A High Temperature Reaction

The pyrimidine (154) (9.3 g, 31 m.moles) was added to the reactor in the liquid phase over a period of 1 hr. The initial reactor temperature was 169°C rising to 174°C and the nitrogen flow was 100 $mls.min^{-1}$. The product, collected over 16 hrs, weighed 7.4 g, most of which was gaseous, only 2.0 g remaining in the liquid phase on warming to room temperature.

The liquid fraction was found by g.l.c. (G.D.B., silicone elastomer, 78°C) to be composed of a complicated mixture of very volatile components with only traces of material of the same retention time or higher retention time than (154).

The gaseous fraction was not resolved on g.l.c. columns even at low temperature (Pye 452, di-isodecylphthalate, -15°C).

8.9B Low Temperature Reaction

The reaction was repeated at a lower temperature. Thus the pyrimidine (154) (4.5 g, 14.9 m.moles) was added to the reactor (temperature 113°C rising to 114°C) in the usual manner. The addition time was 20 mins. and the nitrogen flow was 80 mls. min^{-1}. The product, a liquid (3.2 g) was collected after 20 hrs. Analysis by g.l.c. (Pye 104, silicone elastomer, 150°C) demonstrated the absence of products with a higher retention time than (154). The major component (1.4 g) was identified as (154) by its g.l.c. retention time and i.r. spectrum and the remainder of the product was a mixture of at least six very volatile components, poorly resolved from each other on available g.l.c. columns.

8.10 The Fluorination of Trifluoro-5-chloropyrimidine (155) with Cobalt III Fluoride/Calcium Fluoride

Three aliquots of (155) were fluorinated under the conditions described below and the liquid products were combined and distilled together. The first aliquot of (155) (10 g, 59.4 m.moles) was reacted, in the usual manner for liquids, with an initial reactor temperature of 146°C rising to 154°C. (Addition time 60 mins; N_2 flow 120 mls.min^{-1}). The product, collected over night (18 hrs) consisted of a liquid fraction (8.8 g) and a gaseous fraction (1.2 g) at room temperature. G.l.c. (Pye 104, silicone elastomer, 150°C) indicated the product to consist mainly of a component with the same retention time as starting material with minor amounts of compounds with higher retention time.

A ^{19}F n.m.r. spectrum of the crude product confirmed that it consisted mainly of (155) (>70%). The gaseous fraction was extremely susceptible to hydrolysis and was not investigated further.

A second aliquot of (155) (5.6 g, 3.3 m.moles) was reacted at 170°C, rising to 182°C, (N_2 flow 100 mls.min^{-1}, addition time 40 mins). The product consisted, at room temperature, of 4.3 g. of liquid and 1.0 g of gaseous material. G.l.c. analysis (Pye 104, silicone elastomer, 150°C) indicated the proportion of (155), in the liquid, to have dropped to approximately 15%, the remainder of liquid consisting of a complex mixture of products more volatile than (155) (40% of the liquid) and two less volatile components (20% and 20%).

Finally, a third aliquot of (155) (8.7 g, 51.6 m.moles) was fluorinated at 178°C rising to 183°C (N_2 flow 80 mls.min^{-1}, addition time 1.5 hrs). The product had a similar composition to that of the second aliquot. The liquid fraction was combined with those from the previous fluorination (total 16.8 g) and the mixture was distilled (concentric tube) to give:-

Fraction 1, b.p. <113.5°C (4.2 g) found by g.l.c. (G.D.B., silicone elastomer, 25°C) to be a very complicated mixture of components of short retention times.

Fraction 2, b.p. 113.5-115°C (3.1 g) identified by its spectra and retention time as starting material (155).

Fraction 3, b.p. 78-79.5°C (at 18 mm Hg pressure, 0.7 g) found by g.l.c. (Autoprep Col 0, 70°C) to be a mixture of at least three compounds and some starting material. An attempted g.l.c. separation was unsuccessful and these compounds were not identified.

Fraction 4, 7.1 g collected from 90 to 92°C (18 mm Hg pressure) and identified as a mixture of dimeric compounds of empirical formula $C_8N_4F_{12}Cl_2$. [Found: C, 21.5%; F, 50.5%; Cl, 15.5%; M, 450; P:P+2:P+4 = 100:66:11; $C_8N_4F_{12}Cl_2$ requires Cl, 15.72%; F, 50.55%; M, 450; P:P+2:P+4 = 100:66:11]. i.r. spectrum No. 6.

8.11 The Fluorination of Perfluoro-4,5-di-isopropylpyridazine (167) with Cobalt III Fluoride/Calcium Fluoride

The pyridazine (167) (11.2 g, 24.8 m.moles) was sublimed into the reactor in the manner described for solids (Section 8.4). The solid was heated to 108°C and passed into the reactor, as the vapour, through a delivery arm maintained at 143°C by a heating tape. The N_2 flow was 200 mls.min^{-1} and the reactor temperature was 163°C rising to 169°C, the addition taking 3hrs.

The product, a liquid (10.1 g), was collected after a further 14 hrs and was found by g.l.c. (G.D.B., silicone elastomer 78°C) to contain three components. The reaction was repeated with three further aliquots of (167) under closely similar conditions and the combined product (42.6 g) was separated into its components by distillation (concentric tube microdistillation apparatus) at atmospheric pressure. The first component (b.p. 74.5°C to 75.5°C) was identified as perfluoro-2,3-dimethylpentane (170) (4.0 g). [Found: C, 21.5%; F, 78.1%; P-F, 369, C_7F_{16} requires 21.67%; F, 78.33%; M, 388], i.r. spectrum No. 7, ^{19}F n.m.r. spectrum No. 7.

The second component (24.2 g) (b.p. 118°C to 118.5°C) was identified as a 36:64 mixture of cis- and trans-perfluoro-2,3,4,5-tetramethylhex-3-ene (168) and (169) respectively. [Found: C, 23.8%; F, 75.8%; P-F, 481, $C_{10}F_{20}$ requires C, 24.02%; F, 75.98%; M, 500], i.r. spectrum No. 8;

^{19}F n.m.r. spectrum No. 8.

The third component (7.2 g) b.p. 136°C to 138°C was identified as perfluoro-2,3,4,5-tetramethylhexane (171). [Found: C, 22.0%; F, 77.3%; P-F, 519, $C_{10}F_{22}$ requires C, 22.32%; F, 77.68%; M, 538], i.r. spectrum No. 9, ^{19}F n.m.r. spectrum No. 9.

8.12 The Fluorination of Perfluoro-3,5-di-isopropylpyridazine (174) with Cobalt III Fluoride/Calcium Fluoride

The pyridazine (174) (10.1 g, 22.3 m.moles) was fluorinated in the usual manner for liquids with a reactor temperature of 132°C rising, upon completion of the addition (50 mins) to 138°C (N_2 flow 150 mls.min^{-1}).

The product, a liquid (8.5 g) was collected over a period of 48 hrs. Analysis by g.l.c. (F_{21}, silicone elastomer, 25°C) revealed three components which were separated by preparative g.l.c. (F_{21}, silicone elastomer, 25°C).

The first component (39% of the product by g.l.c.) was identified as a mixture of either cis or trans-perfluoro-2,3,6-trimethylhept-3-ene (175) or (176) and at least one other unidentified compound, also thought to be a perfluorodecene and detectable only by ^{19}F n.m.r. spectroscopy which indicated it to be <15% of the mixture. No difference in the composition of material trapped as the first half of the g.l.c. peak compared with the later half could be detected by ^{19}F n.m.r. spectroscopy. [Found: F, 76.2%; M, 500, $C_{10}F_{20}$ requires F, 75.78%; M, 500], i.r. spectrum No. 10, ^{19}F n.m.r. spectrum No. 10.

The second component (37% by g.l.c.) was also found by ^{19}F n.m.r. to contain one main compound and at least (<10% of the mixture) one other, again thought to be a perfluorodecene. The main compound was identified as either cis or trans perfluoro-2,5,6-trimethylhept-3-ene (177 or 178). [Found: F, 76.0%; M, 500, $C_{10}F_{20}$ requires,F, 75.98%; M, 500], i.r. spectrum No. 11, ^{19}F n.m.r. spectrum No. 11.

The third component was identified as starting material (174).

8.13 The Fluorination of Perfluoro-2,5-di-isopropylpyrazine (184) with Cobalt III Fluoride/Calcium Fluoride

The pyrazine (184) (10.4 g, 22.9 m.moles) was sublimed into the reactor in the usual manner for solids. The reactor temperature was 156°C, rising to 159°C and the N_2 flow was 300 mls.min^{-1}. Addition took 2 hrs and the product (9.6 g) was collected after a further 15 hrs, as a colourless crystalline solid at room temperature. Analysis by g.l.c. (G.D.B., silicone elastomer, 78°C) revealed two components, the minor of which was identified by g.l.c./mass spectroscopy as starting material (184) (10.7% of the product).

The major component (7.0 g) was isolated by recrystallising from cyclohexane to give large, well-formed crystals of perfluoro-2,5-di-isopropyl-1,4-diazacyclohexa-1,4-diene (185) (7.0g); m.p. 43-45°C uncorr. [Found: C, 24.4%; N, 6.1%; F, 69.3%; M, 490, $C_{10}N_2F_{18}$ requires C, 24.51%;, N, 5.72%; F, 69.7%;, M, 490]; i.r. spectrum No. 12, ^{19}F n.m.r. spectrum No. 12.

8.14 Attempted Fluorinations of Cyanuric Fluoride (188) with Cobalt III Fluoride/Calcium Fluoride

Using the technique adopted for liquid substrates (188) (12.4 g, 91.8 m.moles) was passed into the reactor which was at an initial temperature of 110°C (temperature after addition 110°C, nitrogen flow 300 mls.min^{-1}, addition time 2.25 hrs). After 20 hrs, 11.3 g of product had been trapped, which was found upon analysis by g.l.c. and i.r. spectroscopy to contain (188) only.

A second aliquot of (188), (9.7 g, 71.8 m.moles) was added to the reactor at the higher initial temperature of 219^{o}C, rising to 220^{o}C (addition time 1 hr, N_2 flow 300 mls.min^{-1}). The product (8.9 g), collected after a further 18 hrs, was once again found by g.l.c. analysis and i.r. spectroscopy to contain starting material (188) only.

Finally, a third aliquot of (188) (9.6 g, 71.1 m.moles) was added to the reactor at an initial temperature of 328^{o}C rising to 329^{o}C (N_2 flow 300 mls.min^{-1}, addition time 1.5 hrs). The product (8.8 g), collected after a further 16 hrs, was found by g.l.c. analysis (G.D.B. silicone elastomer, 78^{o}C) and i.r. spectroscopy to contain only traces (<2%) of new products, which were of very short retention time.

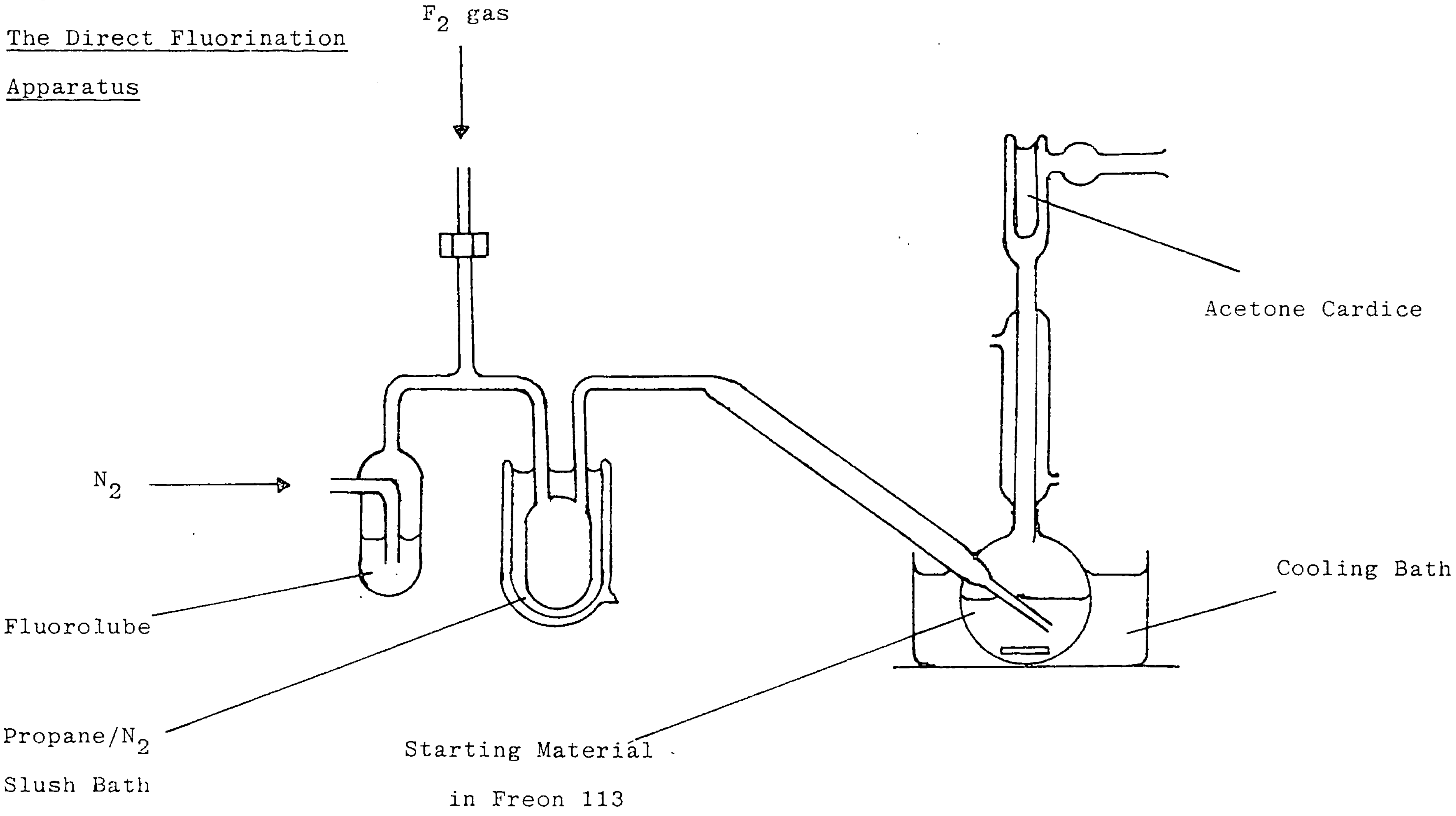
8.15 Experimental Procedure for Direct Fluorinations

Direct fluorinations were performed by passing fluorine, heavily diluted with dry nitrogen, through solutions of the compound to be fluorinated, in 'Freon 113' (Freon 113 is the DuPont trade name for 1,2,2-trifluorotrichloroethane). The apparatus was designed so that the fluorine did not come into contact with any materials other than dry glass, passivated copper, brass and 'Fluorolube' (a heavy fluorinated kerozene produced by I.C.I.). A drawing of the apparatus is presented below in Diagram 8.2.

The glassware was dried in the oven prior to use and allowed to cool whilst being purged with nitrogen. The fluorine line was then also connected to the glassware and the generator switched on at 5 amps and allowed to produce fluorine gas for 30 mins in order

Figure 8.2

The Direct Fluorination Apparatus



to remove any ingressed moisture from the electrolyte. It was suspected that oxygen difluoride produced from such moisture might be the cause of the explosions that have been reported by other workers when performing direct fluorinations and indeed, several explosions were experienced in the present work before adopting these precautions. Tatlow has also suggested that moisture in fluorine cell electrolytes is responsible for the acid fluorides often present among the products of direct fluorinations.[186]

As a secondary precaution, the trap in the fluorination apparatus (see Figure 8.2) was cooled with a nitrogen/propane slush bath maintained at $-187^{o}C$ in order to trap any remaining oxygen containing species (F_2 b.pt = $-187^{o}C$; OF_2 b.pt = $-145.3^{o}C$).

Blast screens, heavy gloves and protective clothing were employed at all stages of these experiments, of course.

After this pre-electrolysis, the generating cell was temporarily switched off and, after waiting 10 mins for the nitrogen purge to remove fluorine gas from the apparatus, a flask, containing a solution of the substrate in freon 113 and a magnetic follower, was connected to the apparatus so that the nitrogen and fluorine would pass through the liquid. A water cooled reflux condenser and an acetone/cardice cooled, cold finger condenser were placed at the flask exit, the latter above the former, in order to minimise losses of solvent, substrate or products. The final exit of the apparatus was guarded by a calcium chloride tube.

After cooling the contents of the reaction flask in a cooling bath and with vigorous stirring the fluorine generator was switched on again (2 amps, 1.3 g. $F_2.hr^{-1}$) and fluorine was passed through the solution, until an amount calculated to be equivalent to the addition of two fluorine atoms to the substrate had been passed. The freon solvent functioned both as a diluent of the substrate and also, by refluxing, as a heat sink for the reaction. It was dried, prior to use, by distilling from P_2O_5, in grease free apparatus, collecting the fraction at b.pt. 47°C.

The fluorolube trap through which the nitrogen entered the line prevented back diffusion of fluorine. After passing sufficient fluorine, the generator was switched off and the apparatus was purged with the nitrogen flow for a further 10 min.

8.16 Direct Fluorination of Perfluoro-4-isopropylpyridine (189)

The pyridine (189) (4.1 g, 12.8 m.moles) was dissolved in dry 1,1,2-trifluorotrichloroethane (7.2 g) and the solution was placed in the fluorination apparatus described above and cooled (-20°C) in an acetone/cardice bath. Fluorine gas (1.3 $g.hr^{-1}$, 12.6 $mls.min^{-1}$, a generator current 2 amperes) mixed with dry nitrogen (4.5 $mls.min^{-1}$, 3.1 g hr^{-1}) was bubbled through the vigorously stirred solution. Crackling sounds thought to be due to minor explosions were heard during the reaction.

After 24.4 mins (i.e. two equivalents of fluorine), the current was switched off, whilst the nitrogen purged residual fluorine from the apparatus. The flask was then removed and allowed to attain room temperature behind the blast screen. After standing for 30 mins the product (7.4 g) was analysed by g.l.c. (G.D.B., di-isodecylphthalate 78°C). The proportion of solvent (30% of the mixture) had dropped as a result of evaporation. Starting material (64% of the mixture by g.l.c.) was the only other major component with traces of two other components (1% and 2% respectively by g.l.c.). The first had identical retention times to perfluoro-4-isopropyl-1-azacyclohexa-1,3-

diene (121) on silicone gum rubber and di-isodecylphthalate g.l.c. columns whilst the second had shorter retention times. Material which had solidified on the cold finger during reaction (1.5 g) was identified as solvent (248) only.

8.17 Direct Fluorination of Perfluoropyrimidine (156)

Into the fluorination apparatus was placed perfluoropyrimidine (156) (5 g, 32.9 m.moles) and dry 1,1,2-trichlorotrifluoroethane (10 g). Following the usual procedure, fluorine was bubbled through the vigorously stirred solution at a rate of 47.25 m.moles hr^{-1}. The solution was maintained at $-20^{o}C$ (generator set at 3 amps giving 18.75 $mls.min^{-1}$). The fluorine was diluted with dry nitrogen (30 mls min^{-1}). The generator was switched off after 50 mins equivalent to the passage of 46.7 m.moles of fluorine.

The product (9.6 g) was analysed by g.l.c. (Pye 104, silicone gum rubber, $100^{o}C$) which revealed only three major components. The first two were isolated by distillation through a short (15 cm x 1 cm) vigreux column and identified by ^{19}F n.m.r. and g.l.c. as solvent (4.5 g) and starting material (156) (2.1 g). The residue was a nearly colourless oil (2.0 g) which boiled above $150^{o}C$ and was indicated by g.l.c. (Pye 104, silicone gum rubber, $150^{o}C$) to be mainly the third component. Most of the oil crystallised on standing and the crystals were purified by sublimation onto a cold finger ($40^{o}C$, 0.01 mm Hg) to give white crystals of perfluoro-2,2'-bi-1,3-diazacyclohexa-3,6-dienyl (195) (1.4 g), m.pt. 56^{o}-$57^{o}C$ (uncorr.). Found: C, 27.7%; N, 16.8%; F, 55.9%; M, 342. $C_8N_4F_{10}$ requires C, 28.0%; N, 16.38%; F, 55.54%, M 342. ^{19}F n.m.r. spectrum No. 13. Owing to rapid hydrolysis, a satisfactory i.r. spectrum was not obtained.

8.18 Direct Fluorination of Perfluoro-4,6-di-isopropylpyrimidine (152)

Into the fluorination apparatus was placed (152) (5 g, 11.1 m.moles) and 1,1,2-trifluorotrichloroethane (15 mls). Following the described procedure, fluorine gas, generated at 3 amps (≡47.25 m.moles hr^{-1} or 18.75 $mls.min^{-1}$) diluted with nitrogen (30 $mls.min^{-1}$), was bubbled into the vigorously stirred solution which was maintained at -10°C. The fluorine was stopped after 37 mins, equivalent to the passage of 29.1 m.moles of fluorine. The product was examined by mass spectroscopy/g.l.c. (silicone gum rubber, 165°C) and solvent (248) and starting material (152) were the only components detected. The bulk of the solvent was distilled off using a short vigreux (15 cm x 1 cm) column to leave a residue (5.2 g) which ^{19}F n.m.r. confirmed as mainly (152) with traces of residual solvent. Also high temperature g.l.c. (Pye 104, silicone gum rubber, 250°C) did not indicate the presence of components of higher retention time than (152).

8.19 The Direct Fluorination of Perfluoro-4,5-di-isopropylpyridazine (167)

The pyridazine (167), (2.9 g, 6.4 m.moles) and excess of Freon 113 (210 mls) as solvent, were placed in an earlier form of the fluorination apparatus, which differed from that already described, in that it did not have an F_2O trap. The solution was cooled to -5°C and stirred vigorously, with a 'teflon'-coated magnetic follower, whilst fluorine (generated at 5 amps, 69.7 $mls.min^{-1}$) diluted with dry nitrogen (46 $mls.min^{-1}$) was bubbled through it for a period of 60 mins (85.5 m.moles).

After the fluorine flow had ceased, the nitrogen flow was continued a further 15 mins in order to purge the apparatus, after which the reaction flask was allowed to stand for 30 mins and attain room temperature.

Material collected on the cold finger (1.4 g) consisted of Freon 113 only, as revealed by g.l.c. (G.D.B., silicone gum rubber, 40°C) and i.r. The flask contents were distilled (30 cm x 1.5 cm column packed with pyrex helices) and, after removal of the solvent, a residue (1.7 g) was obtained which gave only one major component on g.l.c. analysis (G.D.B., silicone gum rubber, 40°C) with traces of products of higher retention time. The major component was isolated by preparative g.l.c. (Autoprep., silicone gum rubber, 30°C) and was identified as a 1:1.8 mixture of cis and trans perfluoro-2,3,4,5-tetramethylhex-3-enes (168) and (169) by comparison of its g.l.c. retention times and ^{19}F n.m.r. spectrum with the product produced by fluorinating (167) with CoF_3/CaF_2 described in Section 3.10.

CHAPTER 9

EXPERIMENTAL FOR CHAPTER FIVE

9.1 Reaction of Perfluoro-4-isopropyl-1-azacychlohexa-1,3-diene (121) with the Perfluoroisopropyl Carbanion

To a dry evacuated, round bottomed, three necked flask, equipped with a gas inlet, a serum cap and communicating via a condensing trap to a collapsible gas bladder was added hexafluoropropene (249) (18 g, 120 m.moles). The hexafluoropropene was condensed into the well, which was then isolated from the flask. Dry nitrogen was admitted into the flask to return it to atmospheric pressure. Against the nitrogen flow was added CsF (c.a. 1.0 g), a magnetic stirrer and dry tetraglyme (10 mls). The flask was re-evacuated and the solvent de-gassed after which the hexafluoropropene was re-admitted and (121) (4.5 g, 12.6 m.moles) was added by injecting through the serum cap. The mixture was stirred vigorously at room temperature for 17 hrs. The volatile product was removed by distillation from the solvent at reduced pressure. The liquid (22.5 g) was found by g.l.c. to consist of two components in addition to dimers and trimers of hexafluoropropene. The mixture was distilled at atmospheric pressure (concentric tube) to give:

(1) a complex mixture of oligomers of hexafluoropropene, boiling below 112°C (11.6 g);

(2) a fraction (2.0 g) collected between 112 and 113°C, which was identified by comparison of i.r. spectra as starting material (121);

(3) a fraction (3.9 g) collected at 177°C which was identified as <u>perfluoro-2,3,4-tri-isopropyl-1-aza-</u>

cyclohexa-1,3-diene (201). [Found: F, 72.5%; M, 657, $C_{14}NF_{25}$ requires F, 72.28%; M, 657], λ_{max} 231 nm, $\varepsilon = 3.89 \times 10^3$ cyclohexane, i.r. spectrum 13, ^{19}F n.m.r. spectrum 14. U.v. spectrum No. 2. B.pt. = 177°C.

9.2 The Defluorination of Perfluoro-2,3,4-tri-isopropyl-1-azacyclohexa-1,3-diene (201)

The diene (201) (3.5 g, 5.3 m.moles) was placed in a dry flask equipped with a nitrogen inlet capillary and boiling chips. The flask was placed at the end of a silica tube (16 m.m. o.d.) which was packed along 45 cm of its length with coarse iron filings heated to 340°C by an enveloping furnace. The diene (201) was heated until it began to reflux in the apparatus and, by passing dry nitrogen through it (50 mls.min^{-1}), it was carried as a vapour over the iron filings. The product (0.7 g) was trapped at liquid air temperature and was found by g.l.c. to consist of one major component (91%) and a less volatile minor component (9%). The product partially crystallised on standing and g.l.c. indicated that the crystals were the major component which was identified as perfluoro-2,3,4-tri-isopropylpyridine (203) (0.5 g). [Found: F, 70.5%; M, 619, $C_{14}NF_{23}$ requires F, 70.58%; M, 619]. i.r. spectrum 14 ^{19}F n.m.r. spectrum 15.

The minor component has not been identified.

9.3 The Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Methanol

In a dry 100 ml two-necked flask containing a magnetic stirrer, continuously purged with dry nitrogen and equipped with a serum cap, was added dry ether (5 mls) anhydrous sodium carbonate (1 g, 9.4 m.moles) and (160) (1.0 g, 2.4 m.moles). Stirring vigorously, methanol (0.2 ml; 0.16 g, 5.2 m.moles) dissolved in dry ether (5 mls) was added by injecting from a syringe over a period of 10 mins. Stirring was continued at room temperature for 30 mins after which the mixture was refluxed for 30 mins. The solvent was then distilled off through a vigreux column (16 cm) to leave a crude white solid. The residue was sublimed onto a cold finger (0.05 mm Hg, 70°C) to give white crystals of 1,1'-bi-2-methoxypentafluoro-1,3-diazacyclohex-2-enyl (212) (0.4 g). [Found: C, 26.9%; N, 12.7%; F, 51.5%; M, 442, $C_{10}N_4H_6O_2F_{12}$ requires C, 27.16%; N, 12.67%; F, 51.56%; M, 442], i.r. spectrum 15, n.m.r. spectrum 16.

9.4 Reaction of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) with Methanol

In a dry 100 ml two-necked flask containing a magnetic stirrer, continuously purged with dry nitrogen and equipped with a serum cap and a reflux condenser, was placed dry ether (5 mls), anhydrous sodium carbonate (1.0 g, 9.4 m.moles) and the -1,3-diene (121) (2.2 g, 6.2 m.moles). Dry methanol (0.3 mls, 0.25 g, 7.7 m.moles) dissolved in dry ether (5 mls) was injected dropwise from a syringe with stirring over a period of 15 min. Stirring was continued for another 45 mins after which the mixture was refluxed for a further 30 mins. After reaction, the solvent was removed by distillation through a short (16 cm) vigreux column and the residual liquid was vacuum transferred from the sodium salt residue. The transferred material was found, by g.l.c., to consist of one major component (70%), two unidentified minor components (10%) and methanol (20%). The mixture was separated (G.D.B., silicone elastomer, 120°C) to give a pure sample of the major component which was found to be 2-methoxy-4-(heptafluoroisopropyl)pentafluoro-1-azacyclohexa-1,3-diene (1.2 g). [Found: C, 29.5%; N, 3.9%; F, 61.5%; H, 1.1%;, M, 369. $C_9NOH_3F_{13}$ requires C, 29.28%;, N, 3.79%;, F, 61.77%; H, 0.82%; M, 369]. i.r. spectrum 18, ^{19}F n.m.r. spectrum 17. λ_{max} = 213 nm, $\varepsilon = 6.07 \times 10^3$. U.v. spectrum No. 3.

9.5 The Reaction of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) with Methoxide Ion

In a dry three necked flask, equipped with a gas inlet, a serum cap, a reflux condenser and a magnetic stirrer was placed, against a flow of dry nitrogen, dry methanol (20 mls, an excess). After a brief wash in methanol, sodium (0.6 g, 26 m.moles) was added, piece by piece, against the nitrogen flow until a clear solution, equivalent to 26 m.moles of methoxide ion, was obtained. The diene (121) (2.3 g, 6.4 m.moles) was slowly added to the solution whilst the latter was stirred vigorously. The stirring was continued overnight after which the volatile contents of the flask were transferred in vacuo. The transferred material was found by g.l.c. to consist of methanol only and the products, which were relatively involatile, had remained in the flask. The material in the flask was extracted into methylene chloride, filtered and examined by g.l.c./mass spectroscopy (Micromass, silicone elastomer, 150°C) and found to consist of a mixture of at least six polysubstituted products.

9.6 Attempted Reaction of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153) with Methanol

The apparatus described for experiment 9.4 was used. To the dry flask, against a flow of dry nitrogen, was added (153) (2.0 g, 4.1 m.moles), sodium dried ether (20 mls), and anhydrous sodium carbonate (1 g). Methanol (0.165 mls, 4.0 m.moles) dissolved in ether (5 mls) was added dropwise from a syringe over a period of 10 mins. The mixture was magnetically stirred throughout the reaction. After one hour, the mixture was refluxed for a further hour, cooled and filtered. The solvent and unreacted methanol were distilled off to leave a liquid residue (1.9 g) which was shown by g.l.c. and i.r. to consist of starting material only.

9.7 Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Phenol

To a dry, round bottomed, 100 ml, two-necked flask equipped with a magnetic stirrer, a serum cap and a reflux condenser was added, against a flow of dry nitrogen, the dimer (^{160}) (1.0 g, 2.5 m.moles) dissolved in dry ether (10 mls) and triethylamine (0.4 g, 5 m.moles). The solution was stirred vigorously whilst phenol (0.45 g, 5 m.moles), dissolved in ether (10 mls), was added slowly through the serum cap. White material precipitated slowly from the solution. The stirring was continued for 12 hrs after which the solvent was removed by distillation. The residue was extracted with an excess of ethylacetate from which crystals (0.5 g) were deposited upon evaporation. The material (m.pt. 177^{o}C) was only sparingly soluble in a range of solvents and a satisfactory ^{19}F n.m.r. spectrum was not obtained. On the basis of mass spectral and i.r. evidence (i.r. spectrum No. 17) it is thought likely that the material is 1,1'-bi-2-phenoxyhexafluoro-1,3-diazacyclohex-2-enyl (216).

9.8 Reaction of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) with Phenol

The same apparatus as for reaction 9.4 was used. Against a flow of dry nitrogen, dry ether (5 mls), freshly distilled triethylamine (0.21 mls, 2.85 m.moles) and (121) (1.0 g, 2.8 m.moles) were added to the flask. Stirring vigorously, phenol (0.26 g, 2.8 m.moles) dissolved in dry ether (5 mls) was added dropwise, from a syringe, over a period of 15 mins. The stirring was continued for 30 mins and then the mixture was refluxed for a further 30 mins. The contents of the flask were then washed with water, dried ($MgSO_4$) and the solvent was removed by distillation. The remaining crude solid was then purified by sublimation (0.05 m.m. Hg, 40^{o}C) to give a white crystalline solid identified as 2-phenoxy-4-(heptafluoroisopropyl)-pentafluoro-1-azacyclohexa-1,3-diene (219) (0.8 g). [Found: C, 40.1%; N, 3.3%;, H, 1.2%;, F, 52.9%; M, 431, $C_{14}NH_5OF_{12}$ requires C, 38.99%; N, 3.25%; H, 1.17%; F, 52.88%; M, 431], i.r. spectrum 18. N.m.r. spectrum 18.

9.9 Hydrolysis of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)

In a 20 ml round-bottomed flask equipped with a reflux condenser and a magnetic stirrer, were placed (160) (1 g, 2.4 m.moles), water (1 g, 55.5 m.moles), acetone (5 mls) and magnesium carbonate (0.35 g, 4.15 m.moles). The mixture was refluxed, with stirring, for 24 hrs. The product was filtered ether (20 mls) was added and the whole was washed twice with water. Upon removal of the solvent, a solid (0.8 g) remained which was recrystallised ($CHCl_3$) to yield 1,1'-bi-3H-2,4-diketotetrafluoro-1,3-diazacyclohexyl (218) (0.7 g). Found: C, 25.9%; N, 15.3%; F, 41.5%; M, 370. $C_8N_4O_4H_2F_8$ requires, C, 25.96%; N, 15.14%; F, 41.07%;

M, 370], i.r. spectrum No. 19, ^{19}F n.m.r. spectrum No. 19.

9.10 Hydrolysis of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121)

To a 10 ml, round-bottomed flask equipped with a reflux condenser was added (121) (0.9 g, 2.6 m.moles), water (2 mls, 111 m.moles) and acetone (5 mls). The mixture was refluxed for 7 hrs after which the solvent and excess water were removed by vacuum transference, leaving a white solid. The solid was purified by sublimation onto a cold finger (0.005 mm Hg, 90°C) to crystals (0.4 g) identified as 1H-2,6-diketo-4-(heptafluoroisopropyl)trifluoro-1-azacyclohex-3-ene (218). [Found: C, 27.7%; F, 56.7%; M-F, 314, $C_8NO_2HF_{10}$ requires C, 28.8%; F, 57.0%; M, 333], i.r. spectrum 20, ^{19}F n.m.r. spectrum 20.

9.11 Hydrolysis of Perfluoro-4-isopropyl-1-azacyclohexa-1,4-diene (122)

Using the same method as for the -1,3-diene (121),(122) (1.0 g., 2.8 m.moles) reacted with water (2 mls, 111 m.moles) in acetone (5 mls) to give a crude white solid from which crystals (0.3 g) were obtained by sublimation (0.005 mm Hg, 105°C). Comparison of the i.r. and ^{19}F n.m.r. spectra showed the product to be identical to that produced from the -1,3-diene (121).

9.12 Attempted Hydrolysis of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153)

Using the same method as described for the hydrolysis of (121) in 9.10, the diene (153) (1.0 g, 2.0 m.moles) was refluxed in aqueous acetone (acetone 10 mls, water 1 ml, 5.5 m.moles) for 16 hrs. Upon distilling the product through a vigreux column, no involatile residue remained and the distillate (0.9 g.) boiling at 126°C was indicated by g.l.c. and comparison of spectra to consist of starting material (153) only.

9.13 Attempted Acidic Hydrolyses of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153)

To a 25 ml conical flask, equipped with a reflux condenser and a magnetic stirrer, was added (153) (2.5 g, 5.1 m.moles) and concentrated sulphuric acid (10 mls, 7.7 molar). The contents were refluxed for 16 hrs stirring vigorously to emulsify, as much as possible, the two immiscible liquids. The product still comprised two immiscible phases and the organic layer (2.5 g), after separation in a dropping funnel, was shown by comparison of the g.l.c. retention time and i.r. spectrum to be unchanged (153).

The reaction was repeated under more vigorous conditions. Thus, into a carius tube (10 mls) was placed (153) (2.8 g, 5.7 m.moles) and oleum (9.9 g) containing the equivalent of 25% free SO_3. The tube was sealed under vacuum and placed in a mechanical shaker to mix the two immiscible phases. The tube was heated to 145°C for 17 hrs, with continuous shaking after which it was found that two immiscible phases remained. The organic layer (2.7 g) was shown by comparison of the respective i.r. spectra and g.l.c. retention times to be identical to the starting material. Upon adding the residual oleum to excess ice-water, no organic material separated.

9.14 Reactions of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Fluoride Ion

9.14A Reaction without a solvent

The dimer (160) (1.0 g, 2.25 m.moles) was transferred under vacuum into a carius tube (35 mls capacity) containing dry caesium fluoride (1 g, 6.5 m.moles). The tube was sealed under vacuum and heated at 170°C for 3 hrs. The product (1.0g) was removed from the tube by vacuum transference and was found, by g.l.c. (silicone rubber 100°C, Pye 104) to consist of starting material (62%), and one other product (32%) which was isolated by preparative g.l.c. (Autoprep Col 'O', 40°C) and identified as perfluoro-4-methyl-1,2,5,7-tetra-azatricyclo$[5.3.1.0^{2,6}]$undec-4-ene (222) (0.3 g). [Found: C, 23.1% N, 13.7%; F, 63.6%; M, 418, $C_8N_4F_{14}$ requires C, 22.98%; N, 13.40%; F, 63.62%; M, 418]. i.r. spectrum 21, ^{19}F n.m.r. spectrum 21.

9.14B Reaction of (160) with Caesium Fluoride in Tetrahydrothiophendioxide at 140°C

The dimer (160) (4.1 g, 10.0 m.moles) was transferred under vacuum into a carius tube (35 mls) containing dry caesium fluoride (1 g) and dry tetrahydrothiophendioxide (15 mls). The tube was sealed under vacuum and heated at 140°C for 2 hrs. After reaction the products were removed by vacuum transference and examined by g.l.c. (G.D.B. Col A, 78°C). Three components were present. After separation by preparative g.l.c., the most abundant component (50%) was shown by comparison of i.r. spectra to be starting material. The second component (27% of the product) could not be identified. Its mass spectrum gave a parent ion at m/e = 423 and analysis indicated the empirical formula $C_8N_3F_{15}$.

Its i.r. spectrum contained a band at 1696 cm^{-1} and the ^{19}F n.m.r. spectrum gave six signals at 57.00, 95.46, 99.65, 101.95, 139.06 and 141.84 p.p.m.

The third component (23% of the product) was identified as the tricyclic compound (222) by comparison of i.r. spectra.

9.14C Reaction of Dimer (160) with Fluoride Ion at 180°C in Tetrahydrothiophendioxide

The dimer (160) (1.8 g, 4.3 m.moles) was transferred under vacuum from a $P_2O_5/MgCO_3$ mixture to a flat bottomed carius tube equipped with a magnetic stirrer and containing tetrahydrothiophendioxide (10 mls) as a solvent. The tube was sealed under vacuum and heated at 180°C for 3 hrs whilst vigorously stirring its contents. Upon transferring the products from the reaction vessel under vacuum a liquid (0.8 g) identified by g.l.c. and comparison of i.r. spectra as the unknown product of experiment 9.14B was isolated. No water insoluble phases remained in the residue apart from a fine white powder (0.3 g) identified by i.r. as silica. Gaseous products (c.a. 0.5 g) were also produced.

9.15 Reaction of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) with Caesium Fluoride

Into a dry, flat bottomed carius tube (80 mls capacity) containing a magnetic stirrer, was placed dry caesium fluoride (0.5 g) and tetraglyme (15 mls). (121) (2 g, 5.6 m.moles) was vacuum transferred into the tube which was then sealed under vacuum and heated at 75°C for 2 hrs, stirring the contents vigorously. The product, obtained by vacuum transference, was shown by g.l.c. to consist of two components in the ratio 71:29. After separating by preparative g.l.c. (F_{21}, Col 'O', 20°C) the major component was identified as starting material (0.9 g) and the second component as the -1,4-diene (122) (0.2 g) by comparison of the respective i.r. and ^{19}F n.m.r. spectra.

9.16 Reaction of Perfluoro-4-isopropyl-1-azacyclohexa-1,4-diene (122) with Caesium Fluoride

(122) (1.0 g, 2.8 m.moles) was reacted with caesium fluoride in the same manner as (121) at 80°C for 2 hrs. The product was found by g.l.c. and ^{19}F n.m.r. spectroscopy to consist of a mixture of (121) and (122) in approximately the same ratio as when the -1,3-diene had been the starting material.

9.17 Attempted Reaction of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153) with Caesium Fluoride

Into a dry flat-bottomed carius tube containing a magnetic stirrer (85 mls capacity), was placed dry tetraglyme (10 mls) and caesium fluoride (1 g). The diene (153) (0.9 g, 1.8 m.moles) was added by vacuum transference and the tube was sealed under vacuum and reacted at 50°C for 15 hrs. After vacuum transferring the product (0.9 g) from the solvent it was found by comparing its g.l.c. retention time and i.r. spectrum with those of authentic material, that it consisted of unchanged (153).

9.18 Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Chloride Ion

In a dry, flat-bottomed carius tube (60 mls capacity), was placed a magnetic stirrer, dry lithium chloride (1.0 g, 23.6 m.moles) and dry tetrahydrothiophendioxide (15 mls). The tube was evacuated and the solvent allowed to de-gas, after which (160)

(3.3 g, 7.9 m.moles) was added by vacuum transference from a mixture of P_2O_5 and NaF. The tube was sealed under vacuum and heated at 112°C for 12 hrs whilst its contents were stirred vigorously. The product (3.1 g) was isolated by vacuum transference from the solvent and lithium salts. It was a liquid which partially crystallised on standing (2.4 g of crystals were isolated by recrystallising at 0°C and the product was identified as 1,1'-bi-2-chlorohexafluoro-1,3-diazacyclohex-2-enyl (229). [Found: C, 21.5%; N, 12.1%; F, 50.2%; Cl, 15.8%; M, 450, $C_8N_4F_{12}Cl_2$ requires C, 21.30%; N, 12.42%; F, 50.55%; Cl, 15.72%; M, 450], i.r. spectrum 23, ^{19}F n.m.r. spectrum 22, m.pt. 38-39°C (uncorrected).

Using the same method (160) was reacted with a slightly lower proportion of LiCl. Thus (160) (4.6 g, 11 m.moles) was reacted with LiCl (1.0 g, 23.6 m.moles) in tetrahydrothiophendioxide (15 mls) at 130°C for 18 hrs. The product (4.8 g) was combined with the mother liquor of the first reaction and contained four components (g.l.c.). The most abundant (85%) was isolated by fractionation under reduced pressure collecting at 92-94°C (22 mm Hg) and was shown by comparison of its i.r. spectrum with that of a sample from the first experiment to be (229). The other components were not isolated in a pure state. Of these, the most abundant was less volatile than (229) and comprised 8% of the product. M.s/g.l.c. of fractions rich in this component indicated a parent ion at m/e = 466 and the isotope ratio P:P+2:P+4 was 10:10:3, indicating the presence of three chlorine atoms. The remaining component (7%) was more volatile than (229) and gave a parent ion at m/e = 434 and its isotope ratio P:P+2 = 3:1 indicated one chlorine atom. Traces of a compound with P = 482 and intensity ratio P:P:2:P+4:P+6 =

10:13:6:1, indicating a tetrachloro compound, were also detected.

9.19 Defluorination of 1,1'-bi-2-chlorohexafluoro-1,3-diazacyclohex-2-enyl (229)

(229) (1.8 g, 4 m.moles) was placed in a dry flask where it was vaporised at 85°C into a stream of dry nitrogen (50 mls.min^{-1}). The gas stream was fed through a silica tube (16 m.m. i.d.) packed along 45 cm of its length with coarse iron filings which were heated to 445°C by an enveloping furnace. The product was removed from the nitrogen at liquid air temperature. After a day, all the material had passed through the tube. A liquid product (0.8 g) was obtained. It consisted of one major component (85%) and two unidentified minor components. The major component was isolated by g.l.c. (G.D.B., Col O, 80°C) and was identified as 2-chlorotrifluoropyrimidine (228) (0.4 g). [Found: C, 28.8%; N, 16.3%; F, 33.5%; Cl, 21.5%; M, 168, $C_4N_2F_3Cl$ requires C, 28.51%; N, 16.62%; F, 33.82%; Cl, 21.04%; M, 168], λ_{max} = 212 nm, $\varepsilon = 9.76 \times 10^3$ cyclohexane, i.r. spectrum No. 24, ^{19}F n.m.r. spectrum No. 23, u.v. spectrum No. 4.

CHAPTER 10

EXPERIMENTAL TO CHAPTERS 6 and 7

10.1 Introduction

In this chapter the experimental for Chapters 6 (photolyses) and 7 (miscellaneous reactions) is given. The photolytic work was, as mentioned in Chapter 6, performed in co-operation with R. Middleton. All the photolyses were carried out with a 120 watt Hanovia low-pressure mercury arc which gives virtually monochromatic radiation of 253.7 nm wavelength.

10.2 Photolysis of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121)

Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) (4.3 g, 12.0 m.moles) was placed in clean dry silica tube and de-gassed, prior to sealing the tube under vacuum. The tube (25 cm long and 2 cm in diameter) was then irradiated at 253.7 nm for 116 hours.

The product (3.9 g) was removed from tube by vacuum transference. It was a colourless liquid at room temperature and analysis by g.l.c. (G.D.B., silicone gum rubber, 78^{o}C) indicated the presence of two major components and some minor components. The mixture was separated by distillation (concentric tube). The major component (70%, b.pt. 98.5^{o}C) was identified as perfluoro-6-methyl-5-methylene-2-azahepta-1,3-diene (234). [Found: Analysis results inconsistent; M, 357, $C_8F_{13}N$ requires C, 26.91%; N, 3.92%; F, 69.17%; M, 357]. ^{19}F n.m.r. spectrum No. 24, i.r. spectrum No. 25.

None of the other components were isolated in a pure enough state to be identified.

10.3 Photolysis of Perfluoro-2,3,4-tri-isopropyl-1-azacyclohexa-1,3-diene (201)

Into a clean dry silica tube (29 cm x 2.8 cm dimensions) was placed (201) (0.5 g, 0.81 m.moles). After de-gassing the contents, the tube was sealed under vacuum and irradiated at 253.7 n.m. for 203 hrs. The tube was then opened and the product (0.5 g) removed by vacuum transference. It was shown by g.l.c. and i.r. spectroscopy to consist of starting material only.

10.4 Mercury Sensitized Photolysis of Perfluoro-2,5-di-isopropyl-1,4-diazacyclohexa-1,4-diene (185)

To a clean dry silica tube, of dimensions 22 cm by 2.8 cm was added a small drop (c.a. 0.5 g) of mercury. Perfluoro-2,5-di-isopropyl-1,4-diazacyclohexa-1,4-diene (185) (1.0 g, 2.0 m.moles) was then transferred to the tube under vacuum. After de-gassing the contents to exclude oxygen, the tube was sealed under vacuum and irradiated, in the usual manner, at 253.7 nm with a 120 watt source, for a period of 335 hrs. Slight tarring of the tube contents, after this time, indicated that some reaction had taken place.

The tube was opened and the products were transferred under vacuum. Upon warming to room temperature some of the material volatilized and was collected in a gas storage bulb. The volatile product was identified as perfluoroisobutyronitrile (242) from its mass spectrum and by comparison of its i.r. spectrum with that of an authentic sample.[203]

The material remaining in the liquid phase (0.6 g) was analysed by g.l.c. and was found to contain one major (80%) component and two minor components. The two minor components (together <10%) were identified as (242) and starting material

(185) by comparison of g.l.c./mass spectra with those of authentic samples. The major component was isolated from the mixture by preparative g.l.c. (Autoprep., di-isodecylphthalate, 40^{o}C). It was identified as perfluoro-4-methyl-3-methylene-2-azapent-1-ene (241) although a pure sample was not obtained because of its extreme susceptibility to hydrolysis. Analysis indicated the presence of hydrolysed material. M, 295, $C_6F_{11}N$ requires M, 295 (but a peak at m/e = 272 also indicated the presence of the isocyanate hydrolysis product) ^{19}F n.m.r. spectrum No. 25.

10.5 Mercury Sensitized Photolysis of Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153)

To a clean dry silica tube (28 cm high, 2.7 cm wide) was added perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153) (1.5 g, 3.1 m.moles) and a small drop of mercury. The liquid was dé-gassed, to remove atmospheric oxygen and then irradiated at 253.7 nm, using a 120 watt source, for 117 hrs. After reaction the contents of the tube had discoloured and the volatile products (1.5 g) were removed by vacuum transference, a colourless liquid being obtained.

Analysis by g.l.c. revealed four major components and traces of other material. The mixture was separated by preparative g.l.c. (Autoprep. silicone gum rubber, 80^{o}C) and the first two components were identified as (242) (9%) and (241) (15%) by comparison of their g.l.c. retention times, i.r. spectra and mass spectra with those of authentic samples. The third component (24%) was identified as starting material (153) in the same way. The fourth component (48%) was identified as <u>perfluoro-2,8-dimethyl-7-methylene-4,6-di-azanona-3,5-diene</u> (243). [Found

F, 69.6%; M, 490, $C_{10}F_{18}N_2$ requires F, 69.8%; M, 490]. ^{19}F n.m.r. spectrum No. 26, i.r. spectrum No. 26.

10.6 Mercury Sensitized Photolysis of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)

Into a clean dry silica tube (21.0 cm x 2.7 cm), containing a small drop (c.a. 0.5 g) of mercury, was placed perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) (1.0 g, 2.5 m.moles). The contents of the tube were thoroughly de-gassed before it was sealed under vacuum. The tube was then irradiated at 273.7 nm using a 120 watt source for a period of 227 hrs. The product (1.0 g) was then transferred from the tube under vacuum and analysis by g.l.c. and i.r. indicated it to contain starting material (160) only.

10.7 Mercury Sensitized Photolysis of Perfluoro-1-azacyclohex-1-ene (161)

Into a clean dry silica tube (22 cm long, 2.8 cm diameter) was placed a small drop of mercury (c.a. 0.25 g) and (161) (2.6 g, 10.6 m.moles). After de-gassing the contents, to remove dissolved oxygen, the tube was sealed under vacuum and irradiated under the usual conditions (253.7 nm, 120 watt source) for 357 hrs. The tube was then opened and its contents removed by vacuum transference. They were found to consist solely of starting material, by comparison of the g.l.c. retention times and i.r. spectra.

10.8 Defluorinations of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160)

The defluorinating apparatus consisted of a silica tube (internal bore 16 m.m.) packed for 45 cm of its length with coarse iron filings (283 g), heated externally by an enveloping electric furnace and purged with dry nitrogen. The starting material (160) (4.1 g, 9.8 m.moles) was passed over the iron filings (at 345^{o}C) as a vapour in the nitrogen flow (46 mls.min^{-1} contact time 118 sec). The product (1.1 g), a liquid, was trapped from the gas flow at liquid air temperature. Two days were required to pass all compound (160) by this method. Analysis of the product by g.l.c. revealed one major component, which was shown, by comparison of its i.r. spectrum with that of an authentic sample, to be tetrafluoropyrimidine (1.0 g) (156).

The same experiment was performed at a lower temperature. Thus (160) (1.7 g, 4.1 m.moles) was passed over iron filings at 257^{o}C in a stream of dry nitrogen (43 mls.min^{-1}) to give, after two days, a liquid product (0.9 g). The product was found to contain two major components, by g.l.c., with small amounts of other components. Upon separation (F21 Col A, 70^{o}C), the major components were identified as starting material (160) (0.5 g) and tetrafluoropyrimidine (156) (0.2 g), by comparison of their i.r. spectra with those of authentic samples. The most abundant of the minor components was indicated by its g.l.c. peak area to comprise c.a. 5% of the product and was indicated, by mass spectroscopy/g.l.c., to have a parent ion at m/e = 380.

10.9 Attempted Reaction of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Mercury

Into a clean dry carius tube (10 mls) was placed (160) (1.0 g, 2.4 m.moles) with mercury (1.4 g, 7.0 m.moles). The tube was sealed under vacuum and heated at 240^{o}C for 59 hrs. Upon opening the tube a liquid product (0.9 g) was obtained by vacuum transference. It was found by g.l.c. and i.r. to consist of unchanged (160).

The reaction was attempted at a higher temperature. Thus into a clean dry carius tube of 12 mls capacity was placed (160) (1.2 g, 2.9 m.moles) and mercury (1.2 g, 6.0 m.moles). The tube was sealed under vacuum and heated at 400°C for 4.75 hrs. Upon opening the tube volatile products were recovered by vacuum transference. On warming to room temperature the bulk of the product vaporised only 0.2 g remained in the liquid phase. The liquid was found by g.l.c./mass spectroscopy to consist of a complicated mixture of products of lower molecular weight than (160). The gas was unresolved by g.l.c. Recovered mercury weighed 1.2g.

10.10 Attempted Reactions of Perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with Nitric Oxide

The dimer (160) (2.3 g, 5.5 m.moles) was placed in a carius tube (232 mls) by vacuum transference from P_2O_5 and de-gassed. Nitric oxide (0.3 g, 10.5 m.moles) was then admitted to the tube which was then sealed under vacuum and heated at 180°C for 12 hrs. The product consisted of 0.1 g of gas, identified as unreacted nitric oxide by i.r. spectroscopy, and 2.2 g of liquid indicated by g.l.c. and i.r. to be unreacted (160) only.

At a higher temperature (345°C for 16 hrs) in the same tube, 2 g (6.3 m.moles) of (160) similarly failed to react with 0.33 g (11.2 m.moles) of nitric oxide.

10.11 Defluorination of a Mixture of Cis and Trans-perfluoro-2,3,4,5-tetramethylhex-3-ene (168) and (169)

Into a 25 ml, two-necked, pear-shaped flask was placed a mixture of cis and trans-perfluoro-2,3,4,5-tetramethylhex-3-ene (168 and 169, 3.5 g, 7m mole The liquid was slowly vaporised by dry nitrogen (24 mls.min^{-1}) and the vapour was then passed through a silica tube (45 cm by 1.4 cm) which contained loosely packed coarse iron filings (c.a. 280 g) maintained at 310^{o}C by an enveloping furnace. The evaporation took 9 hrs, 45 mins and the product (2.0 g) was collected by trapping at liquid air temperature. G.l.c. analysis (G.D.B., silicone gum rubber, 25^{o}C) indicated two major components and at least six minor components. The mixture was separated by preparative g.l.c. (F21, silicone gum rubber, 20^{o}C) but an insufficient amount of the first major (15%) component was recovered for it to be identified. The second major component (70%) was obtained as a 90% pure fraction by careful peak chopping and identified as as perfluoro-2,3,4,5-hexa-2,4-diene (245). [Found: F, 74.4%; M, 462, $C_{10}F_{18}$ requires F, 74.0%; M, 462]. ^{19}F n.m.r. spectrum No. 27, i.r. spectrum No. 27.

APPENDIX 1

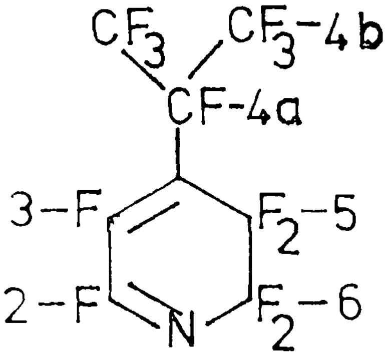
^{19}F and ^{1}H N.m.r. Spectra

The following abbreviations have been used in Appendix 1:

ax. = axial
eq. = equatorial
D = doublet
T = triplet
Q = quartet
Sp = septet

1. Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121)

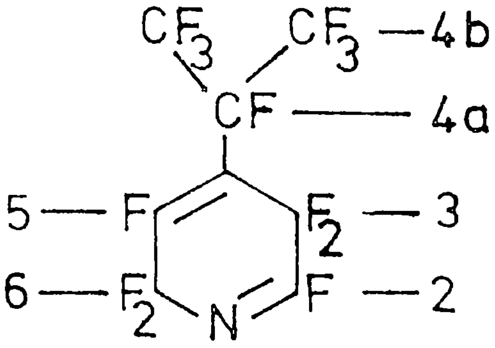
Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
52.55	D($J_{2.3}$ = 20)	1	2
76.76	D($J_{4b.3}$ = 17.5) of D($J_{4b.4a}$ = 6) of T($J_{4b.5}$ = 6)	6	4b
102.68	D($J_{6.4a}$ = 5.5)	2	6
107.5	D($J_{3.2}$ = 20) of D($J_{3.4a}$ = 20) of Sp($J_{3.4b}$ = 17.5)	1	3
114.62	D($J_{5.4a}$ = 35) of multiplets	2	5
185.08	Broad	1	4a



Recorded neat at 40°C with external $CFCl_3$ reference

2. Perfluoro-4-isopropyl-1-azacyclohexa-1,4-diene (122)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
58.12	T($J_{2,3}$ = 26)	1	2
78.44	D($J_{4b,4a}$ = 24) of multiplets	6	4b
88.2	D($J_{6,5}$ = 24)	2	6
101.06	Broad	1	5
103.1	Broad	2	3
188.67	Broad	1	4a

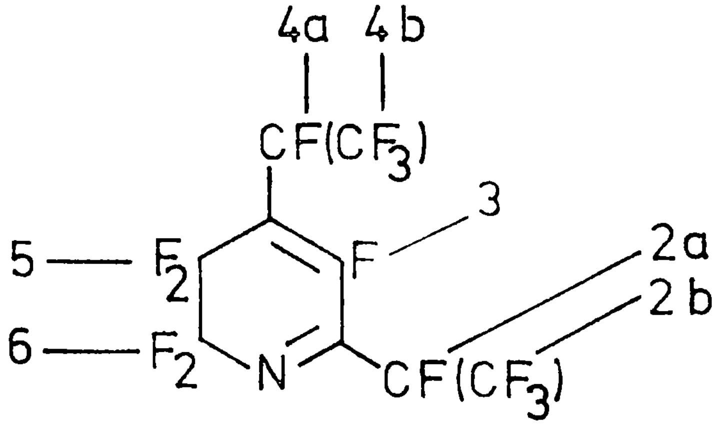


Recorded neat at 40°C with external $CFCl_3$ reference.

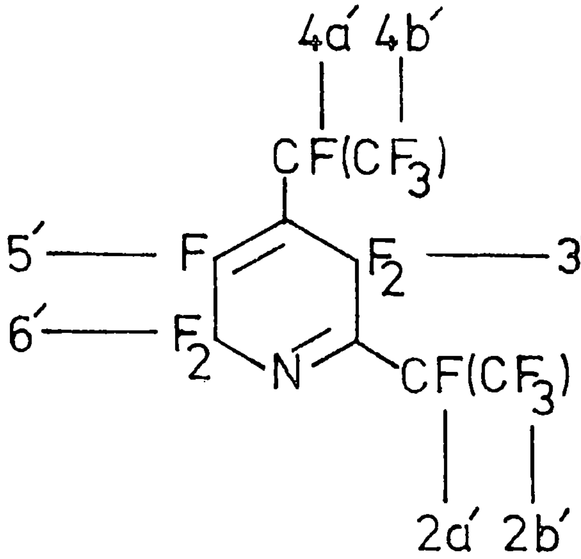
3. An Equimolar Mixture of Perfluoro-2,4-di-isopropyl-1-azacyclohexa-1,4-diene (128) and Perfluoro-2,4-di-isopropyl-1,3-diene (127)

Shift p.p.m..	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
75.46	D(J = 7) of D(J = 6.5)	6	2, 2b', 4b or 4b'
76.45	D(J = 5) of T(J = 3.5)	6	2b, 2b', 4b or 4b'
76.88	D(J = 20) of D(J = 11.5) of	6	2b, 2b', 4b or 4b'
77.58	D(J = 24) of D(J = 6) of T(J = 3.5)	6	2b, 2b', 4b or 4b'
91.02	D($J_{6'.5'}$ = 26)	2	6'
98.42	D($J_{3'.2a'}$ or $J_{3'.4a'}$ = 37.5) of D($J_{3'.2a'}$ or $J_{3'.4a'}$ = 37.5)	2	3'
101.26	Multiplet	1	3 or 5'
c.a. 103	Broad	c.a. 1	3 or 5'
109.72	T($J_{6.5}$ = 8)	2	6
111.76	Multiplet	2	5
c.a. 184	Broad	c.a. 1	4a
186.61	D($J_{2a.3}$ = 68) of Multiplets	1	2a
187.87	T($J_{2a'.3'}$ or $J_{4a'.3'}$ = 37)	1	2a' or 4a'
191.74	T($J_{2a'.3'}$ or $J_{4a'.3'}$ = 39)	1	2a' or 4a'

(127)



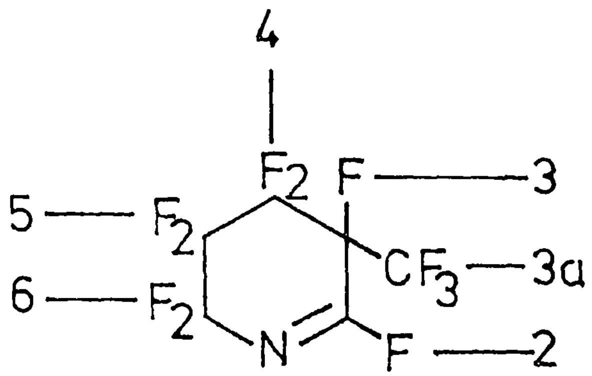
(128)



Recorded neat at 40°C
with external $CFCl_3$
reference

4. Perfluoro-3-methyl-1-azacyclohex-1-ene (135)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
41.0	Broad	1	2
72.23	Broad	3	3a
93.16	D($J_{6ax.6eq}$ = 242)	1	6 ax.
101.10	D($J_{6eq.6ax}$ = 242)	1	6 eq.
127.63	D($J_{4ax.4eq}$ or $J_{5ax.5eq}$ = 313)	1	4 ax. or 5 ax.
132.59	D($J_{4ax.4eq}$ or $J_{5ax.5eq}$ = 293)	1	4 ax. or 5 ax.
137.51	D($J_{4eq.4ax}$ or $J_{5eq.5ax}$ = 293)	1	4 eq. or 5 eq.
148.64	D($J_{4eq.4ax}$ or $J_{5eq.5ax}$ = 313)	1	4 eq. or 5 eq.
177.43	Partially resolved doublet ($J_{3.2}$ = 24)	1	3



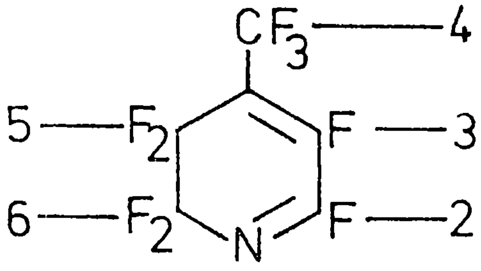
(135)

Run neat at 40°C with external $CFCl_3$ reference

5. Perfluoro-4-methyl-1-azacyclohexa-1,3-diene (140)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
52.26	D($J_{2.3}$ = 18.5)	1	2
61.93	D($J_{4a.3}$ = 22) of T($J_{4a.5}$ = 6.5)	3	4a
103.95	Broad	2	6
114.83	Q($J_{3.4a}$ = 22) of D($J_{3.2}$ = 18.5) of T($J_{3.5}$ = 16)	1	3
117.83	D($J_{5.3}$ = 16) of Q($J_{5.4a}$ = 6.5)	2	5

Run neat at 40°C with
external $CFCl_3$ reference

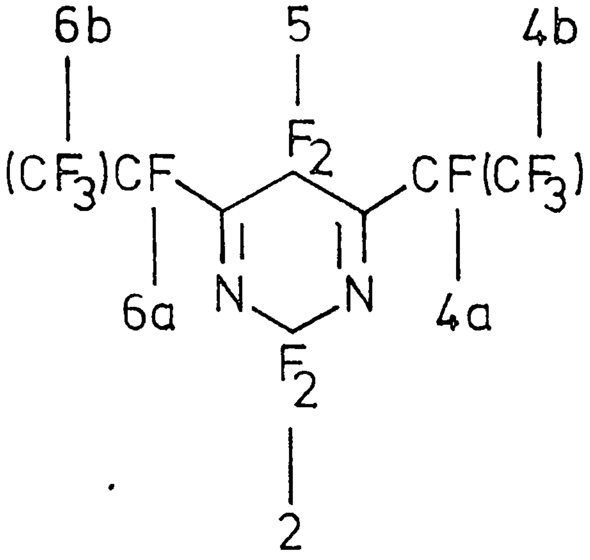


(140)

6. Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-3,6-diene (153)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
74.33	Singlet	2	2
77.92	D($J_{4b.4a}$ = 6) of T($J_{4b.5}$ = 3)	12	4b and 6b
114.32	T($J_{5.4a}$ = 31) of multiplets	2	5
184.72	T($J_{4a.5}$ = 31) of Sp($J_{4a.4b}$ = 6)	2	4a and 6a

Run neat at 40°C with external $CFCl_3$ reference

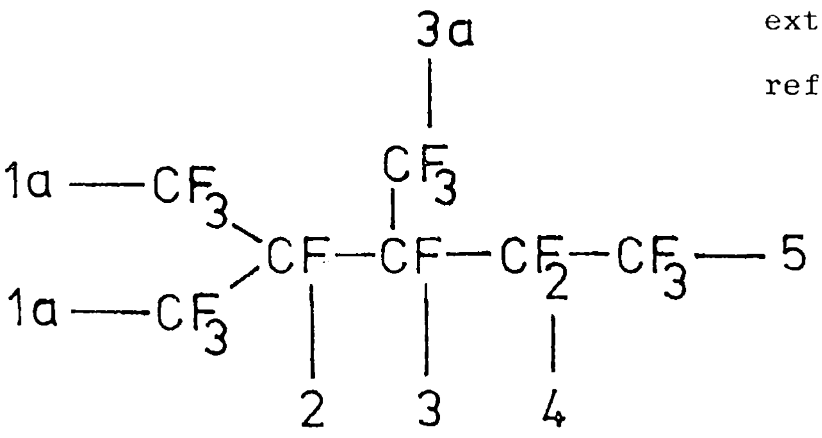


(153)

7. Perfluoro-2,3-dimethylpentane (170)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
72.62	Broad, assymetrical	9	1a overlapping 3a
83.19	Multiplet	3	5
115.44	Multiplet	2	4
177.93	Broad	1	2 or 3
181.99	Multiplet	1	2 or 3

Run neat at 40°C with external $CFCl_3$ reference



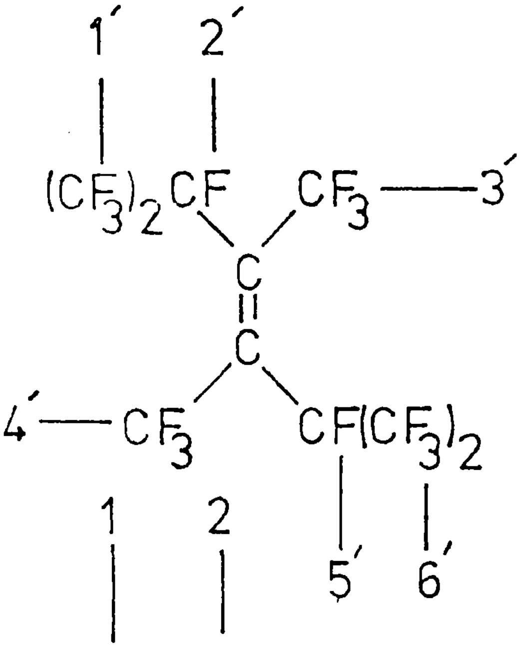
(170)

8. A Mixture of Cis- and Trans-perfluoro-2,3,4,5-tetramethylhex-3-ene (168) and (169) (Cis:trans = 36:64)

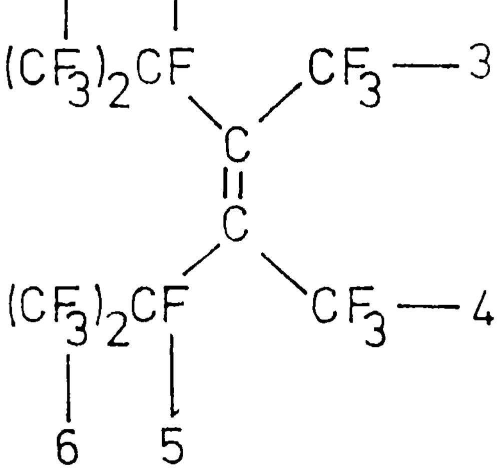
Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
57.0	D($J_{3',5'} \equiv J_{4',2'} = 50$)	12 combined	3' and 4'
57.64	Broad		3 and 4
72.25	Broad, assymetric	24	1 and 6 overlapping 1' and 6'
159.34	Broad	4 combined*	2 and 5
161.45	Q($J_{2',4'} \equiv J_{5',3'} = 50$)		2' and 5'

*Intensity ratio (2+5):(2'+5') = 36:64

Run neat at 40°C with external $CFCl_3$ reference



(169)

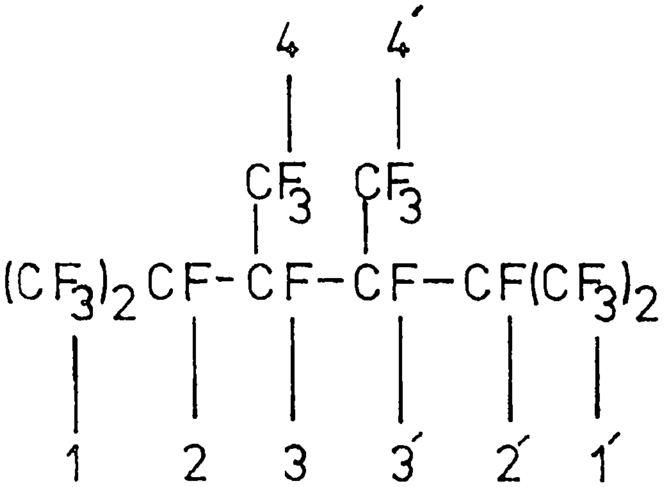


(170)

9. Perfluoro-2,3,4,5-tetramethylhexane (171)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
69.52	Broad	12	1 and 1'
72.62	Broad	6	4 and 4'
166.5	Broad	2	2 and 2' or 3 and 3'
170.32	Broad	2	2 and 2' or 3 and 3'

Run neat at 40°C with external $CFCl_3$ reference

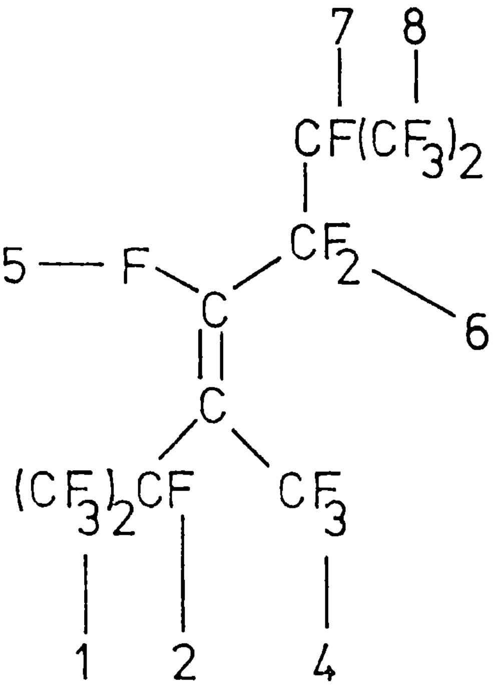


$(CF_3)_2CF\text{-}CF(CF_3)\text{-}CF(CF_3)\text{-}CF(CF_3)_2$

10. Cis- or Trans-perfluoro-2,3,6-trimethylhept-3-ene (175) or (176)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
62.41	Multiplet	3	4
75.82	Multiplet	6	8
77.32	D($J_{1.5}$ = 29)	6	1
89.11	Broad	1	5
107.18	Broad	2	6
180.83	Q($J_{2.4}$ = 30)	1	2
184.73	Broad	1	7

Run neat at 40°C with external $CFCl_3$ reference

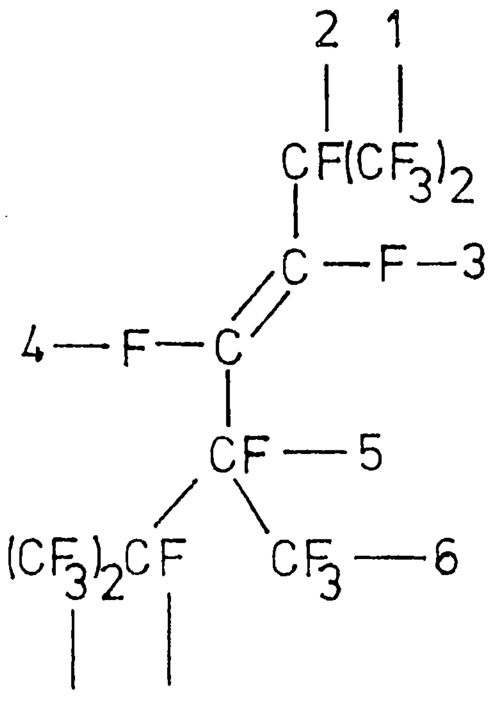


(or cis)

(176)

11 Cis or Trans-perfluoro-2,5,6-trimethylhept-3-ene (177) or (178)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
70.9	Broad, assymetric	9	6 overlapped by 1 or 8
73.9	Broad	6	1 or 8
126.5	Broad	1	3 or 4
128.7	Broad	1	3 or 4
194.5	Broad	1	2 or 5 or 7
201.2	Broad	1	2 or 5 or 7
207.6	Multiplet	1	2 or 5 or 7



(or cis)

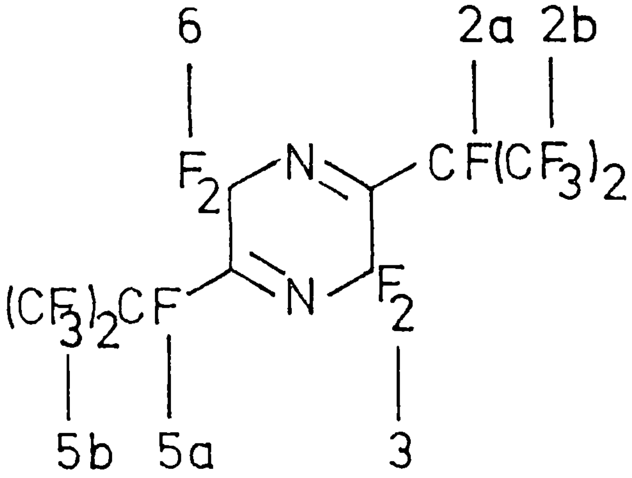
(178)

Run neat at 40°C with external $CFCl_3$ reference

12 Perfluoro-2,5-di-isopropyl-1,4-diazacyclohexa-1,4-diene (185)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
74.02	D($J_{2b.2a} \equiv J_{5b.5a} = 6$) of T($J_{2b.3} \equiv J_{5b.6} = 3$)	12	2b and 5b
85.70	D($J_{3.2a} \equiv J_{6.5a} = 29$) of Sp($J_{3.2b} \equiv J_{6.5b} = 3$)	4	3 and 6
189.09	T($J_{2a.3} \equiv J_{5a.6} = 29$) of Sp($J_{2a.2b} \equiv J_{5a.5b} = 6$)	2	2a and 5a

Recorded as a solution in hexadeuteroacetone at 40°C with external $CFCl_3$ reference

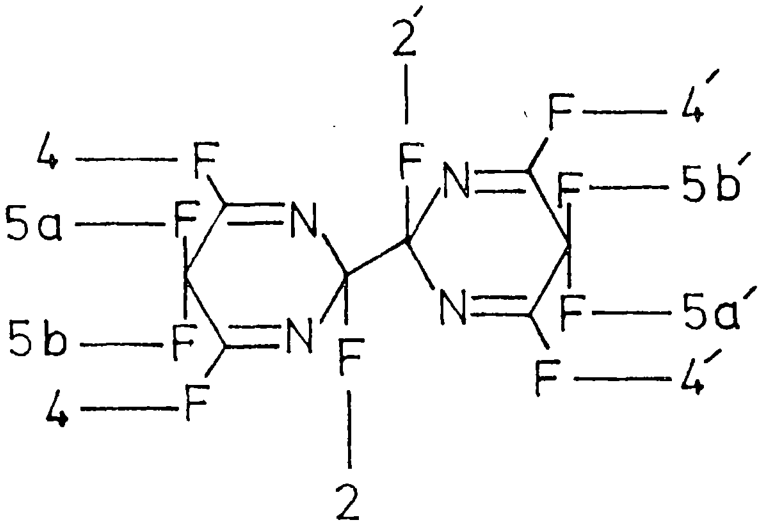


(185)

13. Perfluoro-2,2'-bi-1,3-diazacyclohexa-3,6-dienyl (195)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
60.39	D($J_{4.5b} \equiv J_{4'.5b'}$ = 24) of D($J_{4.5a} \equiv J_{4'.5a'}$ = 24) of T($J_{4.2} \equiv J_{4'.2'}$ = 3)	4	4 and 4'
118.33	Broad	2	2 and 2'
120.93	T($J_{5b.4} \equiv J_{5b'.4'}$ = 24) of D($J_{5b.2} \equiv J_{5b'.2'}$ = 4)	2	5b and 5b'
121.22	T($J_{5a.4} \equiv J_{5a'.4'}$ = 24)	2	5a and 5a'

Recorded as a solution in hexadeuteroacetone at 40°C with external $CFCl_3$ as reference

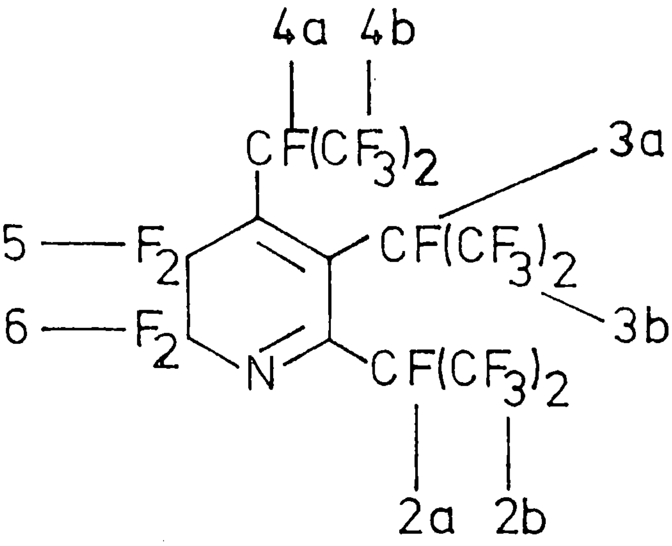


(195)

14. Perfluoro-2,3,4-tri-isopropyl-1-azacyclohexa-1,3-diene (201)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
66.93	Multiplet	3	2b, 2c, 3b, 3c 4b and 4c
68.92	Multiplet	3	
72.55	Multiplet	3	
76.54	Broad, assymetric	9	
107.88	D($J_{6ax.6eq.}$ = 220)	1	6 ax.
117.42	D($J_{6eq.6ax.}$ = 220)	1	6 eq.
121.73	D($J_{5ax.5eq.}$ = 316)	1	5 ax.
131.38	D($J_{5eq.5ax.}$ = 316)	1	5 eq.
154.52	Multiplet	1	2a, 3a and 4a
170.99	Multiplet	1	
182.62	Multiplet	1	

Recorded neat at 40°C with external $CFCl_3$ as reference

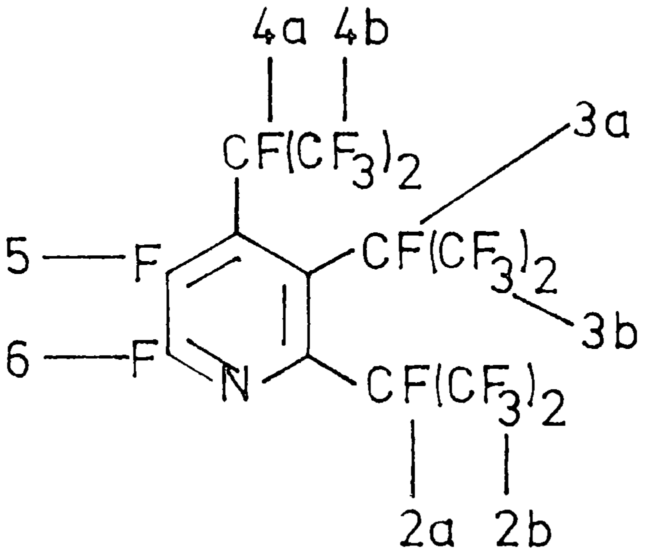


(201)

15. Perfluoro-2,3,4-tri-isopropylpyridine (203)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
69.33	Multiplet	6	3b or 2b
71.03	Multiplet	6	3b or 2b
72 65	D($J_{4b.5}$ = 25)	6	4b
76.71	D($J_{6.5}$ = 25)	1	6
125.64	D($J_{5.6}$ = 25) of Sp($J_{5.4b}$ = 25)	1	5
143.14	Multiplet	1	2a, 3a and 4a
170.32	Multiplet	1	
172.42	Multiplet	1	

Recorded as a solution in $CFCl_3$ at 40°C



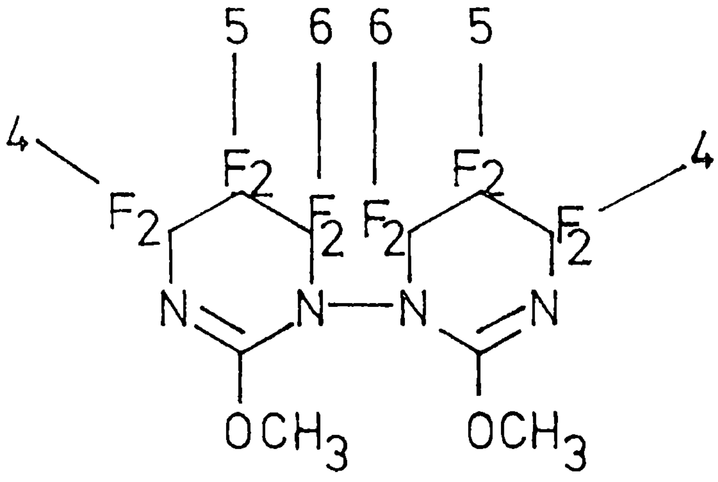
(203)

16. 1,1'-bi-2-methoxyhexafluoro-1,3-diazacyclohex-2-enyl (212)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
92.4	D($J_{4ax.4eq.}$ or $J_{6ax.6eq.}$ = 570)	1	4 ax. or 6 ax.
95.3	D($J_{4eq.4ax.}$ or $J_{6eq.6ax.}$ = 570)	1	4 eq. or 6 eq.
97.9	D($J_{4ax.4eq.}$ or $J_{6ax.6eq.}$ = 196)	1	4 ax. or 6 ax.
111.2	D($J_{4eq.4ax.}$ or $J_{6eq.6ax.}$ = 196)	1	4 eq. or 6 eq.
135.7	D($J_{5ax.5eq.}$ = 254) of multiplets	1	5 ax.
138.1	D($J_{5eq.5ax.}$ = 254) of multiplets	1	5 eq.

^{1}H = Singlet at 3.12 p.p.m.

Recorded as a solution in d_6-acetone at 40°C with external $CFCl_3$ and T.M.S. references



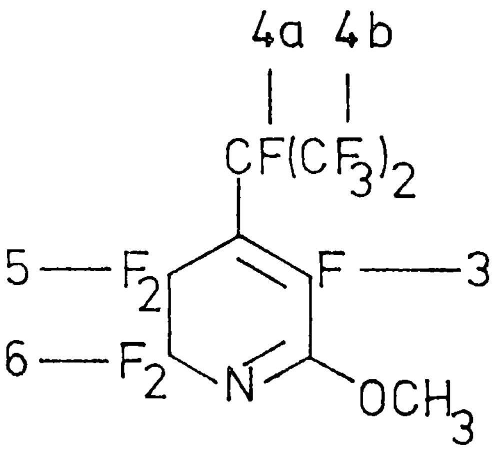
(212)

17. 2-methoxy-4-(heptafluoroisopropyl)pentafluoro-1-azacyclohexa-1,3-diene (213)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
79.2	D($J_{4b,3}$ = 18.5) of D($J_{4b,4a}$ = 7) of T($J_{4b,5}$ = 5)	6	4b
99.5	T($J_{6,5}$ = 6)	2	6
105.9	D($J_{3,4a}$ = 14) of Sp($J_{3,4b}$ = 18.5)	1	3
115.3	D($J_{5,4a}$ = 27) of Sp($J_{5,4b}$ = 5) of T($J_{5,6}$ = 6)	2	5
177.2	T($J_{4a,5}$ = 27) of Sp($J_{4a,4b}$ = 7)	1	4a

^1H = singlet at 3.13 p.p.m.

Recorded neat at 40°C
with external $CFCl_3$
and T.M.S. references.



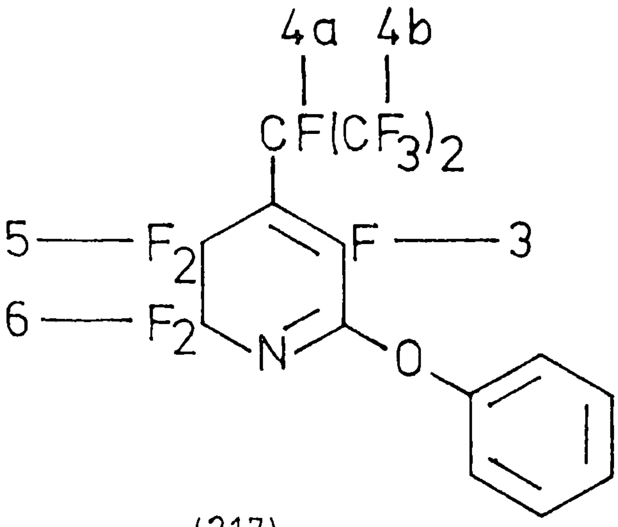
(213)

18. 2-phenoxy-4-(heptafluoroisopropyl)pentafluoro-1-azacyclohexa-1,3-diene (217)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
77.6	D($J_{4b,3}$ = 16) of D($J_{4b,4a}$ = 6) of T($J_{4b,5}$ = 5)	6	4b
100.1	T($J_{6,5}$ = 7)	2	6
105.1	Sp($J_{3,4b}$ = 16) of D($J_{3,4a}$ = 14)	1	3
115.4	Multiplet	2	5
177.0	Multiplet	1	4a

^{1}H = broad 7.11 p.p.m.

Recorded as a solution in diethylether at 40°C with external $CFCl_3$ and T.M.S. reference

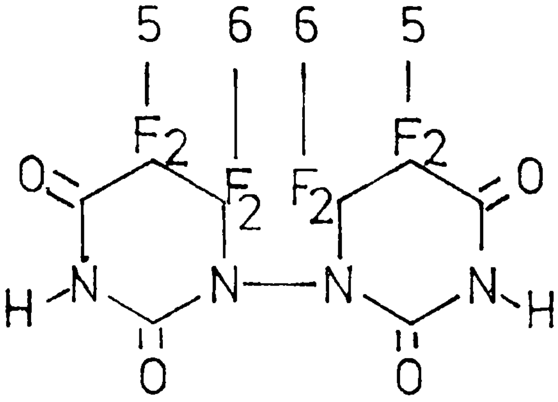


(217)

19. 1,1'-bi-3H-2,4-diketotetrafluoro-1,3-diazacyclohexyl (218)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
98.72	D($J_{6ax.6eq.}$ = 187)	1	6 ax.
105.41	D($J_{6eq.6ax.}$ = 187)	1	6 eq.
120.71	D($J_{5ax.5eq.}$ = 285)	1	5 ax.
130.07	D($J_{5eq.5ax.}$ = 285)	1	5 eq.

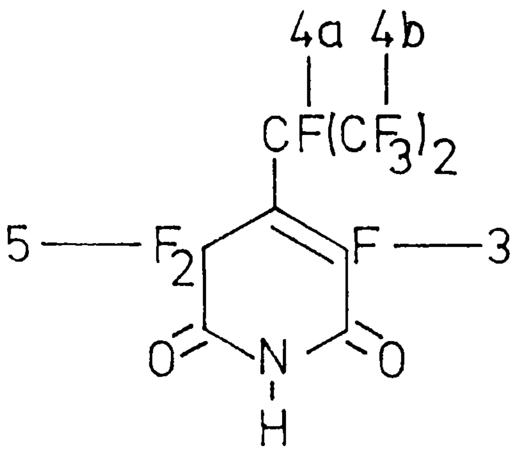
Recorded as a solution in tetraglyme at 40°C with external $CFCl_3$ reference



20. 1-H-2,6-diketo-4-(heptafluoroisopropyl)trifluoro-1-azacyclohex-3-ene (219)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
75.49	D($J_{4b,3}$ = 23) of D($J_{4b.4a}$ = 7) of T($J_{4b.5}$ = 3)	6	4b
93.69	D($J_{5.4a}$ = 34) of Multiplets	2	5
c.a.100.4	Broad	c.a. 1	3
185.51	T($J_{4a.5}$ = 34) of Multiplets	1	4a

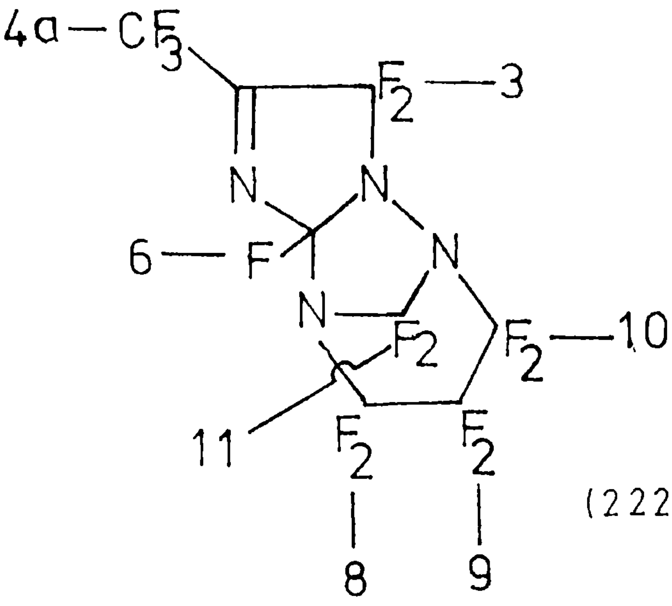
Recorded as a solution in tetraglyme at 40°C with external $CFCl_3$ reference



(219)

21. Perfluoro-4-methyl-1, , ,7-tetraazatricyclo[5.3.1.$0^{2,6}$]-undec-4-ene (222)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
58.6	Singlet	3	4a
88.3	D($J_{11ax.11eq.}$ = 234)	1	11ax.
98.6	D($J_{11eq.11ax.}$ = 234)	1	11eq.
93.8	D(J = 139)	1	3,8,10 or 11
115.1	D(J = 139)	1	
105.3	D(J = 90)	1	
106.3	D(J = 90) over a Singlet	2	6 overlain by 3,8,10 or 11
125.1	Singlet	2	3,8,10 or 11
130.0	D($J_{9ax.9eq.}$ = 260)	1	9ax.
137.0	D($J_{9eq.9ax.}$ = 260)	1	9eq.

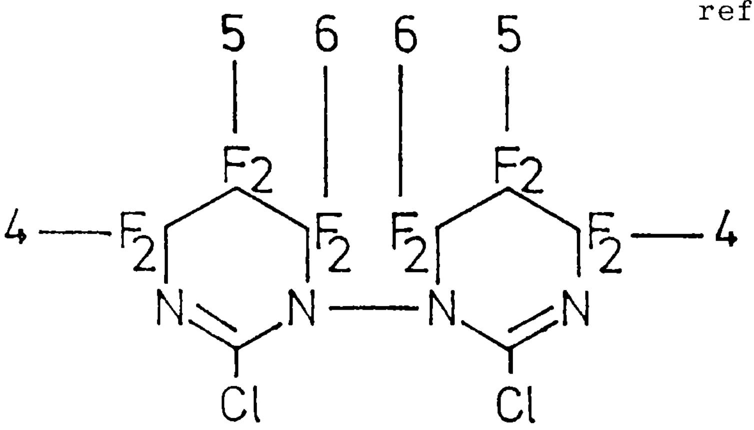


(222)

22. <u>1,1'-bi-2-chlorohexafluoro-1,3-diazacyclohex-2-enyl (229)</u>

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
91.05	D($J_{4ax.4eq.}$ or $J_{6ax.6eq.}$ = 198)	1	4 ax. or 6 ax.
93.02	D($J_{4ax.4eq.}$ or $J_{6ax.6eq.}$ = 237)	1	4 ax. or 6 ax.
102.76	D($J_{4eq.4ax.}$ or $J_{6eq.6ax.}$ = 237)	1	4 eq. or 6 eq.
129.98	D($J_{4eq.4ax.}$. or $J_{6eq.6ax.}$ = 198)	1	4 eq. or 6 eq.
131.76	D($J_{5ax.5eq.}$ = 266)	1	5 ax.
141.43	D($J_{5eq.5ax.}$ = 266)	1	5 eq.

Recorded as neat liquid at 40°C with external $CFCl_3$ reference



(229)

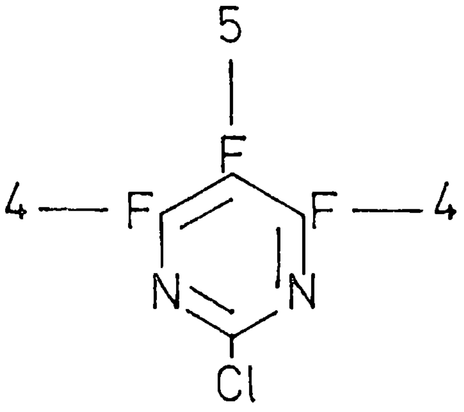
23. 2-chlorotrifluoropyrimidine (228)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
74.52	D($J_{4.5}$ = 20)	2	4
172.61	T($J_{5.4}$ = 20)	1	5

Recorded neat at 40°C

with external $CFCl_3$

reference

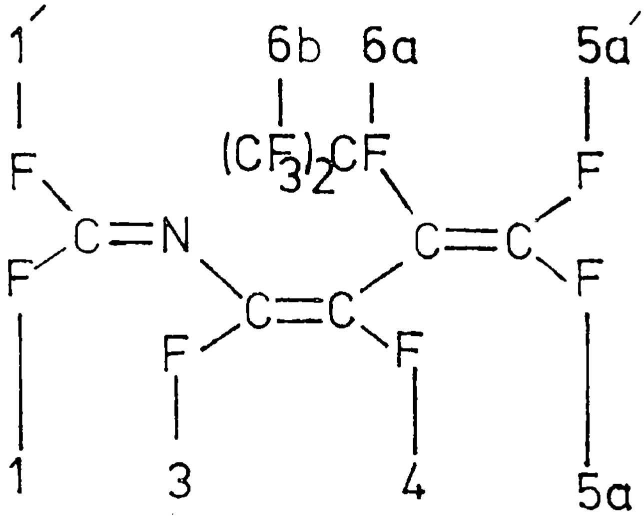


(228)

24. Perfluoro-6-methyl-5-methylene-2-azahepta-1,3-diene (234)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
32.9	Broad	1	1 or 1'
51.2	Broad	1	1 or 1'
78.19	Multiplet	6	6b
96.12	Broad	1	5a or 5a'
113.8	Broad D($J_{4,3}$ = 18)	1	4
114.3	Broad	1	5a or 5a'
136.7	D($J_{3,4}$ = 18) of T($J_{3,1}$ = 7.5)	1	3
186.4	Broad	1	6a

Recorded at 40°C with external $CFCl_3$ reference

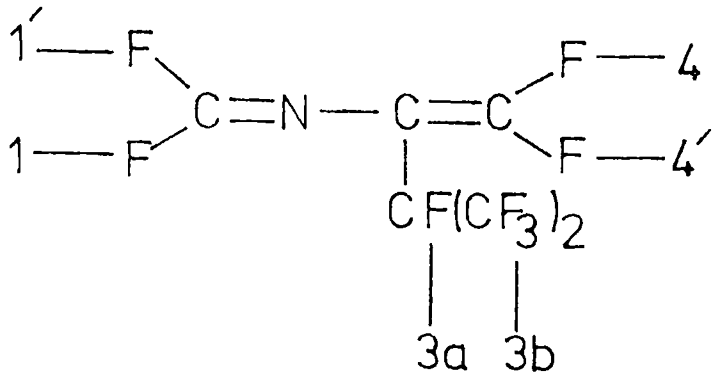


(234)

25. Perfluoro-4-methyl-3-methylene-2-aza-pent-1-ene (241)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
42.6	Broad	1	1 or 1'
55.9	Broad	1	1 or 1'
78.88	Singlet	6	3b
83.05	D($J_{4.4'}$ = 29) of T($J_{4.1}$ or $J_{4.1'}$ = 15)	1	4
92.99	D($J_{4'.3a}$ = 59) of D($J_{4'.4}$ = 29)	1	4'
187.0	Broad D($J_{3a.4'}$ = 59)	1	3a

Recorded neat at 40°C with external $CFCl_3$ reference

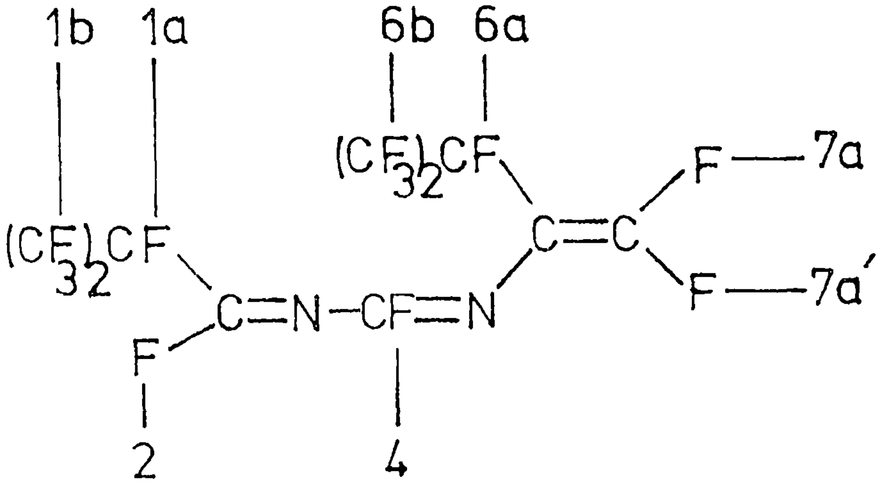


(241)

26. Perfluoro-2,8-dimethyl-7-methylene-4,6-diazanona-3,5-diene (243)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
41.78	Singlet	2	2 and 4
76.62	Multiplet	6	1b or 6b
77.67	D($J_{7a.7a'}$ = 26)	1	7a
77.93	Multiplet	6	1b or 6b
91.32	D($J_{7a'.6a}$ = 62) of D($J_{7a'.7a}$ = 26)	1	7a'
182.2	Sp($J_{1a.1b}$ = 7)	1	1a
185.9	D($J_{6a.7a'}$ = 62) of Sp($J_{6a.6b}$ = 6)	1	6a

Recorded neat at 40°C with external $CFCl_3$ reference

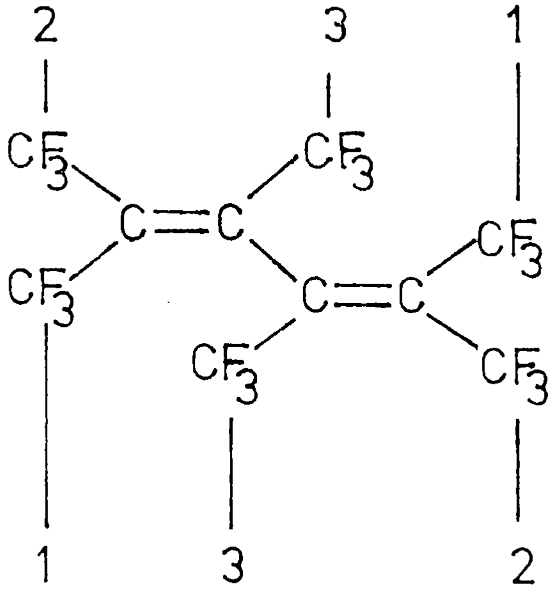


(245)

27. Perfluoro-2,3,4,5-tetramethylhexa-2,4-diene (245)

Shift p.p.m.	Fine Structure Coupling Constants in Hz	Relative Intensity	Assignment
78.33	Broad	3	3
79.89	Broad, assymetric	6	1 and 2

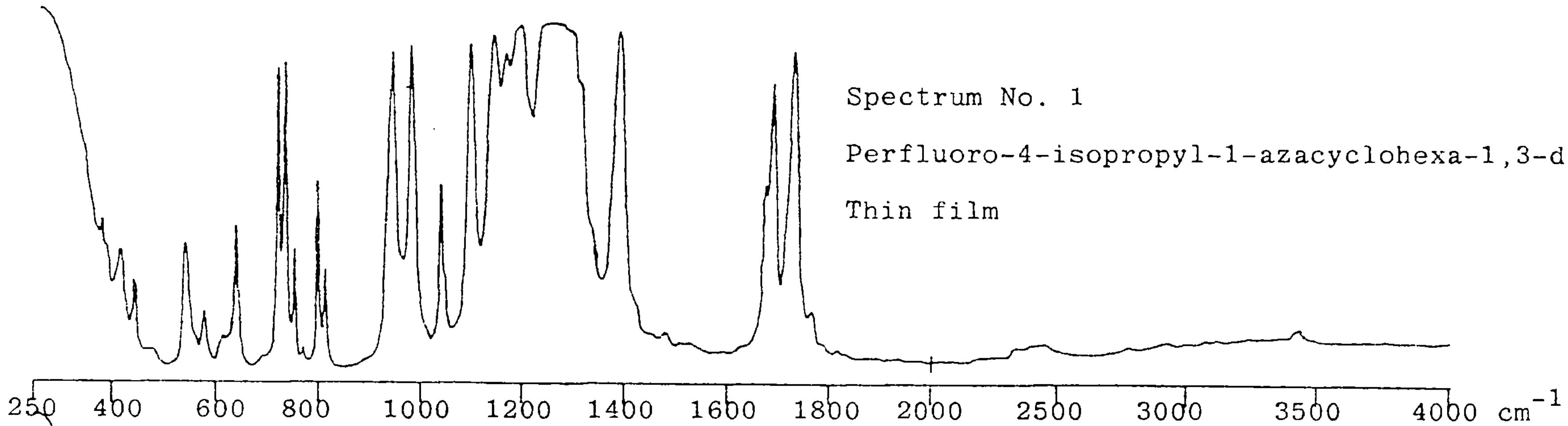
Recorded neat at 40°C with external $CFCl_3$ reference



(245)

APPENDIX 2

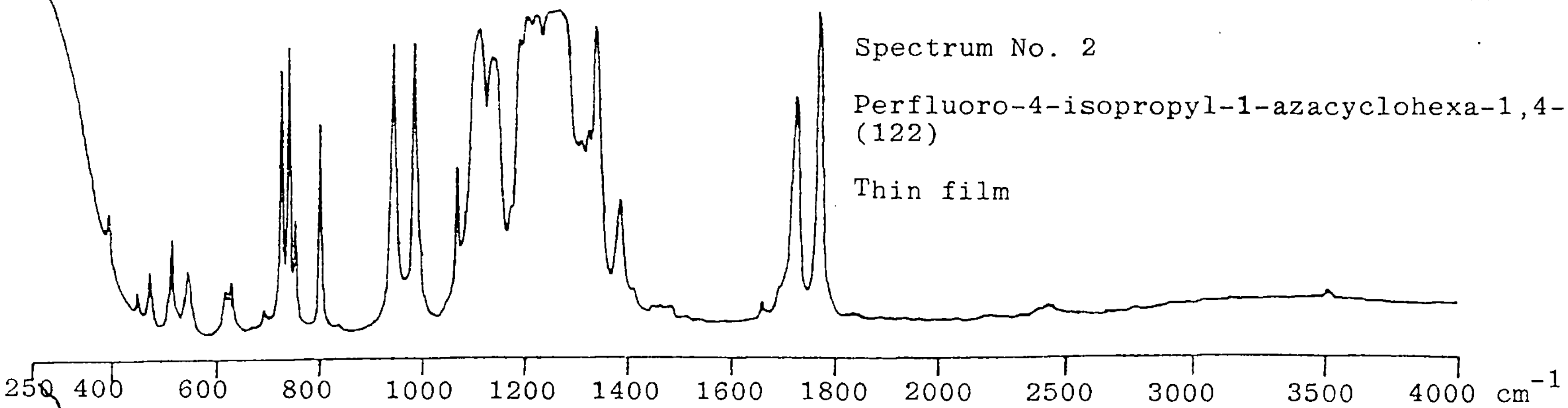
Infra Red Spectra



Spectrum No. 1

Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene

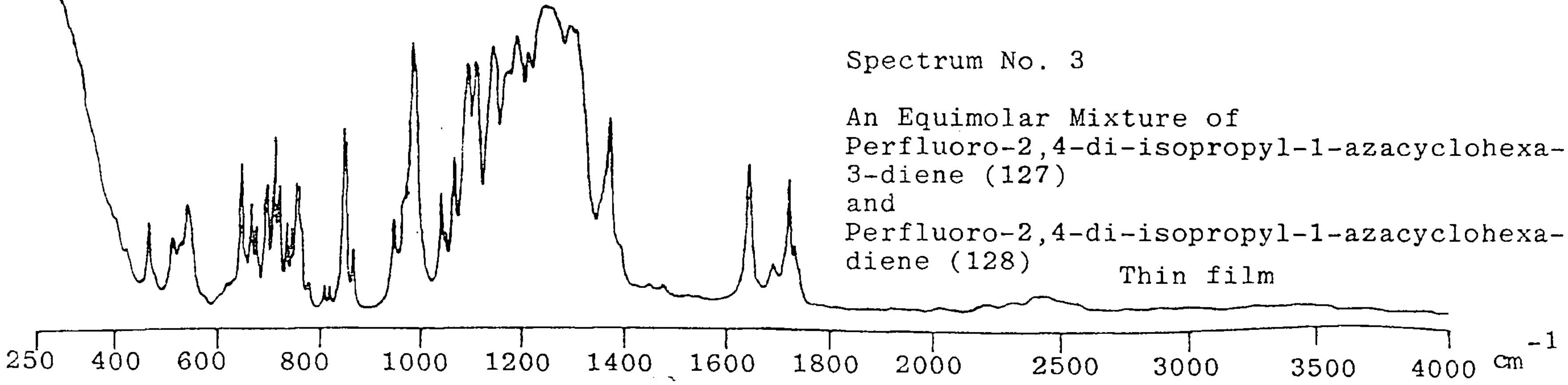
Thin film



Spectrum No. 2

Perfluoro-4-isopropyl-1-azacyclohexa-1,4-diene (122)

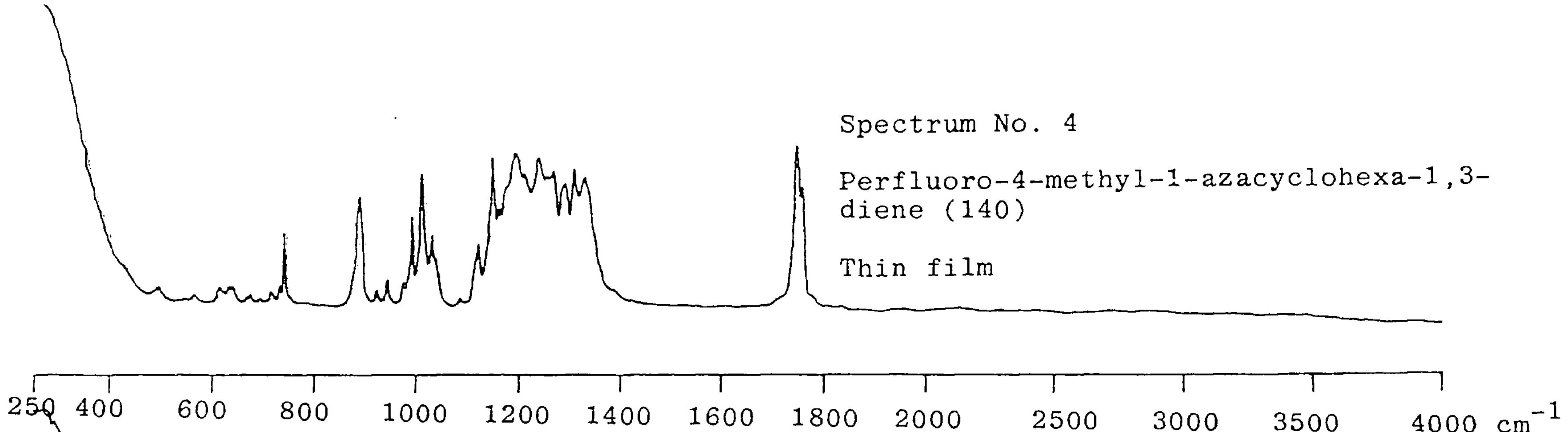
Thin film



Spectrum No. 3

An Equimolar Mixture of
Perfluoro-2,4-di-isopropyl-1-azacyclohexa-1,3-diene (127)
and
Perfluoro-2,4-di-isopropyl-1-azacyclohexa-1,4-diene (128)

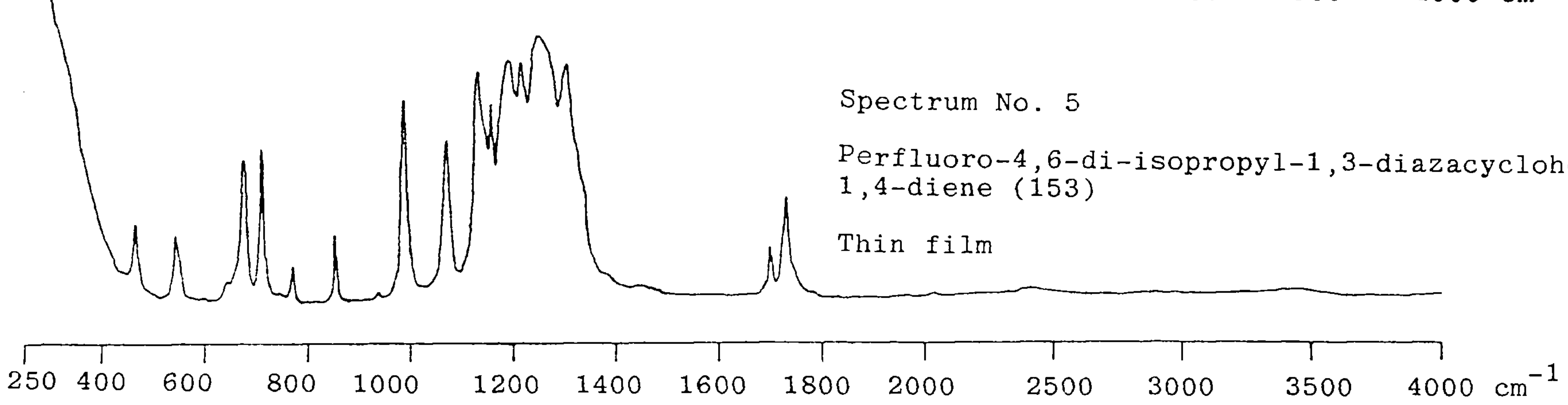
Thin film



Spectrum No. 4

Perfluoro-4-methyl-1-azacyclohexa-1,3-diene (140)

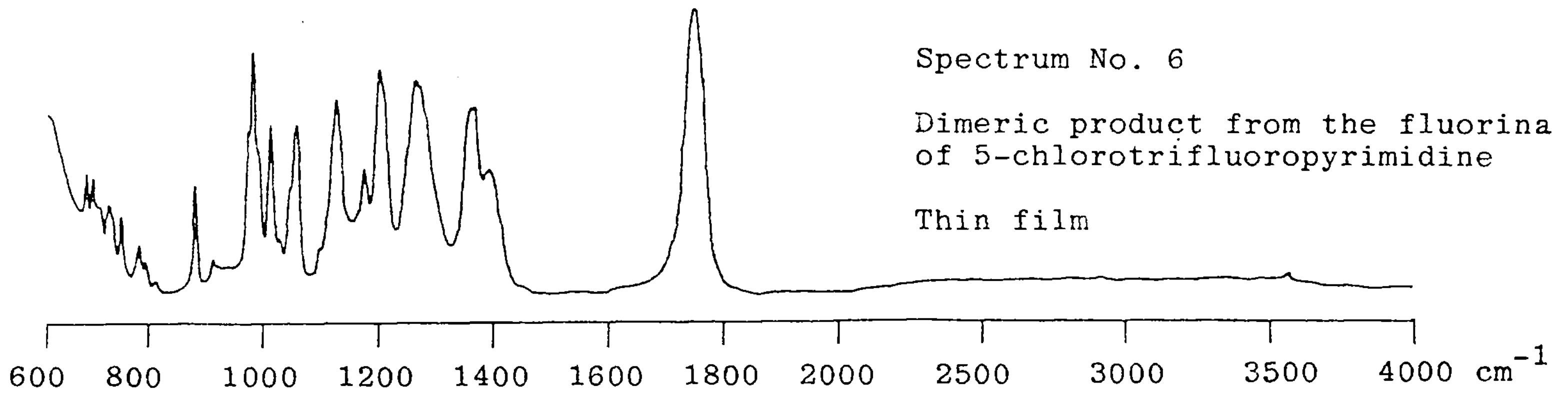
Thin film



Spectrum No. 5

Perfluoro-4,6-di-isopropyl-1,3-diazacyclohexa-1,4-diene (153)

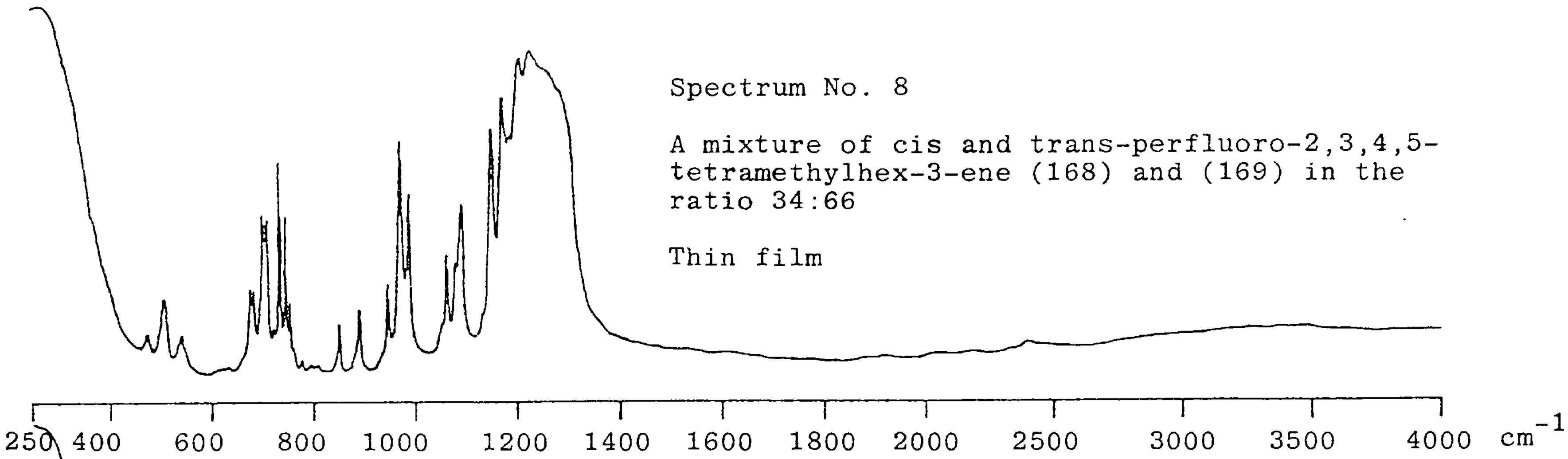
Thin film



Spectrum No. 6

Dimeric product from the fluorination of 5-chlorotrifluoropyrimidine

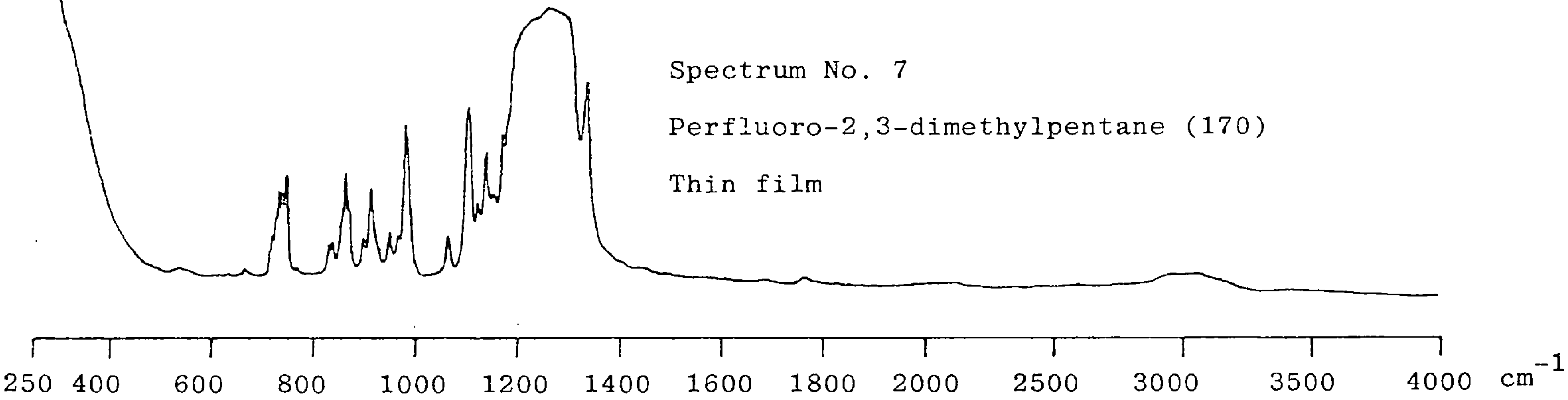
Thin film



Spectrum No. 8

A mixture of cis and trans-perfluoro-2,3,4,5-tetramethylhex-3-ene (168) and (169) in the ratio 34:66

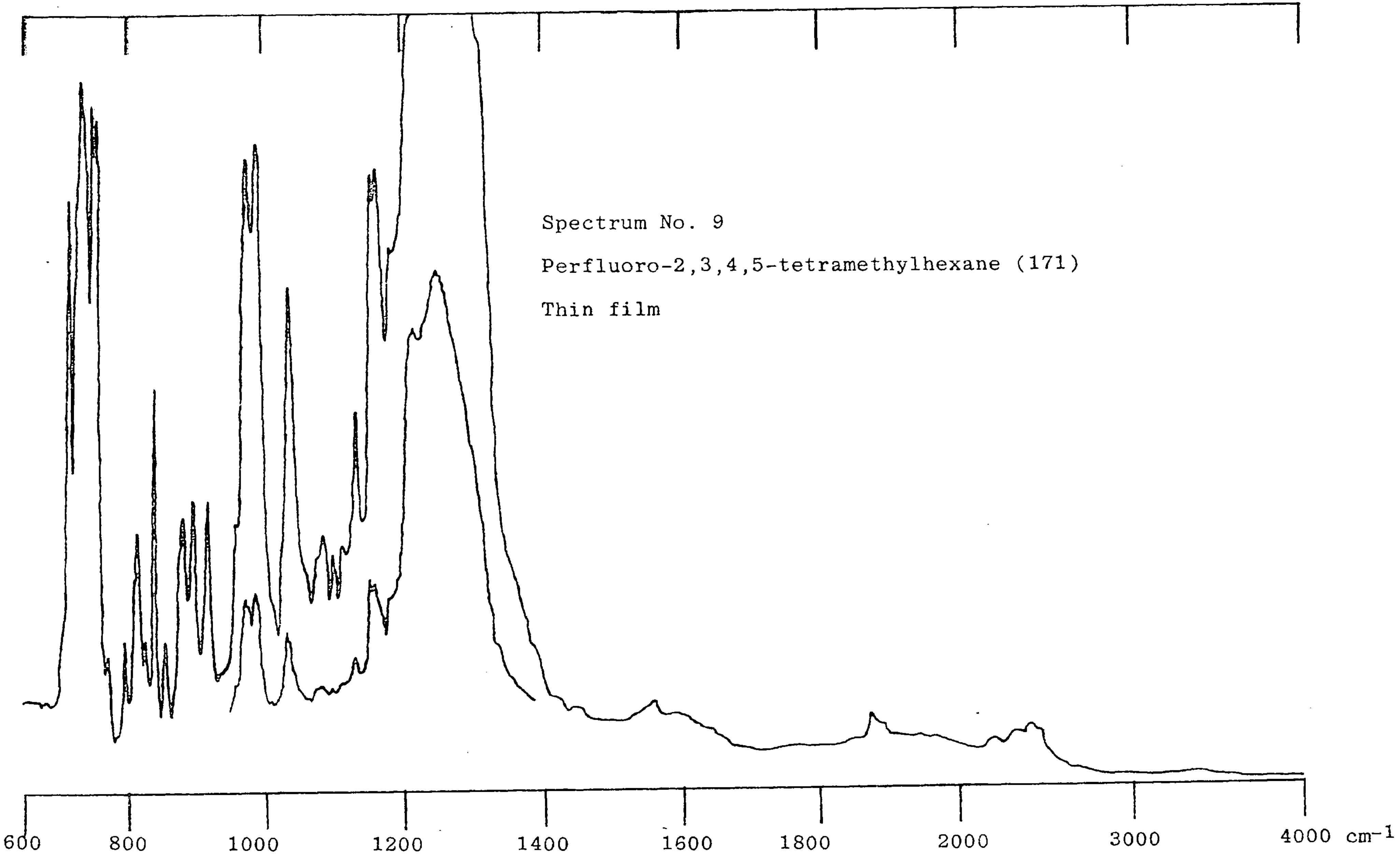
Thin film



Spectrum No. 7

Perfluoro-2,3-dimethylpentane (170)

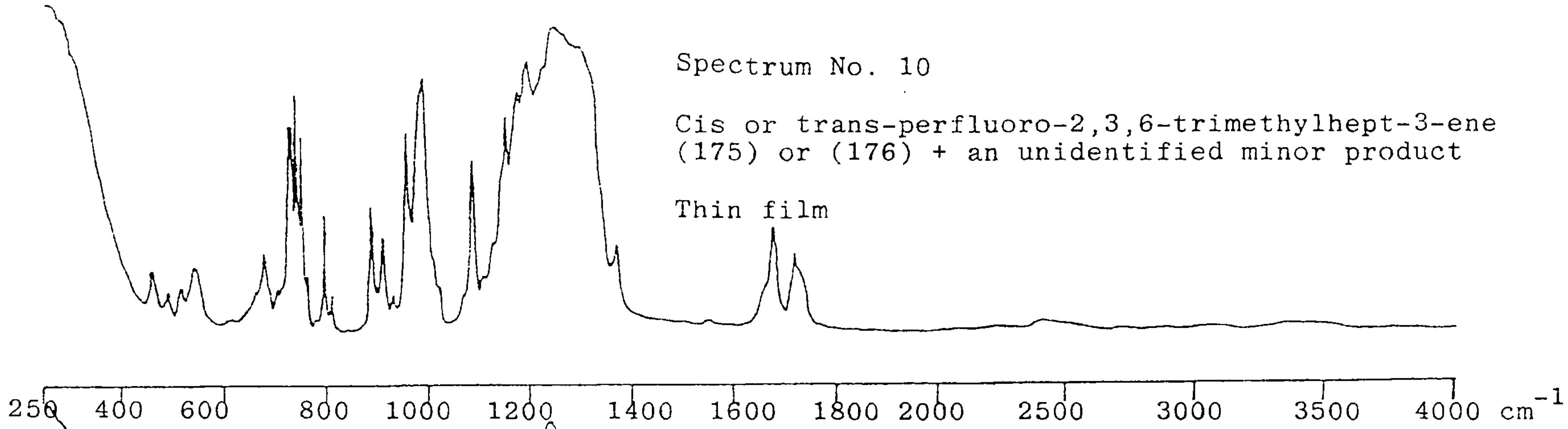
Thin film



Spectrum No. 9

Perfluoro-2,3,4,5-tetramethylhexane (171)

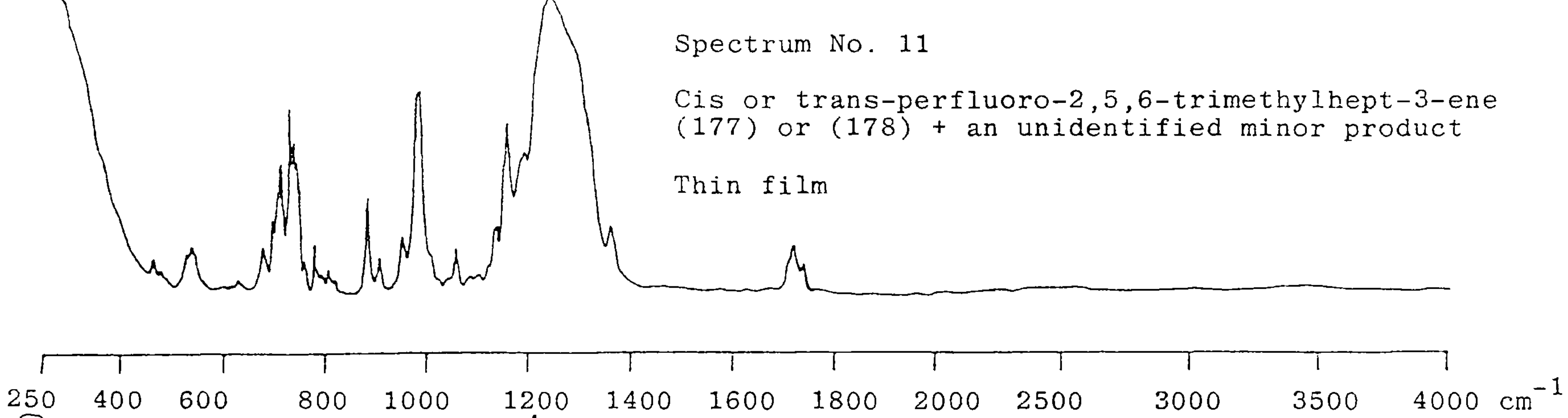
Thin film



Spectrum No. 10

Cis or trans-perfluoro-2,3,6-trimethylhept-3-ene (175) or (176) + an unidentified minor product

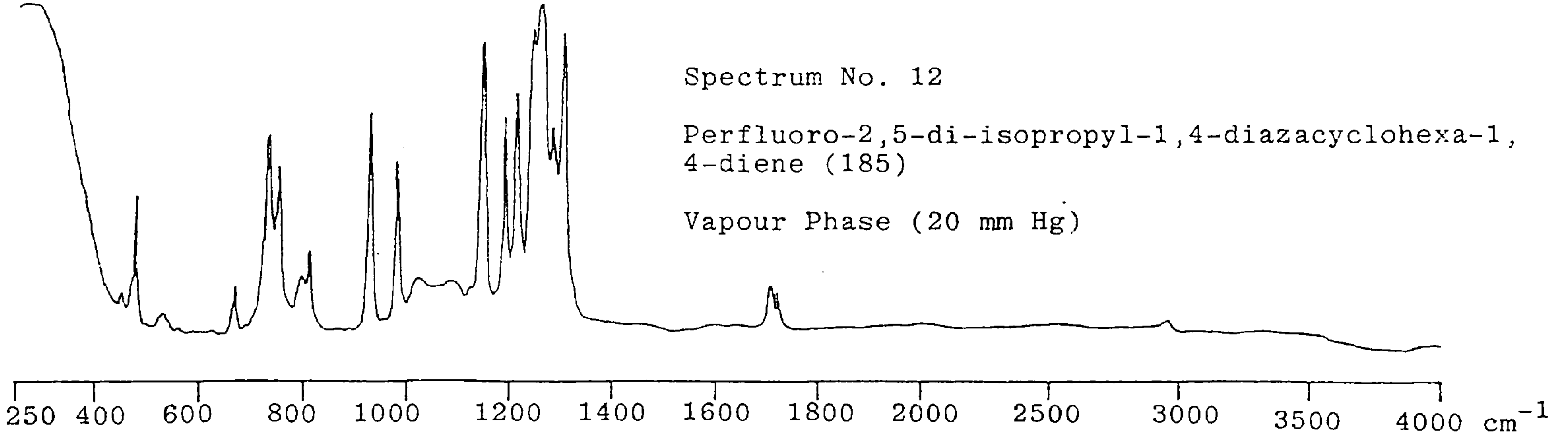
Thin film



Spectrum No. 11

Cis or trans-perfluoro-2,5,6-trimethylhept-3-ene (177) or (178) + an unidentified minor product

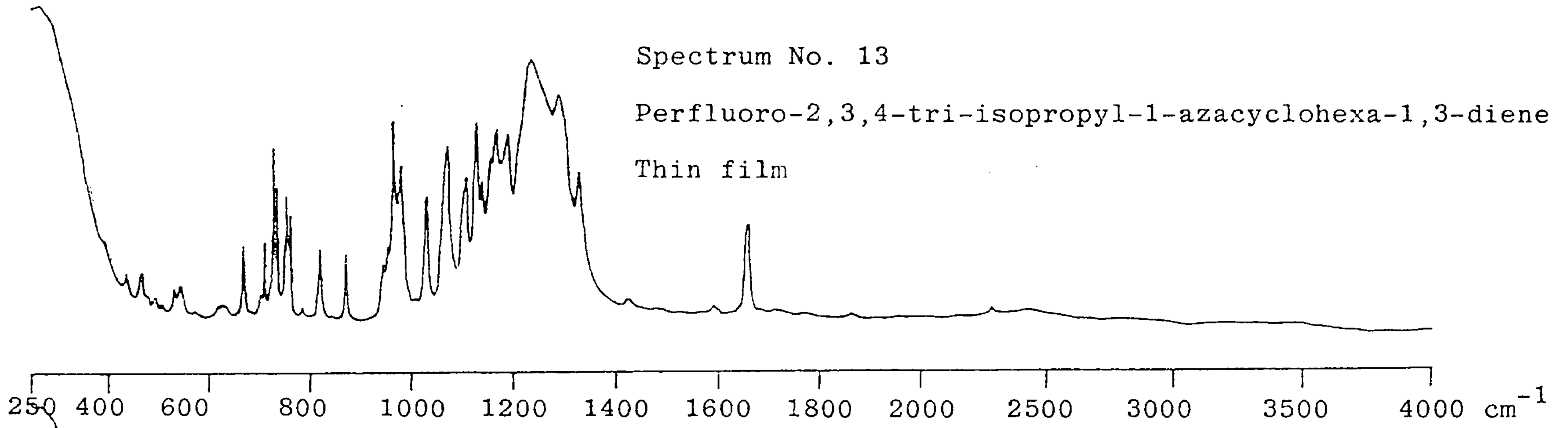
Thin film



Spectrum No. 12

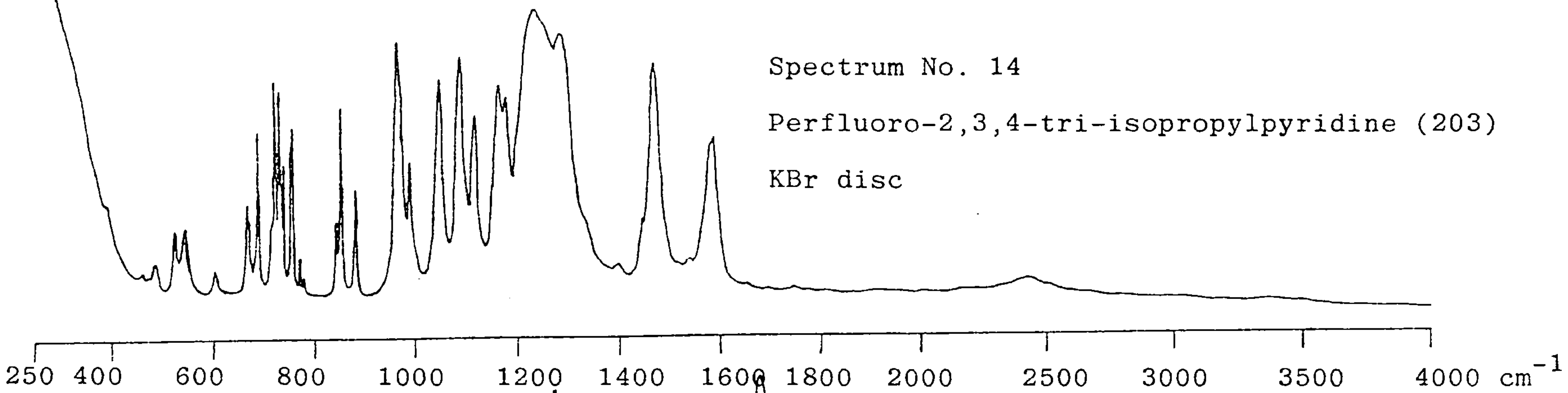
Perfluoro-2,5-di-isopropyl-1,4-diazacyclohexa-1,4-diene (185)

Vapour Phase (20 mm Hg)


Spectrum No. 13

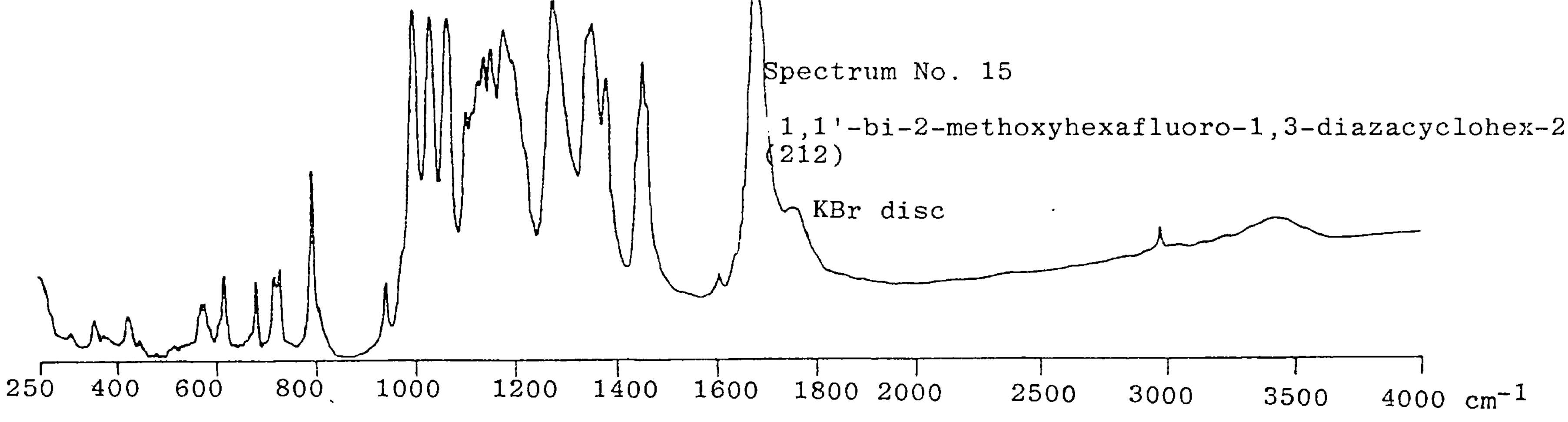
Perfluoro-2,3,4-tri-isopropyl-1-azacyclohexa-1,3-diene (201)

Thin film


Spectrum No. 14

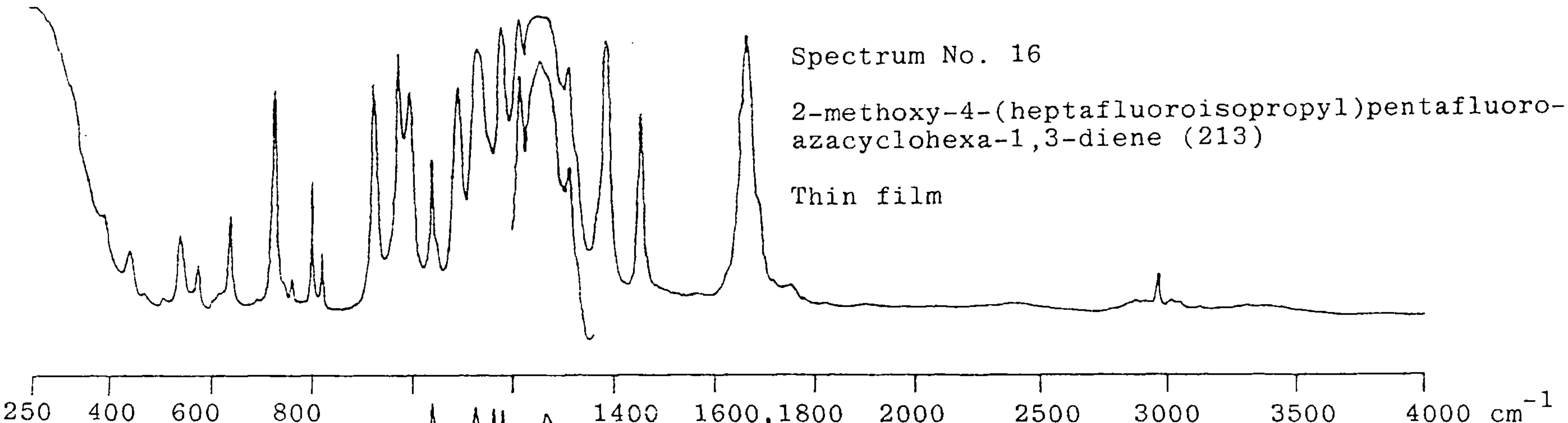
Perfluoro-2,3,4-tri-isopropylpyridine (203)

KBr disc


Spectrum No. 15

1,1'-bi-2-methoxyhexafluoro-1,3-diazacyclohex-2-enyl (212)

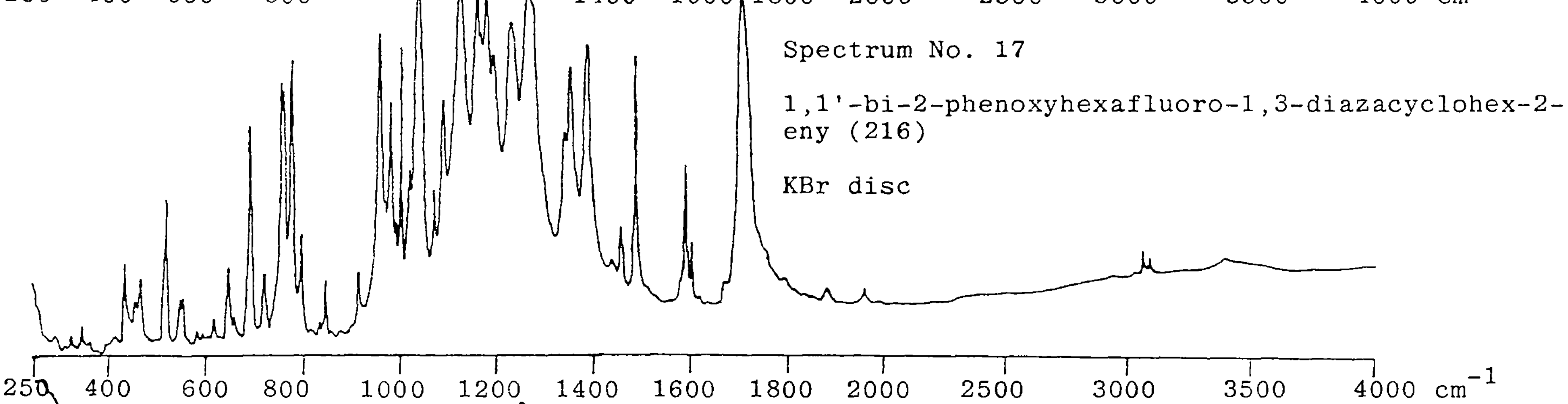
KBr disc



Spectrum No. 16

2-methoxy-4-(heptafluoroisopropyl)pentafluoro-1-azacyclohexa-1,3-diene (213)

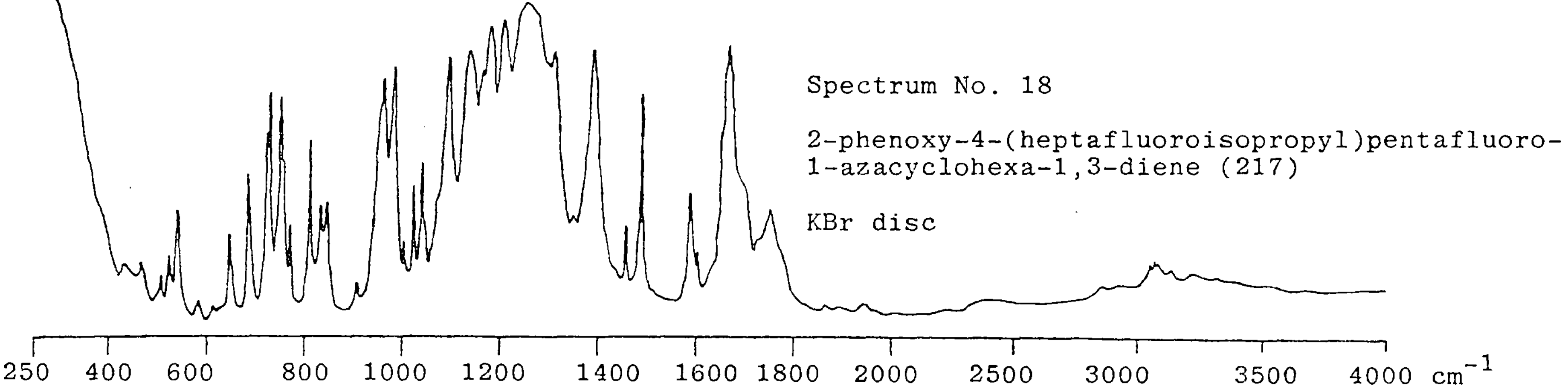
Thin film



Spectrum No. 17

1,1'-bi-2-phenoxyhexafluoro-1,3-diazacyclohex-2-eny (216)

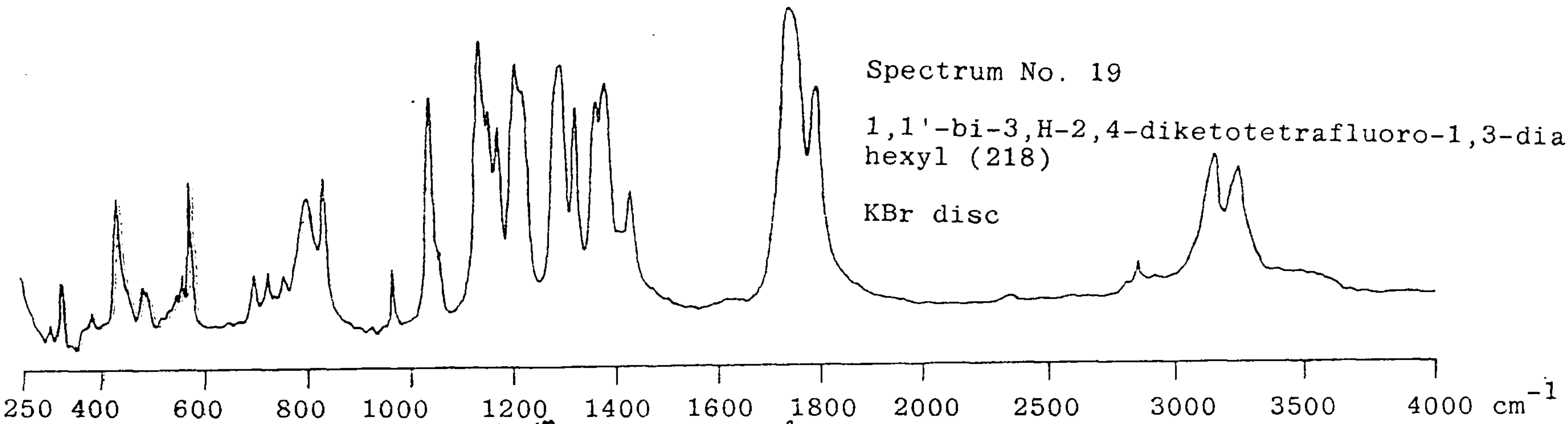
KBr disc



Spectrum No. 18

2-phenoxy-4-(heptafluoroisopropyl)pentafluoro-1-azacyclohexa-1,3-diene (217)

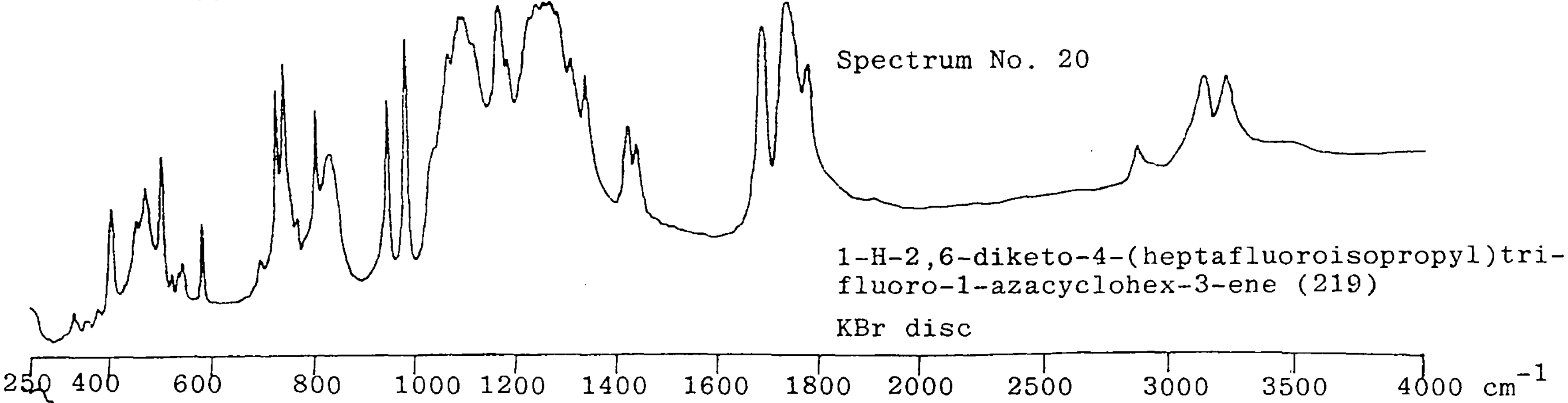
KBr disc



Spectrum No. 19

1,1'-bi-3,H-2,4-diketotetrafluoro-1,3-diazacyclohexyl (218)

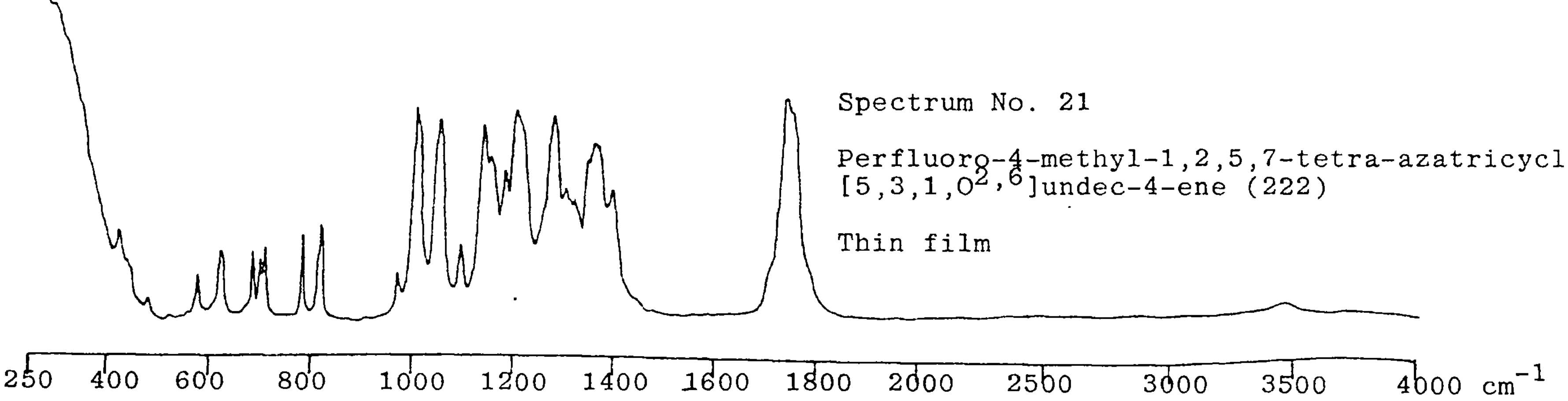
KBr disc



Spectrum No. 20

1-H-2,6-diketo-4-(heptafluoroisopropyl)trifluoro-1-azacyclohex-3-ene (219)

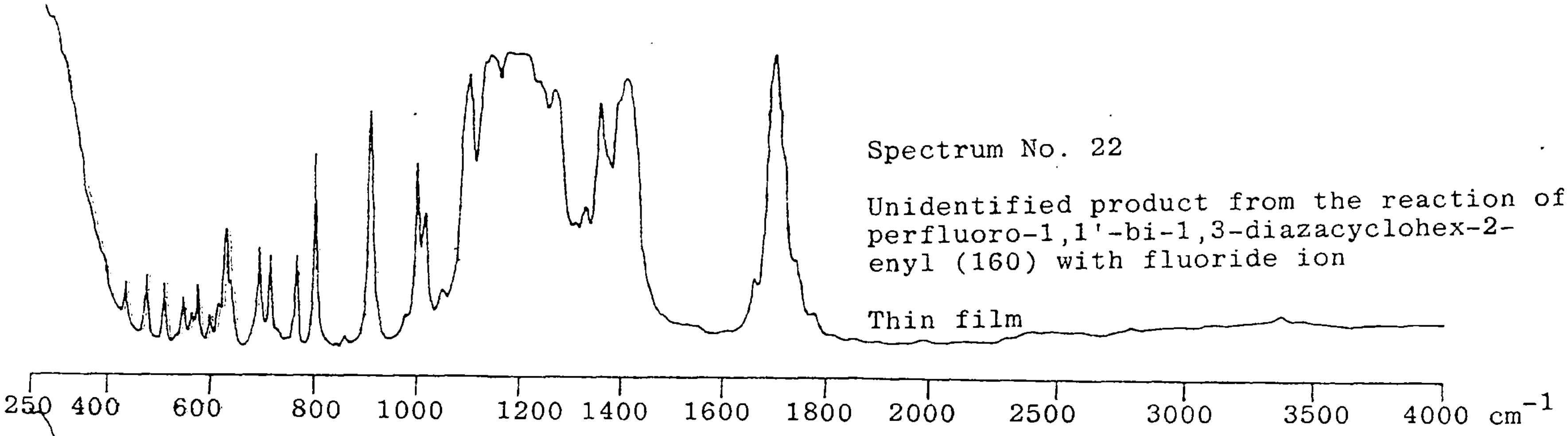
KBr disc



Spectrum No. 21

Perfluoro-4-methyl-1,2,5,7-tetra-azatricyclo [5,3,1,$0^{2,6}$]undec-4-ene (222)

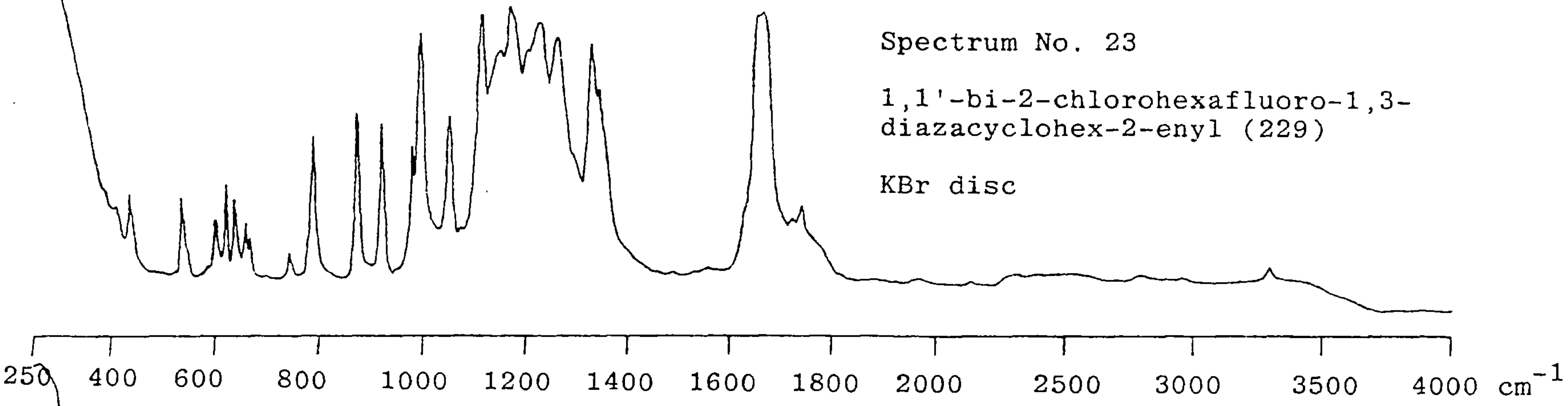
Thin film



Spectrum No. 22

Unidentified product from the reaction of perfluoro-1,1'-bi-1,3-diazacyclohex-2-enyl (160) with fluoride ion

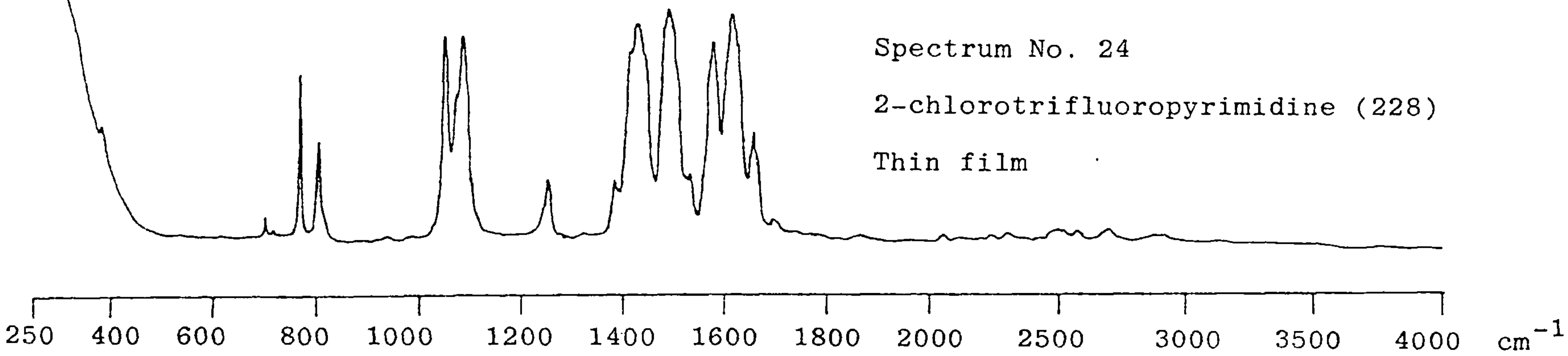
Thin film



Spectrum No. 23

1,1'-bi-2-chlorohexafluoro-1,3-diazacyclohex-2-enyl (229)

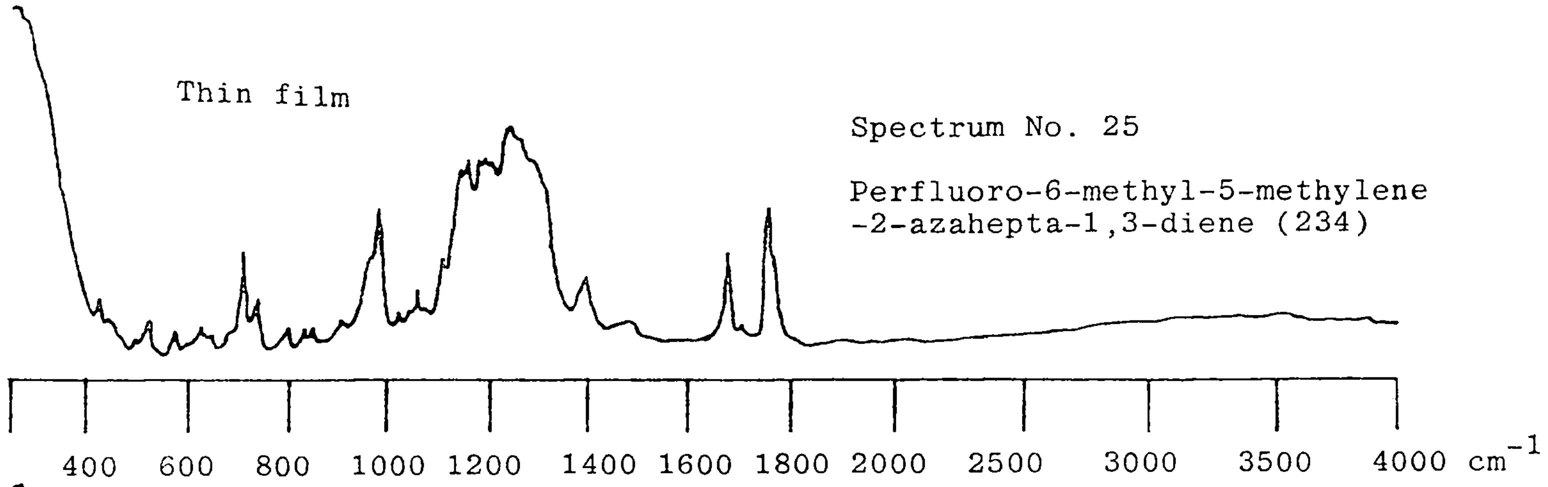
KBr disc



Spectrum No. 24

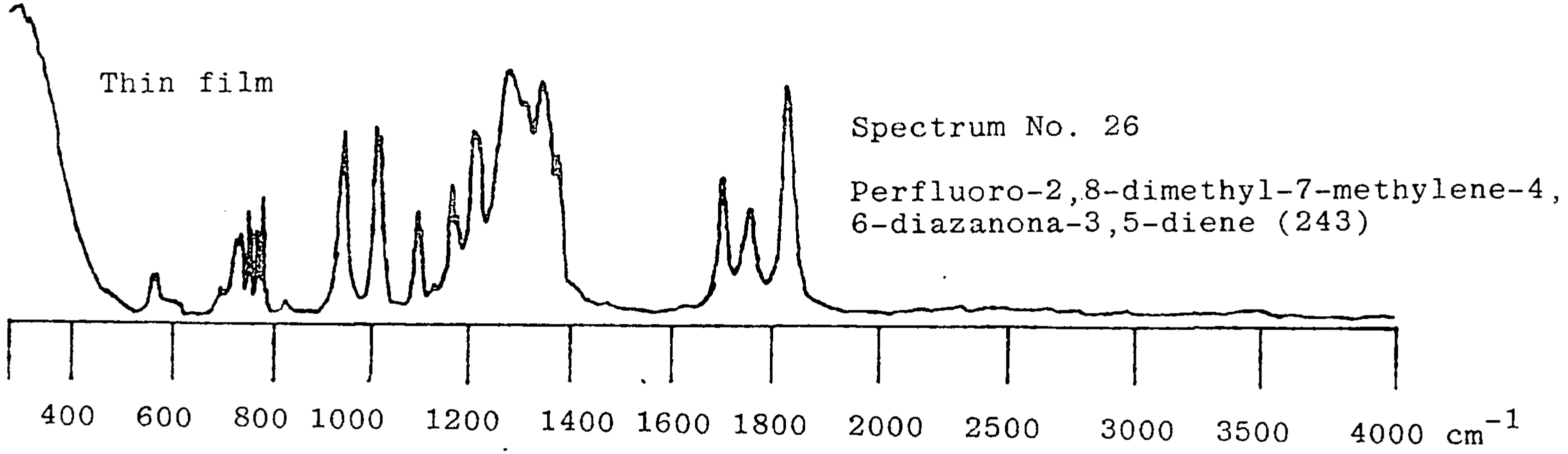
2-chlorotrifluoropyrimidine (228)

Thin film



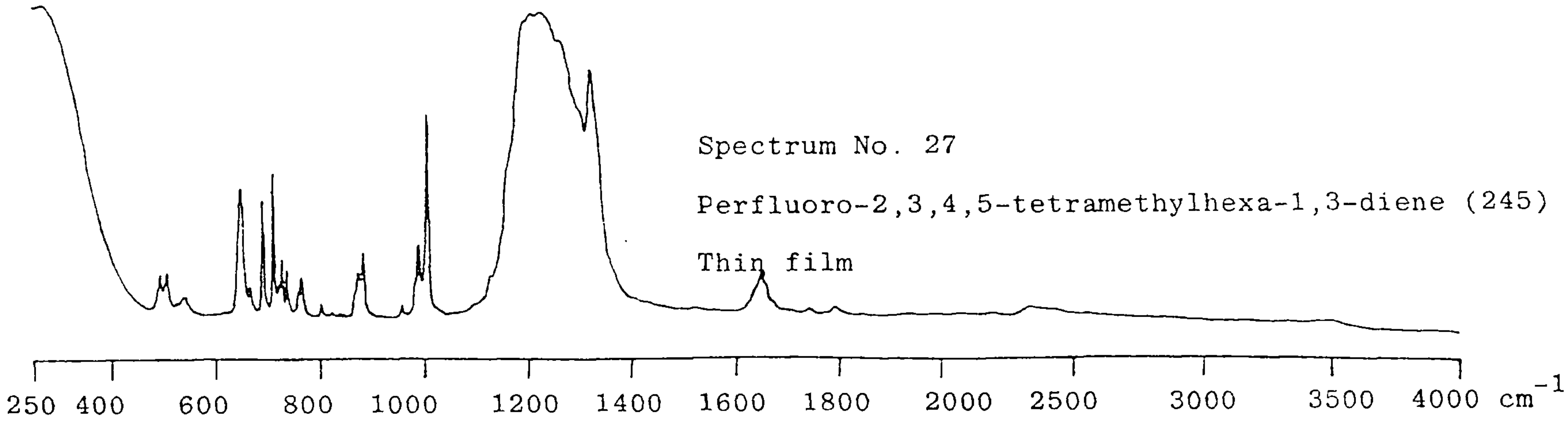
Spectrum No. 25

Perfluoro-6-methyl-5-methylene-2-azahepta-1,3-diene (234)



Spectrum No. 26

Perfluoro-2,8-dimethyl-7-methylene-4,6-diazanona-3,5-diene (243)



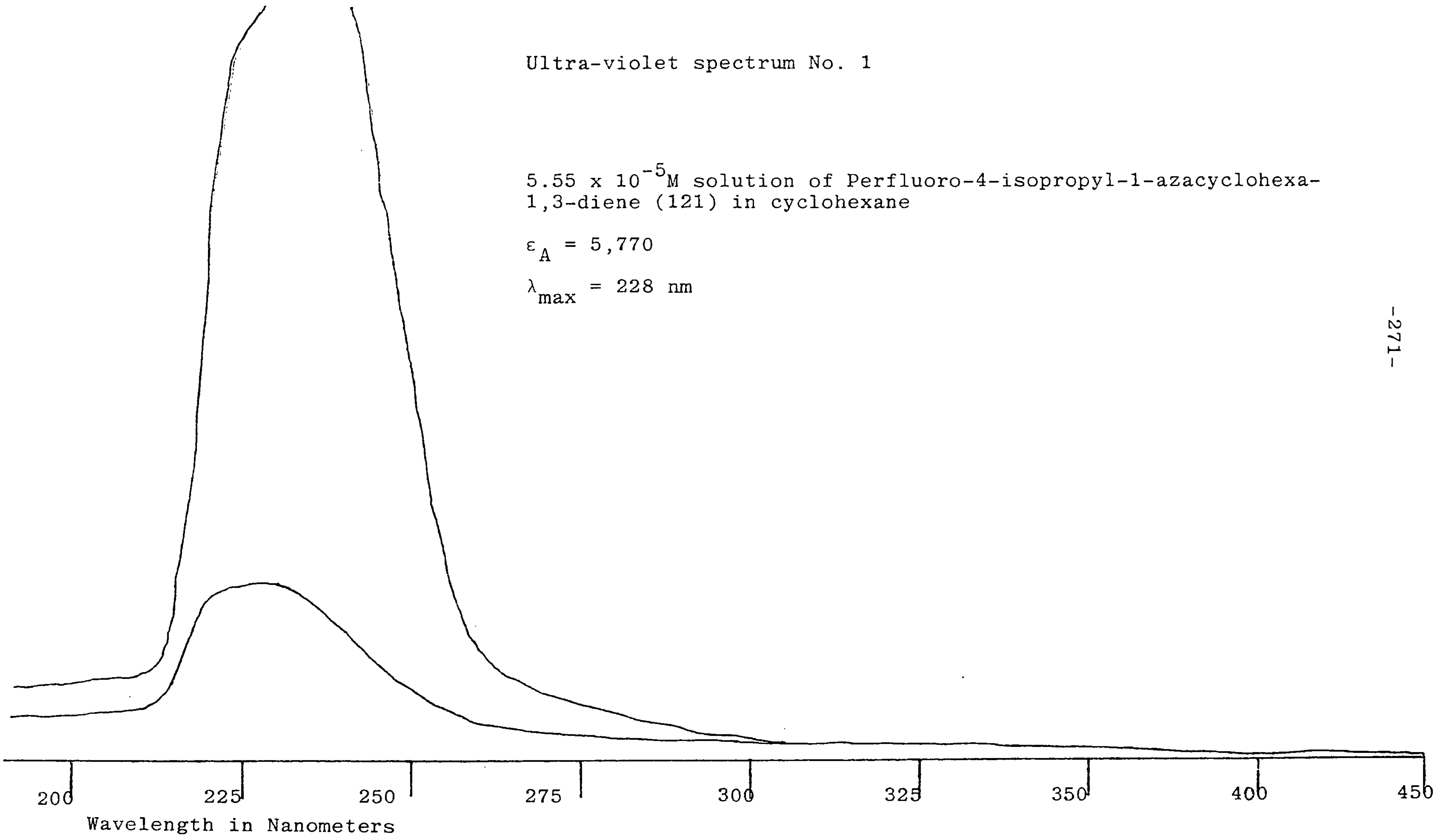
Spectrum No. 27

Perfluoro-2,3,4,5-tetramethylhexa-1,3-diene (245)

Thin film

APPENDIX 3

Ultra Violet Spectra

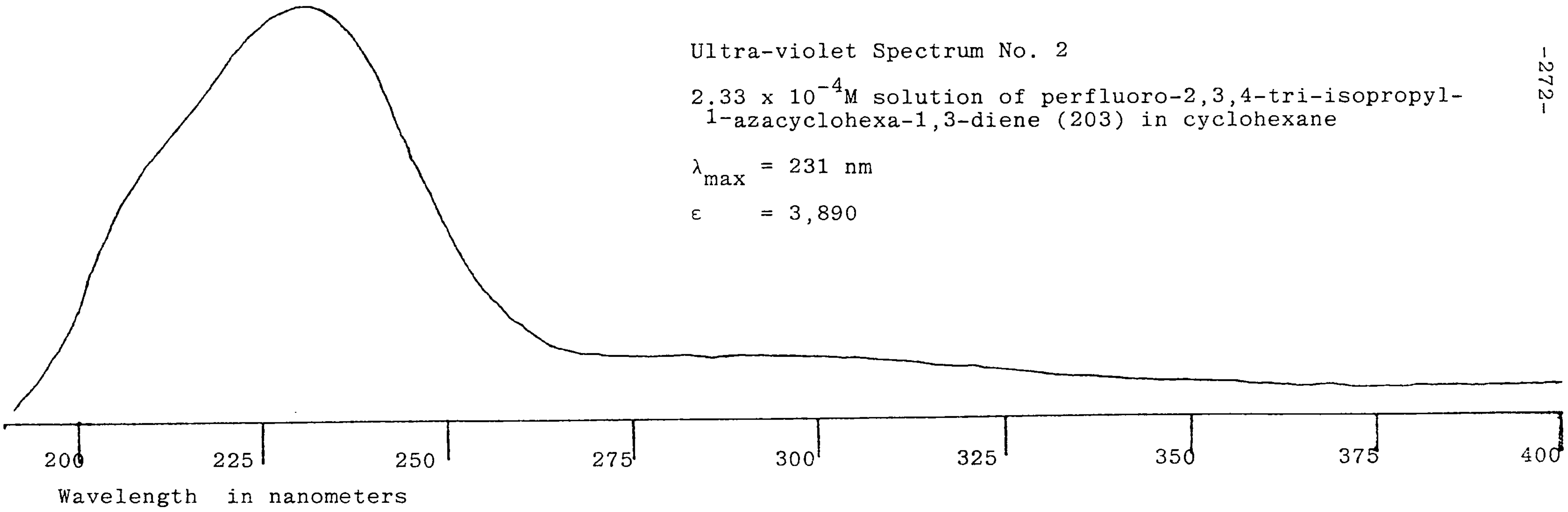


Ultra-violet spectrum No. 1

5.55×10^{-5}M solution of Perfluoro-4-isopropyl-1-azacyclohexa-1,3-diene (121) in cyclohexane

$\varepsilon_A = 5{,}770$

$\lambda_{max} = 228$ nm

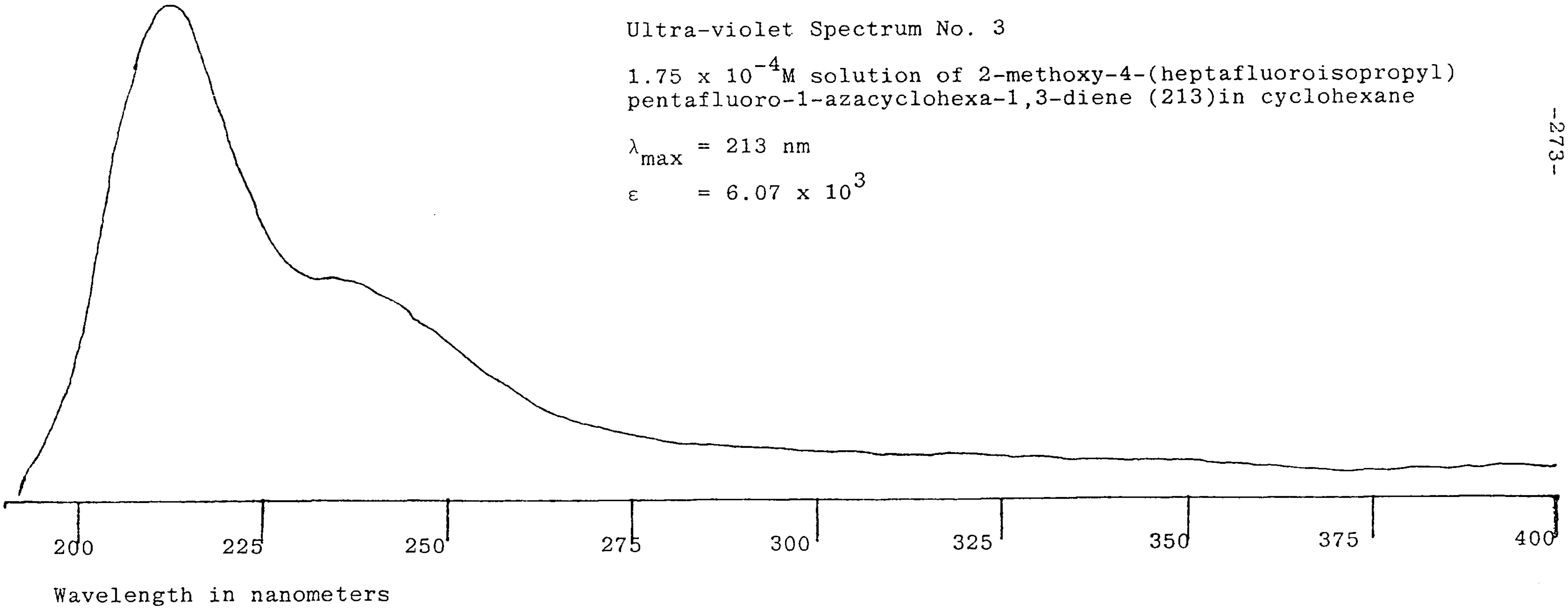


Ultra-violet Spectrum No. 2

2.33 x 10^{-4}M solution of perfluoro-2,3,4-tri-isopropyl-1-azacyclohexa-1,3-diene (203) in cyclohexane

λ_{max} = 231 nm

ε = 3,890



Ultra-violet Spectrum No. 3

1.75 x 10^{-4}M solution of 2-methoxy-4-(heptafluoroisopropyl) pentafluoro-1-azacyclohexa-1,3-diene (213)in cyclohexane

λ_{max} = 213 nm

ε = 6.07 x 10^3

Ultra-violet spectrum No. 4

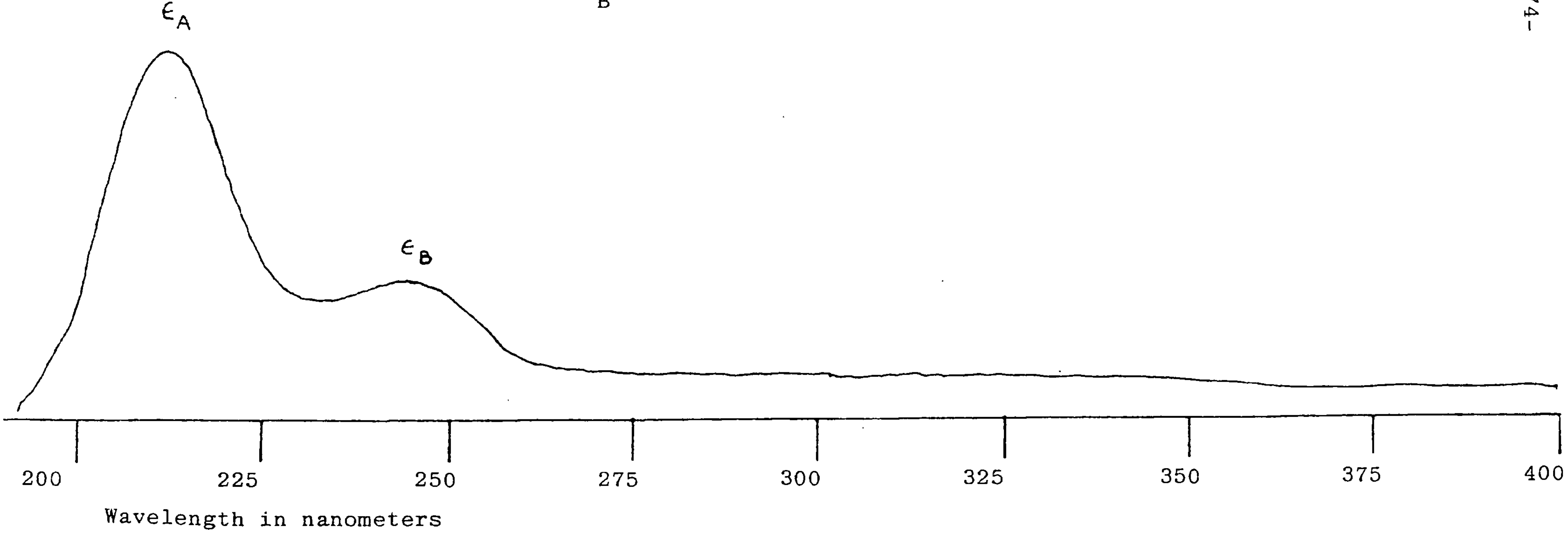
A 7.5×10^{-5}M solution of 2-chlorotrifluoropyrimidine (328) in cyclohexane

$\lambda_{maxA} = 212$ nm

$\varepsilon_{A} = 9.76 \times 10^{3}$

$\lambda_{maxB} = 244$ nm

$\varepsilon_{B} = 2.88 \times 10^{3}$



APPENDIX FOUR

Comparisons of Infra Red and Ultra Violet Spectra.

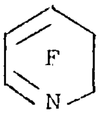
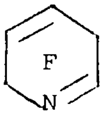
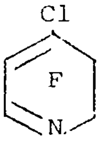
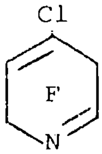
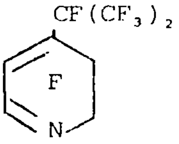
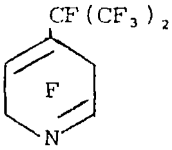
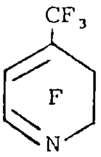
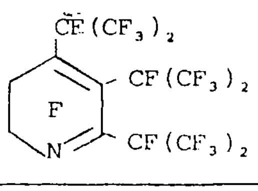
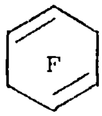
a) Infra Red Spectra

Upon comparing the infra red spectra of a series of polyfluoro - 1 - azacyclohexa - 1,3 - and - 1,4 - dienes (table A4-1 below) it becomes apparent that both types of diene give rise to either one or two strong absorptions between 1600 and 1800cm^{-1}. However, it may be significant that in the cases 1,2 and 3 where a - 1,3 - diene may be compared with the analogous - 1,4 - diene bearing the same substituents, the - 1,3 - diene has an absorption at lower frequency than either of the absorptions of the - 1,4 - diene, presumably arising from a vibration mode affected by the lowering of bond orders on conjugating the two π bonds. A similar effect is noted for perfluorocyclohexa - 1,3 - and - 1,4 - dienes as in case 6 and it appears therefore that infra red data may be used to distinguish polyfluoro - 1 - azacyclohexa - 1,3 - and - 1,4 - dienes provided they bear identical substituents.

It would be of interest to see if this diagnostic criterion is applicable to case 4, the - 4 - methyl - diene, which, although unambiguously indentified as a - 1,3 - diene by other means, has it's lowest energy absorption at 1745cm^{-1}. It is therefore required that the equivalent, as yet unknown, - 1,4 - diene would have two absorptions at even higher frequency.

TABLE A4-1

Diene Infra Red Absorption Frequencies (cm^{-1})

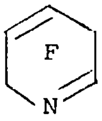
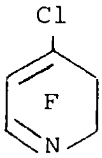
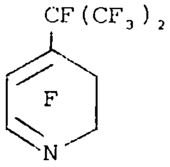
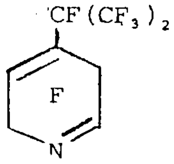
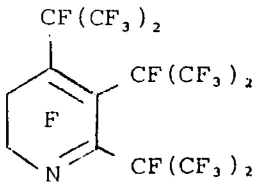
Case	- 1,3 - dienes	- 1,4 - dienes
1	1700,1750; Ref: 192 	1750,1750; Ref: 192 
2	1660,1705; Ref: 163 	1715,1754; Ref: 163 
3	1687,1775; this thesis 	1742,1767; this thesis 
4	1745,1756; this thesis 	Not known
5	1657, - ; this thesis 	Not known
6	 1713,1753; Ref: D.E.M. Evans and J. C. Tatlow; J.C.S.,'54, 3779	 1739,1739; Ref: D.E.M. Evans and J.C. Tatlow; J.C.S.'54, 3779

b) Ultra Violet Spectra

The limited data in table A4-2 below indicate that polyfluoro-1-azacyclohexa -1,3 - and -1,4 - dienes may be readily distinguished by their ultra violet spectra. Thus, in every case, the -1,3-dienes give reasonably strong absorptions ($\epsilon > 1800$) at wavelengths between 228 and 248nm whereas, at least where the data is reported, the corresponding -1,4-dienes do not appear to absorb significantly above 228nm.

TABLE A4-2

Ultra-Violet Spectra of Dienes

Case	-1,3-dienes (Absorptions in nm's)	-1,4-dienes (Absorptions in nm's)
1	 λmax = 233nm ϵ = 1800, Cyclohexane Ref: D.E.M. Evans and J.C. Tatlow; J.C.S., '54, 3779	 Spectrum not reported
2	λmax 248nm ϵ = 9380 Cyclohexane Ref: 163 	λ max 217nm (end absorption?) Cyclohexane ϵ = not reported Ref: 163 
3	λmax = 228nm ϵ = 5770 Cyclohexane Ref: This thesis 	No maximum at longer wave-length than 222nm Cyclohexane Ref: this thesis 
4	 λmax = 231nm ϵ = 3890 Cyclohexane Ref: This thesis	Not known
5	 λmax = 256nm ϵ = 3160 Diethylether Ref: D.E.M. Evans and J.C. Tatlow; J.C.S., '54, 3779	 No absorbtion in the 250nm region. Diethylether Ref: D.E.M. Evans and J.C. Tatlow; J.C.S., '54,3779

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