The chemistry of heptafluoroquinoline and related systems

Bell, Stephen Leslie

UNIVERSITY OF DURHAM

A THESIS

entitled

THE CHEMISTRY OF HEPTAFLUOROQUINOLINE AND RELATED SYSTEMS

submitted by

STEPHEN LESLIE BELL, B.Sc.

(Grey College)

A candidate for the degree of Doctor of Philosophy

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To my Mother and Father.

'What good shall it do you, unless what I say contains something by way of revelation, or enlightenment, or prophecy or instruction?'

I Corinthians 14, v.6

The New English Bible

ACKNOWLEDGEMENTS

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Thanks are also due to the University of Durham who supported this work through a Research Studentship.

MEMORANDUM

The work described in this thesis was carried out at the University of Durham between October 1969 and October 1972. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

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

S.L. Bell, R.D. Chambers, W.K.R. Musgrave, and J.G. Thorpe, J. Fluorine Chem., 1971/2, 1, 51.

SUMMARY

The Chemistry of Heptafluoroquinoline and Related Systems

Some ^{19}F n.m.r. measurements on a series of hexafluoroantimonate salts of a number of perfluoro-N-heteroaromatic compounds and of the bases with acid have enabled a qualitative comparison of the base strengths of these compounds to be made. The results indicate that a dominant factor controlling the base strength is the number of fluorine atoms ortho to the ring nitrogen. Quantitative comparison of the basicities was not possible in most cases but the ^{19}F n.m.r. spectra of pentafluoropyridine in various strong acids have indicated that the H_o of half protonation is about -10.

Investigations into the nucleophilic substitution in heptafluoroquinoline have shown that substitution at the 4-position is sterically hindered and increasingly bulky nucleophiles preferentially substitute at the 2-position. Disubstitution is almost exclusively under the control of the ring nitrogen but subsequent substitution is significantly affected by substituents present in the ring. Electron withdrawing substituents strongly activate the 6-position in the carbocyclic ring whereas with electron donating substituents substitution only occurs in the 7-position.

Fluoride ion catalysed attack of perfluoroisobutene on heptafluoroquinoline gives rise to a single monosubstituted product, perfluoro-2-t-butylquinoline and a single disubstituted product, perfluoro(2,6-di-t-butylquinoline). In contrast attack by carbanions generated from tetrafluoroethylene has given rise to inseparable mixtures of products.

The attempted formation of derivatives of heptafluoroquinoline by intermediate lithium compounds or Grignard reagents generated from 2-bromohexafluoroquinoline and 2,4-dibromopentafluoroquinoline has in every case given rise to considerable tar formation and shown it not to be a viable route to derivatives.

Preliminary investigation into the formation of perfluoro(5,6,7,8-tetrahydroquinoline) by halogen exchange of heptachloroquinoline with potassium fluoride at elevated temperatures has indicated that chlorine addition may be an important step in the saturation of the carbocyclic ring. Initial nucleophilic substitution reactions have shown the 2- and 4-positions to be of comparable reactivity but of more reactivity than heptafluoroquinoline.

The variable temperature ^{19}F n.m.r. spectra of some perfluoro-t-butyl compounds has been investigated and no barrier to rotation is apparent. A rationale of the observed barriers to rotation of perfluoro-ethyl,-isopropyl, and-t-butyl compounds is given, based on qualitative consideration of the energies of the rotational ground states and transition states. The explanation has been extended to account for the relative proportion of the conformers of some perfluoroisopropyl-pyridines and -quinolines.

CONTENTS

Page

CHAPTER 4 - Some Aspects of the Chemistry of Heptafluoroquinoline

EXPERIMENTAL

CHAPTER 7

Page

APPENDICES

GENERAL INTRODUCTION

Investigations into fluorocarbon chemistry have been an increasingly important area of both academic and industrial research over the past three decades. The reason for this is that hydrogen in a hydrocarbon compound can be extensively or completely replaced by fluorine without serious distortion of the carbon skeleton and so, reactions of the resultant fluorocarbon compounds, in contrast to the reaction of the analogous chlorocarbon compounds, are not controlled by steric effects although they are of some importance. Thus a chemistry based on carbon and fluorine rather than carbon and hydrogen is possible.

The considerable interest in fluorocarbon chemistry arises because of the quite different electronic environments of functional groups in a fluorocarbon compound caused by the substantial difference between hydrogen and fluorine. Thus new compounds with often quite different reactions are available to test current theories of reaction processes and factors affecting reactivity. Aromatic hydrocarbon compounds react with olefins by electrophilic attack, in contrast, however, aromatic fluorocarbon compounds react with fluoro-olefins by nucleophilic attack and from this unique opportunity to study two complementary types of chemistry springs the great academic interest in fluorocarbon chemistry.

Furthermore, the extensive replacement of hydrogen by fluorine in a compound often leads to increased stability and this factor has encouraged considerable industrial interest and the preparation of a wide variety of highly inert polymers, lubricants, liquids and gases from aliphatic fluorocarbon compounds. There are as yet no extensive industrial uses of aromatic fluorocarbon compounds but exploratory work with a view to their utilisation continues.

The work described in this thesis is a study of two aspects of fluorine containing compounds. The first is concerned with an investigation of the

factors controlling the base strength of a series of very weakly basic polyfluoro-nitrogen heterocyclic compounds; the second, is to investigate the factors controlling the orientation of nucleophilic substitution and attempt to prepare some functional derivatives of one member of the series, heptafluoroquinoline.

CHAPTER 1

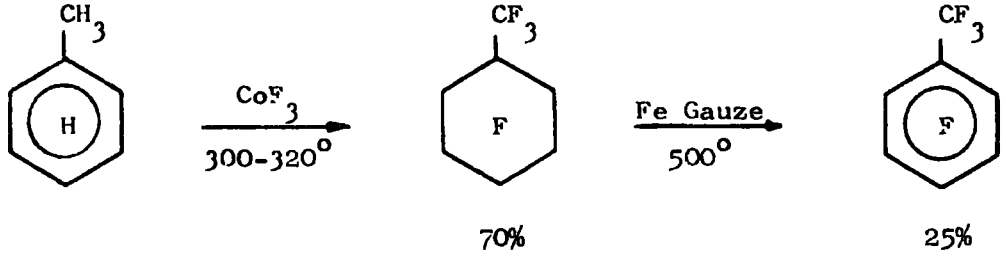
Perfluoroheteroaromatic Compounds Containing Nitrogen

Introduction

During the last decade interest in polyfluorinated organic compounds has been extended to include the polyfluoroheteroaromatic compounds, particularly with nitrogen as the heteroatom. The first of these, pentafluoropyridine, was originally thought to be effectively non basic[1,2], but subsequent observations on other polyfluorinated aza-aromatic compounds have shown that acid induced reactions occur in the chemistry of perfluoroquinoline[3,4], and tetrafluoropyridazine has been found to be particularly susceptible to this type of reaction.[5] It is the purpose of the first part of this work to investigate the qualitative order of basicity of these systems and attempt to elucidate some of the factors controlling the base strength. There follows a discussion of the background material related to this topic.

A. Preparation

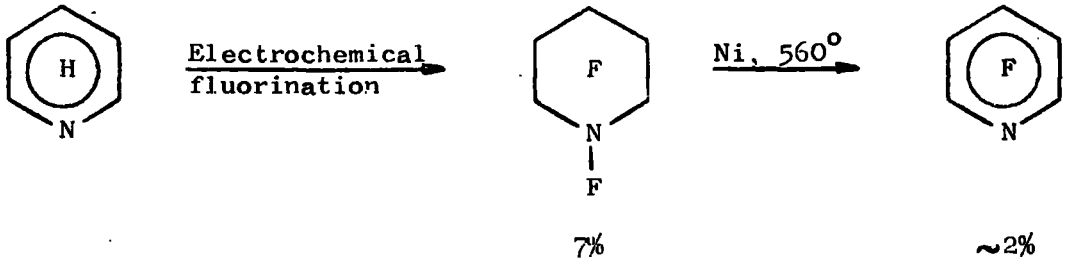
The first preparation of pentafluoropyridine involved direct fluorination of pyridine[1] either by electrolytic fluorination or using cobalt trifluoride as fluorinating agent; methods developed for the preparation of polyfluoroaromatic compounds.



6

The overall yields in the preparation of benzenoid compounds via fully fluorinated cyclic compounds followed by pyrolytic defluorination and

rearomatisation were good but attempted extensions of the method for the preparation of aza-aromatic compounds gave rise to substantial breakdown and low yields of the fully fluorinated heterocyclic compound were obtained.



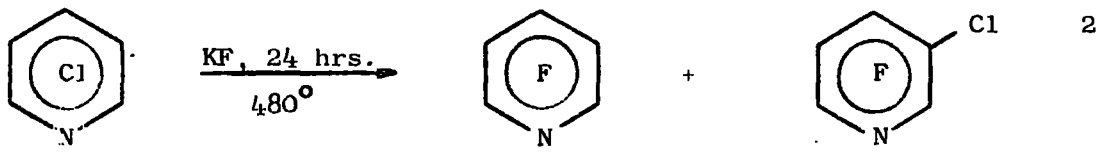
7,8

7%

~2%

The route was not viable as a general preparative method to the polyfluoro-aromatic nitrogen heterocycles.

However a general preparative route was indicated by the preparation of pentafluoropyridine[9,10] by halogen exchange between pentachloropyridine and potassium fluoride in the absence of a solvent, there now being satisfactory



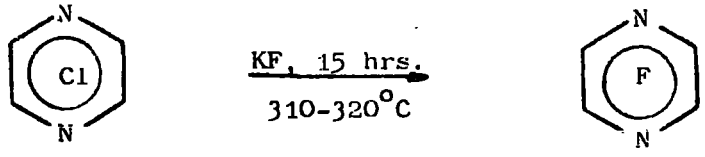
2

70%

10%

preparative routes to the perchlorinated compounds.

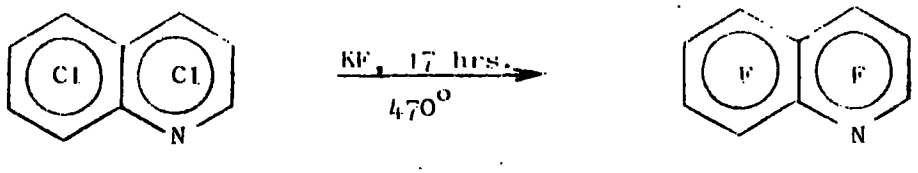
This method has now been extended to the preparation of perfluorinated aza-benzenes and aza-naphthalenes.[2,3,11-16]



16

95%

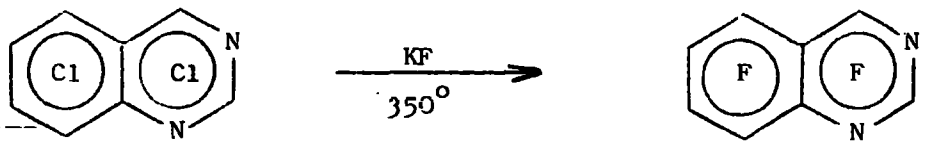
perfluoropyrazine



71%

3

perfluoroquinoline



17

good yield

perfluoroquinazoline

The preparations are normally carried out in nickel lined autoclaves under autogenous pressure. The volatility of the resultant perfluorinated compounds allow them to be vacuum distilled directly from the hot autoclave so eliminating wasteful extraction processes.

B. Nucleophilic substitution

1. Homocyclic compounds

(a) Perfluorobenzenoid compounds

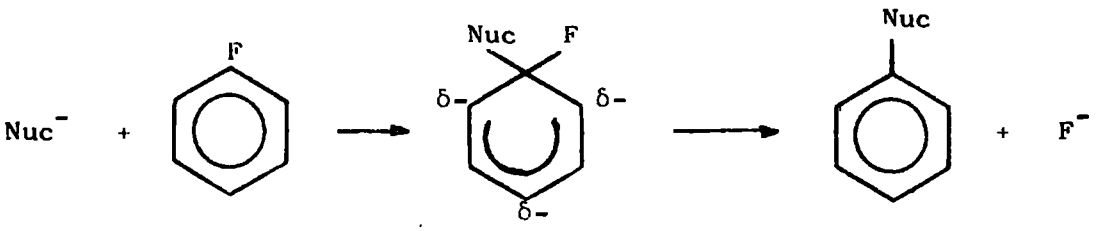
Nucleophilic aromatic substitution takes place readily in hexafluorobenzene with a variety of nucleophiles to give monosubstituted products. Of more interest is the subsequent reaction of monosubstituted pentafluorobenzenes with further nucleophiles where the positional isomerism of the disubstituted products is clearly possible.

The reactions of C_6F_5X with nucleophilic reagents has been extensively investigated[18,19] and in general the rate and position of further substitution depends on the group X already present. For a large number of substituents

($X = H, CH_3, NMe_2, SMe, CF_3, SO_2Me$) attack is largely at the position para to X, for a few ($X = NH_2, O^-$) reaction is predominantly meta and occasionally both meta and para are in comparable amounts (X = OMe, NHMe). In a few cases substitution is largely ortho ($X = NO_2$, nucleophile = amine).

(b) Rationalisation of substitution

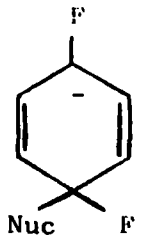
The orientation of nucleophilic aromatic substitution in polyhaloaromatic compounds has been successfully rationalised[20] by consideration of the energies of the transition states using Wheland-type intermediates (1) as models.



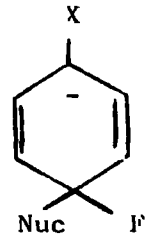
(1)

The rationalisation depends on two assumptions. The first is that the formation of the intermediate is the rate determining step in which bond breaking is of little significance,[21] and the second is that the negative charge in the transition state is greatest on the para carbon. This assumption receives some justification from molecular orbital calculations.[22]

Although fluorine, relative to hydrogen, appears to stabilise an adjacent tetrahedral carbanionic centre, as evidenced by the greatly increased kinetic acidity of α,α-difluorotoluene over that of toluene,[23] in the enforced planar configuration of the aromatic system the fluorine, by lone pair repulsions, destabilises the adjacent negative charge relative to a large number of other substituents and so, if -X destabilises the negative charge less than -F, intermediates of type (2) are less stable than intermediates of type (3) and so substitution takes place predominantly para to the group -X.



(2)



(3)

If -X more strongly destabilises the negative charge then substitution will be predominantly meta.

Now if -X destabilised the negative charge to the same extent as -F then substitution would be in the statistical proportions ortho:meta:para, 2:2:1, and the nearer the influence of -X is to that of fluorine the nearer will be the ratios to the statistical ones.

(c) Orientating effect of specific substituents[20]

In general the nitro, alkyl, and perfluoroalkyl groups will stabilise the adjacent negative charge and so substitution is predominantly para. Similarly the halogens and hydrogen stabilise the negative charge relative to fluorine $F < Cl < Br < I \sim H$ because the repulsion between the halogen lone pairs and the π system (I_π effect) decreases in that order and substitution is again predominantly para.

The magnitude of the I_π effects of nitrogen and oxygen are not derivable from spectroscopic measurements[25] but are assumed to be $N > O > F$ and as evidence pentafluoroaniline is attacked by ammonia slowly to give largely the meta diamine.

Steric interaction between a $-NMe_2$ group and its ortho fluorines, forcing it out of the plane of the ring, reduces the I_π repulsion, those of -OMe and -NHMe being similarly reduced.

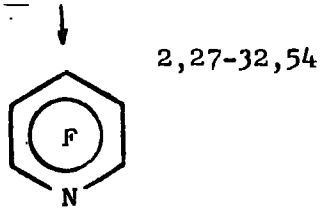
Specific interaction between the nitro group of pentafluoronitrobenzene

and ammonia or monomethylamine nucleophile increases the proportion of ortho attack[26] and steric interactions between incoming nucleophiles and -OMe and -NHMe groups reduces the ortho replacement below that expected.

2. Heterocyclic compounds

(a) Perfluoronitrogen-heteroaromatic compounds

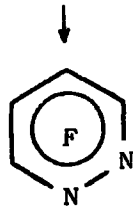
Nucleophilic substitution in a number of perfluorinated nitrogen heterocycles (with a variety of nucleophiles) has been investigated and they have been found to give monosubstituted products at the positions indicated.



2,27-32,54

(4)

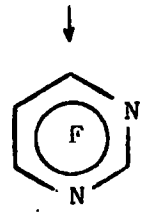
perfluoropyridine



11,32-34

(5)

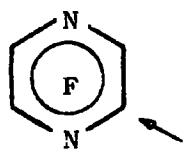
perfluoropyridazine



33,35-37

(6)

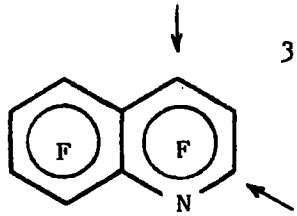
perfluoropyrimidine



12,16

(7)

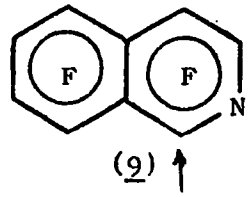
perfluoropyrazine



38-40

(8)

perfluoroquinoline



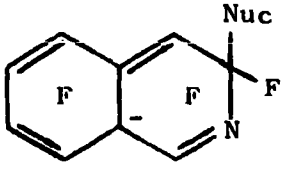
38,39

(9)

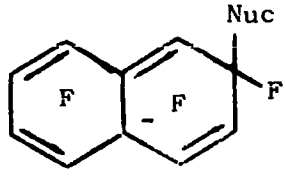
perfluoroisoquinoline

(b) Rationalisation of monosubstitution

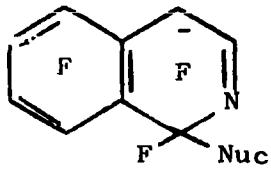
Although control by the repulsive I_π effect of the fluorines predicts the pattern of substitution for (4) to (8) the prediction breaks down for heptafluoroisoquinoline (9) where 3-substitution is predicted (10) analogous to the observed β-substitution in octafluoronaphthalene (11).[41]



(10)



(11)



(12)

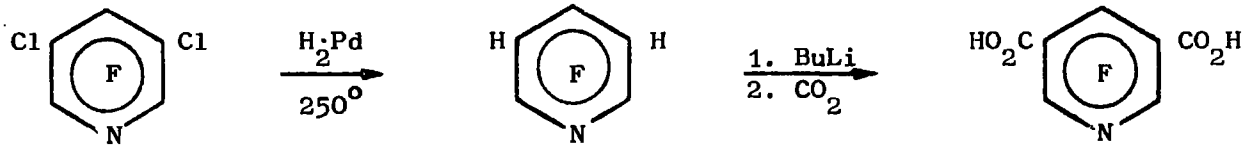
In all cases monosubstitution is observed in the 1-position despite the destabilising para fluorine indicating control by the ring nitrogen. This control by the ring nitrogen is confirmed by the fact that displacement of halogen[42-44] or methylsulphonyl[45] group takes place most readily from the arrowed positions in (4) to (9) in the corresponding hydro compounds.

C. General chemistry of polyfluoroheteroaromatic compounds

Since the development of the halide exchange method for the preparation of a number of polyfluoronitrogen heterocyclic compounds extensive studies of the reactions of these systems have been carried out. Pentafluoropyridine serves as an example of the heterocycles and the chemistry, which has been studied in some detail, is briefly outlined below.

1. Pentafluoropyridine

By careful control of the halogen exchange of pentachloropyridine with potassium fluoride both 3-chlorotetrafluoropyridine (13) and 3,5-dichlorotrifluoropyridine (14) can be obtained.[9] Although nucleophilic displacement of the fluorine[28] occurs readily, they are mainly useful in the synthesis of the otherwise inaccessible 3- and 3,5-disubstituted polyfluoropyridines.[46,47]



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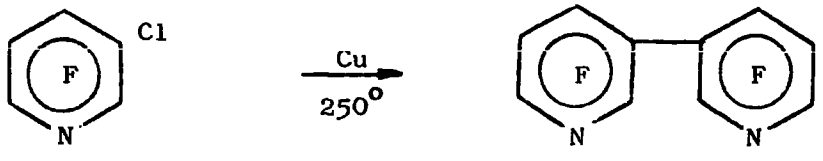


(13)

Pentafluoropyridine itself readily undergoes nucleophilic aromatic substitution reactions and some examples are given in Figure 1.

The 4-bromotetrafluoropyridine is readily obtained from pentafluoropyridine and some of its chemistry is summarised in Figure 2.[29]

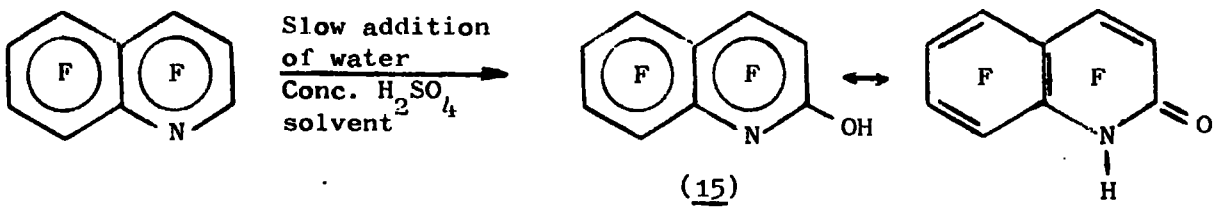
Attack of polyfluorocarbanions, generated in aprotic solvents by the action of caesium fluoride on perfluoro-olefins, gives rise to a number of substituted products of pentafluoropyridine. In the case of hexafluoropropene intermolecular rearrangement of one of the tri-substituted products has been observed. Some of the polyfluoroalkylations are summarised in Figure 3.

2. Acid induced chemistry

An interesting property of the polyfluoroheterocyclic compounds is their ability to undergo acid induced reactions[4,5,51] and it is this type of reaction that leads to an indication of the relative order of base strengths.

(a) In sulphuric acid

Pentafluoropyridine does not, on superficial investigation appear to have any basic properties;[1,2] it does not form a salt when HCl is bubbled through an ethereal solution and solutions in pentane do not give isolable complexes with boron trichloride. However, all of the polyfluoroheterocyclic compounds are soluble in concentrated sulphuric acid and if such solutions are slowly diluted with water, tetrafluoropyrazine, pentafluoropyridine and heptafluoroisoquinoline[49] are precipitated unchanged but high yields of the α-hydroxy compounds of heptafluoroquinoline (15)[3] and tetrafluoropyridazine[5] are precipitated.



(15)

FIGURE 1 2,24,27,29,30,48

Some nucleophilic substitution reactions of pentafluoropyridine

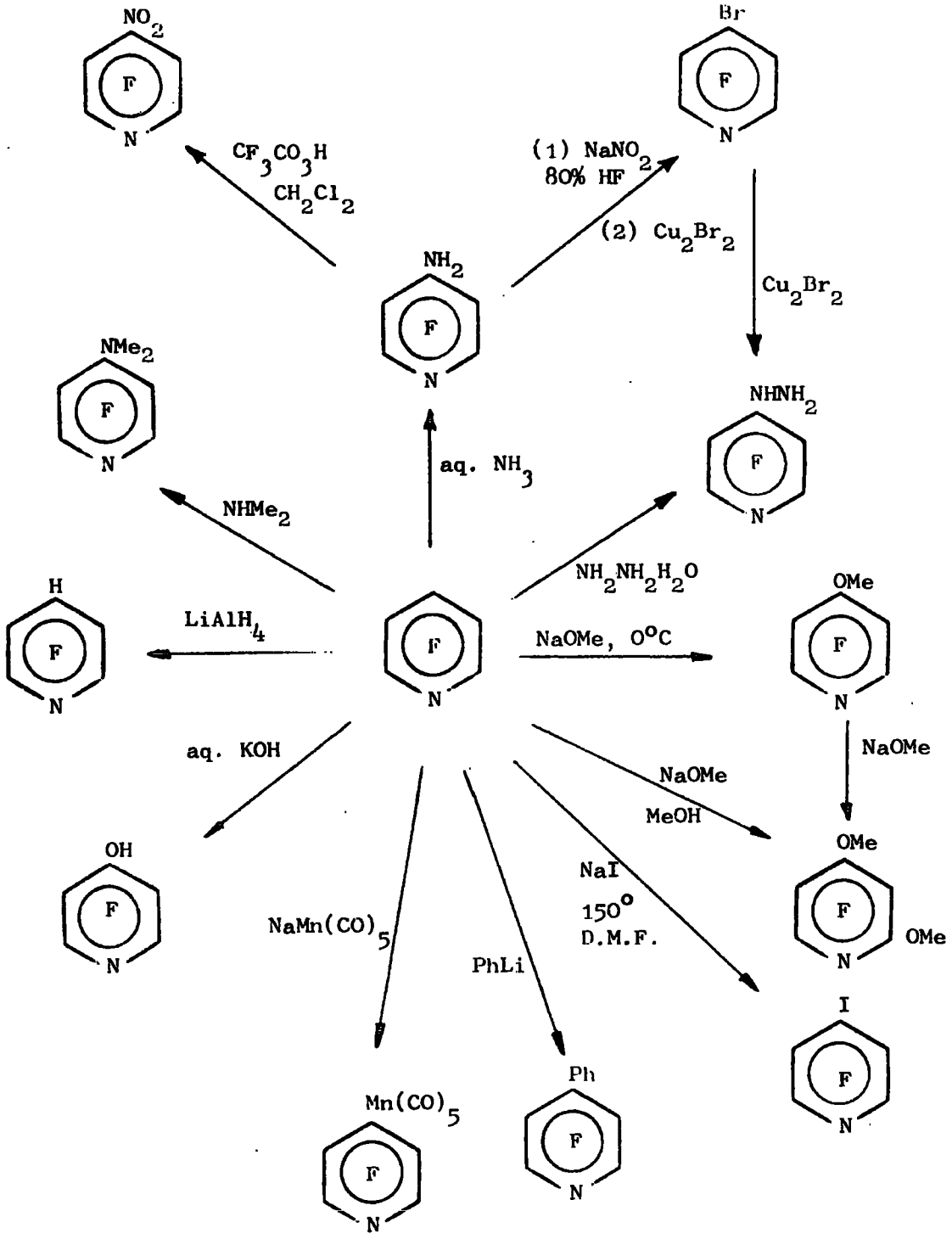


FIGURE 2

Reactions of 4-bromotetrafluoropyridine [24,29]

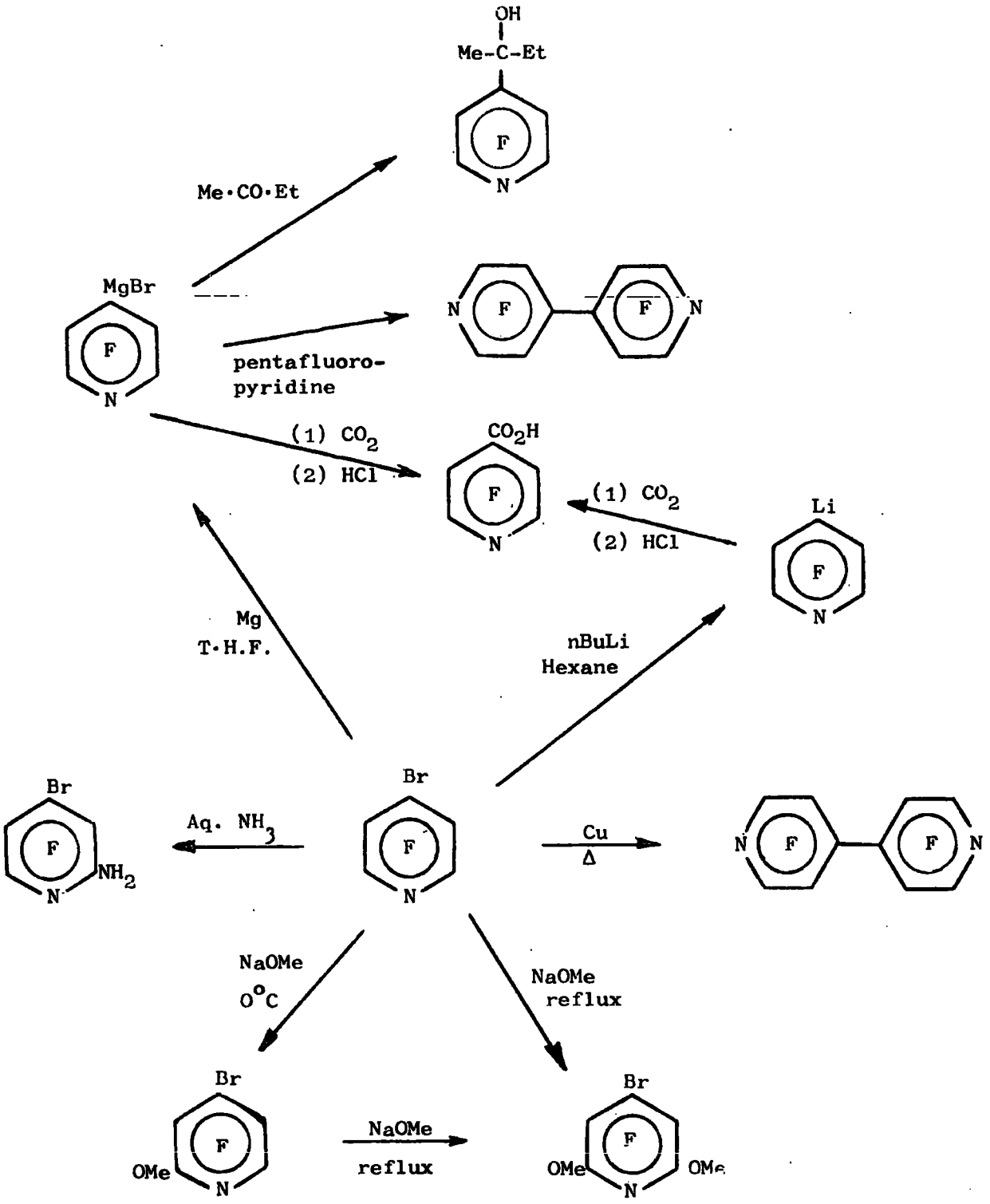
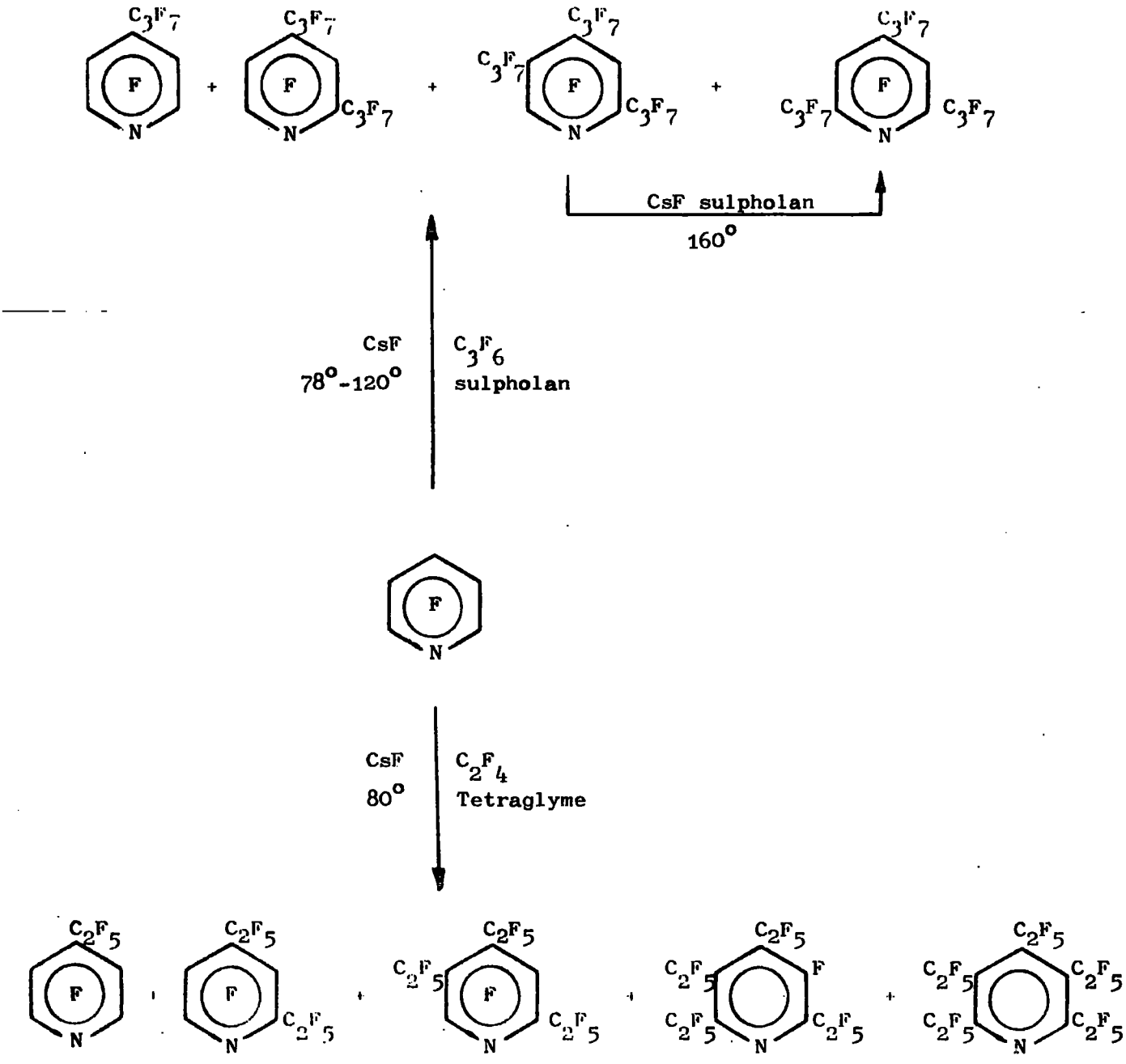
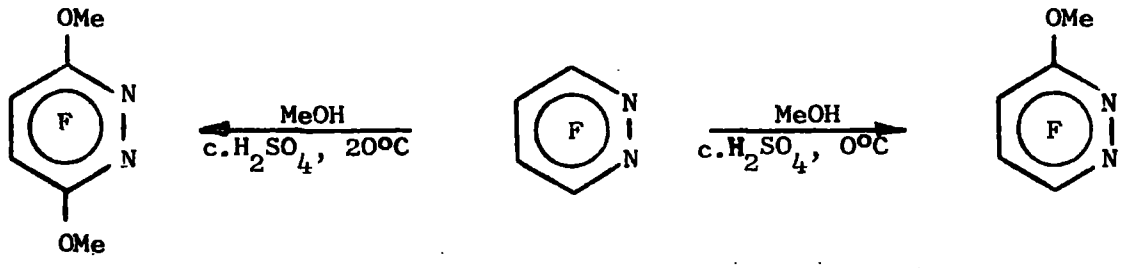


FIGURE 3

Reactions of pentafluoropyridine with perfluorocarbanions [49,50,54]



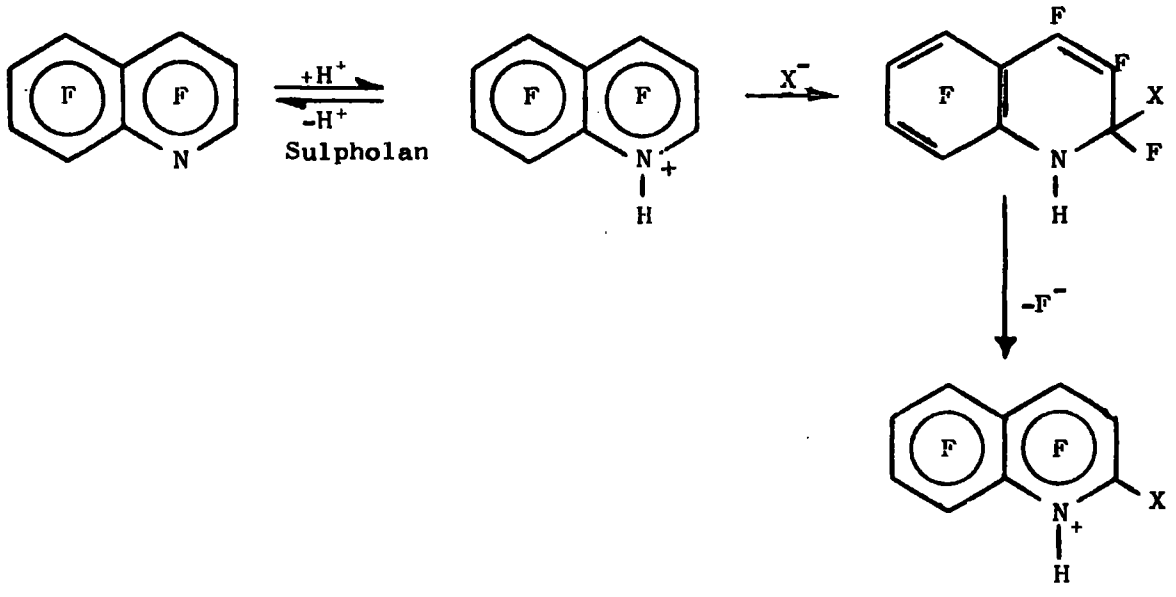
Similarly slow dilution of the sulphuric acid solutions of tetrafluoropyrazine, heptafluoroquinoline and tetrafluoropyridazine with methanol gives the corresponding α-methoxy compounds in good yields.[3,5]



Rapid dilution in both cases leads to only partial displacement.

(b) With hydrogen halides

Attack by the halogen acids on heptafluoroquinoline[4] in very dry sulpholan firstly displaces the fluorine ortho to the aza group and then the para fluorine. This contrasts with nucleophilic substitution on the neutral molecule where the 2- and 4-positions are of similar reactivity to small nucleophiles.[3]



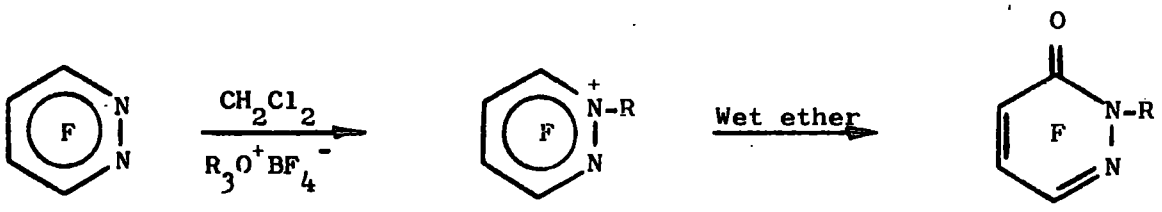
Comparable reactions on pentafluoropyridine[4] yield only traces of substituted products, the monosubstituted product being the 4-halopyridine

but there is no proof that the reaction takes place on the protonated species. Attempted reactions of KCl and KBr in sulpholan on heptafluoroquinoline and pentafluoropyridine[51] again only yield traces of substituted products after prolonged heating although the insolubility of the salts in the medium cannot be ignored.

An ethereal solution of tetrafluoropyridazine is particularly susceptible to attack by hydrogen halides bubbled through the solution,[5] all the fluorines being uncontrollably displaced at room temperature by either HBr or HCl.

(c) Of N-alkylpyridazines

Confirmation that substitution was adjacent to the positively charged nitrogen was obtained[5] by the hydrolysis of two N-alkylpyradazinium tetrafluoroborates yielding 3,4,5-trifluoro-1-alkylpyradazin-6-ones (16).



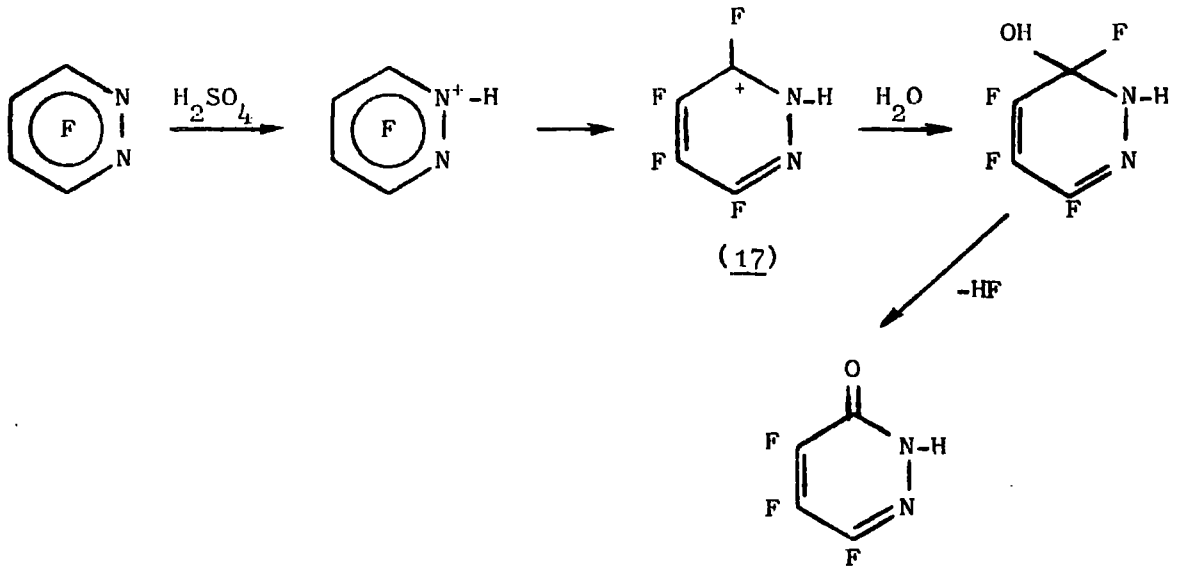
(16)

R = (a) Et
(b) Me

(d) Rationalisation of substitution

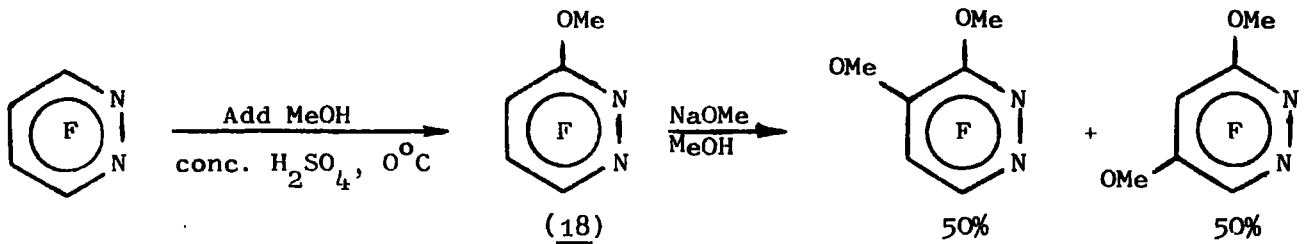
In the reactions of pentafluoroquinoline it is reasonable to suppose that the preferential nucleophilic displacement of the 2-fluorine in the acidic solutions compared with a mixture of 2- and 4-fluorines under basic conditions could be caused either by assistance in the elimination of the fluoride ion by hydrogen bonding or, more likely, to solvent effects.[51] It is unlikely, however, that effects such as these would cause a change from the unique substitution pattern at the 4- and 5-fluorines in basic nucleophilic substitution to the 3- and 6-fluorines under acidic conditions of tetrafluoro-

pyridazine. The activation of the fluorine ortho to the protonated nitrogen is envisaged as either through the inductive effect of the positively charged nitrogen or, in the extreme, by structures such as (17).

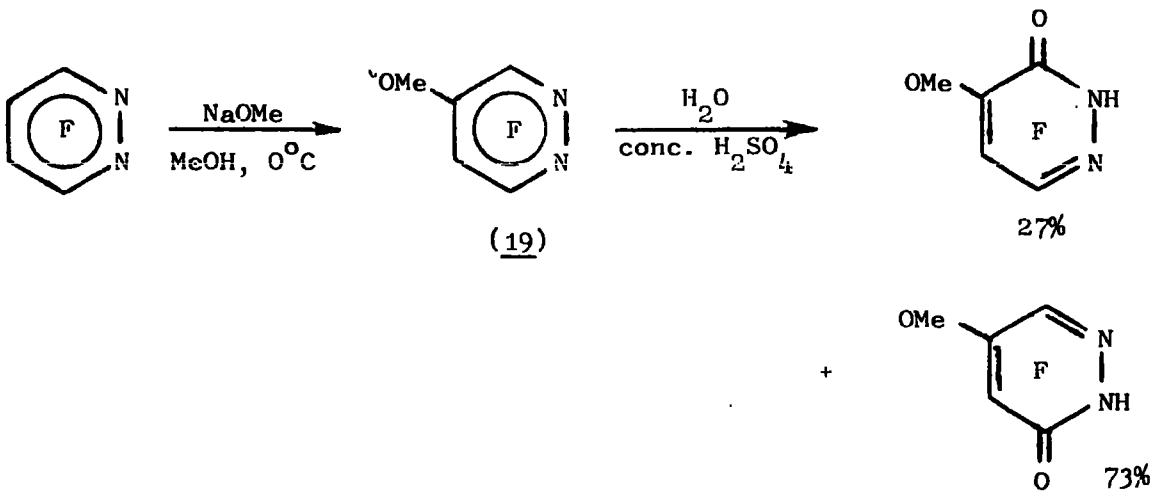


(17)

The possibility of kinetic versus thermodynamic control of the products of substitution does not seem likely as no rearrangements of monomethoxy substituted products were observed[5] when converting the 3-methoxytrifluoropyridazine (18) to disubstituted products under basic conditions or the 4-methoxytrifluoropyridazine (19) to disubstituted products under acidic conditions



(18)



(19)

(e) With Lewis acids

Acid-induced reactions on perfluoro-pyridine and -quinoline have been attempted with Lewis acids and again, substitution has taken place, often with more satisfactory results.

Both boron and aluminium trihalides interact with the polyfluoroheterocycles[52]: pentafluoropyridine and heptafluoroquinoline dissolve in boron trihalides to give pale yellow solutions and both complex with aluminium trihalides to give viscous orange red solutions and in every case, after heating, halogen-substituted products can be isolated.

The most satisfactory preparative reactions were with heptafluoroquinoline and the results are summarised in Table 1.

TABLE 1

Reactions between heptafluoroquinoline and various Lewis acids [52]

Lewis Acid	Proportion	Temp (°C)	Time (hr)	Product Yields (%)			
				I	II	III	IV
BBr_3	excess	150	55			88	
BCl_3	excess	140	128			91	
BCl_3	$^1/_3$ equivalent	140	128	90	5	5	
$AlCl_3$	excess	150	200		90		
$AlBr_3$	excess	150	120		74		
$AlBr_3$	excess	170	120				95
AlI_3	excess	150	160				17

All reactions carried out in sealed carius tubes.

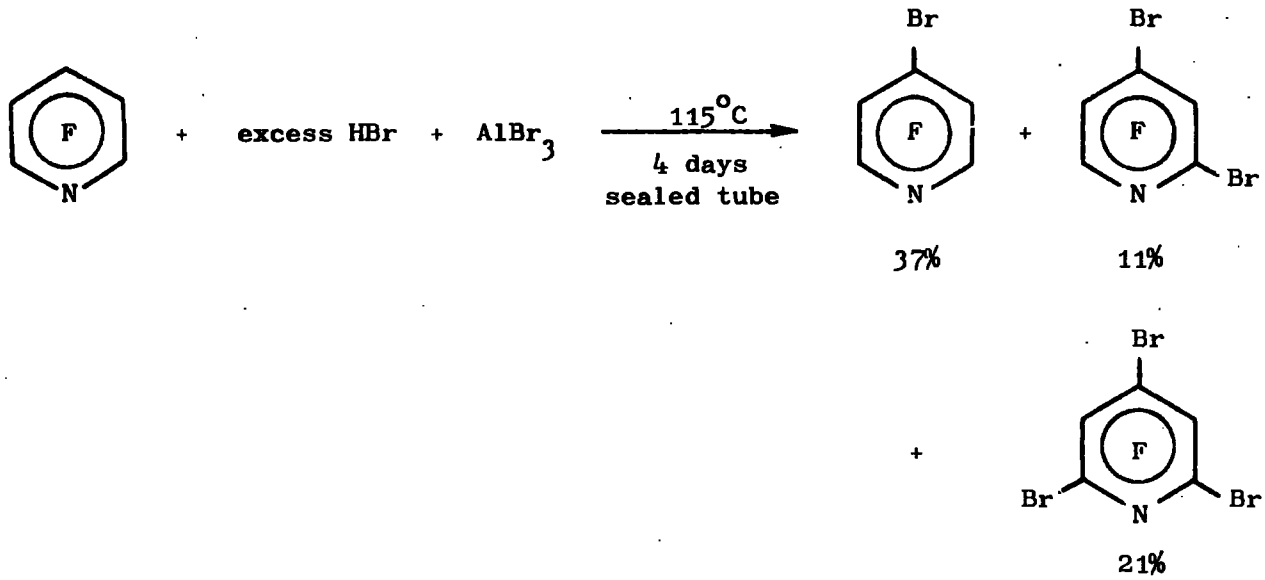
Products: I = heptafluoroquinoline, II = 2-halohexafluoroquinoline

III = 2,4-dihalopentafluoroquinoline, IV = 2,8-dihalopentafluoroquinoline

The formation of the 2,8-dihalopentafluoroquinoline can be envisaged as an intramolecular reaction between heptafluoroquinoline and a co-ordinated aluminium trihalide dimer.[53]

(f) With super acids

Aluminium halides and pentafluoropyridine form tars at elevated temperatures, but the addition of one equivalent of the corresponding protic acid to give a system of higher acidity gives better yields of the substituted products than formed by the protic acids alone,[52] presumably because of greater protonation of the pyridine.



(g) Inferred order of basicity

Table 2 summarises the reactions of the various perfluorinated nitrogen heterocycles with water when in concentrated sulphuric acid, with hydrogen halides, and with hydrogen halide-aluminium trihalide mixtures. If these reactions are sensitive to the change in basicity in the expected way then the relative order of basicities will be:-[4] tetrafluoropyridazine > heptafluoroquinoline > heptafluoroisoquinoline > pentafluoropyridine, tetrafluoropyrazine.

TABLE 2

Relative reactivities of some perfluoro-nitrogen heterocycles towards various acidic reagents

	H_2SO_4 solution add water slowly	Hydrogen halide in sulpholan	Hydrogen halide aluminium halide mixture
Tetrafluoropyridazine	I	I	I
Heptafluoroquinoline	II	II	II
Heptafluoroisoquinoline	IV	III	
Pentafluoropyridine	IV	III	II
Tetrafluoropyrazine	IV		II

I = very reactive to IV = no reaction.

CHAPTER 2

Weak Bases and Highly Acidic Solvents

Introduction

The replacement of hydrogen by halogen in the nitrogen heteroaromatic compounds brings about a marked decrease in their base strength, therefore, increasingly acidic solutions are required for their protonation and the measurement of their basicity. There follows a discussion of the preparation and determination of the acidity of some highly acidic media and their use in the measurement of the strengths of some weak bases.

A. Acidity scales

1. Definition

It was first pointed out by Hammett and Deyrup[55] as far back as 1932, that the then current definitions of acidity were not satisfactory for the description of highly acidic media and proposed the "acidity in terms of a basic indicator" formulation now developed as the acidity function, H_o.

For a basic neutral indicator I, protonated in the acidic medium to form IH^+, the following equilibrium is set up:

$$I + H^+ \rightleftharpoons IH^+$$

For a weak base it is customary[56] to express the basicity as the equilibrium constant of the conjugate acid, K_a so,

$$K_a = \frac{a_{IH^+}}{a_{H^+} . a_I} \qquad a = \text{activity}$$

$$= \frac{f_{IH^+}}{a_{H^+} . f_I} \quad \frac{[IH^+]}{[I]} \qquad f = \text{activity coefficient}$$

Now an acidity function H_o is defined as:

$$H_o = -\log_{10} \frac{a_{H^+} \cdot f_I}{f_{IH^+}}$$

$$\text{so} \quad pK_a = H_o + \log_{10} \frac{[IH^+]}{[I]}$$

normally written as

$$pK_a = H_o + \log Q \qquad \text{Equation 1}$$

2. Measurement

Hammett's method[55] was to calculate the ratio of protonated to non-protonated forms of the indicator by observation of the u.v. absorption spectrum in acidic solution, when the spectra of the protonated and non-protonated forms were both known. If the basicity of the base was known then the acidity of the solution could readily be calculated and vice versa. By starting with very weakly acidic aqueous solutions and using known indicators and then further indicators with overlapping useful ranges Hammett was able, by stepwise comparison, to measure the acidities of the more strongly acidic solutions using the dilute aqueous solutions as the reference point for the scale.

3. Use

The H_o scale is a scale of acidity developed by Hammett and Deyrup[55] and refined by others[57] for a set of primary aniline indicators in sulphuric acid, where the H_o is referred to a standard state of infinite dilution in water and under these circumstances H_o becomes pH. The H_o scale of acidity is critically dependent upon the ratio f_I/f_{IH^+} being constant for a particular type of indicator and in general this has been found to be true. The use of the scale for other types of indicators has necessitated the more general form of Equation 1, i.e.

$$pK_a = H_o + n \log Q \qquad \text{Equation 2}$$

Arnett in his review[56] suggested that the value of n in Equation 2 should be routinely quoted to indicate the degree of similarity of the compounds studied with true Hammett bases and hence the meaning of the pK value. Where n equals unity, pK_a represents the thermodynamic equilibrium constant referred to the standard state free energy of ionisation; where n differs significantly from unity pK_a represents only the H_o at which the base is half protonated and the base must be considered to follow a different acidity function.

B. Highly acidic solvent systems

1. Aqueous sulphuric acid

The acidities of aqueous sulphuric acid solutions range from H_o values of +7 to -11 and attempts to extend the range have been made both with sulphuric acid and other acid systems. Pure sulphuric acid has an acidity of -11[58] but it is possible to increase this to -12·2 by addition of one mole of SO_3.[59] According to the solvent system definition of acids, an acid in a particular solvent system is a compound which increases the concentration of the characteristic cation. SO_3 complexes the HSO_3^- so increasing the concentration of $H_3SO_4^+$.

$$2H_2SO_4 \rightleftharpoons H_3SO_4^+ + HSO_3^- \xrightarrow{+2SO_3} HS_3O_{10}^-$$

2. Non-aqueous sulphuric acid

Efforts to extend the medium acidity ranges available with sulphuric acid into non-aqueous systems were started in 1945 by Hammett[60] who investigated the acidities of nitromethane-sulphuric acid mixtures down to H_o -4.

Arnett[61] in a similar study of the sulphuric acid-sulpholan system was able to investigate the H_o values of the whole range of mixtures and again the solutions were found to be more acidic than the corresponding solutions in water.

3. Other acid systems

Gillespie and co-workers[62,63] have done extensive work on the development and measurement of new highly acidic media. The accurate determination of the acidities of some of these media has necessitated the change from aromatic amine indicators to aromatic nitro indicators but adherence to the Hammett equation has been good.

Acidic systems developed include HF/SbF_5, FSO_3H/SbF_5, H_2SO_4/HSO_3F, H_2SO_4/HSO_3Cl, $H_2SO_4/HB(HSO_4)_4$ and the most acidic yet, the tripartite system $HSO_3F/SbF_5/SO_3$. The H_o of these systems probably ranges below -17 although new indicators are required before consistent values will be available. Some recent values of the acidities are given in Table 3.

TABLE 3

The acidities of some strong acids and strong acid mixtures

Acid	Molar Proportion	H_o	Ref.
HF		-10·2	58
HF/SbF_5	1:3	-15·3	58
HSO_3F		-14·5 (-12·8)	62 (58)
HSO_3F/SbF_5	1:1	~-17·5	58
H_2SO_4/HSO_3F	90% HSO_3F	-13·73	62
$H_2SO_4/HB(HSO_4)_4$	30% $HB(HSO_4)_4$	-13·62	62
$HSO_3F/SbF_5/SO_3$	1:0·33:1·182	at least -16	76

4. Inert diluents

The addition of certain inert solvents has been found not to reduce the H_o of acids appreciably.[64] Particularly useful diluents to circumvent the n.m.r. spectral broadening of HSO_3F and HSO_3F/SbF_5 solutions with decreasing temperature are SO_2 (m.pt. = -72·7°C), SO_2ClF (m.pt. = -124·7°C) and SO_2F_2 (m.pt. = -136·7°C).

C. Basicity measurements

1. Absolute basicity

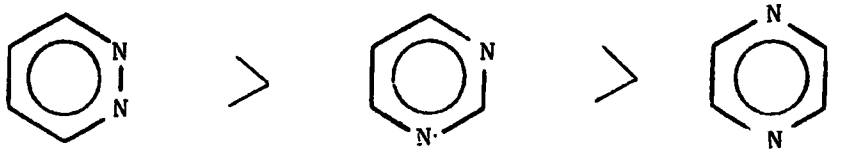
The most accurate measurement of the basicity of a weak base or the acidity of a highly acidic medium is still the method of Hammett[55] where the concentrations of the protonated and unprotonated forms are measured from the u.v. or visible absorption spectrum. The method is limited to those compounds which have suitable u.v. spectra and other methods, often less accurate and indirect, have been used.

Titrations in non-aqueous solvents, conductivity changes and the heats of ionisation in acidic media are quite common but changes in Raman spectrum intensity and the shifts of n.m.r. peaks on protonation have all been used to measure basicity.[65]

2. Relative basicity to Lewis acids

Complementary to the Brønsted basicities of the various nitrogen heterocycles Fratellio[66-68] has measured the relative basicities towards boron Lewis acids. The complexing of the acid results in a downfield shift of the proton n.m.r. spectrum of the base and in most cases ligand exchange in a cooled inert solvent is sufficiently slow on the n.m.r. time scale to observe bound and bulk base molecules independently. Direct integration yields the stoichiometry of the complex and a direct measure of the relative donor strengths of a series of bases towards the particular boron acid.[66,68]

In general the relative basicities of a series of heterocycles parallel the measured proton basicities, steric effects excluded. Towards BF_3 the relative basicities of some diazines were found to be:



(pK_{BH^+} = 2·3 pyridazine > 1·3 pyrimidine > 0·6 pyrazine)

Similarly 4-cyclopropylpyridine and 4-ethylpyridine have similar basicities towards BF_3 (pK_{BH^+} 6·2 and 5·0 respectively).[66] Steric effects are noticeable for the heterocycles substituted α to the nitrogen where interaction between the substituents and the bulky BF_3 becomes apparent.[68] Towards BF_3:

(pK_{BH^+} = 4-methylpyridine 6·02 > 3-methylpyridine 5·68 > pyridine 5·25)

(pK_{BH^+} = 2-methylpyridine 5·97 > 2,6-dimethylpyridine 6·75)

3. Basicities of some heterocyclic compounds

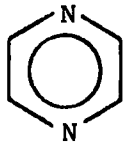
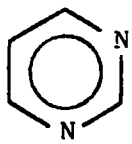
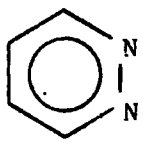
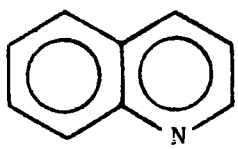
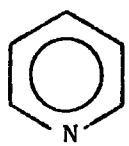
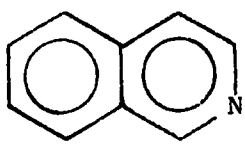
(a) Unsubstituted heterocycles

The basicities of some nitrogen heterocycles are given below in Table 4.

All are relatively weak bases but no adequate explanation of the order has been given. Introduction of a second aza group into pyridine leads to a reduction in base strength in all cases, however this is not simply an inductive effect as that would lead to a reverse order to that observed.

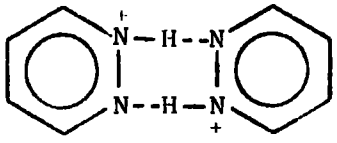
TABLE 4

Base strengths of some N-heteroaromatic compounds [69]

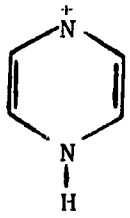
Base		pK_a *
Pyrazine		0·65
Pyrimidine		1·30
Pyridazine		2·33
Quinoline		4·94
Pyridine		5·23
Isoquinoline		5·40

* pK_a in water 20°C

Pyridazine may have enhanced basicity because of stabilisation by structures such as (20)[70] and pyrazine may be weakened by the reluctance of the para nitrogen to accept the positive charge (21)[71]



(20)



(21)

Annelation of a benzene ring to pyridine gives rise to slight variations in the basicity of the aza group, that in isoquinoline being slightly increased, and in quinoline slightly decreased relative to pyridine.

(b) Substituted pyridines

The basicities of some monohalopyridine derivatives have been measured by Brown and McDaniel[72] using the method of Hammett, the results being summarised in Table 5.

TABLE 5

Basicities of various monohalopyridines [72]

Halogen	pK_a 2-halopyridine	pK_a 3-halopyridine
H	+5·17	+5·17
F	-0·44	+2·97
Cl	+0·72	+2·84
Br	+0·90	+2·84
I	+1·82	+3·25

pK_a values 25°C in water

Katritzky and co-workers[73] have extended the data available to polyhalopyridines by the same method and also by measurement of the pH of solutions of their salts. The results are given in Table 6.

TABLE 6

Basicities of some polyhalopyridines [73]

Chloropyridines		Bromopyridines	
Substituted positions	pK_a	Substituted positions	pK_a
3,5	+0·75	3,4,5	+0·45
2,3	-0·85	2,3,4	-1·07
2,6	-2·86	2,4,6	-3·36
2,3,5,6	-5·50	2,3,5,6	-4·90
2,3,4,5,6	-6·02	2,3,4,5,6	-5·23

Temperature not quoted

(c) Substituted quinolines

Data on substituted quinolines are not so extensive but the basicities of a series of monosubstituted quinolines by Knight[74,75] is given in Table 7 (reconverted to the pK_a scale by $pK_a = 14·10 - pK_b$.[74])

TABLE 7

pK_a values of some monosubstituted quinolines at 25°C [74,75]

Group / Position	F	Cl	Br	Me
2	too weak	too weak	0·89	5·52
3	2·46	2·50	2·63	4·38
4	N.A.	3·52	N.A.	5·44
5	3·78	3·44	3·48	N.A.
6	4·10	3·14	3·76	4·99
7	4·10	3·72	3·72	5·14
8	3·18	2·95	2·99	4·74

N.A. - not available

pK_a of quinoline 4·79

4. Factors controlling the basicity

From Tables 5, 6 and 7 it can be seen that, in general, two points emerge.

(i) That the electronegative groups depress the basicity in the order of their electronegativity i.e. F > Cl > Br > I (> H).

(ii) That electron releasing groups increase the basicity.

The most important factor controlling the depression of the basicity is the proximity of the halogen atoms to the nitrogen, the depression of basicity falling off rapidly with increasing distance from the aza centre. In particular, from

Tables 5 and 6, it can be seen that a consistent depression of basicity takes place on substitution of hydrogen for chlorine, displacement of an α hydrogen by chlorine depresses the pK_a by 3·5 to 4·5 units, a β hydrogen by 1·5 to 2·4 units, and a γ hydrogen by 0·5 units for the various chloropyridines. Further evidence can be obtained from the fact that the 3- and 8-bromoquinolines have approximately the same basicity, the halogen being comparable distances from the nitrogen atom.

CHAPTER 3

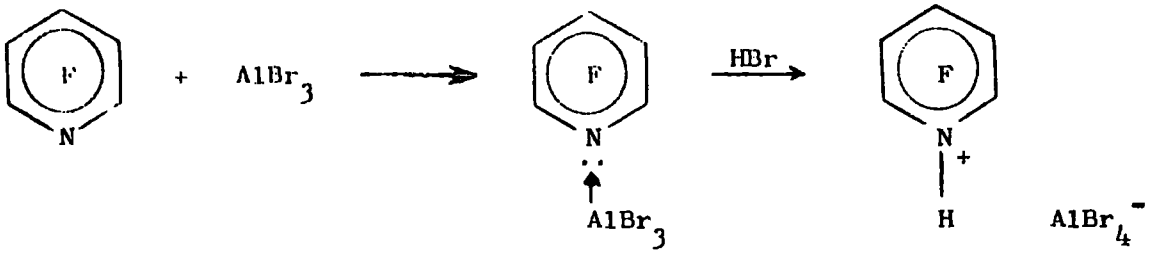
Comparison of the Base Strengths of Some Polyfluoroheterocyclic Compounds

Introduction

The first attempts at the preparation of a salt of pentafluoropyridine[1] by bubbling hydrogen chloride gas into an ethereal solution did not produce any precipitate and so pentafluoropyridine was considered to be only very weakly or effectively non-basic. Later reactions on other polyfluorinated nitrogen heterocycles as described in Chapter 1.C.2, in particular of heptafluoroquinoline[3] and tetrafluoropyridazine[5], showed that interactions with acidic reagents and indeed acid induced reactions were possible and attempts to prepare isolable salts by reaction with acids stronger than hydrogen chloride in ether were attempted.

A. Preparation and isolation of salts

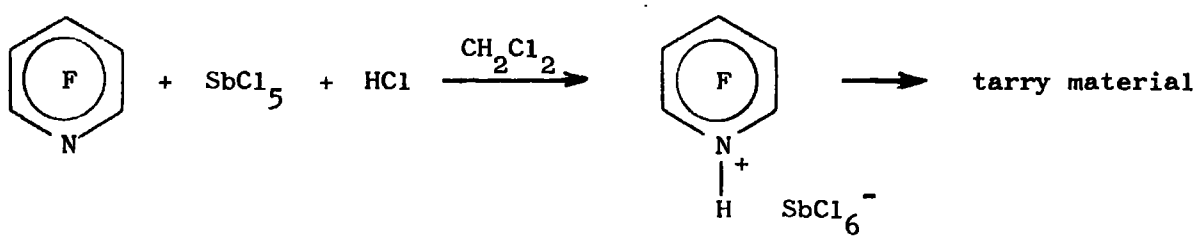
It was noticed[51], in the attempted preparation of substituted pyridines by reacting pentafluoropyridine with a mixture of aluminium tribromide and hydrogen bromide, that, after sealing the three reactants into a Carius tube, the aluminium tribromide dissolved in pentafluoropyridine to give an orange red solution and on shaking thoroughly to mix in the hydrogen bromide the coloured liquid turned to an off-white solid. This was explained as possibly the two stage process given below.



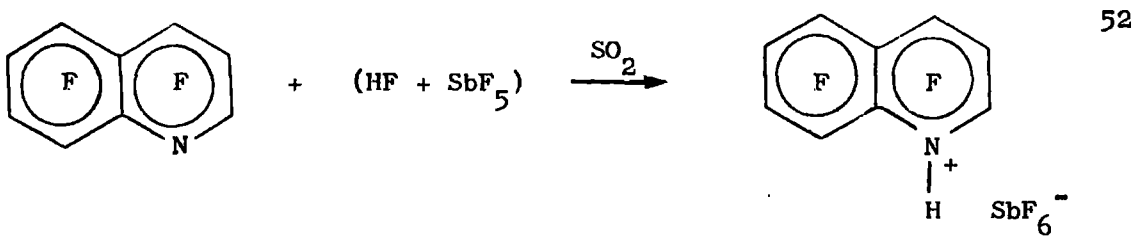
orange red solution white solid

Other perfluorinated azo-aromatic compounds similarly all give the highly coloured mixtures with the very acidic aluminium trihalides[52] without the hydrogen halide.

In an attempt to prepare isolable salts[52] pentafluoropyridine was dissolved in methylene chloride with an equimolar amount of antimony pentachloride. On saturating this solution with hydrogen chloride a white crystalline solid was formed but before isolation it darkened to a tarry material presumably because of halogen exchange.



The problem of halogen exchange was readily overcome by using hexafluoroantimonic acid, prepared by mixing together equimolar proportions of anhydrous hydrogen fluoride and antimony pentafluoride. The solvent used was sulphur dioxide. The isolation of white crystalline salts of perfluoro-pyrazine, -pyridine, -quinoline, -isoquinoline, and 3,5-dichlorotrifluoropyridine was achieved in quantitative yields.[52]



52

The salts were highly susceptible to moisture, immediately decomposing on contact with moist air, and so were stored in a nitrogen glove box.

B. Proof of N-protonated salt formation

Since pentafluoropyridine in particular was believed to be such a weak

base it was necessary to confirm that N-protonation had indeed taken place. The first most noticeable feature is that all the salts are white crystalline solids highly soluble in, but recrystallisable from, sulphur dioxide. The infrared spectra of the compounds in dry nujol all had bands attributable to N-H stretch and a broad band at 666 cm^{-1} characteristic of the hexafluoroantimonate ion; an ion shown by Olah[92] to stabilise weakly basic protonated species. The shifts induced in the ultraviolet spectra on solution in sulphuric acid[3] are comparable with those induced in the corresponding hydrocarbon systems which are known to be N-protonated.

The n.m.r. spectra of the salts in sulphur dioxide and of the parent bases dissolved in various strong acids are discussed in detail later, but the generally well resolved spectra with the peaks shifted, but very similar in general overall shape to those of the free base, are consistent only with N-protonation.

In contrast to the polyfluorinated nitrogen bases, hexafluorobenzene does not dissolve in concentrated sulphuric acid but in the more acidic medium, antimony pentafluoride in fluorosulphuric acid, forming radical cations.[77] The ^{19}F n.m.r. spectra of the polyfluorinated bases in these acidic solvents, with the exception of tetrafluoropyrazine in fluorosulphuric acid-antimony pentafluoride mixtures, are not consistent with the formation of the radical cations.

C. ^{19}F n.m.r. spectra of the salts

Table 7 gives the ^{19}F n.m.r. data for the hexafluoroantimonate salts of some polyfluoroaza-aromatic compounds dissolved in sulphur dioxide where a comparison with the free base is made.

The spectral data was interesting in comparison with the non-fluorinated heterocyclic ions and also in comparison with fluorobenzenonium ions.

TABLE 7

^{19}F n.m.r. data of the hexafluoroantimonate salts of some perfluoroheterocyclic compounds *

Tetrafluoropyrazine †

Base	95·9
Salt	90·9
δ =	-5·0

Pentafluoropyridine †

	(2,6)	(4)	(3,5)
Base	89·5	135·0	163·5
	m	J = 13·8, 18·0 Hz.	m
Salt	97·8	107·1	156·4
	m	J = 21·6, 27·3 Hz.	m
δ =	+8·3	-28·9	-7·1

3,5-Dichlorotrifluoropyridine †

	(2,6)	(4)
Base	71·1	96·8
	$J_{2,4}$ = 14 Hz.	$J_{4,2}$ = 14 Hz.
Salt	79·1	68·1
	$J_{2,4}$ = 25·3 Hz.	$J_{4,2}$ = 25·3 Hz.
δ =	+8·0	-28·7

Heptafluoroquinoline †

	(2)	(4)		(5)				
Base	75·0	126·5		148·5	151·0	154·2	157·5	163·7
Salt	78·1	95·2	138·1	140·0	147·7	150·7	159·4	
δ =	+3·1	-31·3		-8·5				

Heptafluoroisoquinoline†

	(1)	(3)					
Base	63·5	99·3	141·6	147·3	148·0	155·3	157·5
Salt	69·1	113·9	133·2	134·8(8)	142·7	147·1	150·3
δ =	+5·6	+14·6					

Tetrafluoropyridazine

	(3,6)	(4,5)
Base	90·7	144·6
Salt	80·1	121·2
δ =	-10·6	-23·4

* Solvent SO_2, -30°C in all cases. Shifts (in p.p.m.) relative to $CFCl_3$ in a capillary tube, assignments in parenthesis, m = multiplet, δ = difference between chemical shift recorded and that of the free base.

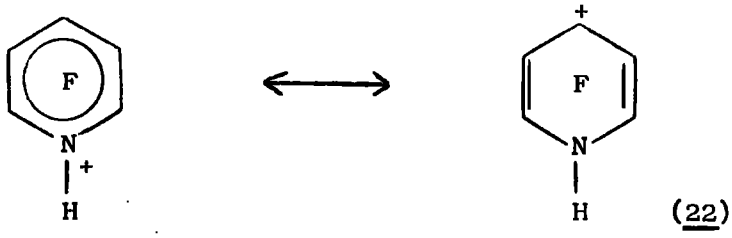
† = reference 59.

A simple approach would anticipate that the fluorine atoms in all positions would be deshielded as evidenced by a downfield shift in the ^{19}F n.m.r. peaks on protonation. Examination of Table 7 shows that for pentafluoropyridine the ortho positions in fact move upfield, the meta positions slightly downfield and the para fluorine moves substantially downfield on protonation of the nitrogen. The same general shifts are noted for the other compounds.

The rather surprising upfield shift of the ortho position has previously been noted in the hydrocarbon series for the ^{13}C n.m.r. spectra,[78] indicating that either the electron density ortho to ring nitrogen may increase on protonation[79] or, alternatively, changes in the C-N bond order occur.[78] The

proton shift[80] of the ortho position, although not upfield, is much smaller than the downfield shift of the meta and para protons.

It has been concluded, from calculations which included the pi electrons and the sigma electron framework, that mixing of ground state and low lying excited states[81] occurs and that changes in bond order[78] take place on protonation. Nevertheless, if it is accepted that the charge lies principally on the carbon atom which is para to nitrogen, then this provides a simple qualitative model (22) which accounts for the large downfield shift of that fluorine.



(22)

The ^{13}C and ^{19}F internal shifts on protonation of pyridine (Table 8)[78] are very large in comparison with the ^{1}H shifts and the parallel behaviour of the ^{13}C and ^{19}F shifts on protonation may show, at least quantitatively, that the ^{19}F shifts can be used to reflect the electron distribution in charged systems in comparison with the uncharged species. The correlation between the ^{13}C and ^{19}F data for the mono-protonated diazine systems does not appear to be so good.[78]

The increase in the value of the coupling constants to the para fluorine could be compared with the enormous increase in coupling noted on the formation of carbonium ions by protonating substituted benzenes.[82,83] This increase in the coupling may indicate some charge localisation on the para fluorine, i.e. the system has some degree of carbonium ion character.

TABLE 8

Changes in ^{1}H, ^{13}C and ^{19}F chemical shift induced in some nitrogen bases on mono-protonation [78]

Pyridine		(2,6)	(3,5)	(4)
	^{1}H †	-1·08	-1·71	-1·75
	^{13}C †	+7·78	-5·04	-12·42
	^{19}F *	+8·3	-7·1	-28·9
Pyrazine		(2,3,5,6)		
	^{1}H †	-0·41		
	^{13}C †	+2·67		
	^{19}F*	-5·0		
Pyridazine		(3,6)	(4,5)	
	^{1}H †	-0·08	-0·84	
	^{13}C †	+1·10	-10·08	
	^{19}F *	-10·5	-22·6	
Pyrimidine		(2)	(4,6)	(5)
	^{1}H †	-0·59	-0·78	-1·14
	^{13}C †	+7·28	-1·33	-3·04
	^{19}F *	-2·5	-14·4	-12·0

† Shift induced on protonating the hydrocarbon compound

* Shift induced on protonating the perfluorinated compound.

D. N.m.r. spectra of salt-base mixtures

Because of the considerable differences in the peak positions of the ^{19}F n.m.r. spectra of the salts of polyfluorinated aza-aromatic compounds and the parent base (Table 7) it seemed feasible to identify whether a known base was protonated in a particular acidic mixture and so compare the proton acceptor qualities of several bases.

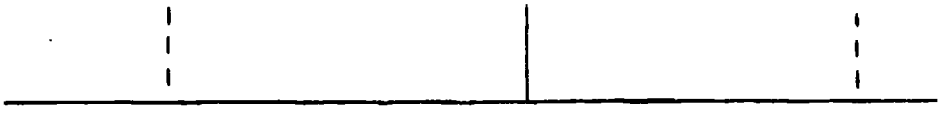
1. Addition of 3,5-dichlorotrifluoropyridine to a solution of its hexafluoroantimonate salt

The first requirement was to investigate the change in ^{19}F n.m.r. spectrum on the addition of free base to a solution of its conjugate acid (the salt) in an inert solvent. The base 3,5-dichlorotrifluoropyridine was chosen because of the simple, fully analysed spectra of the salt and of the free base. In order to have a consistent reference for all the ^{19}F n.m.r. spectra, $CFCl_3$ sealed in a capillary tube was used so eliminating problems of interaction between reference and possible free acid.

Free base was added slowly to a solution of 3,5-dichlorotrifluoropyridinium hexafluoroantimonate in sulphur dioxide. The ^{19}F n.m.r. spectrum of the salt slowly shifted from the salt positions towards the positions in the free base, the 4-fluorine upfield, the 2,6-fluorines downfield. The shift is shown against volume of free base added in Graph 1.

Graph 2 shows the position of the 2,6-fluorine resonance plotted against the position of the 4-fluorine resonance for the mixtures.

Graphs 3 and 4 show the volume of 3,5-dichlorotrifluoropyridine added to the solution of the salt plotted against the value of the ratio $\frac{1}{Q}$ where Q is given by

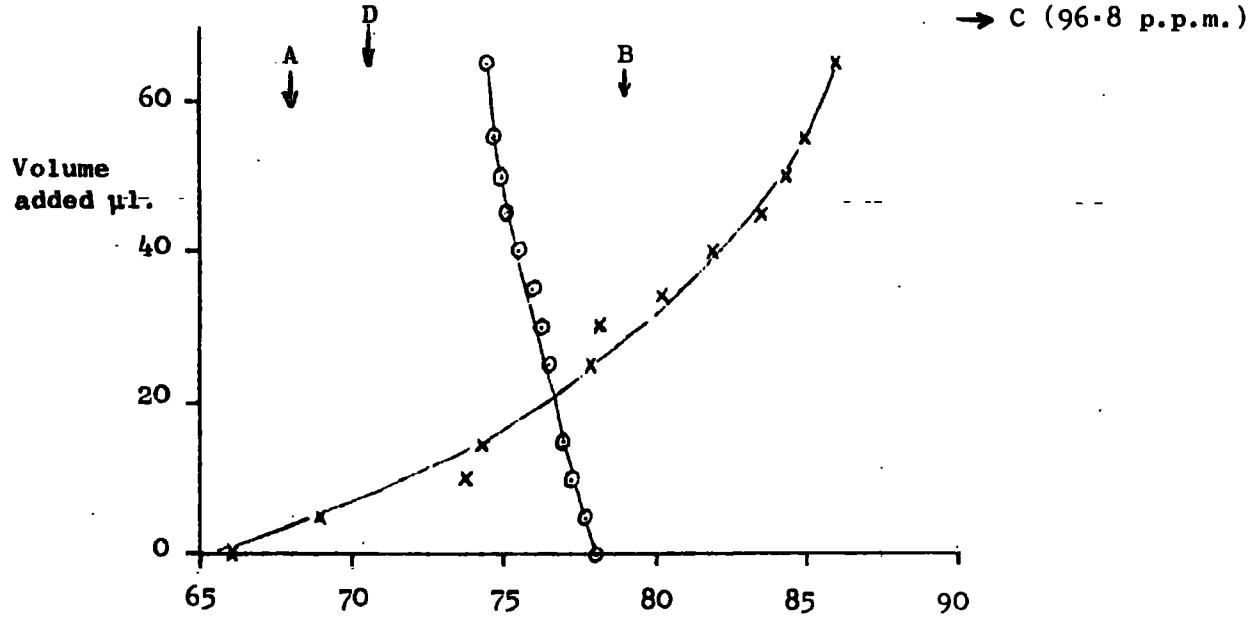


A	B	C
N.m.r. shift of peak in pure salt	N.m.r. shift of intermediate peak in mixture	N.m.r. shift of peak in pure base

$$Q = \frac{B-C}{A-B}$$

GRAPH 1

Shift of ^{19}F n.m.r. peak positions of 3,5-dichlorotrifluoropyridinium hexafluoroantimonate in SO_2 against volume of 3,5-dichlorotrifluoro-pyridine added



x = positions of triplet resonance and ⊙ = positions of doublet resonance after successive additions of base.

Letters denote peak positions of pure components.

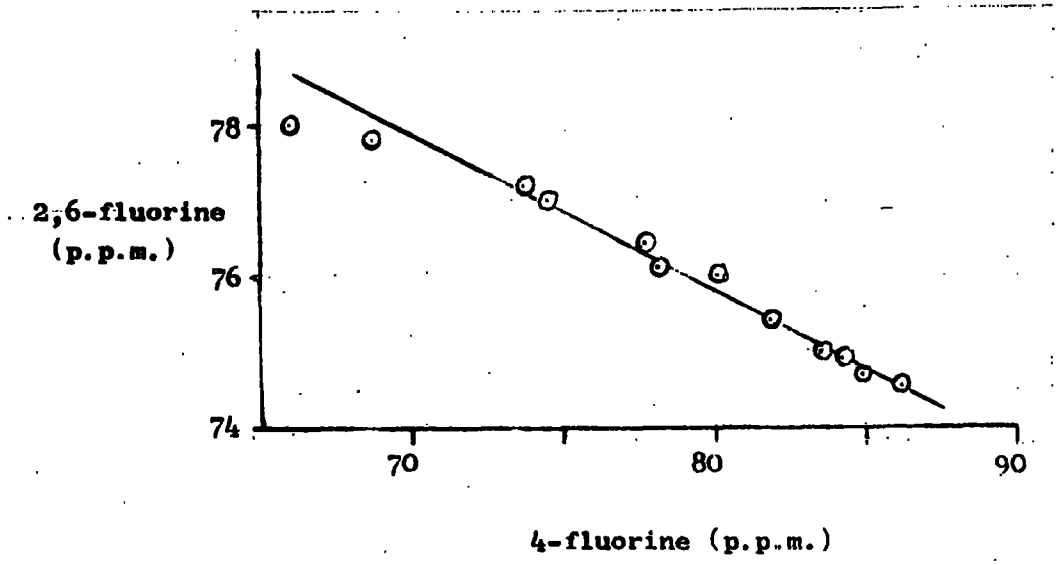
Protonated base : (4), A; (2,6), B

Non-protonated base : (4), C; (2,6), D

Assignments in parenthesis

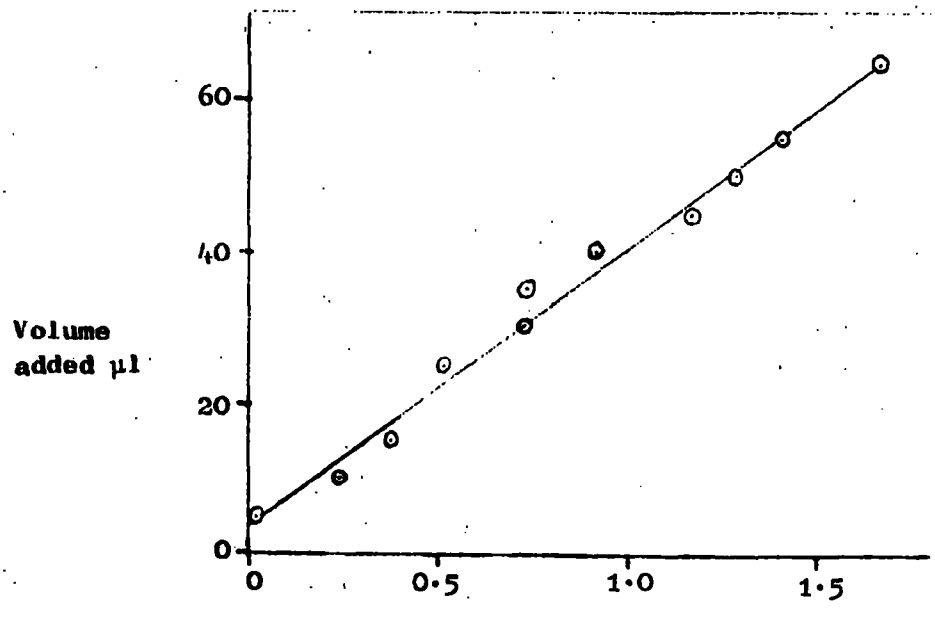
GRAPH 2

Shift of 2,6-fluorine resonance plotted against shift of 4-fluorine resonance for various mixtures of 3,5-dichlorotrifluoropyridine and its hexafluoroantimonate salt



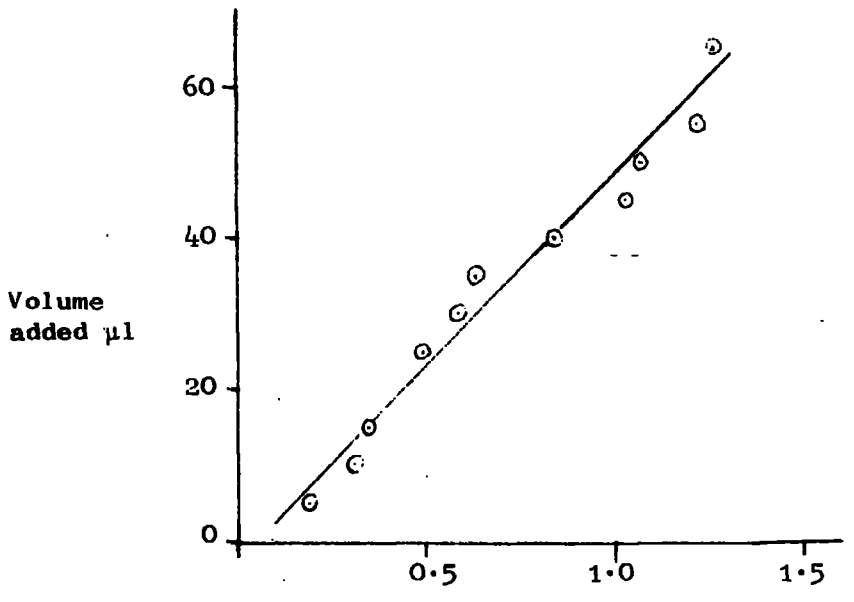
GRAPH 3

Graph of volume of 3,5-dichlorotrifluoropyridines added to a solution of its hexafluoroantimonate salt against $\frac{1}{Q}$ calculated from the position of the 4-fluorine resonance



GRAPH 4

Graph of volume of 3,5-dichlorotrifluoropyridine added to a solution of its salt against $\frac{1}{Q}$ calculated from the position of the 2,6-fluorine resonance



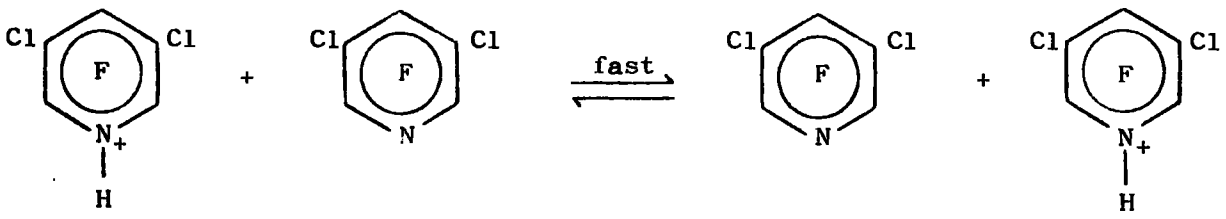
The ratio Q was calculated for both the 4-fluorine (Graph 3) and the 2,6-fluorines (Graph 4). Although both graphs are similar, Graph 3 (from the 4-fluorine) has the least scatter of points about the line.

Variation of the temperature of the recording of the n.m.r. spectra of the mixtures down to the freezing point of the solvent SO_2 produced no appreciable change in the peak shapes or the positions of the resonances.

2. Interpretation

The interpretation of the results is as follows. Graph 1 shows that progressive additions of free base to a solution of the salt shift the positions of the resonances towards those of the base. The very nearly linear Graph 2 shows that to a very good approximation a shift in the position

of the triplet resonance is accompanied by a proportionately equal shift of the doublet resonance. These results are consistent with there being rapid exchange of the proton between the nitrogen atoms within the mixture from -15 to -70°C.



Each base molecule is indistinguishable from any other and so the n.m.r. spectrum is intermediate between that of the salt and that of the base. Moreover, the position of the intermediate peak in the spectrum is directly related to the relative concentrations of the protonated and non-protonated forms,[84] i.e.

$$\frac{1}{Q} = \frac{\text{shift of intermediate peak from corresponding peak in pure salt}}{\text{shift of intermediate peak from corresponding peak in pure base}}$$

$$= \frac{[\text{free base}]}{[\text{protonated base}]}$$

This is confirmed to be true by Graphs 3 and 4 where the volume of base added is plotted against $\frac{1}{Q}$ for both resonances. The straight line graphs, extrapolating through the origin show that the volume of added base was indeed proportional to the concentration of the free base in the mixture as estimated from the n.m.r. spectrum, the concentration of protonated base in the mixture remaining, to a first approximation, constant.

The results show that for 3,5-dichlorotrifluoropyridine in particular that:

(a) rapid exchange of the protons between base molecules occurs,

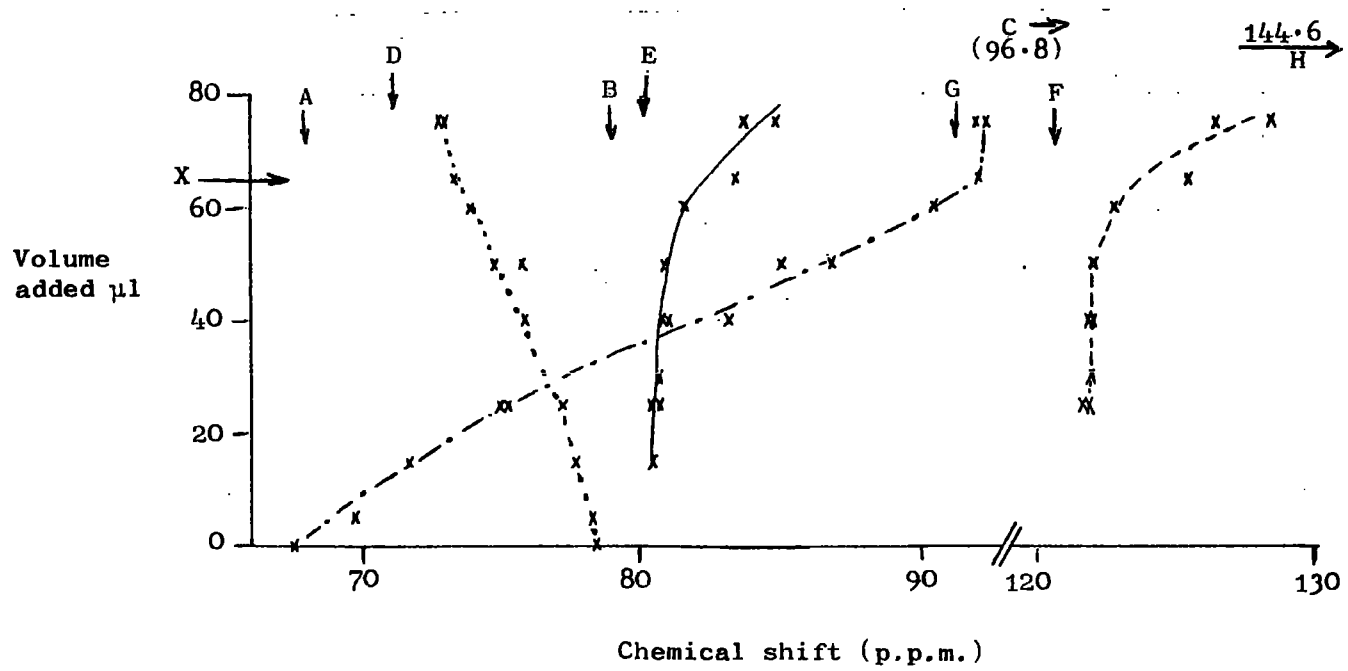
(b) the relative proportions of protonated and non-protonated forms in a mixture is readily estimated from the intermediate peak positions.

3. Addition of tetrafluoropyridazine to a solution of 3,5-dichloro-trifluoro-pyridinium hexafluoroantimonate in SO_2

This next experiment showed that a comparison of base strengths was possible using the peak positions. The addition of tetrafluoropyridazine to a solution of 3,5-dichlorotrifluoropyridinium hexafluoroantimonate in sulphur dioxide caused a shift in the spectrum of the pyridine in exactly the same way as in the previous experiment i.e. free pyridine base had been created in the mixture by the addition of the stronger base, tetrafluoropyridazine. After further addition of the pyridazine the n.m.r. spectrum of the pyridazine could be observed downfield of the free base in SO_2 at a position coincident with the salt, prepared in SO_2. Further additions of base gave a spectrum of increased intensity but relatively invariant position for the pyridazine, the spectrum of the pyridine shifting towards that of the base after each addition. At the point X on the Graph 5 a change in the slopes of the lines is evident and this is approximately where one equivalent of tetrafluoropyridazine has

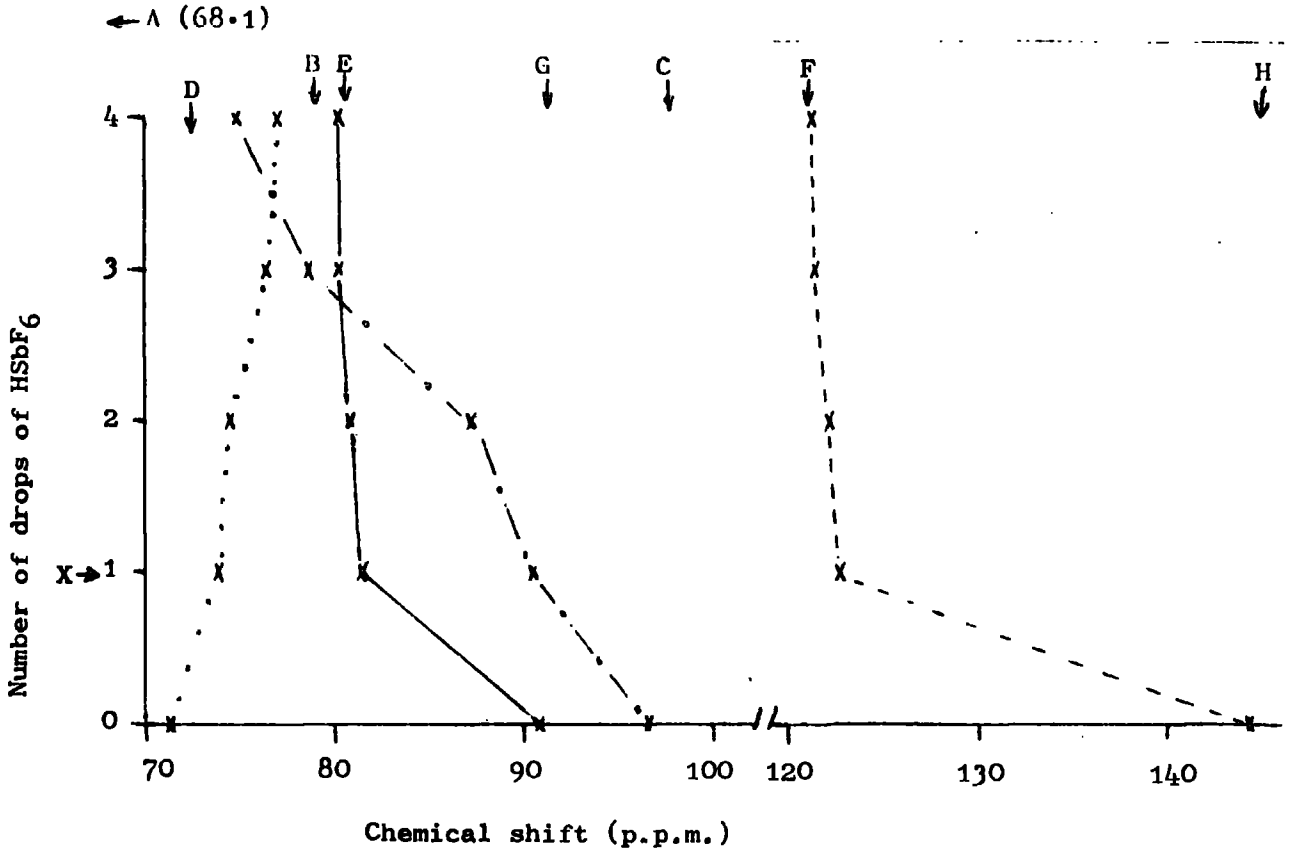
GRAPH 5

Change in the ^{19}F n.m.r. spectrum of 3,5-dichlorotrifluoropyridinium hexafluoroantimonate in SO_2 on the addition of tetrafluoropyridazine



GRAPH 6

Change in the n.m.r. spectrum of a mixture of 3,5-dichlorotrifluoropyridine and tetrafluoropyridazine in SO_2 on the addition of $HSbF_6$



Legend for Graphs 5 and 6

Signals of the two bases denoted thus:

3,5-dichlorotrifluoropyridine, (4) — · — · —, (2,6) ·····

tetrafluoropyridazine, (3,6) ———— (4,5) - - - -

Letters denote positions of resonances for pure protonated and non-protonated forms of the bases:

3,5-dichlorotrifluoropyridine, protonated; (4), A; (2,6), B

non-protonated; (4), C; (2,6), D

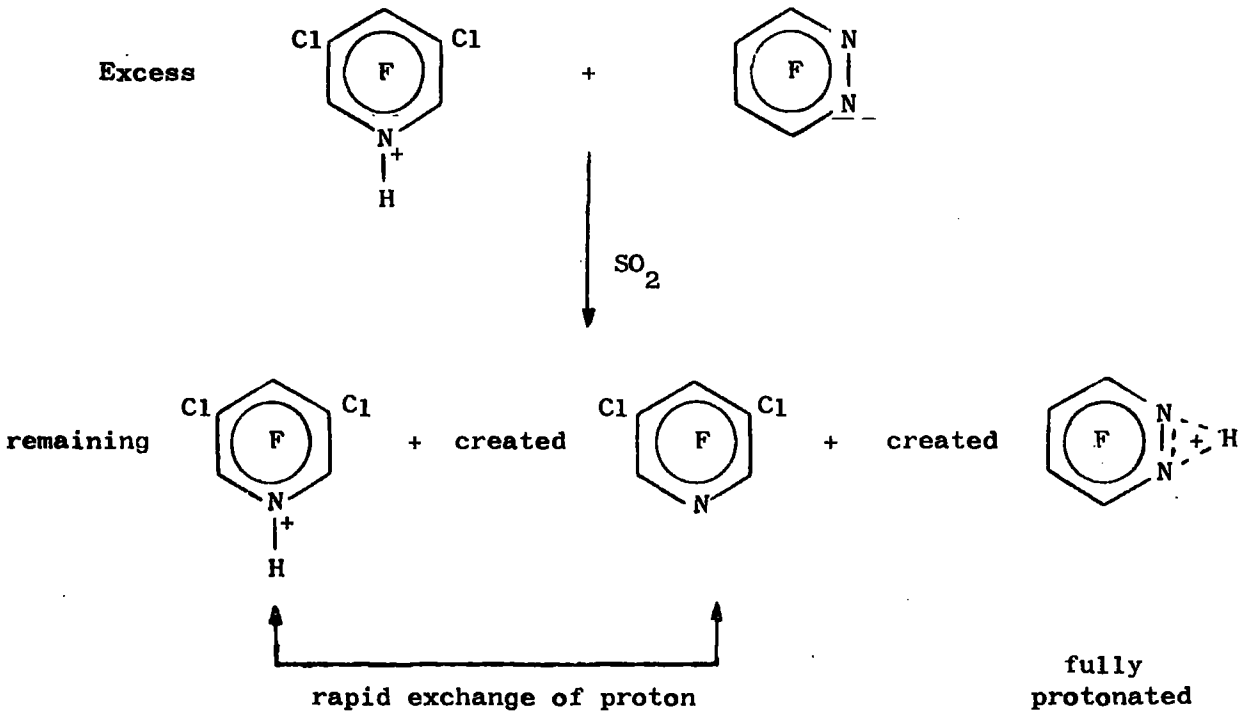
tetrafluoropyridazine, protonated; (3,6), E; (4,5), F

non-protonated; (3,6), G; (4,5), H.

Assignments in parenthesis, shifts relative to $CFCl_3$ in a capillary tube.

been added. The mixture is thus an equimolar mixture of protonated tetrafluoropyridazine and non-protonated 3,5-dichlorotrifluoropyridine. The addition of further tetrafluoropyridazine only shifts the tetrafluoropyridazine spectrum to a position intermediate between the protonated and non-protonated spectra.

The peak shifts are readily understood by reference to Equation 3.



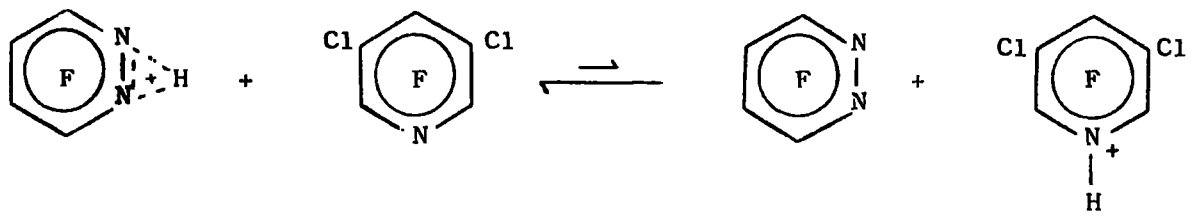
Equation 3

The equilibrium constant for the reaction (Equation 4) is large and so tetrafluoropyridazine is a substantially stronger base than 3,5-dichlorotrifluoropyridine.

Equation 4

When the equivalence point is reached nearly all the acid has been transferred to the tetrafluoropyridazine and so the additional free tetrafluoropyridazine exchanges with the created tetrafluoropyridazine salt to giveaspectrum intermediate between salt and base forms.

A reverse experiment of adding 3,5-dichlorotrifluoropyridine to a solution of tetrafluoropyridazinium hexafluoroantimonate showed no appreciable shift of the salt peaks and the pyridine spectrum appeared in the positions expected for the free base, changing little with increasing additions of 3,5-dichlorotrifluoropyridine.



From the above results it is apparent that in a mixture of 3,5-dichlorotrifluoropyridine and tetrafluoropyridazine with a deficiency of acid almost all of the acid resides on the tetrafluoropyridazine and very little on 3,5-dichlorotrifluoropyridine so proving the former to be the stronger base.

4. Other pairs of bases

Similar reactions between salts of pentafluoropyridine, 3,5-dichlorotrifluoropyridine, and perfluoroquinoline in sulphur dioxide with added perfluoropyridazine, -quinoline, and -pyridazine respectively proved that in each case the added base was the stronger:

i.e. base strengths

perfluoropyridazine > 3,5-dichlorotrifluoropyridine
> perfluoropyridine
> perfluoroquinoline

perfluoroquinoline > 3,5-dichlorotrifluoropyridine

A reaction between the hexafluoroantimonate salt of pentafluoropyridine and 3,5-dichlorotrifluoropyridine showed that protonated and non-protonated forms of both bases co-existed in comparable amounts in the one solution, i.e. they are of similar basicity.

Closer examination of the ratios of protonated to non-protonated forms showed that in each case 3,5-dichlorotrifluoropyridine was apparently the more protonated (see below, Section E).

5. Alternative method for the comparison of base strengths

Because of the problems of preparation and handling of the very moisture sensitive salts and the occasional precipitation from strong solutions of salt and base, particularly with the higher molecular weight solid bases, an alternative technique was developed which obviated the repeated use of the glove box and eliminated the problems of adding solid base to a solution of a salt in SO_2. The method is described more fully in Chapter 7 but was, in outline, to add a deficiency of acid to an approximately equimolar mixture of the two bases under study in sulphur dioxide. From the peak shapes and positions before and after the additions of acid and a knowledge of the effects on the n.m.r. spectrum of the protonation of the two bases it was possible to assign the peaks and identify the (more) protonated base.

The method gave essentially the same final result as previously when using 3,5-dichlorotrifluoropyridine/tetrafluoropyridazine mixtures. On addition of acid to such a mixture the n.m.r. spectrum of 3,5-dichlorotrifluoropyridine appeared unaltered but the spectrum of the tetrafluoropyridazine moved towards that of the tetrafluoropyridazinium hexafluoroantimonate. Further additions of acid increased that shift until the peak positions were almost coincident with those expected for the salt. The addition of more acid at this point (X) then caused a shift in the peak positions of the 3,5-dichlorotrifluoropyridine towards those of its hexafluoroantimonate salt. The shifts

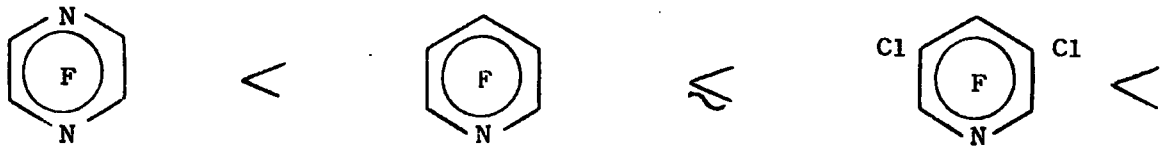
are outlined diagrammatically in Graph 6.

The following pairs of bases were studied and the first named found to be the stronger:

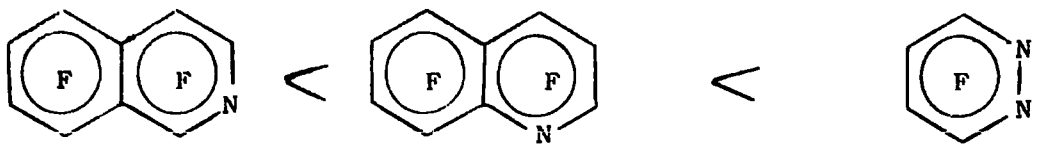
tetrafluoropyridazine	> 3,5-dichlorotrifluoropyridine
	> heptafluoroquinoline
	> heptafluoroisoquinoline
heptafluoroquinoline	> tetrafluoropyrazine
	> heptafluoroisoquinoline
heptafluoroisoquinoline	> 3,5-dichlorotrifluoropyridine
	> pentafluoropyridine
pentafluoropyridine	> tetrafluoropyrazine
3,5-dichlorotrifluoropyridine	> tetrafluoropyrazine

6. Overall order of basicity

The measurements of the relative basicity of the compounds led to a consistent order of base strength given below.



tetrafluoropyrazine pentafluoropyridine 3,5-dichlorotrifluoropyridine



heptafluoroisoquinoline heptafluoroquinoline tetrafluoropyridazine

E. Attempted extension to quantitative ratios of the basicity

Because of the success of the qualitative comparison of the base strengths of the series of polyfluorinated heterocyclic compounds, attempts were made to give quantitative estimates of the ratios of the base strengths.

The equilibrium in the n.m.r. tube can be considered, for two bases, A and B, by three linked equations.

$$AH^+ \overset{K_1}{\rightleftharpoons} A + H^+$$

$$BH^+ \overset{K_2}{\rightleftharpoons} B + H^+$$

$$AH^+ + B \overset{K_3}{\rightleftharpoons} A + BH^+$$

Now k_1 is a measure of the basicity of A and likewise k_2 of B:

$$K_1 = \frac{a_A \cdot a_{H^+}}{a_{AH^+}}$$

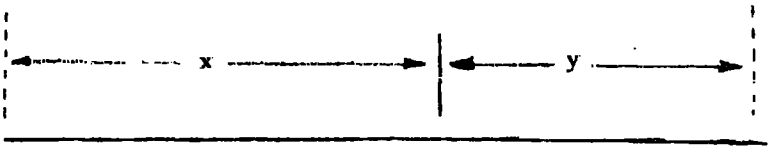
$$K_2 = \frac{a_B \cdot a_{H^+}}{a_{BH^+}}$$

$$K_3 = \frac{a_A \cdot a_{BH^+}}{a_{AH^+} \cdot a_B} = \frac{K_1}{K_2}$$

Now because the chemical shift of a particular peak in the n.m.r. spectrum of AH^+ is significantly different from that of A and the proton is in rapid exchange then

$$Q = \frac{[\text{protonated base}]}{[\text{non-protonated base}]} = \frac{y_a}{x_a} \text{ for A and } \frac{y_b}{x_b} \text{ for B.}$$

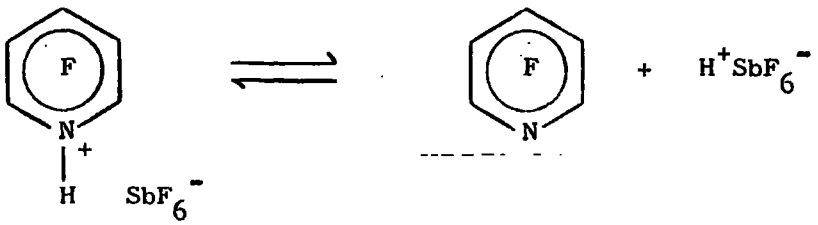
84



position of peak of protonated form — intermediate peak in a mixture — position of peak of non-protonated form

Therefore $k_3 = \frac{x_a}{y_a} \times \frac{y_b}{x_b} \simeq \frac{k_1}{k_2}$ Equation 5

The positions of the n.m.r. peaks of the pure base in SO_2 could readily be measured accurately but the peaks of the salt in SO_2 may well not be those of the undissociated salt.



The n.m.r. peak positions of the undissociated salt were estimated by suppression of the ionisation by the addition of further amounts of $HSbF_6$ to a solution of the salt in SO_2 until no appreciable further shift of the n.m.r. peaks occurred. The shifts were generally small and are given in Table 9.

TABLE 9

Estimated n.m.r. peak positions for some of the undissociated salts of polyfluoroheterocyclic compounds

	Base	Salt	'Undissociated' salt
Heptafluoroisoquinoline (1)	63·5	69·1	69·8
Pentafluoropyridine (4)	135·0	107·1	106·3
3,5-dichlorotrifluoropyridine (4)	96·8	68·1	66·3
Tetrafluoropyrazine	95·9	90·9	80·9 *

Assignment in parenthesis; solvent SO_2, $-30^{\circ}C$

* See Chapter 3, section E.3.

1. Values of some ratios

Equation 5 given above enables the ratio of the base strength of two compounds to be calculated from the positions of the peaks in the ^{19}F n.m.r. spectrum. Substitution into this equation of values of x_a and y_a from an assigned peak in the spectrum of one of the bases and x_b and y_b of an assigned peak in the spectrum of the other base enables the ratio of base strengths, k_3, to be calculated.

Analysis of the shift positions known from the spectra of all the previous pairs of bases studied enabled the ratios of the base strengths of all of the bases to be calculated. Only one pair of bases gave a consistent ratio throughout, that of 3,5-dichlorotrifluoropyridine to pentafluoropyridine being $8{\cdot}8\pm1{\cdot}0$:1 corresponding to a pK_a difference of about 0·95.

The ratios of the basicities of the other pairs of bases were larger and much less accurate but very approximately the ratios were:

3,5-dichlorotrifluoropyridine:heptafluoroisoquinoline, 20 to 40 : 1

$\Delta\ pK_a$ 1·2 to 1·6

pentafluoropyridine:tetrafluoropyrazine

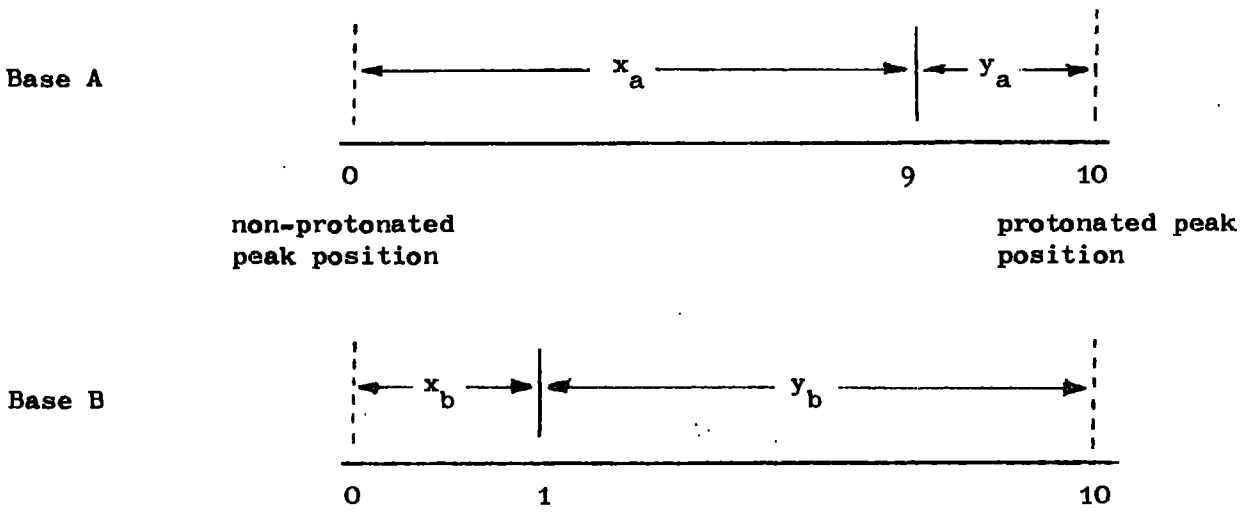
and heptafluoroquinoline:heptafluoroisoquinoline were both of the order of 100 : 1 corresponding to a pK_a difference of $\sim$2.

2. Inaccuracies

The large variations in the values of the ratios of the basicities of the compounds can be explained by the uncertainties in the values obtained for the ratio of protonated to non-protonated forms of a base outside the range 20 to 80% protonation. Outside this range the ratio is critically dependant on the actual value of the shift of a particular assigned fluorine. If the base is nearly fully protonated then the difference in shift between the fully protonated form and that in the mixture will be small and this will

dominate the calculation of the ratio. Likewise, if the base is almost non-protonated the difference between the shift of the free base and that of the peak in the mixture will be small and in this case this term will dominate the calculation of the ratio.

As a fictitious example consider two bases with nominal ratio of basicity of 80:1, where the ^{19}F n.m.r. shifts between the protonated and non-protonated forms of the two bases are 10 p.p.m. Consider the ^{19}F n.m.r. peaks in the partially protonated mixture to be 9 p.p.m. from the non-protonated peak for one base and 1 p.p.m. for the other as below:



Now the ratio of basicities as given by Equation 5 is

$$\frac{x_a}{y_a} \cdot \frac{y_b}{x_b} = \frac{9}{1} \times \frac{9}{1} = 81$$

Consider now if the intermediate peak of A is just 0·1 p.p.m. nearer the fully protonated position and the corresponding peak of B is 0·1 p.p.m. nearer the non-protonated position.

Now the ratio is $\frac{9{\cdot}1}{0{\cdot}9} \times \frac{9{\cdot}1}{0{\cdot}9} = 102$

If the movement in each case is in the opposite direction the ratio is

$$\frac{8.9}{1.1} \times \frac{8.9}{1.1} = 65$$

Thus an error or variation in the positions of both intermediate peaks of just 1% of the separation of protonated and non-protonated peaks gives a variation in the final ratio of 20 to 25%.

Because of unknown solvent effects all peaks are liable to small variations from their expected positions, indeed the values of the n.m.r. shifts of the pure protonated and non-protonated bases are not known in the particular medium of the ratio measurement and this small variation will cause large variations in the final calculation of the ratio of the base strengths when one or both of the bases are not between 20 and 80% protonated. Variations in the internal shift positions of the pure protonated and pure non-protonated forms of a based with small changes in solvent have previously been found for acetophenone.[85]

Consider an equimolar mixture of two bases with one equivalent of strong acid. Table 10 gives the proportions of each of the bases protonated for various differences in pK_a values.

TABLE 10

ΔpK_a	Ratio of basicities	% protonated 1st base	% protonated 2nd base
0	1:1	50	50
0.6	4:1	67	33
1.0	10:1	76	24
2.0	100:1	91	9
3.0	1000:1	97	3

From the Table it can be seen that to keep within the requirement of about 20 to 80% protonation for both bases they must have a pK_a difference of less than 2.

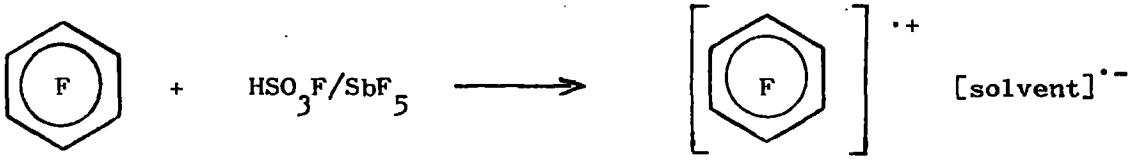
3. Tetrafluoropyrazine anomaly

Of the bases studied in sulphur dioxide, all but tetrafluoropyrazine on the progressive additions of acid (either $HSbF_6$ or HSO_3F/SbF_5) gave sharp n.m.r. spectra which shifted from the positions in the free base towards, and in some cases beyond, the position of the peaks in the salt to a position formulated as the n.m.r. spectrum of the undissociated salt, with little change thereafter.

Tetrafluoropyrazine likewise shifted beyond the position as found for the salt in sulphur dioxide to a position assigned to the undissociated salt but then, on further addition of acid the signal vanished to reappear as a sharp signal only on further addition of free base.

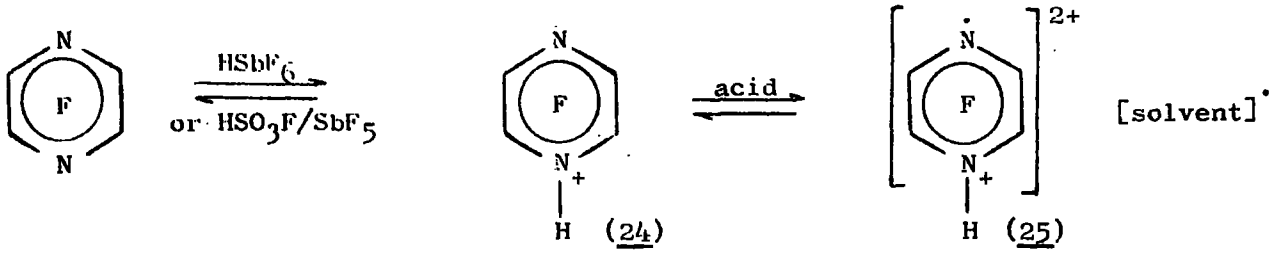
No n.m.r. spectrum attributable to any tetrafluoropyrazine species could be seen on examination of a solution of tetrafluoropyrazine in fluorosulphuric acid-antimony pentafluoride mixtures.

As previously mentioned hexafluorobenzene does not dissolve in concentrated sulphuric acid but does dissolve in the stronger acid, HSO_3F/SbF_5, not protonating but forming the radical cation (23).[77]



(23)

A similar reaction may well be taking place with the very weakly basic monoprotonated tetrafluoropyrazine (24).



(24) (25)

The production of the radical di-cation (25) will destroy the n.m.r. signal but addition of further base will reverse the equilibria so reforming the n.m.r. signal of the mono-cation (24).

Crude attempts to observe the e.s.r. signal failed but more expert opinion[86] suggested that more refined attempts may well not have given a simple conclusive result.

F. Factors affecting the base strength of the polyfluorinated aza-aromatic compounds

One of the more noticeable features of the physical properties of the perfluorinated aza-aromatic compounds compared with the hydrocarbon series (Table 11) is that, despite the considerable increase in molecular weight, a decrease in boiling point occurs showing a decrease in the cohesive forces of the molecules because of the large reduction in basicity.

TABLE 11

Boiling points and molecular weights of perfluoroaromatic compounds in comparison with the hydrocarbon analogues [1,3,36,87]

Compound	Hydrocarbon		Fluorocarbon		$B.pt._F - B.pt._H$
	B.pt. °C	M.wt.	B.pt. °C	M.wt.	°C
Benzene	80·1	78	80·2	186	+0·1
Toluene	106	92	102-3	236	-3
p.Xylene	138	106	117-8	286	-20
Pyridine	115·5	79	83·3	169	-32
Quinoline	237·1	129	205	255	-32
Isoquinoline	243·2	129	212	255	-31
1,2-diazine	208	80	117	152	-90
1,3-diazine	123·5	80	89	152	-34

1. Inductive effect of fluorine

The most significant factor determining the base strength of the polyfluorinated compounds appears to be the number and proximity of the fluorine atoms to the nitrogen. As clearly shown (Chapter 2.C.4) for the polychloro-aza-cyclic compounds the influence of a particular halogen in the heterocyclic ring is to decrease the basicity, the depression of basicity being ortho $\gg$ meta $\gg$ para to the aza centre. The same effect is evident in the fluorocarbon series. Table 12 gives the number of effective ortho, meta and para fluorines of the series of aza-aromatics, considering the protonation of the diazines to be purely on one nitrogen.

TABLE 12

Number of fluorines ortho, meta and para to the protonated nitrogen for a series of polyfluoro-aza-aromatic compounds

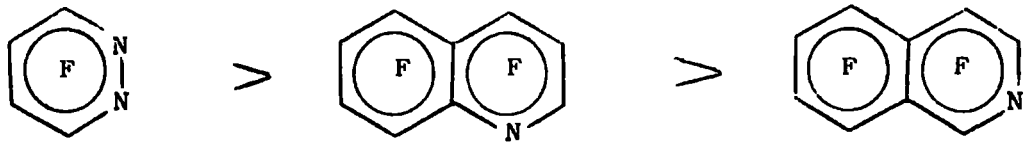
	ortho	meta	para
Tetrafluoropyridazine *	1	2	1
Heptafluoroquinoline	1	2†	1
Heptafluoroisoquinoline	2	1	
Pentafluoropyridine	2	2	1
Tetrafluoropyrazine *	2	2	

* Considering one nitrogen only to be protonated

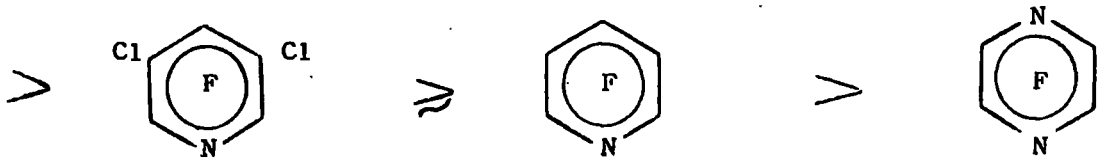
† Considering the 3 and 8 positions equivalent [74]

Ignoring the differences in basicity of the hydrocarbon series (Chapter 2.C.3.a) the order of basicity, repeated below, can be rationalised in terms of the number and proximity of the fluorine atoms to the nitrogen.

Order of base strength



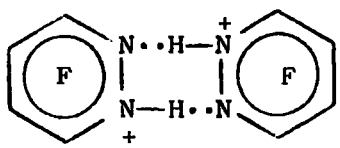
perfluoro -pyridazine -quinoline -isoquinoline



3,5-dichlorotrifluoropyridine perfluoro-pyridine -pyrazine

From Table 12 it would be expected that perfluoro-pyridazine and -quinoline would be substantially stronger bases than the others, each having only one ortho fluorine, perfluoroisoquinoline would be next having two ortho fluorines but only one meta fluorine and perfluoro-pyridine and -pyrazine would be the weakest.

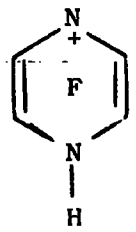
Thus it can be seen that the observed order of basicity is explicable on the basis of the reduction of basicity caused by the fluorine atoms in the various positions. The cumulative small basicity reductions caused by the fluorines in the carbocyclic ring could explain the lower basicity of perfluoro-quinoline with respect to perfluoropyridazine. Alternatively or additionally stabilisation of the protonated pyridazine by structures such as (26), as invoked for the hydrocarbon series[70] could account for its increased basicity



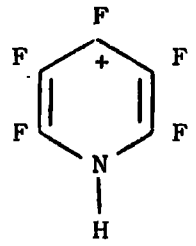
(26)

Reference to work by Brown and McDaniel[70] shows that meta chlorines decrease the basicity less than meta fluorine atoms and so it is understandable that 3,5-dichlorotrifluoropyridine is a stronger base than pentafluoropyridine.

The weakness of tetrafluoropyrazine compared with pentafluoropyridine can be explained by the reluctance of the para nitrogen (27), compared with a para fluorine (28), to accept the positive charge; the argument used to explain the basicity order in the hydrocarbon series.[71]



(27)



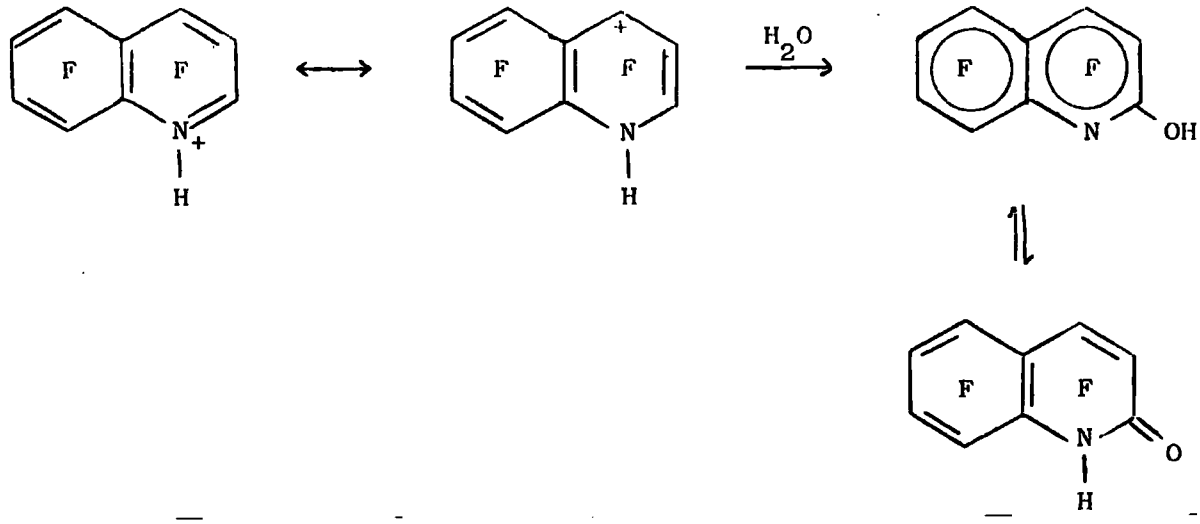
(28)

G. Comparison of relative basicity and susceptibility towards acid induced reactions

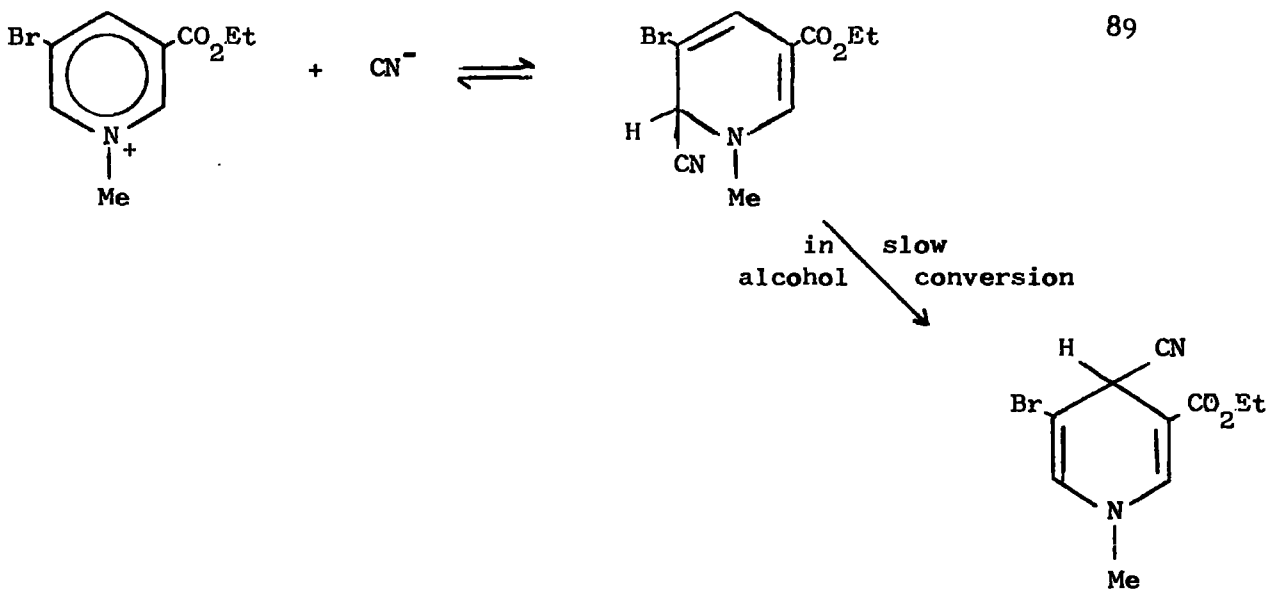
The order of susceptibility of these polyfluoroheterocyclic compounds towards acid induced reactions (Chapter 1.C.2.g.) correlates well with the relative order of base strength found. This underlines that the acid induced reactions do occur on the protonated species and are not merely caused by acid assistance in the removal of fluoride ion.

H. Comparison of n.m.r. internal shifts on protonation and position of acid induced attack

From the n.m.r. internal shifts on protonation it was concluded that the positive charge was probably largely localised on the para fluorine where possible. Acid induced attack by various nucleophiles on heptafluoroquinoline in particular have shown that exclusively ortho mono-substitution takes place.[3]



Quite clearly the ground state electronic distribution as deduced from the ^{19}F n.m.r. spectrum gives no indication of the positions of maximum reactivity unless product formation is thermodynamically controlled. There is no evidence of thermodynamic rearrangements of derivatives of either perfluoropyridazine[5] or perfluoroquinoline from this type of reaction although there are other examples of rearrangement when the addition step is reversible.[89,90]



89

I. Estimates of absolute values of basicity

Table 13 gives a list of the peak positions of the series of perfluorinated heterocycles in various highly acidic solvents with the values for the n.m.r. peaks of the salts and free bases repeated for comparison.

From Equation 1 (Chapter 2.A.1), the basicity of a particular base and the acidity of the solvent are related by

$$H_o = pK_a + \log Q \qquad Q = \frac{[\text{protonated form}]}{[\text{non-protonated form}]}$$

Now if the following approximations are made:

- that the n.m.r. peak shifts for the non-protonated base are those of the neat base (or in acetone),

- that the n.m.r. peak shifts of the protonated form are those of the base dissolved in the strongest acid, HSO_3F/SbF_5,

then an estimate of Q can be calculated.

These approximations are crude in that they do not allow for solvent effects other than caused by protonation, a poor approximation as can be seen by noting the non-parallel behaviour of the 2- as compared with the 4- and 5-positions of perfluoroquinoline in the various solvents (Table 13). The anomalous shifts of the 2-fluorine may be caused by some specific interaction either with the solvent generally or possibly the counter ion, SbF_6^-, an effect previously noted for pyridinium ions.[91]

It can readily be seen from Table 13 that tetrafluoropyridazine and heptafluoroquinoline are essentially fully protonated in all three solvents, whereas pentafluoropyridine, tetrafluoropyrazine and tetrafluoropyrimidine are only partially protonated in sulphuric and fluorosulphuric acids.

The logarithm of the ratios of the protonated to non-protonated forms (logQ) as calculated from the n.m.r. shifts are given in Table 14.

TABLE 13

^{19}F n.m.r. peak positions for some perfluoroheterocyclic compounds in various acidic solvents

Tetrafluoropyrazine

	(2,3,5,6)	δ =
Base in SO_2	95·9	
Salt in SO_2	90·9	-5·0
H_2SO_4	93·7	-2·2
HSO_3F	92·6	-3·3
HSO_3F/SbF_5	no peak	

Pentafluoropyridine

	(2,6)	δ =	(4)	δ =	(3,5)	δ =
Base in SO_2	89·5		135·0		163·5	
Salt in SO_2	97·8	+8·3	107·1	-28·9	156·4	-7·1
H_2SO_4	91·8	+2·3	126·0	-9·0	160·0	-3·5
HSO_3F	97·4	+7·9	109·4	-25·6	156·7	-6·8
HSO_3F/SbF_5	96·4	+6·9	102·8	-32·2	154·5	-9·0

Heptafluoroquinoline

	(2)	δ =	(4)	δ =		(5)	δ =				
Base in SO_2	75·0		126·5			148·5		151·0	154·2	157·5	163·7
Salt in SO_2	78·1	+3·1	95·2	-31·3	131·8	140·0	-8·5	147·7	150·7	159·4	
H_2SO_4	86·1	+11·1	92·1	-34·4	134·1	136·3	-12·2	144·9	146·5	156·0	
HSO_3F	85·3	+10·3	91·5	-35·0	134·1	136·0	-12·5	143·8	146·2	156·0	
HSO_3F/SbF_5	77·3	+2·3	90·5	-36·0	135·0	137·7	-10·8	145·5	151·2	158·2	

Tetrafluoropyrimidine

	(2)	δ =	(4,6)	δ =	(5)	δ =
Base in SO_2	47·6		73·0		173·3	
H_2SO_4	46·1	-1·5	67·9	-5·1	168·7	-4·6
HSO_3F	46·4	-1·2	63·1	-9·9	166·6	-6·7
HSO_3F/SbF_5	45·1	-2·5	58·6	-14·4	161·3	-12·0

Tetrafluoropyridazine

	(3,6)	δ =	(4,5)	δ =
Base in SO_2	90·7		144·6	
Salt in SO_2	80·1	-10·6	121·2	-23·4
H_2SO_4	80·2	-10·5	121·4	-23·2
HSO_3F	81·0	-9·7	123·0	-21·6
HSO_3F/SbF_5	80·3	-10·4	122·0	-22·6

Shifts in p.p.m. relative to $CFCl_3$ in a capillary tube, assignments in parenthesis, δ = difference between chemical shift recorded and that of the free base

TABLE 14

Values of logQ for various bases in H_2SO_4 and HSO_3F

	perfluoro-pyrazine	perfluoro-pyrimidine	perfluoro-pyridine	perfluoro-quinoline
H_2SO_4	-0·3 (0·5)	-0·1 (0·8)	-0·4 (0·4)	1·3 (21)
HSO_3F	0·1 (1·2)	0·3 (2·1)	0·6 (3·8)	1·5 (35)

Values of Q in parenthesis

Assuming that the values do not change appreciably on extrapolation to infinite dilution and that the H_o values for sulphuric and fluorosulphuric acids are -11·0 [58] and -12·8 [58] or -14·5 [62] then perfluoro-pyrazine, -pyridine and -pyrimidine all have basicity values (i.e. H_o at half protonation) between these values with perfluoropyrazine the weakest (most negative). Heptafluoro-quinoline will have a value around -10 and perfluoropyridazine substantially more (less negative) than this.

Considering the crudeness of the method, the value for pentafluoropyridine compares surprisingly well with an estimate calculated from values of the depression of basicity caused by halogen substitution[72] assuming the effects of substitution to be cumulative,[97] i.e. ortho substitution of hydrogen for fluorine, depression of 5·6 units of pK_a/fluorine, meta depression 2·2 units and para depression estimated at 0·5 units.

Total depression of basicity for pentafluoropyridine

= 2 ortho + 2 meta + 1 para

= 16·1 units of pK_a.

The pK_a of the hydrocarbon is +5·2 [69] giving the basicity of pentafluoropyridine to be -10·9.

It is noteworthy that the depression of basicity caused by one ortho fluorine is larger than the range of basicities of the parent hydrocarbon series so allowing the neglect of differences in basicity of the parent molecules in Section F.1.

CHAPTER 4

Some Aspects of the Chemistry of Heptafluoroquinoline

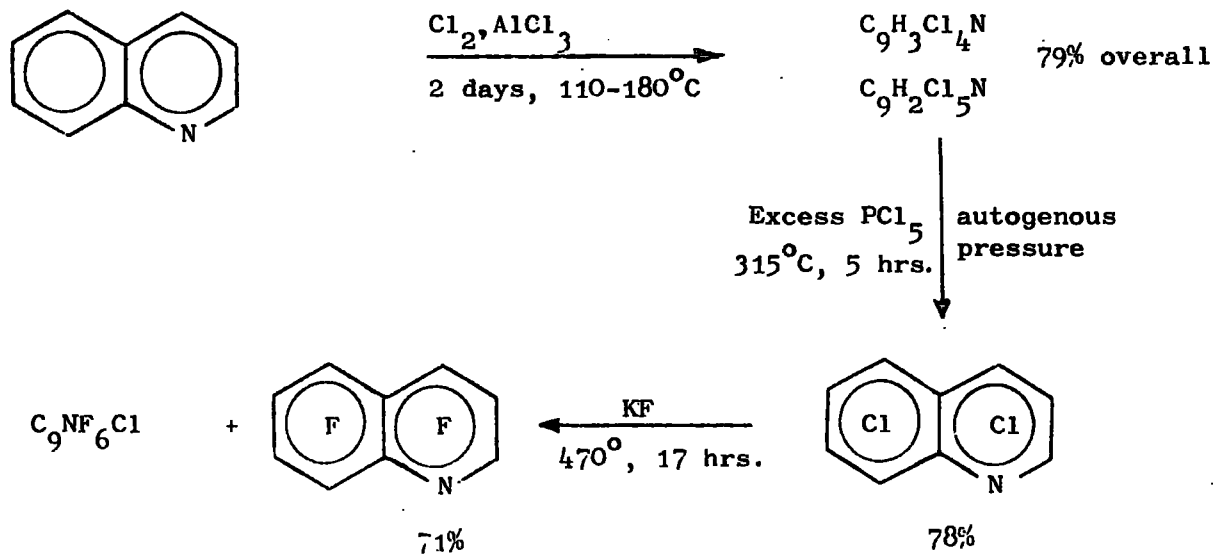
Introduction

A satisfactory preparative route to heptafluoroquinoline is available and preliminary work on nucleophilic substitution has previously been completed. The introduction outlines this work and other closely related background work.

A. Previous work

1. Preparation

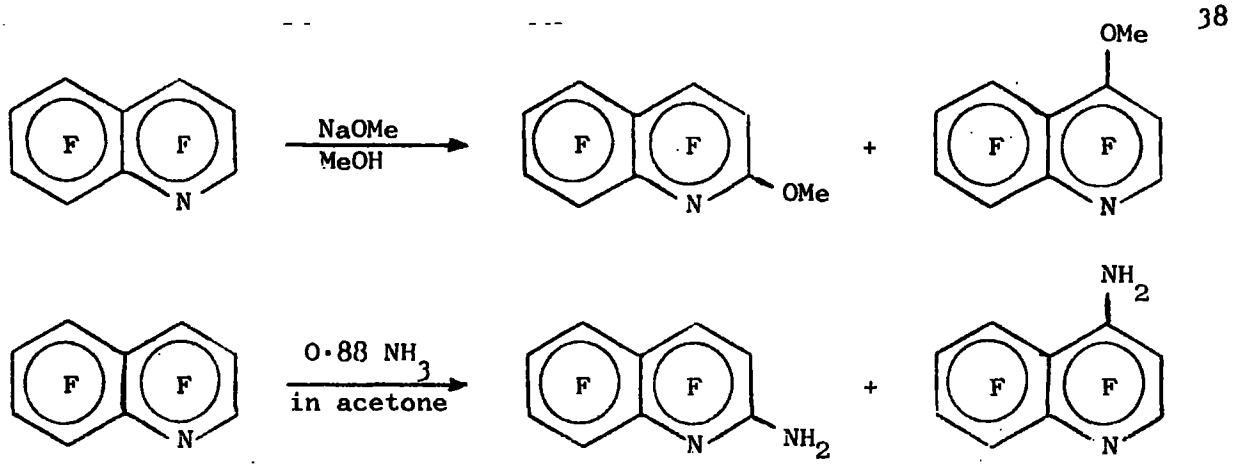
As described in Chapter 1, heptafluoroquinoline is readily prepared in good yield from quinoline itself by a two step chlorination procedure followed by halogen exchange of heptachloroquinoline with potassium fluoride without solvent in an autoclave.[3]



The heptachloroquinoline is obtained pure by distillation at atmospheric pressure (b.pt. 205°C).

2. Nucleophilic substitution [38]

Heptafluoroquinoline is susceptible to nucleophilic aromatic substitution under mild conditions, the fluorine atoms ortho and para to the nitrogen being particularly reactive. Sodium methoxide in methanol readily displaces these fluorine atoms to give a mixture of monosubstituted products with some di-substituted pentafluoroquinoline.[38] Ammonia in acetone likewise displaces the 2- or 4-fluorine atoms rapidly at room temperature to give a mixture of monosubstituted products.[38]



Recent kinetic work has shown that heptafluoroquinoline is more reactive to nucleophilic substitution in that it reacts with sodium methoxide at a substantially faster rate than does pentafluoropyridine under the same conditions.[97]

3. Comparison with nucleophilic substitution in hydrocarbon heterocycles

Comparison of the nucleophilic substitution of heptafluoroquinoline and nucleophilic displacement of halogen from mono- and di-halogenated quinolines show strong similarities.

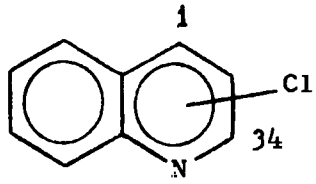
Figure 4 gives some of the relative rates of substitution in some of the halogenated pyridines and quinolines for piperidino-dehalogenation and methoxy-dehalogenation.[93]

Kinetic studies have shown that in general the rates of reactions with neutral molecules are strongly dependant on solvent polarity particularly

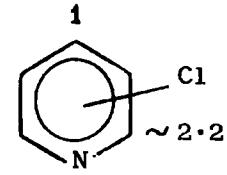
FIGURE 4

Relative rates of halogen displacement for some halopyridines and quinolines [93]

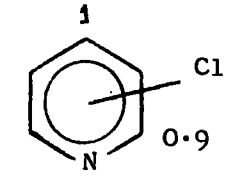
1. Neutral nucleophiles - piperidine



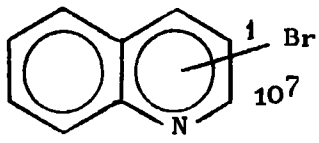
in piperidine 86·5°C



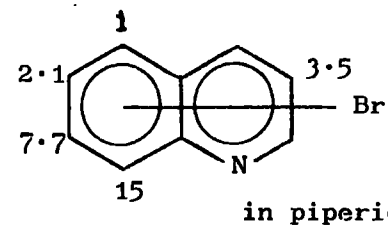
in piperidine 122-125°C



in alcohol 75·2°C

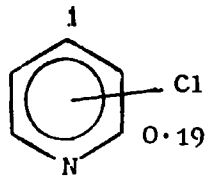


in piperidine 72·5°C

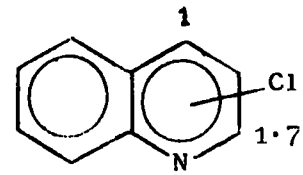


in piperidine 200°C

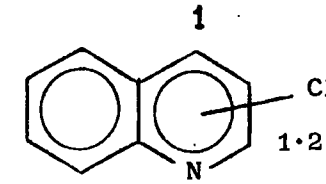
2. Charged nucleophiles



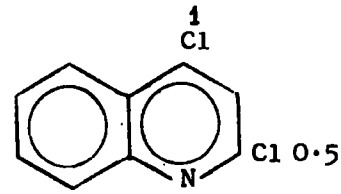
EtO^- 90°C



EtO^- 70°C

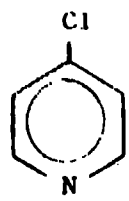


MeO^- 70°C



MeO^- 75·2°C

3. Annelation effects (EtO^-, 20°C)



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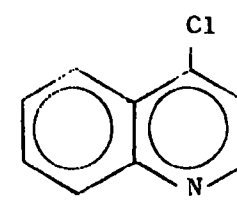
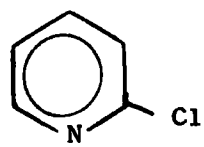


7·5



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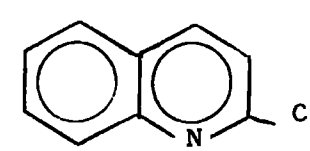


290

substitution of the position para to the activating aza group.[93] Some values for the piperidino-dechlorination of 2- and 4-chloroquinolines in various solvents are given below (Table 15).

TABLE 15

Rates of piperidino-dechlorination of chloroquinolines [94]

Solvent	2-Cl *	4-Cl *
Toluene	0·04	too small
Piperidine	0·31	0·009
Methanol	0·26	0·29

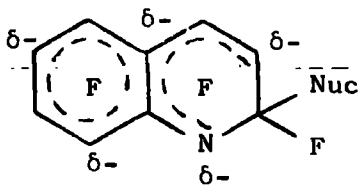
* 10^4K l.mole^{-1} sec.$^{-1}$ at 86·5°C

The rate of displacement of halogen from monohaloquinoline is about seven orders of magnitude faster from the 2- and 4-positions than from any of the remaining positions.[93] This correlates well with displacement of fluorine from heptafluoroquinoline which takes place readily from the 2- and 4-positions at room temperature, further displacement taking place only from the carbocyclic ring at reflux temperatures.

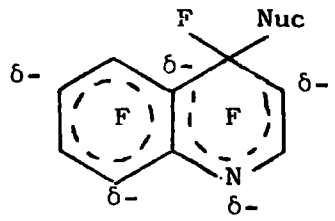
The effect of annelation of a benzene ring to a chloropyridine to form the corresponding chloro quinoline causes a rate enhancement particularly at the 2-position. This rate enhancement is ascribed to the greater delocalisation available for the negative charge in the Wheland intermediate.[95] Corresponding rate enhancement, of about the same order of magnitude for the 4-position, is noticeable in competition reactions between heptafluoroquinoline and pentafluoropyridine.[38]

4. Orientation of substitution

The identification of the two monomethoxylated substitution products of heptafluoroquinoline as the 2- and 4-substituted isomers and the subsequent methoxylation to form solely the 2,4-disubstituted pentafluoroquinoline[38] is entirely as expected with the control of substitution being by the aza group, the Wheland intermediates where the negative charge can be delocalised onto the nitrogen being the more stable.

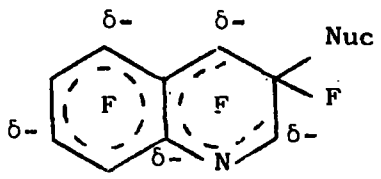


2-substitution

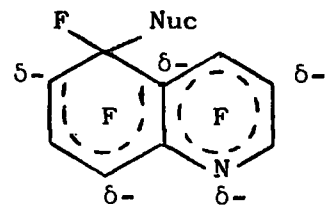


4-substitution

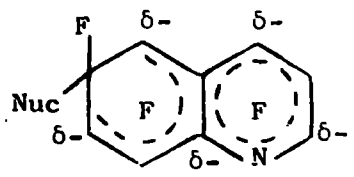
Of the remaining possible isomers of substitution only substitution at the 5- and 7-positions can be stabilised by delocalisation of the charge of the Wheland intermediate onto the aza nitrogen.



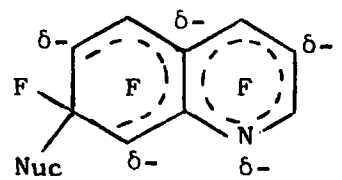
3-substitution



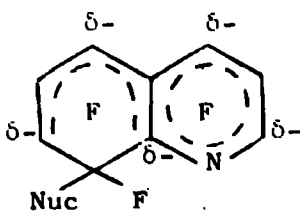
5-substitution



6-substitution



7-substitution



8-substitution

No stabilisation of the intermediates of substitution at the 3-, 6- and 8-positions is possible by delocalisation of the charge onto the nitrogen.

Thus, assuming control is purely by the nitrogen, the ease of substitution at the various positions will be, 2,4 > 5,7 > 3,6,8. If a group is substituted into the ring that is able to stabilise the negative charge on an adjacent carbon then it will exert an influence on the stabilisation of the various intermediates. If it is in the 3-, 6- or 8-positions it will assist the nitrogen in the stabilisation of the negative charge and so may enhance the reactivity of the 2-, 4-, 5- and 7-positions. If the group is in the 2-, 4-, 5- or 7-positions it will activate the 3-, 6- and 8-positions and, if stabilisation of the charge is sufficiently large, may direct substitution into the 3-, 6- or 8-positions.

A perfluoroalkyl group is able to stabilise an adjacent carbanionic centre by its powerful electron withdrawing effect and as will be discussed later two perfluoroalkyl groups in the 2- and 4-positions are able to control further substitution into the 6- and 3-positions overriding the effect of the nitrogen.

5. Structure determination

The structure determination of the various possible isomers of perfluoroquinoline derivatives by chemical techniques has not been very successful[96] and the proof of structure has largely been from interpretation of the ^{19}F n.m.r. spectra. Heptafluoroquinoline has seven non-equivalent fluorine atoms with strong coupling between some of the nucleii leading to a complex spectrum which has only now been fully analysed. Before this work commenced the 2-fluorine had been identified from its resonance in a strongly deshielded position, the 4-fluorine from comparison with pentafluoropyridine and the 5-fluorine from the strong peri coupling with the 4-fluorine.[38]

From the results of the full analyses of the ^{19}F n.m.r. spectra of some of the substituted polyfluoroquinolines (discussed later) it has now been possible

to complete a full analysis of the ^{19}F n.m.r. spectrum of heptafluoroquinoline, (analysis completed by Dr. R.S. Matthews).

B. Nucleophilic displacement of fluorine

1. Monosubstitution

Attack on heptafluoroquinoline by nucleophilic reagents readily gives rise to monosubstitution products with varying proportions of the 2- and 4-isomers. The proportions of the monosubstituted products formed, as determined from integration of the n.m.r. spectrum of the crude mixtures of products, are given in Table 16.

TABLE 16

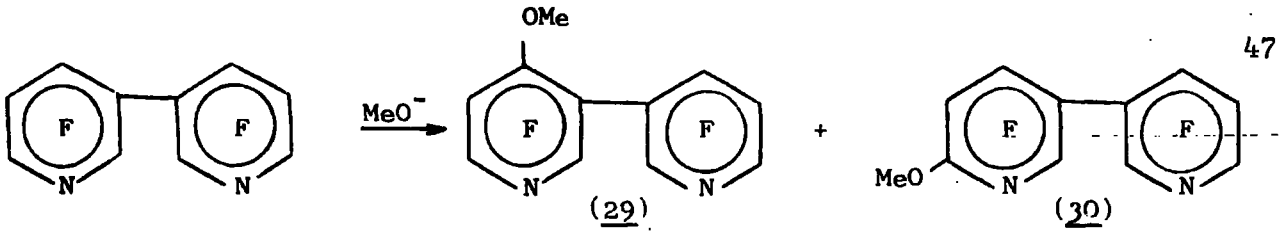
Relative proportions of 2- and 4-substituted hexafluoroquinolines

Nucleophile/Solvent	Dielectric constant	2-isomer	4-isomer
NAOMe/MeOH [38]	32·6	75	25
NaOMe/^{t}BuOH	10·9	> 95	
NH_3/acetone [38]	20·7	50	50
NH_3/diethyl ether	4·3	60	40
$NHEt_2$/acetone	20·7	> 95	
BuLi/hexane	1·9	> 95	
BuLi/ether	4·3	90	10

From the variations it is apparent that the solvent is important in determining the ratios of the two monosubstituted products formed.

It has previously been noted that attack by sodium methoxide on perfluoro-(3,3'-bipyridyl) was particularly solvent dependant.[47] Attack by sodium

methoxide in methanol gives the 4-substituted product (29) whereas in tert-butanol largely the 6-substituted product (30) is formed. Similar steric effects are noted on the formation of dimethoxylated products from substitution of 4-methoxyheptafluoro-3,3'-bipyridyl with methoxide ion in methanol leading to an equimolar mixture of the 4,4'- (31) and the 4,6'- (32) products whereas in tert-butanol only the 4,6'-product is formed.



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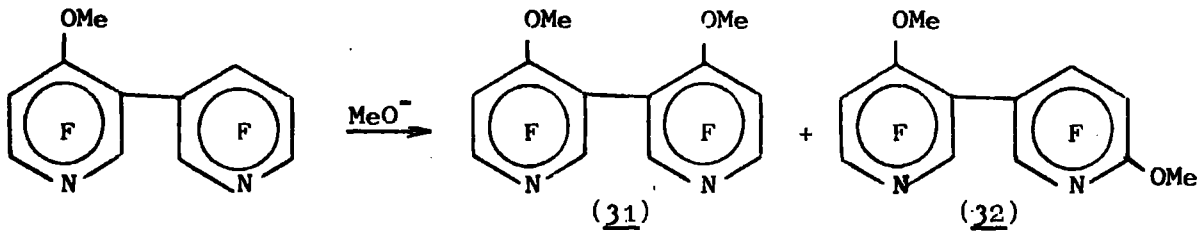
Solvent MeOH	95%	
Solvent ^{t}BuOH	20%	80%

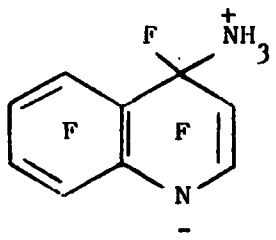


Solvent MeOH	50%	50%
Solvent ^{t}BuOH		95%

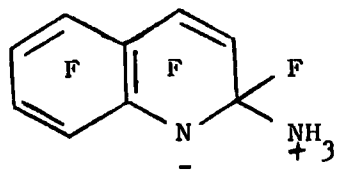
The explanation advanced was that the more bulky tertiary butanol solvates the methoxide ion giving a larger attacking nucleophile than when solvated by methanol. In the case of attack on the perfluoroquinoline system the 4-position is subject to steric hindrance caused by the 5-peri fluorine and so attack occurs more readily at the 2-position, ortho to nitrogen.

The steric restrictions of substitution of fluorine by diethyl amine in comparison with ammonia in the same solvent (acetone) are also apparent. Substitution is again more than 95% at the less sterically hindered 2-position with the bulkier diethylamine.

The small variation in the ortho/para ratio of products on changing from acetone to ether for the reaction between heptafluoroquinoline and ammonia may well be caused by the change in dielectric constant of the medium. Because ammonia is a neutral molecule, charge separation in the intermediate species and the dielectric constant of the medium will be important in determining the relative energies of the two intermediates. The low dielectric constant of ether will result in least energy of the intermediate with least charge separation, the 2-substituted product (34). In the medium of high dielectric constant, acetone, the energy difference between the two intermediates (33, 34) will be minimal.



(33)



(34)

Comparison of the relative rates of 2- and 4-substitution for sodium methoxide and ammonia in heptafluoroquinoline with the corresponding relative rates for the 2- and 4-substitution in various 5-substituted trifluoropyrimidines[98] shows an interesting reversal from the quinoline to the pyrimidine system, (Table 16 and Table 17). In all cases of reaction of 4-substituted trifluoropyrimidines there is always preferential attack by ammonia at the least sterically hindered 2-position, compared with attack by sodium methoxide. In heptafluoroquinoline the opposite is true, there being proportionally more reaction by ammonia at the more sterically hindered 4-position.

The methanolysis of the trifluoropyrimidines was considered to be 'normal', and the relative enhancement of 2-substitution by ammonia, ignoring possible effects of charge separation, was considered to be caused by hydrogen bonding

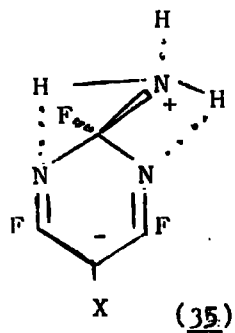
TABLE 17

Reactions of various 5-X-trifluoropyrimidines with nucleophiles [98]

Nucleophile	Group X	2-substituted product	4-substituted product
$MeOH/Na_2CO_3$	H	33	67
NH_3		67	33
$MeOH/Na_2CO_3$	Cl	6	94
NH_3		9	91
$MeOH/Na_2CO_3$	CN	90 *	10 †
NH_3		100 *	0 †
Statistical proportions		$33\frac{1}{3}$	$66\frac{2}{3}$

* 2,4 isomer, † 4,6 isomer

to the aza groups from the ammonia in the intermediate complex (35),[98]



X = H, Cl, CF_3, CN

(35)

there being understandably less enhancement in the positions ortho to only one ring nitrogen. In the case of substitution in heptafluoroquinoline, enhancement of attack by ammonia ortho to ring nitrogen will be slight but the greater effect will be the steric hindrance to attack at the 4-position by

sodium methoxide, which is probably a bulkier nucleophile than ammonia.

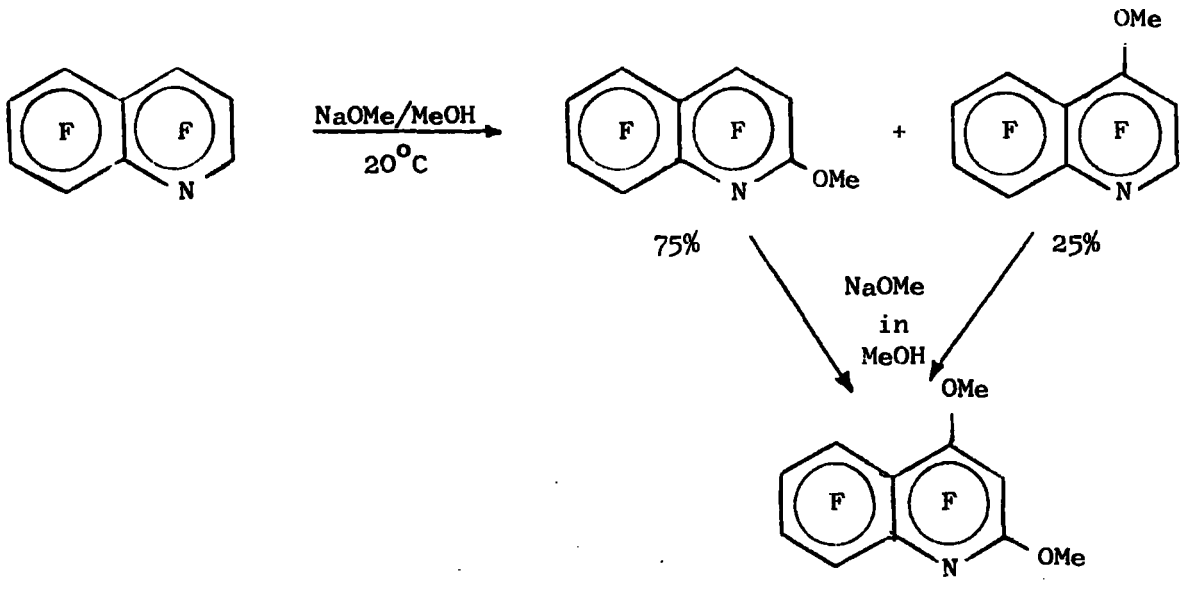
This may be a gross oversimplification of the substitution as comparison of the proportions of substitution of the fluorines by charged nucleophiles and by uncharged nucleophiles, where solvent effects are often large and highly specific,[93] may be very misleading.

The attack of butyl-lithium on heptafluoroquinoline was found to be slightly solvent dependant on changing from ether to hexane and there can be two possible explanations of this. The first in that n-butyl-lithium in hexane exists mainly in a hexameric form[99] which may be much bulkier than the dimeric form found in ether[100] solution. The results is that only the smaller nucleophile (i.e. in ether) will be able to attack to any appreciable extent in the 4-position. The resultant product from a reaction in hexane will be almost completely the 2-substituted product whereas a mixture of products will be formed from the reaction in ether, as was found.

The alternative argument is that the very weakly basic heptafluoroquinoline is able to co-ordinate with the highly electron deficient n-butyl-lithium so holding the reagent in a favourable position for attack at the 2-position. On the other hand n-butyl-lithium is sufficiently strongly solvated by ether[100] to prevent the co-ordination of a molecule of heptafluoroquinoline with the result that attack occurs mainly at the 2- and 4-positions in ether. Such co-ordination compounds have previously been noted between heptafluoroquinoline and the aluminium trihalides.[52] These alternative arguments have been advanced to account for the solvent dependancy of attack of n-butyl-lithium on pentachloropyridine.[101]

2. Disubstitution

Further reaction of either of the monomethoxyhexafluoroquinolines with one equivalent of sodium methoxide gives rise to the formation of a single disubstituted product, the 2,4-dimethoxypentafluoroquinoline.[38]



38

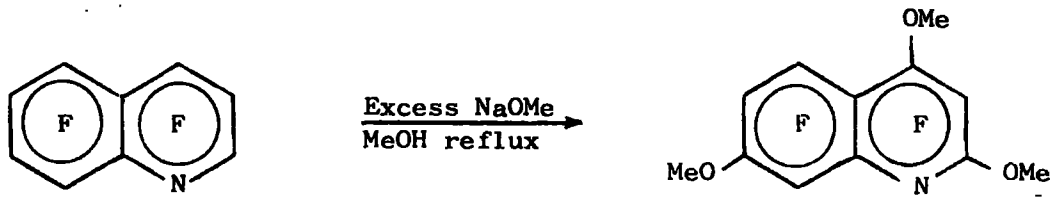
Nucleophilic substitution in heptafluoroquinoline, with the exception of a few special cases where other factors clearly control the substitution, gives rise to entirely the 2,4-disubstituted pentafluoroquinoline. Two examples of a disubstituted product not the 2,4-isomer are when heptafluoroquinoline reacts with dry aluminium halides to form the 2,8-dihalopentafluoroquinoline where specific co-ordination of the quinoline with the aluminium takes place[52] and also the formation of perfluoro-2,6-di-isopropylquinoline which was formulated as formed from the loss of a perfluoroisopropyl group from the perfluoro(2,4,6-tri-isopropylquinoline).[40] Thus the aza group can be clearly seen to control the orientation of substitution up to the disubstituted product.

3. Polysubstitution

(a) Polymethoxylation

The reaction of either 2,4-dimethoxypentafluoroquinoline or heptafluoroquinoline under reflux conditions with an excess of sodium methoxide in methanol yielded a white crystalline solid which had hitherto been unidentified.[96] It was essentially a single isomer as no additional peaks could be seen in the ^{19}F n.m.r. but it obtained a glassy appearance before melting.

Inspection of the ^{1}H n.m.r. of the compound showed three equal intensity bands, a singlet assigned to the 2-methoxy group, a doublet assigned to the 4-methoxy group and a doublet of doublets for the additional methoxy group. This showed the group to be flanked by two ring fluorine atoms and so to be in the 6- or 7-position.



In order to assign the position of the third methoxy group it was necessary to fully analyse the ^{19}F n.m.r. spectra of 2-methoxyhexafluoroquinoline and 2,4-dimethoxypentafluoroquinoline in order to assign the individual carbocyclic ring fluorine resonances to provide a basis for substituent chemical shift calculations and also to provide coupling constant measurements for a comparison between the three methoxy compounds.

The method of applying substituent chemical shifts induced by a particular substituent in a particular environment to the ^{19}F n.m.r. peak positions of a suitable reference compound and so predicting the chemical shifts of a related compound, has been widely used for the identification of many polyfluorinated compounds, generally with good results.

A suitable reference compound for the trimethoxytetrafluoroquinoline is clearly the 2,4-dimethoxypentafluoroquinoline and the substituent chemical shifts (s.c.s.) for the methoxy group in the carbocyclic ring were taken as the shifts induced in hexafluorobenzene[102] on substituting one of the fluorines for a methoxy group. They are ortho shift -4 p.p.m., meta shift +3 p.p.m. and para shift +2 p.p.m.

Calculation of the chemical shifts of all four possible isomers in only one case gives predicted shifts that correlate with those found (see Table 18).

TABLE 18

Chemical shifts of various 2,4,Y-trimethoxytetrafluoroquinolines calculated from 2,4-dimethoxypentafluoroquinoline

Position	Shift in unsubstituted compound	5-MeO	6-MeO	7-MeO	8-MeO
5	146·7	(MeO)	142·7	149·7	148·7
6	153·2	149·2	(MeO)	149·2	156·2
7	158·1	161·1	154·1	(MeO)	154·1
8	163·5	165·5	166·5	159·5	(MeO)

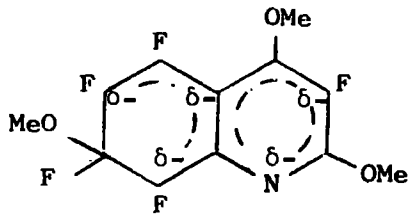
Shifts measured 146·6, 147·9, 157·0 p.p.m.

Reference $CFCl_3$

The shifts recorded most closely fit those calculated for 2,4,7-trimethoxytetrafluoroquinoline with none of the other calculated spectra fitting at all well.

Further proof is obtained from the consistency of the coupling constants within the quinoline ring system, largely unaffected by substitution. The coupling constants measured closely correlate with those of the 2,4-dimethoxypentafluoroquinoline (see Appendix I) and also serve to confirm the assignment of the three fluorine resonances as 147·9 p.p.m. - 5 fluorine (calculated 149·7), 146·6 p.p.m. - 6 fluorine (calculated 149·2) and 157·0 p.p.m. - 8 fluorine (calculated 159·5).

The formulation of the trimethoxy product as the 2,4,7-trimethoxytetrafluoroquinoline is entirely in accordance with the aza group directing the site of nucleophilic attack (35), the 2- and 4-methoxy groups merely deactivating the



(36)

system to nucleophilic attack.

(b) In perfluoro(2,4-di-isopropylquinoline)

The displacement of the 2- and 4-fluorine atoms in heptafluoroquinoline by the deactivating, electron repelling methoxide groups has been seen to reinforce the controlling effect of the nitrogen and direct further substitution into the 7-position. Replacement of the 2- and 4-fluorine atoms by the activating, electron withdrawing perfluoroisopropyl groups enhances the reactivity of the positions not enhanced by the nitrogen atom.

Perfluoro(2,4-di-isopropylquinoline) rapidly reacted with one equivalent of sodium methoxide in methanol to give a single monomethoxylated product.

The application of substituent chemical shifts to the four carbocyclic ring fluorine atoms of perfluoro(2,4-di-isopropylquinoline) to calculate the chemical shifts for all four possible isomeric compounds led to the unambiguous identification of the compound as 2,4-di-heptafluoroisopropyl, 6-methoxytetrafluoroquinoline (36) (Table 19). The substituent chemical shifts were assumed to approximate to those caused by the substitution of a methoxy group into hexafluorobenzene.

TABLE 19

Calculated chemical shifts of various methoxy derivatives of perfluoro(2,4-di-isopropylquinoline)

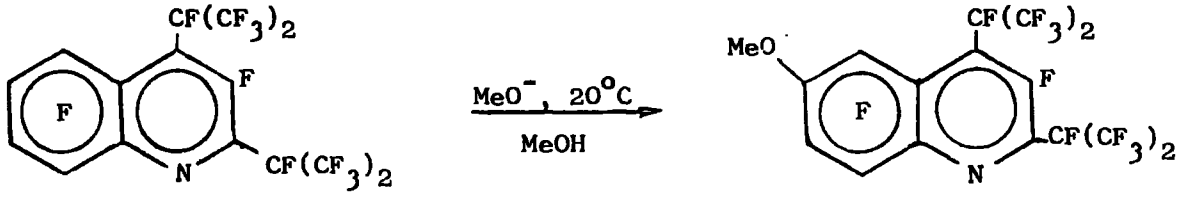
Position	Shifts of unsubstituted compound	5-MeO	6-MeO	7-MeO	8-MeO
5	131·0	(MeO)	127·0	134·0	133·0
6	147·5	143·5	(MeO)	143·5	150·5
7	153·7	156·7	149·7	(MeO)	149·7
8	145·3	147·3	148·3	141·3	(MeO)

Comparison of shifts for 6-substitution

	5-F	7-F	8-F
Calculated	127·0	149·7	148·3
Observed	125·6	~149·1	~149·1

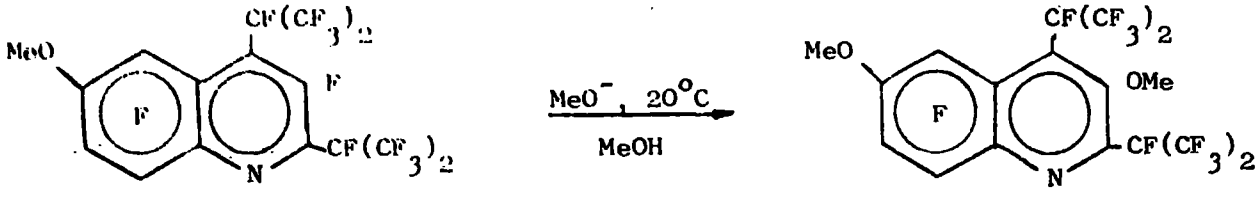
Shifts relative to $CFCl_3$, substituent chemical shifts from Reference 102.

Calculations of calculated and observed spectra are again good. The peak assignments can be further confirmed from comparison of the various measured coupling constants (see Appendix I).



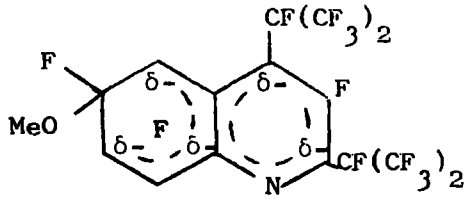
(36)

This monomethoxylated product (36) reacted rapidly with a further equivalent of sodium methoxide to give a single dimethoxylated product. From the greatly simplified ^{19}F n.m.r. spectra of both the 2- and 4-heptafluoroisopropyl groups the compound was identified as the 2,4-diheptafluoroisopropyl, 3,6-dimethoxytrifluoroquinoline (37).



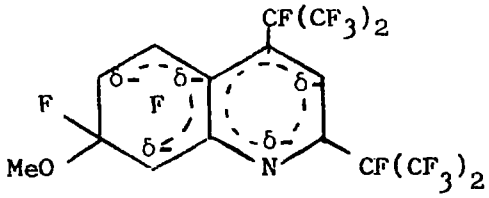
(37)

Rationalisation of the initial substitution at the 6-position is apparent from the Wheland intermediates (38) and (39).



(38)

6-substitution



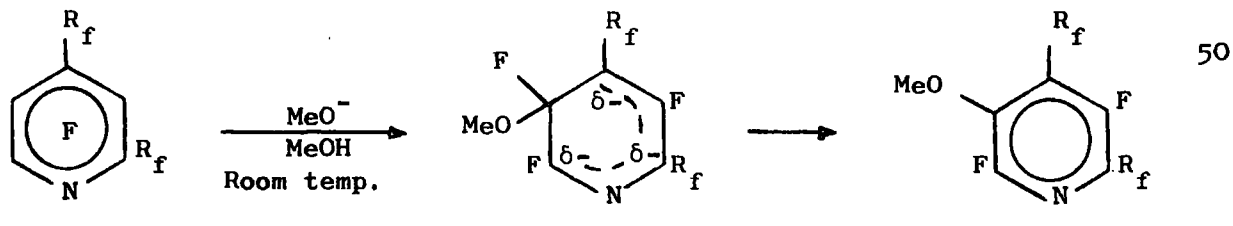
(39)

7-substitution

Stabilisation of the negative charge during 6-substitution is by two perfluoropropyl groups whereas during 7-substitution stabilisation is only by the aza nitrogen. Thus the two perfluoroisopropyl groups override the directing influence of the nitrogen and substitution occurs in the 6-position.

That conversion to the dimethoxylated product involves displacement of the 3-fluorine demonstrates that ortho activating effect of the perfluoroisopropyl groups exceeds the directing influence of the aza centre in the carbocyclic ring.

These reactions provide another clear example of control of substitution by the strongly electron withdrawing substituents rather than by the aza centre. A previous example of control of substitution by the strongly electron withdrawing substituents can be found in the reactions of pentafluoropyridine derivatives where perfluoro(2,4,-di-isopropylpyridine) reacts rapidly with methoxide ion at the 5-position,[50] 2,4-dimethoxytrifluoropyridine reacting at the 6-position, control being by the aza group.[27]



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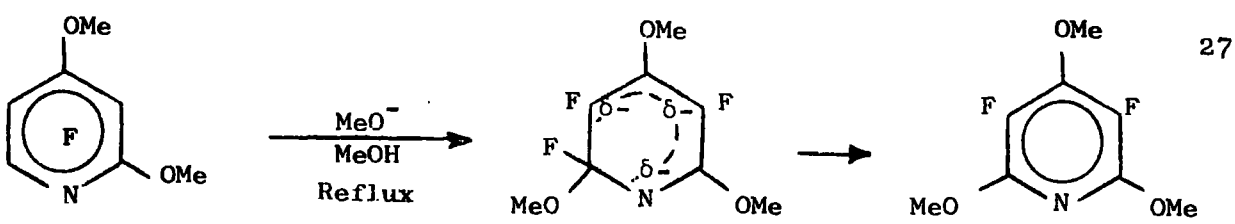
R_f = (i) $CF(CF_3)_2$
(ii) CF_2CF_3



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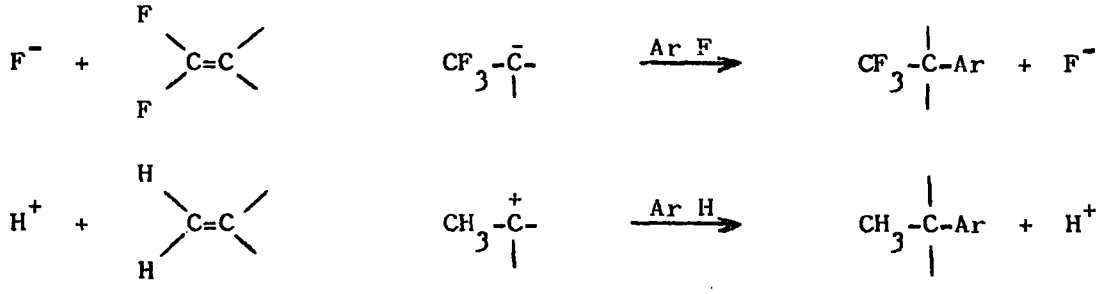
The strong deactivating effect of the methoxy group compared with the perfluoroalkyl group is readily apparent in that substitution by methoxide ion takes place readily at room temperature in the perfluorodialkylated pyridines and quinolines but further substitution in the dimethoxylated heterocycles takes place only at reflux temperatures.

Several attempts at the substitution of perfluoroalkyl groups ($-C_2F_5$, iso-C_3F_7, sec.-C_4F_9, iso-C_4F_9) into dimethoxypentafluoroquinoline were unsuccessful, presumably because of the deactivating effect of the methoxide groups.

C. Polyfluoroalkylation

1. Introduction

Nucleophilic substitution in activated fluoroaromatic compounds with polyfluoroalkylanions generated from fluoride ion and polyfluoro-olefins has been found to be widely applicable to the preparation of polyfluoroalkyl substituted aryl compounds. This type of reaction can be seen to be complementary to the Friedel-Crafts type of reaction in the hydrocarbon system.



Extensive work with a variety of olefins and substrates has shown that of the sources of fluoride ion as initiating agent the less economically attractive caesium fluoride is considerably more efficient than potassium fluoride in promoting reaction.[104]

The choice of solvent required for the reaction is less clear cut, but of the dipolar aprotic solvents studied the glymes and sulpholan have been found

to be effective although there is no correlation between solvent and yield or extent of substitution.[103,104]

A thorough investigation of the polyfluoroalkylation of activated polyfluoro-arynes,[54] -pyridines,[49,50,54] -pyridazines[33] and -pyrimidines[106] has recently been extended to perfluoroquinoline by a detailed study of the perfluoroisopropylation of heptafluoroquinoline with caesium fluoride and hexafluoropropene at atmospheric pressure.[40] The results of this work is summarised in Figure 5.

2. Substitution by tetrafluoroethylene

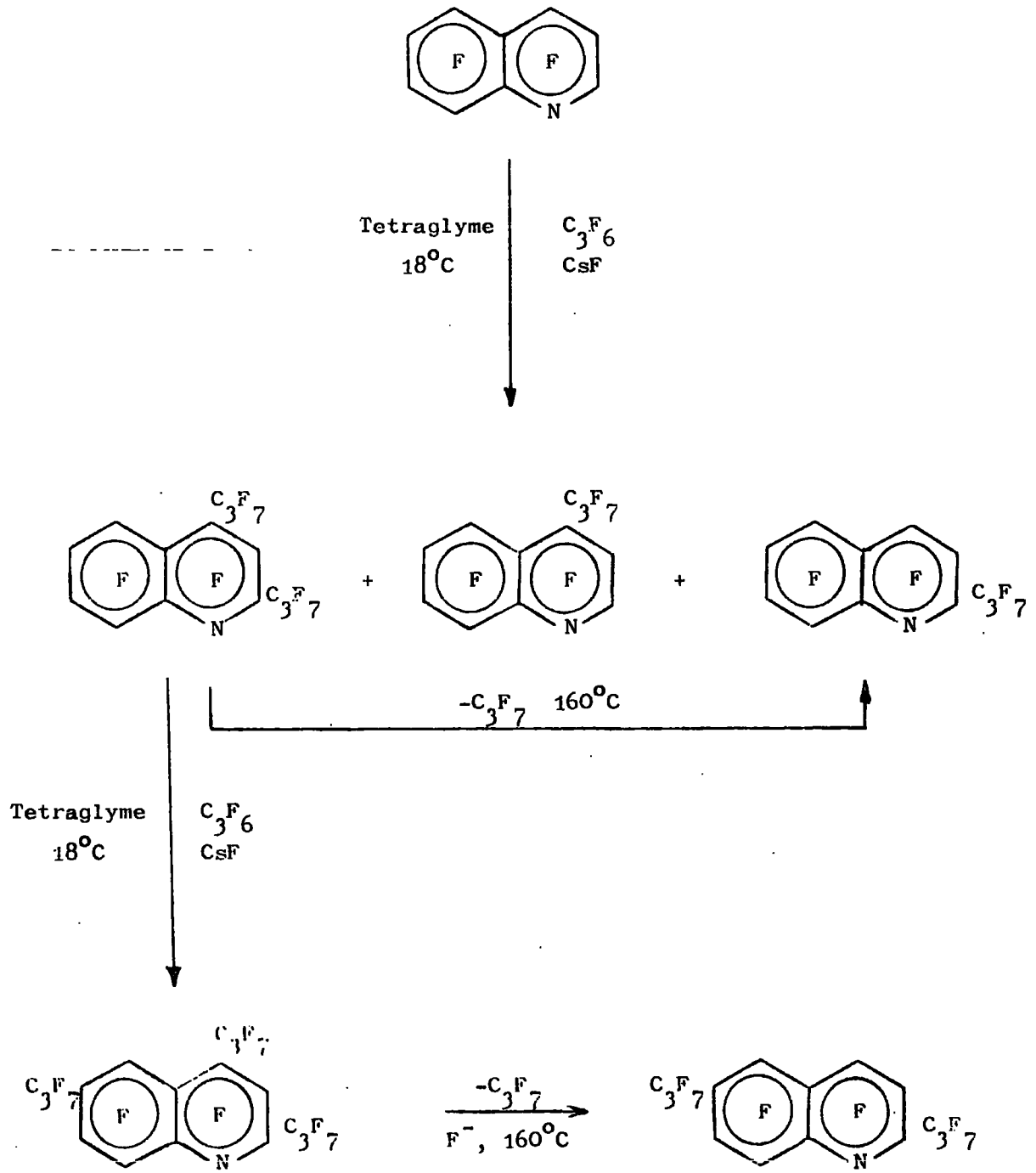
In order to extend the work on the polyfluoroalkylation of heptafluoroquinoline the reactions with the pentafluoroethyl anion, generated from tetrafluoroethylene and caesium fluoride, were studied.

Reaction took place readily at temperatures even as low as room temperature and take up of the tetrafluoroethylene as evidenced by a decrease in the volume of gas in the reservoir (see Experimental) was considerable within a few hours. In all cases colouring of the solution, generally attributed to complex formation between the caesium fluoride, olefin, and substrate in the solvent,[108] was evident. After all reactions, however, the work up of the solution gave rise to the isolation of a very complex mixture of products.

Considerable effort was extended to attempt to prepare less complex mixtures of products by careful control of the conditions of the reaction. Both sulpholan and tetraglyme were used as solvents and various combinations of temperature, time of reaction and proportion of olefin were used with little improvement in the complexity of the mixture. The reactions of longer time, higher temperature, and higher proportion of olefin resulted in a smaller proportion of heptafluoroquinoline (as determined by vapour phase chromatography) and an increase in the proportion of the components of higher retention time but overall no significant improvement was effected.

FIGURE 5

Reactions between heptafluoroquinoline and the heptafluoroisopropyl anion [40]



Substantial work had previously been done on the development of suitable methods for the separation of the complex mixtures of perfluoroisopropylquinolines particularly on the development of different column packings for preparative scale vapour phase chromatography[40] but even the most useful columns gave only moderate resolution. Preliminary attempted separations or simplifications of the mixtures by distillation, elution chromatography, and low temperature recrystallisation of the oils produced little improvement in complex mixtures. The final step of attempted vapour phase chromatography did not result in the isolation of any pure components of the mixture.

Mass spectroscopy of the mixture showed that there were substantial proportions of components with molecular weights corresponding to the insertion of four tetrafluoroethylene groups (m.wt. = 655) in mixtures prepared at room temperature and an increase in the proportion of penta-substituted product (m.wt. = 755) in mixtures prepared at higher temperatures.

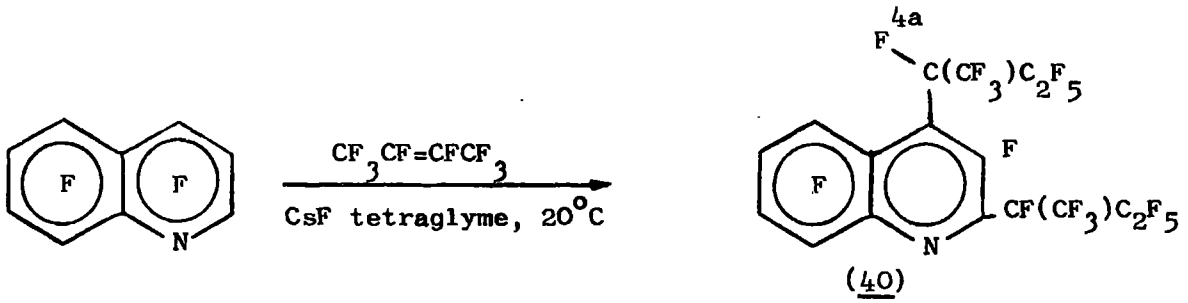
Whereas substitution of heptafluoroisopropyl groups into heptafluoroquinoline gave rise to complex mixtures containing mainly the products shown in Figure 5, substitution by pentafluoroethyl groups will give rise to not only all the analogous pentafluoroethyl products, except possibly those formed by rearrangements, but also the 3-position may well be sufficiently activated for substitution by the smaller pentafluoroethyl nucleophile. Activation such as this towards the smaller nucleophiles has been demonstrated for the perfluoro-(2,4-di-isopropylquinoline).

3. Substitution by octafluorobut-2-ene

Previous work on the substitution of octafluorobut-2-ene into heptafluoroquinoline under high temperatures and pressures[104] had shown that complex mixtures of mono-, di-, tri- and tetra-substituted products were obtained and from the mixture was isolated perfluoro(2,4-di-sec-butylquinoline) (40).

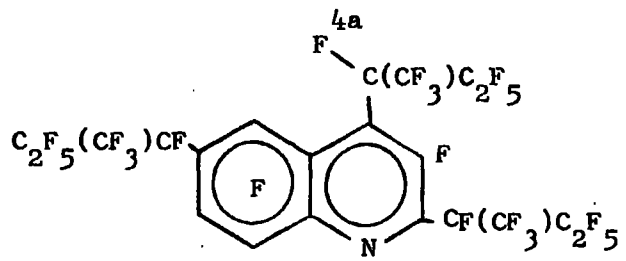
A repeat of the reaction under the more mild conditions of the atmospheric pressure alkylation showed that take up of the olefin occured readily at relatively low temperatures to give a mixture of predominantly two products which were separated and identified as perfluoro(2,4-di-sec-butylquinoline) and a perfluoro(tri-sec-butylquinoline).

Comparison of the very complex spectrum of this product with the disubstituted product (40) showed two of the perfluoroalkyl groups to be in the 2- and 4-positions and the third group to be in the carbocyclic ring.



(40)

+



(41)

Analysis of the high resolution ^{19}F n.m.r. spectrum of (40) allowed the 5-fluorine to be assigned with certainty from the large J_{4a-5} coupling shown. Comparison of the other coupling constants evident with those of perfluoro-(2,4-di-isopropylquinoline) enabled the other resonances to be tentatively assigned, (see Appendix I).

Complete analysis of the high resolution ^{19}F n.m.r. spectrum of (41) was not possible because of the weak signal and broad resonances but the positions of the ring fluorine resonances could readily be ascertained. The large

coupling between the 4a- and 5-fluorine evident in (40) was also evident in (41) so proving the presence of the 5-fluorine. Of the single fluorine resonances only one was sufficiently broad to be able to contain a 200 Hz. coupling, the resonance at around 90 p.p.m. Thus, to be so broad the 5-fluorine must have a perfluoroalkyl adjacent in the 6-position. This is confirmed from its lowfield position; the shift of about 40 p.p.m. downfield from its position in (40) is typical of the ortho shift caused by perfluoroalkyl groups in the carbocyclic ring.[40] The next single fluorine resonance upfield at 109 p.p.m. is assigned to the 3-fluorine from its shape and relatively unmoved position from that in (40), 110 p.p.m. The next single fluorine resonance upfield exists as a doublet (J = 110 Hz.) and a broad resonance in unequal proportions. This is discussed later (Chapter 6) but is assigned to the 7-fluorine with the 6-sec-butyl group existing in two conformers. The remaining single carbocyclic ring fluorine resonance at 148 p.p.m. again exists as two unequal intensity resonances but both are comparatively sharp and so are assigned to the 8-fluorine.

Applying the substituent chemical shifts caused by a 6-perfluoroisopropyl group (as an approximation to those caused by a 6-perfluoro-sec-butyl group) to the tentatively assigned perfluoro(2,4-di-sec-butylquinoline) predicts a spectrum that is consistent with that recorded (Table 20).

TABLE 20

Calculated chemical shifts of perfluoro(2,4,6-tri-sec-butylquinoline)

Compound	5-F	6-F	7-F	8-F
(40)	128	143·6	151·5	145·4
(41) calculated	89	=	130	146
(41) observed	90	=	130-135	148-150

Shifts relative to $CFCl_3$

Substituent chemical shifts, ortho -39 or -21, meta +0·6, (see text)

This 2,4,6-pattern of substitution again is more evidence of the control of substitution by the 2- and 4-perfluoroalkyl groups.

No attempts were made to heat the perfluoro(2,4,6-tri-sec.butylquinoline) to a higher temperature in the presence of caesium fluoride to investigate possible rearrangements.

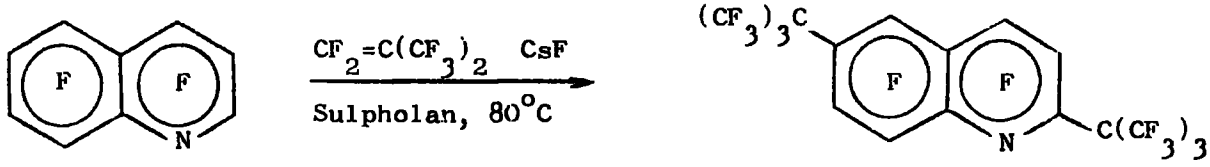
4. Substitution by perfluoroisobutene

Interest in the preparation of perfluoro-t-butylquinolines developed for two major reasons. The first was to complete the series of polyfluoroalkylations of heptafluoroquinoline and secondly in an attempt to investigate some of the rotational isomerism of perfluoroalkyl groups. Variable temperature ^{19}F n.m.r. studies on various perfluoroisopropyl substituted compounds had shown changes in the spectrum attributable to hindrance to the rotation of the perfluoroisopropyl group.[108,109] The symmetrical perfluoro-t-butyl groups are potentially excellent groups for studying the rotational isomerism as different conformers may well have the same ground state energy.

Reaction between excess perfluoroisobutene, caesium fluoride and heptafluoroquinoline at elevated temperatures in sulpholan rapidly produced a disubstituted product. Analysis of the ^{19}F n.m.r. spectrum was as follows.

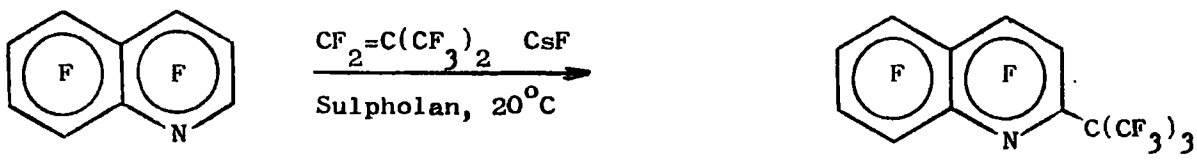
The ^{19}F n.m.r. spectrum contained seven groups of resonances. Two of these were readily assigned to the perfluoro-t-butyl groups because of their intensity corresponding to nine fluorines each. One of these was a doublet and because of the lack of any lowfield single fluorine resonances, characteristic of a ring fluorine ortho to ring nitrogen, was assigned to the 2-position. The other perfluoro-t-butyl group had a sharp triplet resonance and so requires two ortho ring fluorines. Of the five single fluorine resonances, three were very broad and so these were assigned to positions ortho to the perfluoro-t-butyl groups i.e. the 3-position and two other. Of the two remaining well resolved peaks one, at 122·4 p.p.m., showed a coupling of

75 Hz. This coupling was assumed to be the peri-coupling and so the peak was assigned to either the 4- or 5-position. As a corresponding coupling of 75 Hz. was not evident in any of the other resonances it must be presumed to be masked in one of the very broad peaks because of extensive further coupling to an adjacent perfluoro-t-butyl group. The second perfluoro-t-butyl group, as it has two ortho fluorines, must be in the carbocyclic ring and so the sharp resonance at 122·4 Hz. must be assigned to the 4-fluorine. The 5-fluorine must have an adjacent perfluoro-t-butyl group, i.e. in the 6-position, which broadens the 5- and 7-fluorines with extensive coupling, obscuring the $J_{5,4}$ coupling of 75 Hz., so leaving the 8-fluorine as the remaining sharp resonance. Had the perfluoro-t-butyl group been in the 7-position, the large peri-coupling would have been clearly apparent in both the 4- and 5-fluorine resonances. Thus the compound is perfluoro(2,6-di-t-butylquinoline) (42).



(42)

A room temperature reaction afforded mainly a monosubstituted compound, perfluoro(2-t-butylquinoline) (43).

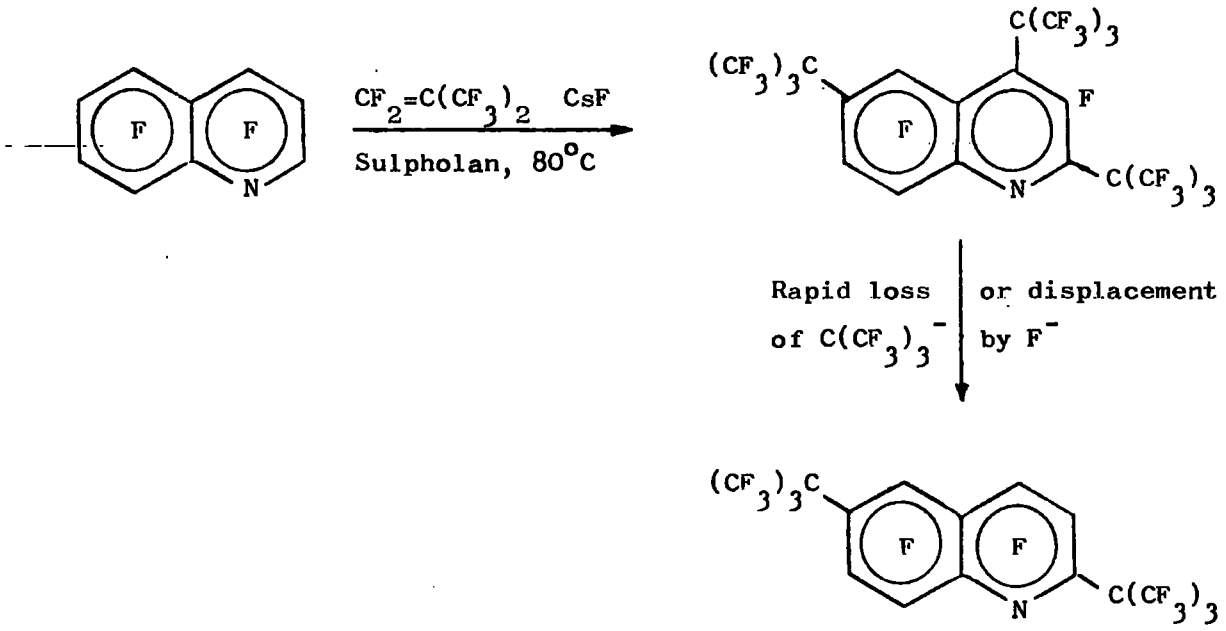


(43)

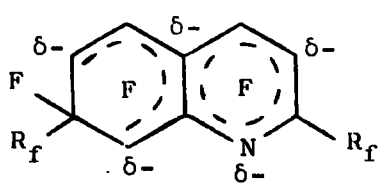
There was no substantial evidence of any other mono- or di-substituted products in either of the reactions.

The formulation of (42) as the sole disubstituted product can be considered from two angles.

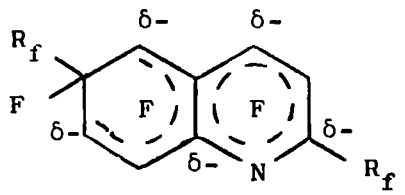
The first is that a route analogous to that of the formation[40] of perfluoro(2,6-di-isopropylquinoline) could be envisaged. Reaction with the excess perfluoro-t-butyl carbanion occurs to yield the 2,4,6-trisubstituted product. High steric strain between the 4-t-butyl group and the 5-peri-fluorine causes rapid loss of the t-butyl group at the temperature of the reaction.



An alternative explanation is that although the 4-position is activated to nucleophilic substitution by the nitrogen, the perfluoro-t-butyl carbanion is too bulky to effect substitution at this sterically crowded position and so substitution occurs directly into position.[6] It is interesting to note that if the disubstituted product is formed via this second route then a perfluoro-t-butyl group in the 2-position is more stabilising towards substitution in the 6-position than the aza group is for substitution at the 7-position, i.e. (44) is more stable than (45).



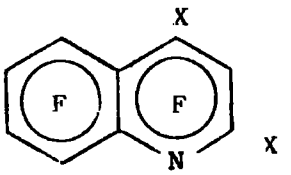
(44)



(45)

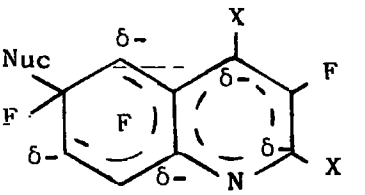
D. Nucleophilic substitution in dihalopentafluoroquinolines*

Nucleophilic substitution in 2,4-dihalopentafluoroquinolines (46) was of interest because of the two possible types of reactions that could take place. The first was that displacement of fluorine from the carbocyclic ring could take place and control of the orientation could either be by the stabilising halogen (47) (i.e. Cl, Br and I are more stabilising than fluorine when attached to carbanionic centre) or by the aza centre (48). The alternative



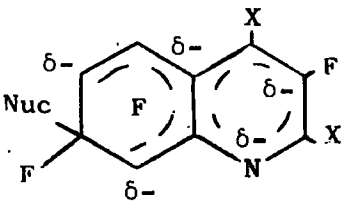
(46)

Nuc^-



(47)

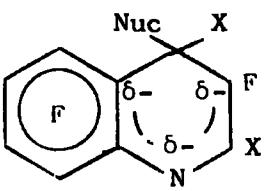
Nuc^-



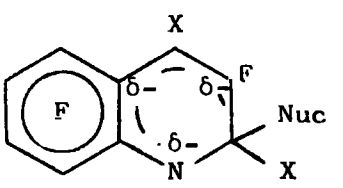
(48)

X = Cl, Br, I

reaction that could take place, the reaction that was observed for displacement by one methoxyl group, was displacement of one of the halogen atoms from the carbocyclic ring, (49), (50).



(49)



(50)

1. Reaction with sodium methoxide

The reaction between 2,4-dihalopentafluoroquinoline and one equivalent of sodium methoxide in methanol gave in each case a low melting solid which was shown by elemental analysis to be a monomethoxymonohalopentafluoroquinoline.

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* Throughout this section the term halogen does not include fluorine unless otherwise stated.

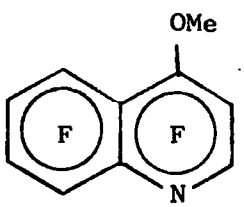
In each case there was preferential displacement of halogen rather than fluorine.

$$C_9NF_5X_2 \xrightarrow[MeOH]{NaOMe} C_9NF_5X(OMe)$$

X = Cl, Br, I

The ^{19}F n.m.r. spectrum indicated in each case that the solid was a mixture of two isomers but these could not be separated by vapour phase chromatography, fractional sublimation or recrystallisation. Nevertheless, the major isomer could be identified from the ^1H spectrum.

It is well established that methoxyl groups in polyfluoroaromatic compounds couple to the ortho fluorine atoms (51) except when adjacent to a ring nitrogen (52) when the ^1H n.m.r. spectrum of the methoxy group is a sharp singlet.[2,38,39]



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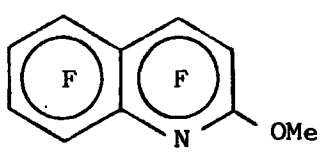


(52)

^1H n.m.r. spectrum

doublet J = 5·5 Hz

singlet

The ^1H n.m.r. spectrum of the mixture of isomeric products from the reactions of each of the dihalopentafluoroquinoline compounds with one equivalent of sodium methoxide showed in each case the major isomer was with the methoxy group in the 2-position (i.e. the spectrum was a sharp singlet). The ^1H n.m.r. spectrum of the minor component, where clearly visible, was a doublet showing the minor component to have the methoxyl group in the 4-position.

The ^{19}F n.m.r. spectrum of the major component of each mixture was fully analysed and is reported in Appendix I. The constancy of coupling values throughout the series, including 2-methoxyhexafluoroquinoline confirms the

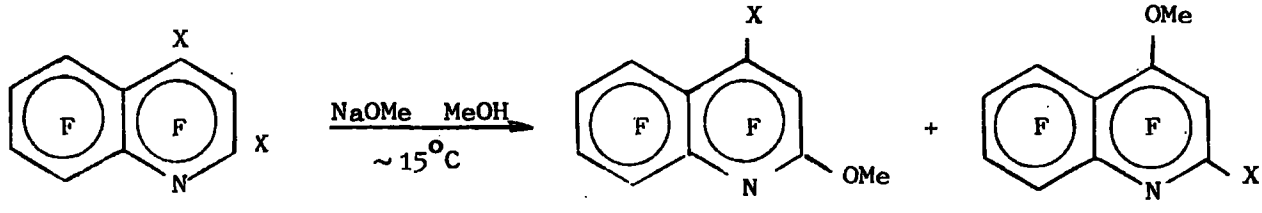
identification of the major component in each case as 2-methoxy,4-halopentafluoroquinoline. The only coupling constant to change through the series is the value of $J_{3,5}$ which increases steadily with the increasing atomic weight of the 4-substituent (Table 21).

TABLE 21

Value of $J_{3,5}$ in some 2-methoxy,4-halopentafluoroquinolines

4-halogen	F	Cl	Br	I
$J_{3,5}$ Hz.	$7\frac{1}{2}$	9	$11\frac{1}{2}$	$14\frac{1}{2}$

Integration of the ^{19}F n.m.r. spectra gave the approximate proportions of the two isomers and the results are given below:



X = F [38]	75%	25%
Cl	< 90%	
Br	75%	25%
I	< 80%	

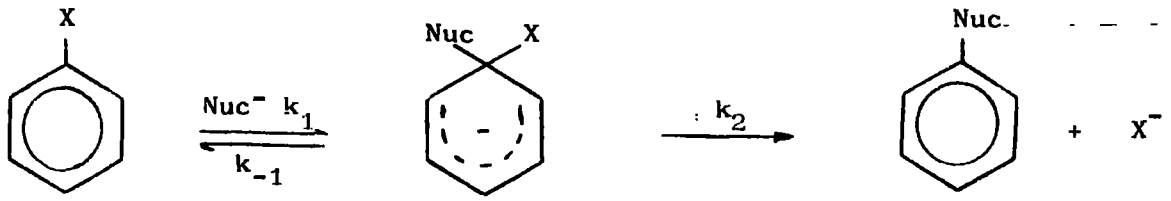
(Proportions by n.m.r. integration ± 5%)

Although the ^{19}F n.m.r. spectrum of the minor component in each mixture could not be fully analysed because of the weak signal the spectrum of the 2-bromo,4-methoxypentafluoroquinoline was very similar to that previously reported for the compound. In particular the ^{1}H spectrum was a doublet with a coupling of 5·0 Hz. to an adjacent fluorine, equal to that previously reported.[69]

2. Mechanism of displacement

The displacement of halogen by sodium methoxide is one of the first examples of preferential unassisted displacement of halogen[110,111] rather than fluorine from polyfluoroarenes but can be rationalised in the following way.

The nucleophilic displacement of halogen from an activated aromatic system takes place generally by a two step mechanism.[21]

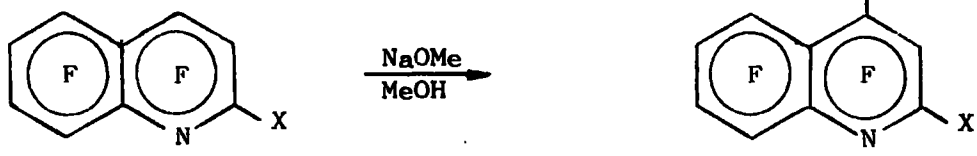


intermediate complex

(53) (54) (55)

The substrate (53) reacts with the nucleophile reversibly to form an intermediate complex (54). This then breaks down with the formation of the product (55) or back to the starting material (53). Either the rate of formation or the rate of decomposition of (54) will be the rate determining step. However, for a substantial number of displacements of halogen from activated aromatic compounds the rate of displacement of fluorine, with its higher carbon-halogen bond dissociation energy[21] (D(Ph-F) = 115 Kcal.mole^{-1}) is much greater than the displacement of other halogens (D(Ph-Cl) = 86 Kcal.mole^{-1}) and so bond breaking in the rate determining step may not be significant. The rate of the displacement is determined by the rate of the complex formation, a rate that is increased by the strongly electron withdrawing effect of fluorine. The rate enhancement of the displacement of fluorine compared with the displacement of chlorine is commonly of the order 10^2 to 10^3 for this type of reaction.[93]

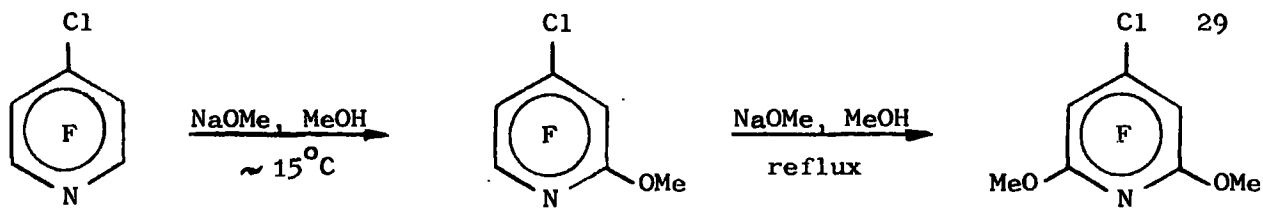
Previous work has shown[112] that attack of sodium methoxide on 2-halohexafluoroquinolines gives exclusively the 4-methoxy,2-halopentafluoroquinoline products showing the increased mobility of fluorine over halogens in this type of reaction.



112

X = (i) Cl
(ii) Br

Similarly reactions of 4-halotetrafluoropyridines with sodium methoxide in methanol lead to successive displacements of fluorine only. Recent kinetic work has shown[113] that the rate of displacement of fluorine from 4-chlorotetrafluoropyridine by methoxide ion is about 2×10^2 times slower than the rate of displacement of the 4-fluorine from pentafluoropyridine and so the rate



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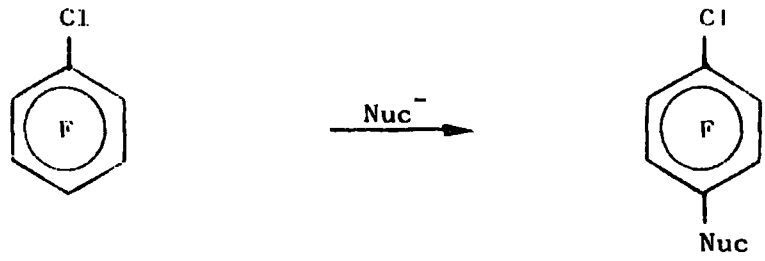
enhancement of fluorine displacement over that of chlorine at the 4-position must be at least this value.

The transmission of activation effects through condensed ring systems has previously been demonstrated for quinoline in the reactions of perfluoro(2,4-di-isopropylquinoline) where substitution in the 6-position was controlled by the heptafluoroisopropyl groups. Chlorine is known to activate the para-fluorine in polyfluoro compounds from the displacement of the para-fluorine in chloropentafluorobenzene.



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The transmission of activation to the carbocyclic ring fluorines as caused by the two chlorine atoms and the aza group is apparently less than the activation of the heterocyclic ring chlorine atoms by the aza group despite the probable enhancement of mobility of the fluorine atom.

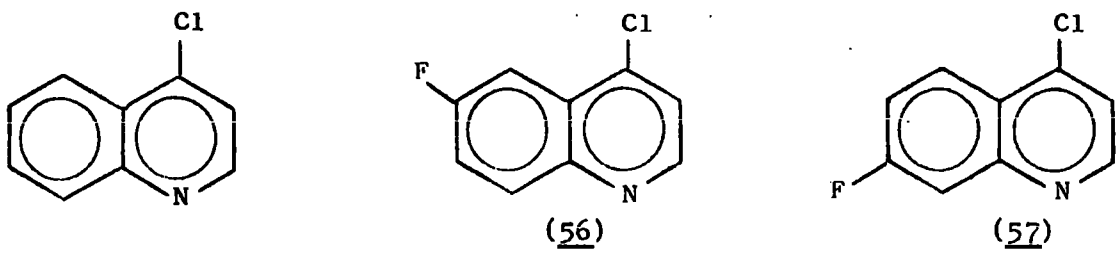
The following order of rates of displacement of halogen or fluorine in quinoline ring systems is proposed:-

displacement of directly activated fluorine > displacement of (other) directly activated halogen > displacement of non-activated (carbocyclic ring) fluorine.

'Directly activated' includes only those groups that are ortho or para to the ring nitrogen.

A previous quantitative example of activation between the quinoline rings, although not exactly comparable with the previous explanation is given by the rate enhancement of chlorine displacement by some carbocyclic ring fluorine atoms in 4-chloromonofluoroquinolines (56) and (57), (Figure 6).

FIGURE 6



(56) (57)

Relative rate:* 1 : 2·1 : 5·0

* Displacement by sodium methoxide in methanol at 75·2°C

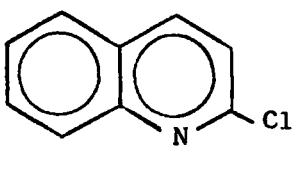
It is interesting to note that only chlorine is displaced in the above reactions.[114]

3. Reactions with excess sodium methoxide

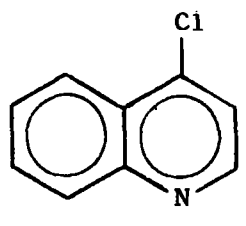
Reactions between the dihalopentafluoroquinolines and excess sodium methoxide in methanol do not appear to be simple in all cases. Vapour phase chromatography indicates at least three products are formed and mass spectrometry indicated the presence of some dimethoxyhalotetrafluoroquinoline compounds in the crude mixtures. Thus the displacement of one of the heterocyclic ring halogens by methoxyl appears to bring a reduction in the reactivity of the remaining halogen; sufficient to make it comparable with the reactivity of the carbocyclic ring fluorines. This reduction in reactivity of the remaining halogen is quite clear in the case of 2,4-dichloroquinoline, (Figure 7).

FIGURE 7

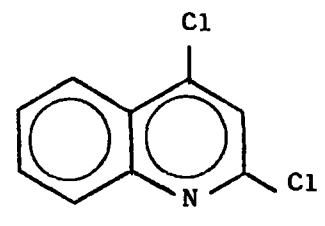
Relative rates of displacement of chlorine in some chloroquinolines* [43,114-116]



1·0

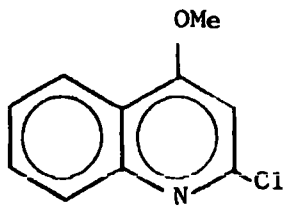


1·11

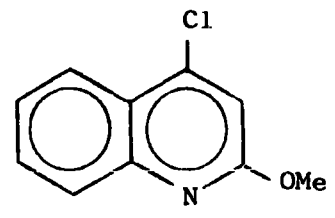


2-position - 39·4

4-position - 74·7



0·22



0·06

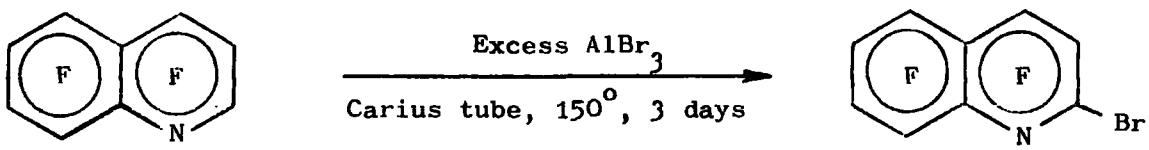
* Displacement by NaOMe in MeOH at 75·2°C

E. Attempted preparation of the lithio derivatives of 2-bromohexafluoroquinoline and 2,4-dibromohexafluoroquinoline

The use of the lithio or Grignard derivatives of 3-hydro-, 4-bromo- and 4-iodo-tetrafluoropyridine has been very valuable in the preparation of a wide variety of derivatives of pentafluoropyridine.[29,30,46] In an attempt to prepare derivatives of polyfluoroquinoline efforts were made to prepare the organometallic derivatives of 2-bromohexafluoroquinoline and 2,4-dibromopentafluoroquinoline.

1. 2-Bromohexafluoroquinoline

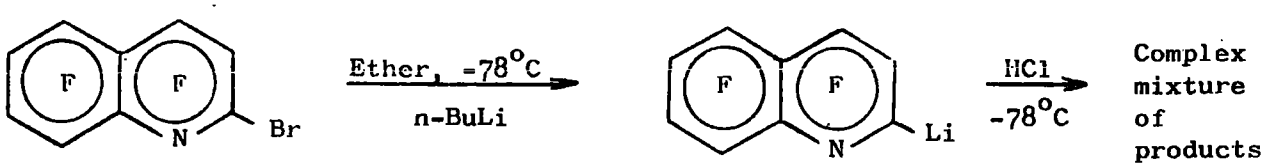
Considerable difficulties were encountered in the attempted preparation of pure 2-bromohexafluoroquinoline by reaction between sublimed aluminium tribromide and heptafluoroquinoline.[51]



51

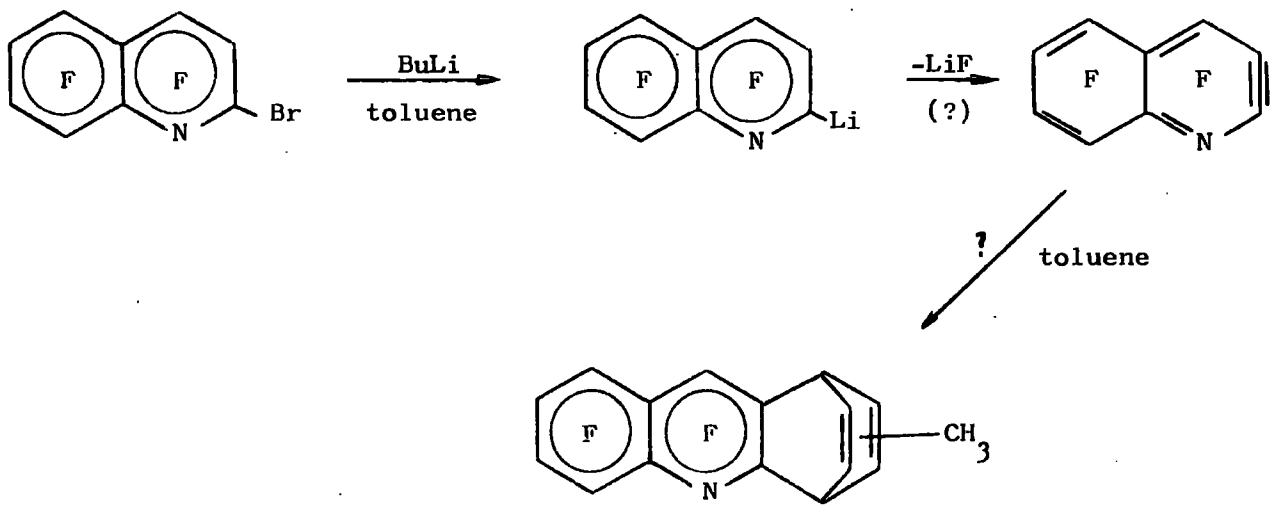
Despite handling the sublimed aluminium tribromide in a glove box the synthesis was very unreliable for reasons that could not be understood.

Attempted lithiation of the compound by metal-halogen exchange with n-butyl lithium in ether, hexane, or mixed solvent and the subsequent hydrolysis, still at -78°C, usually gave dark tars from which could be isolated n-butyl bromide and usually a complex mixture of semi-solid products (as indicated by vapour phase chromatography).

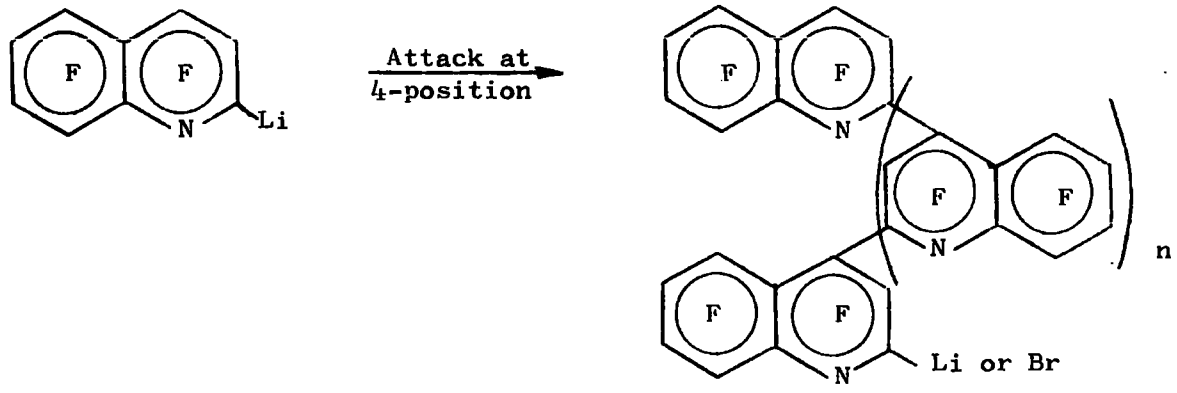


Mass spectrometry of the mixture indicated the presence of a compound of molecular weight corresponding to hexafluoroquinoline. Attempted reactions of the 'lithio compound' with solid carbon dioxide and with mercuric chloride did not yield isolable compounds, only tar formation.

As it is clear that initial bromine-lithium exchange is taking place rapidly at -78°C from the formation of butyl bromide, one possible route of decomposition of the lithium compound is via the heteryne formed by elimination of lithium fluoride. Repeat of the lithiation reaction in toluene as solvent and allowing the mixture to warm to room temperature before hydrolysis failed to form any identifiable compounds, only dark material of featureless i.r. spectrum, presumed polymeric.



Another possible mode of decomposition could be by nucleophilic attack of the lithio compound either on unreacted starting material or other lithio compound at the reactive position with the formation of polymeric material



The attempted preparation of derivatives via the magnesium compounds were not successful as the Grignard reagent could not be prepared.

2. 2,4-Dibromopentafluoroquinoline

In an effort to reduce the possibility of complications in the preparation of 2-lithiohexafluoroquinoline brought about by the presence of a second reactive site in the molecule the monolithiation of 2,4-dibromopentafluoroquinoline was attempted.

2,4-Dibromopentafluoroquinoline, readily prepared by reaction between heptafluoroquinoline and boron tribromide,[51] was reacted with n-butyl lithium in either ether or hexane. In both cases a dark oil was isolated from the work up of the mixture (hydrolysis at -78°C by HCl gas). A moist yellow paste was sublimed from the oil and mass spectrometry indicated the presence of a compound whose molecular weight corresponded to bromopentafluoroquinoline. Vapour phase chromatography indicated the presence of essentially a mixture of two products from the reaction in ether and only one product from reactions in hexane. A reaction in tetrahydrofuran similarly gave a mixture of products.

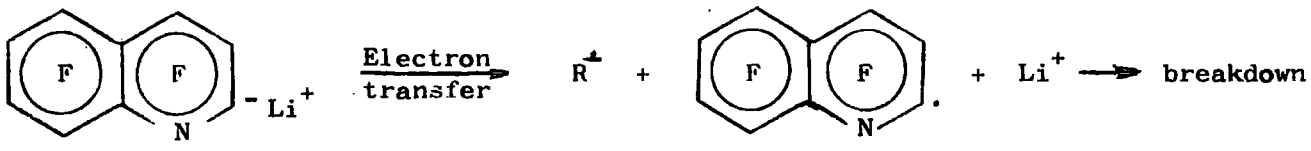
Repeated attempts at the preparation of the bromopentafluoroquinoline and reactions of the lithio compound with solid carbon dioxide, mercuric chloride or trimethyl chlorosilane always gave rise to considerable tar formation and low yields of sublimable material and so this route was abandoned as not viable to derivatives of heptafluoroquinoline.

The attempted formation of Grignard reagents, by metal halogen exchange between methylmagnesium iodide and the 2,4-dibromopentafluoroquinoline at room temperature in ether resulted in the rapid darkening of the solution and no identifiable products could be isolated from its low temperature hydrolysis.

Overall the results do not compare well with the ease of preparation of organometallic derivatives of the various bromo-,[29] iodo-[30] and hydro-pyridines[46] where even the 3,5-dilithiotrifluoropyridine is stable at low temperature.[46]

Likewise it has not been found possible to prepare the Grignard reagent from 4-iodotrifluoropyrimidine,[37] only dark tars being formed after the first difficult initiation step. It was proposed that the difficulty of preparation and subsequent instability of the Grignard reagent depended on the electron withdrawing capacity of the substituent to iodine. Other work[117] within the department has indicated that the preparation of lithio derivatives of other polyhalodiazines similarly gives rise to tar formation.

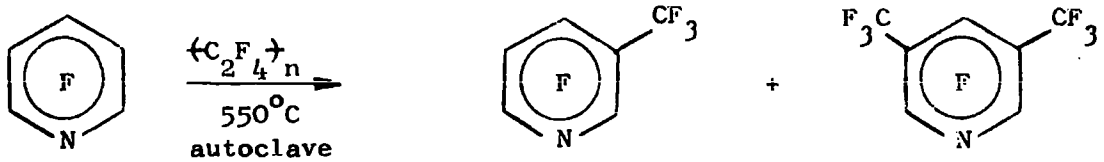
There is the possibility of another decomposition route. This is that the formation of the organolithium compound takes place but is unstable and may break down by electron transfer, possibly to another organic molecule so forming a radical anion and leaving a neutral radical. Breakdown or polymerisation could then readily take place.



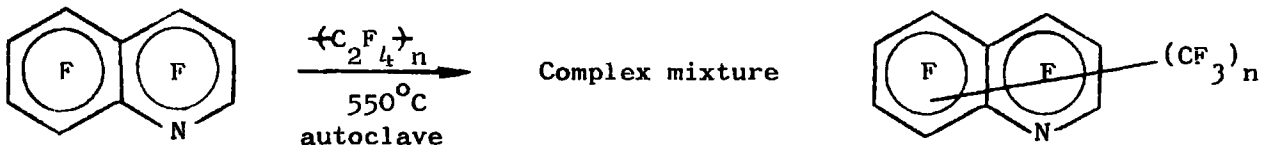
F. Attempted preparation of trifluoromethyl derivatives of heptafluoroquinoline

Russian workers have shown that co-pyrolysis of hexafluorobenzene with polytetrafluoroethylene at 550°C in an autoclave yields mainly perfluorotoluene with a mixture of perfluoroxylenes in which the meta isomer predominates.[118] The method has recently been applied to pentafluoropyridine and shown to be a viable preparative route to 3- and 3,5-bistrifluoromethyl derivatives of pentafluoropyridine.[119]

119



Attempted extension of the method for the preparation of trifluoromethyl derivatives of heptafluoroquinoline resulted in the substitution of up to four groups (as determined by mass spectrometry) but the resulting mixture of products, containing at least eight components, was too complex to be a routine preparative route and so separation was not attempted. Presumably substitution took place readily in the carbocyclic ring.



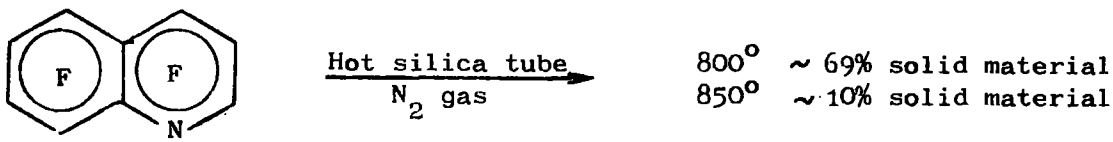
n = up to 4

G. Attempted pyrolysis of heptafluoroquinoline

Recent work on the pyrolysis of various hydrocarbon compounds has shown that quinoline and isoquinoline are interconvertable to a small extent at high temperatures.[120,121]

Because of the current interest in the interconversions of polyfluoro-heterocyclic compounds by pyrolysis[122,123] and photolysis[124] and also because of the often higher stability of the perfluorinated compounds compared with the hydrocompounds the pyrolysis was repeated with perfluoroquinoline.

Chromatographic analysis of the solid products from the pyrolysis over silica at elevated temperatures showed the product to be mainly starting material but with a small amount (5-10%) of a second compound with retention



time on two different stationary phases equal to that of heptafluoroisoquinoline. Attempted preparative scale thick layer chromatography and vapour phase chromatography did not result in sufficient material for characterisation.

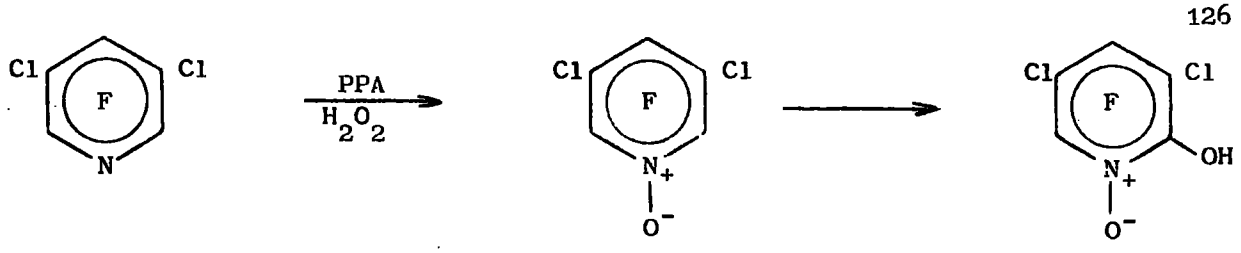
The attempted pyrolysis of heptafluoroisoquinoline by the same procedure gave, at 750°C, 50% of solid material containing ~5% of a material whose retention time was coincident with heptafluoroquinoline although again there was insufficient material for characterisation.

H. Attempted preparation of N-oxides of heptafluoroquinoline

Since the previous unsuccessful attempts at the preparation of N-oxides of heptafluoroquinoline[52] with peroxytrifluoroacetic acid, substantial work has been done on the development of new reagent systems[125,126] for the preparation of N-oxides of weakly basic polyhalogenated species.

In particular, mixtures of 90% hydrogen peroxide in glacial acetic acid and concentrated sulphuric acid and also 90% hydrogen peroxide in polyphosphoric acid (PPA) have been found to be suitable but the application of these reagent systems to heptafluoroquinoline resulted only in the formation of products of hydrolysis.

In view of the fact that 3,5-dichlorotrifluoropyridine was successfully converted to its N-oxide (but was subsequently converted to the 2-hydroxy compound during the work up procedure), the failure to prepare the N-oxide of the stronger base, heptafluoroquinoline, must be ascribed to adverse steric effects from the 8-position or to the rapid formation of a hydroxy compound which may form an N-oxide less readily.



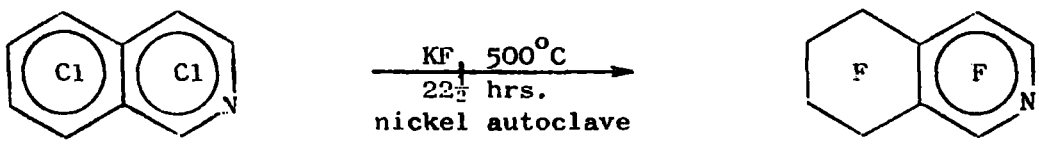
126

CHAPTER 5

The Preparation and Nucleophilic Substitution of perfluoro(5,6,7,8-tetrahydroquinoline)

Introduction

During the preparation of heptafluoroisoquinoline by halogen exchange between heptachloroisoquinoline and potassium fluoride in an autoclave, attempts to reduce the amount of remaining monochlorohexafluoroisoquinoline by increasing the reaction temperature above the normal 420°C had not been successful. Instead they indicated an increase in the proportion of another, more volatile, component of the mixture rather than a decrease in the amount of unchanged monochlorohexafluoroquinoline.[117] At 80°C above the normal preparative temperature this compound was a substantial proportion (~70%) of the product and was isolated and identified as perfluoro(5,6,7,8-tetrahydroisoquinoline)[117] (58).



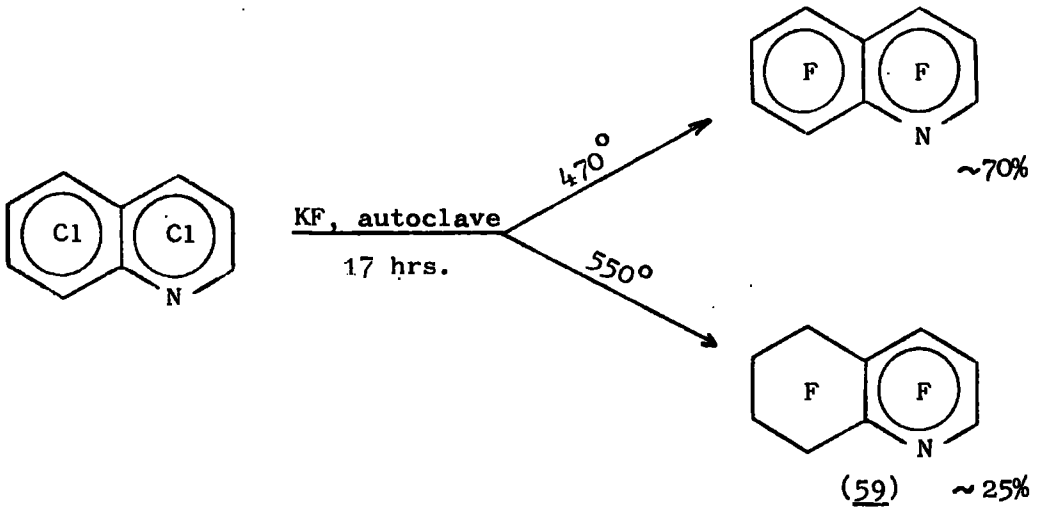
(58)

The present work set out to see if a similar reaction occurred in the preparation of heptafluoroquinoline and, if so, to briefly investigate the mechanism of its formation and its reactivity to nucleophilic attack.

A. Preparation

The preparation of heptafluoroquinoline by halide exchange of heptachloroquinoline with potassium fluoride in an autoclave was repeated and a component of higher volatility than heptafluoroquinoline was present to a small extent in the reaction products. As the temperature of the exchange was increased so the proportion of this product increased until, at about 550°C, it was the

major product of the reaction. Atmospheric pressure distillation of the combined products afforded a pure sample of a clear dense liquid which was identified as perfluoro(5,6,7,8-tetrahydroquinoline), (59).



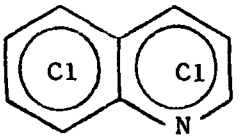
B. Mechanism of formation

1. Exploratory reactions

One of the more likely routes to the saturation of the carbocyclic ring is by radical addition across the double bonds of the carbocyclic ring and subsequent displacement by fluoride ion if necessary to give the fully fluorinated compound. The radical addition of fluorine directly, because of its highly exothermic and generally destructive nature, does not appear to be a route that could account for the formation of an overall 25% of product. The occurrence of free chlorine in the pyrolysis products of polychlorinated compounds has previously been noticed.[86] Addition of chlorine radicals to heptachloroquinoline, heptafluoroquinoline or partially fluorinated compounds may be taking place with subsequent halogen exchange.

The first reactions to test this hypothesis were to seal two equivalents of chlorine into the autoclave with the heptachloroquinoline and potassium fluoride. This was conveniently done by sealing the chlorine into a small glass ampoule and allowing this to rupture under increasing pressure as the

autoclave was heated. Unfortunately no volatile products could be isolated by vacuum transfer from the hot autoclave.

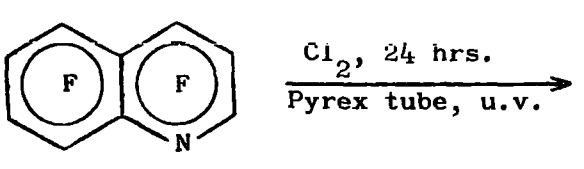


+ Cl_2 $\xrightarrow[470^{\circ},\ 17\frac{1}{2}\text{ hrs.}]{\text{KF}}$ No volatile products

nickel autoclave

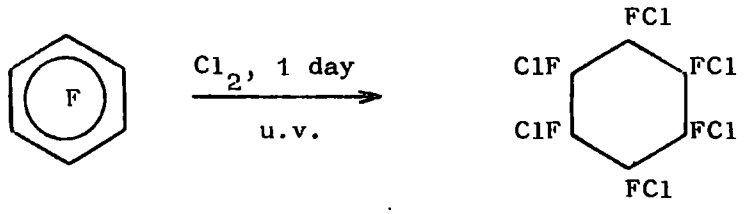
This may be due to three possibilities. The first is that the autoclave leaked in each case. Attack of the copper washer by the chlorine was apparent but from the observation that the hot autoclave was still capable of supporting a vacuum, this did not seem likely. A second possibility was that the glass was attacked by the potassium fluoride giving off hydrogen fluoride which destructively attacked the heptachloroquinoline/heptafluoroquinoline. The final possibility is that the chlorine added to the heptachloroquinoline forming a polychlorinated compound that either broke down readily at the temperature of the reaction or did not exchange with the potassium fluoride to give volatile products. Attempted free radical chlorination of heptachloroquinoline by chlorine initiated by ultraviolet light did not take place in two days either with carbon tetrachloride as solvent or without solvent.

That radical attack on heptafluoroquinoline by chlorine could take place was convincingly proved by the observation that ultraviolet light-initiated attack of a slight excess of chlorine on heptafluoroquinoline sealed in a Pyrex tube readily gave a virtually quantitative yield of a compound of formula $C_9NF_7Cl_4$ identified as 5,6,7,8-tetrachloroheptafluoroquinoline, (60).



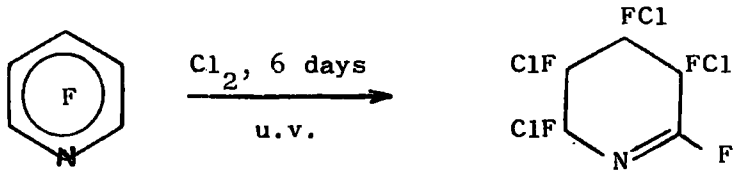
(60)

In general free radical attack on the double bond of a fluorocarbon olefin proceeds smoothly and likewise free radical addition of chlorine to hexafluorobenzene[127] and pentafluoropyridine[128] have been demonstrated.



127

58%



128

99%

The partial chlorination of heptafluoroquinoline giving 5,6,7,8-tetrachloroheptafluoroquinoline in quantitative yields after only one day can be compared with the ease of chlorination of hexafluorobenzene and the extended irradiation required for the chlorination of pentafluoropyridine.

Reaction between this product and potassium fluoride in an autoclave at 470° for 17 hrs., surprisingly gave back mainly heptafluoroquinoline and the chromatographic trace of the products was virtually the same as from the standard preparation of heptafluoroquinoline at that temperature (except no monochlorohexafluoroquinolines). A repeat reaction under much milder conditions (400°, 3 hrs.) still gave mainly heptafluoroquinoline but with a little more of a compound with the same retention time as perfluoro(5,6,7,8-tetrahydroquinoline). This indicated that dechlorination took place rapidly in the clean autoclave.

Thus the mechanism of formation has to be consistent with the following observations.

(i) The proportion of perfluoro(5,6,7,8-tetrahydroquinoline) in the product from reactions of heptachloroquinoline with potassium fluoride increases with increase in temperature,

(ii) 5,6,7,8-tetrachloroheptafluoroquinoline rapidly dechlorinates in a clean autoclave at 400°C and above,

(iii) radical attack of chlorine occurs readily on the carbocyclic ring of heptafluoroquinoline,

(iv) heptafluoroquinoline and perfluoro(5,6,7,8-tetrahydroquinoline) are the only major products from the halogen exchange reactions with heptachloroquinoline,

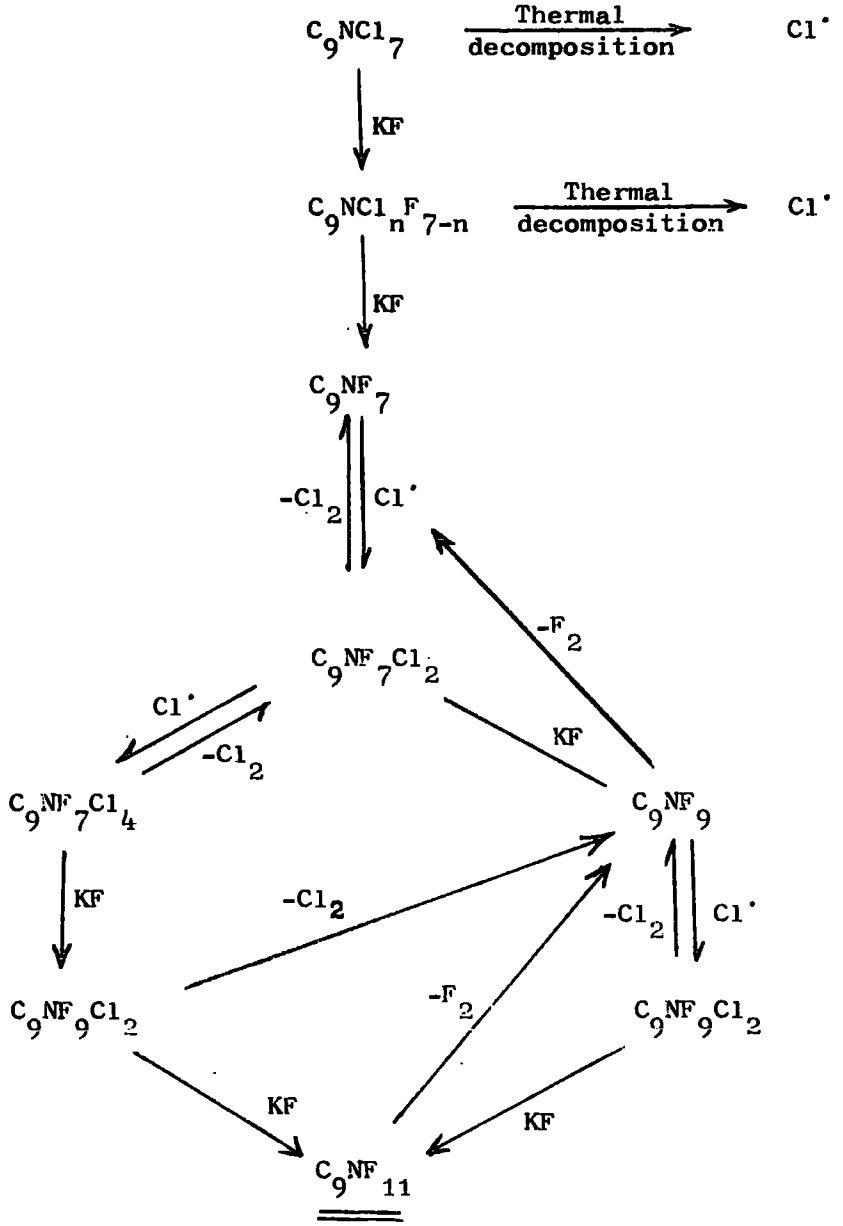
(v) the overall yield of the reaction falls with increase in temperature.

2. Tentative mechanism

On the basis of the observations the following is suggested as the route to the perfluoro(5,6,7,8-tetrahydroquinoline). Thermal breakdown of either heptachloroquinoline or the products of partial exchange with potassium fluoride gives rise to the formation of chlorine atoms. These readily attack the carbocyclic ring of heptafluoroquinoline (or its partially fluorinated analogues) to give a chlorine containing compound which may either add more chlorine to form eventually $C_9NF_7Cl_4$ or exchange with the potassium fluoride to form C_9NF_9. This could in turn be attacked by chlorine and exchange of either of these with potassium fluoride would form the desired product. Thermal dechlorinations and defluorinations would be taking place at the same time and so the whole process would be an equilibrium between all the reactions. An increase in temperature would increase the rate of the dechlorinations and defluorinations but may also increase the rate of halogen exchange and the rate of formation of chlorine atoms. From the observation that the product contains very little, if

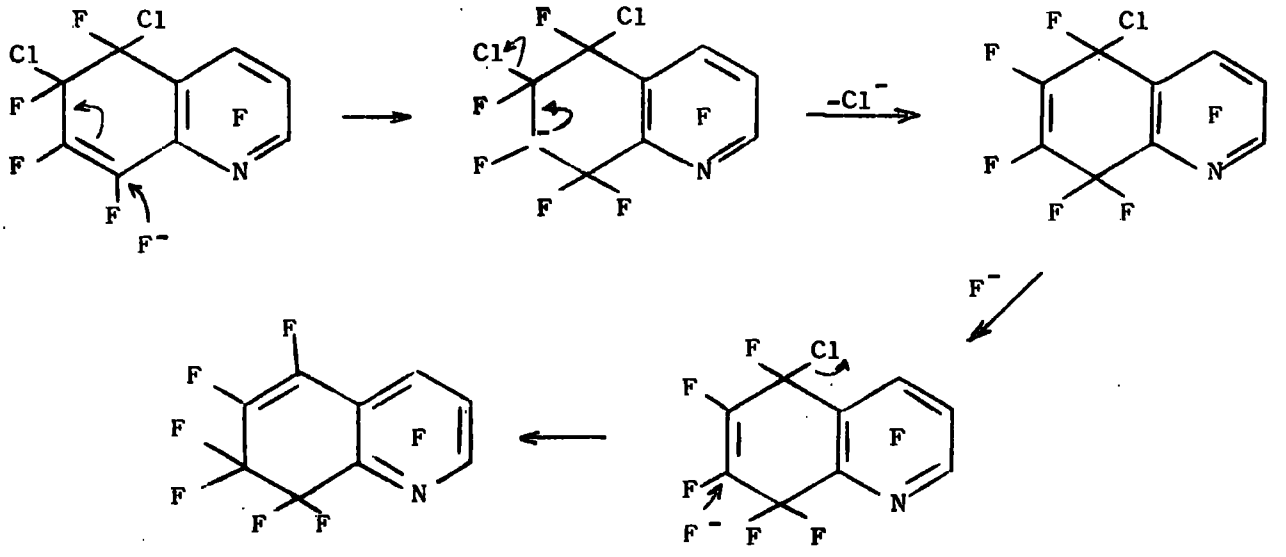
any, product of the general formula C_9NX_9 (X = mixture of Cl andF) then this product must be either rapidly converted to the compound of higher fluorination or chlorination state and/or dechlorinated or defluorinated rapidly. The general overall scheme as applied to heptafluoroquinoline only is outlined in Figure 8. Because of the large excess of potassium fluoride, halogen exchanges will be effectively irreversible.

FIGURE 8



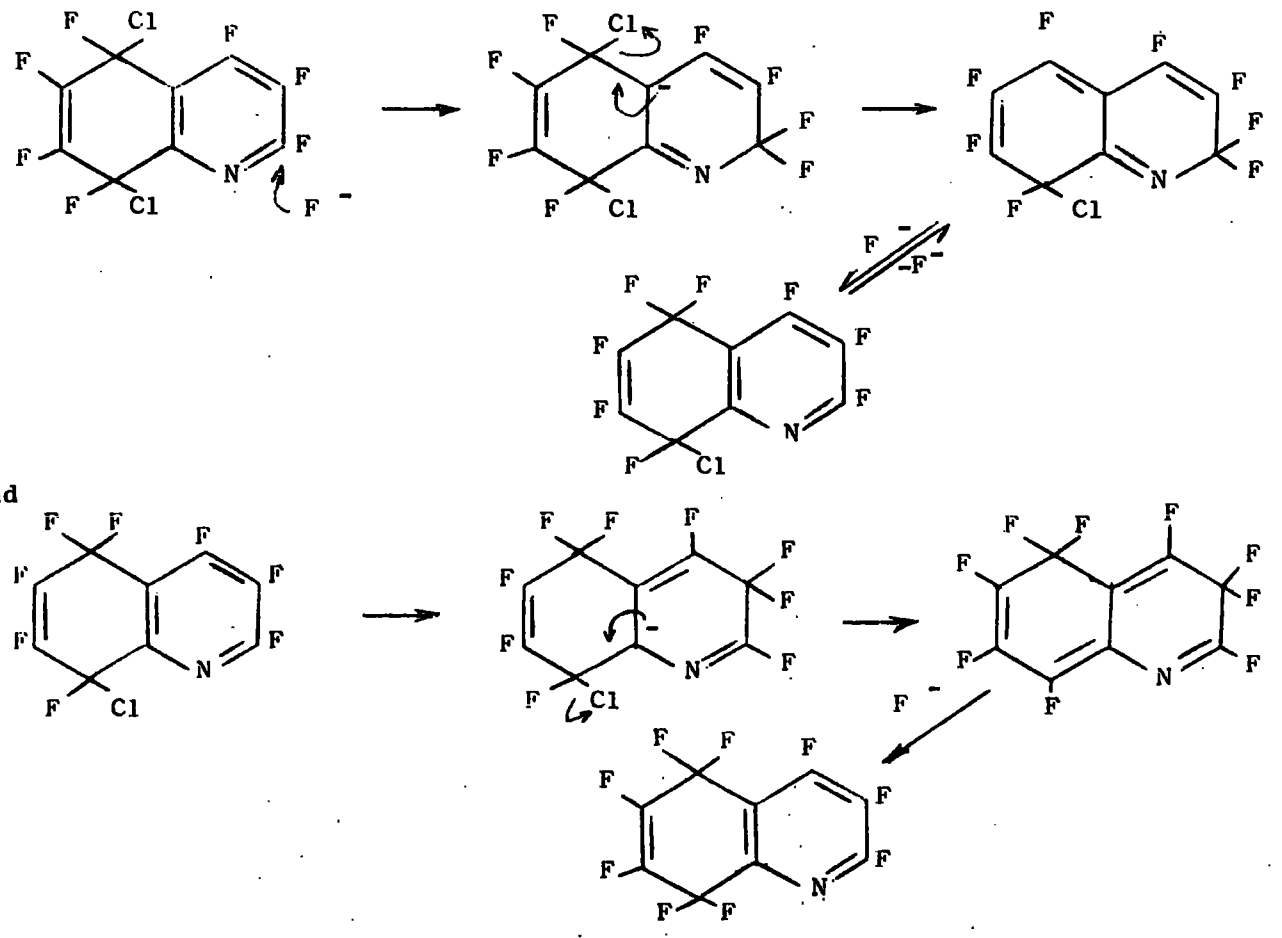
The mechanism of possible halogen displacement in the partially chlorinated product can readily be envisaged as either an S_N2' type mechanism with migration of the double bond (Scheme 1)

Scheme 1

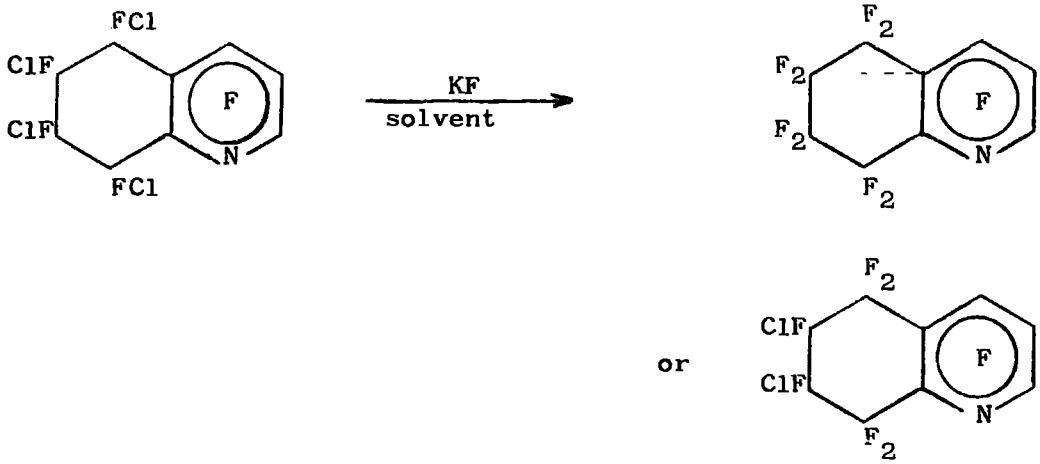


or alternatively by the recently proposed[129-131] pseudo-S_N2' process if the chlorine atoms are in the 5- or 8-positions (Scheme 2).

Scheme 2



This type of mechanism can also account for the displacement of halogen from the 5- and 8-positions even if the carbocyclic ring is saturated. Displacement of chlorine atoms from the 6- and 7-positions when the carbocyclic ring is saturated cannot be accounted for by either of these processes and may be by direct nucleophilic substitution. Experiments that are necessary for the further discussion of the mechanism are given below.



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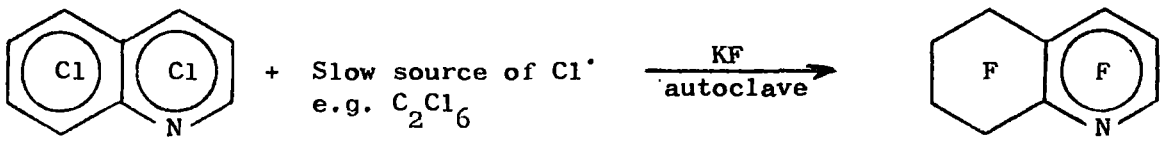


C. ^{19}F N.m.r. spectra

1. Perfluoro(5,6,7,8-tetrahydroquinoline)

The ^{19}F n.m.r. spectrum of perfluoro(5,6,7,8-tetrahydroquinoline) was readily partly assigned from peak area measurements and from comparison with the spectra of pentafluoropyridine and heptafluoroquinoline, Table 22.

The spectrum consisted of seven peaks, four being each twice the intensity of the remaining three. The peaks of intensity corresponding to single fluorines were assigned from their widely spaced positions, the lowfield peak

TABLE 22

^{19}F Chemical shifts of some perfluorinated heterocyclic compounds

	2-fluorine	3-fluorine	4-fluorine
Pentafluoropyridine[132]	88·1	162·6	134·5
Heptafluoroquinoline[40]	75·4	163·6	127·4
Perfluoro(5,6,7,8-tetrahydroquinoline)	72·9	155·8	118·2

Shifts relative to $CFCl_3$

at 72·9 p.p.m., partly broadened from proximity to the nitrogen, was assigned to the 2-fluorine, the peak at 118·2 p.p.m. to the 4-fluorine and the remaining high field peak at 155·8 p.p.m. was assigned to the 3-fluorine. The coupling constants were $J_{2,3}$ = 23 Hz., $J_{2,4}$ = 30·5 Hz., $J_{3,4}$ = 16 Hz. The 3-fluorine also coupled to two other fluorines, J = 3 Hz. and the 4-fluorine coupled to (presumably) the 5-fluorines with a coupling of about 17 Hz.

The four peaks remaining, at 108·8, 113·1, 136·2 and 137·0 p.p.m., were all of equal intensity corresponding to two fluorines and so were assigned to the carbocyclic ring. The splitting of the peaks were all very complex because of the strong couplings between all the fluorine atoms.

2. 5,6,7,8-Tetrachloroheptafluoroquinoline

The ^{19}F n.m.r. spectrum of 5,6,7,8-tetrachloroheptafluoroquinoline, (60), was very complex presumably because of the large number of stereo isomers present. Comparison of the spectrum with perfluoro-5,6,7,8-tetrahydroquinoline allowed two of the resonances to be assigned. The resonance at low field (75·2 p.p.m.) integrating to one fluorine was assigned to the 2-fluorine, the complex band from 85·5 to 101 p.p.m. integrating to two fluorines was assigned

to carbocyclic ring fluorines, a second very complex band from 109 to 125·5 p.p.m. integrating to three fluorines was assigned to the remaining two carbocyclic fluorine atoms and also the 4-fluorine. The remaining resonance at high field (156·2 p.p.m.) integrating to a single fluorine was assigned to the 3-fluorine.

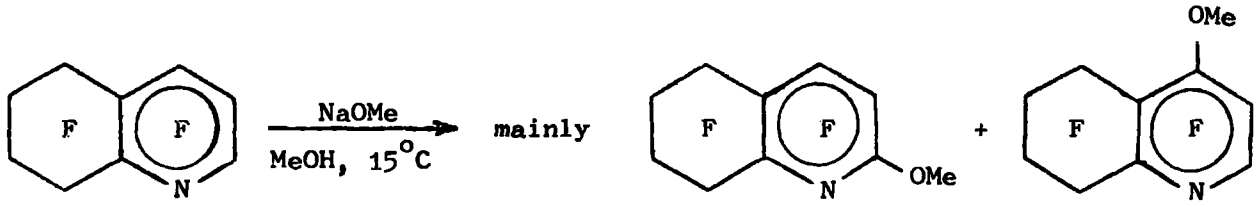
D. Reactions of perfluoro(5,6,7,8-tetrahydroquinoline)

Some preliminary simple reactions on perfluoro(5,6,7,8-tetrahydroquinoline) were carried-out and are discussed below. They are conveniently divided into nucleophilic substitution reactions and other reactions.

1. Nucleophilic substitution

(a) With sodium methoxide

One equivalent of sodium methoxide in methanol reacted rapidly with perfluoro(5,6,7,8-tetrahydroquinoline) (59) to give a mixture of starting material, two monoethers and a small amount of a diether. The two monoethers isolated from the mixture by vapour phase chromatography and readily identified from their ^{19}F n.m.r. spectra as 2- and 4-substituted products. The 2-substituted product (61) was present as about 75% of the monoether mixture,

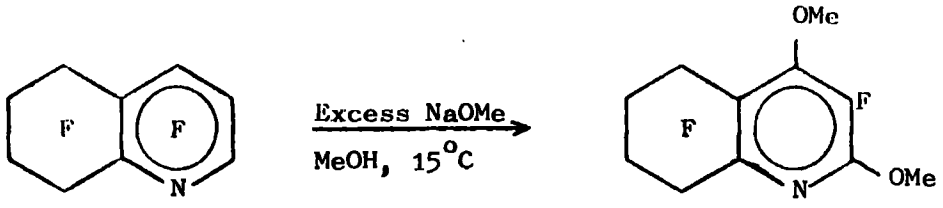


(59) (61) (62)

(quantitative gas chromatography).

Reaction between an excess of sodium methoxide in methanol at room temperature on either (59) or a mixture of the two monosubstituted products gave a single dimethoxylated product (63). This dimethoxylated product was readily identified from its ^{19}F n.m.r. spectrum to be 2,4-dimethoxy,perfluoro-

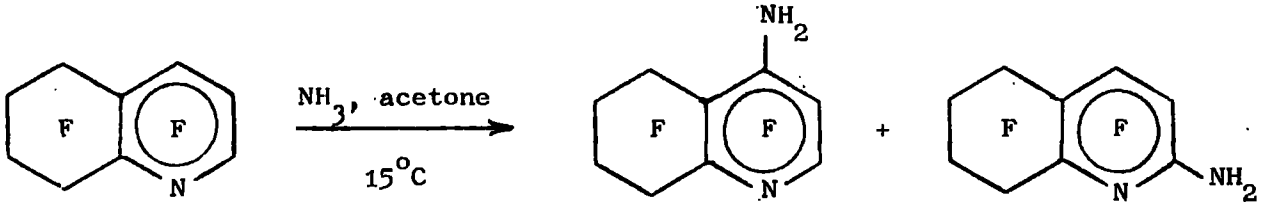
(5,6,7,8-tetrahydroquinoline).



(59) (63)

(b) With ammonia

Reaction between (59) and excess ammonia in aqueous acetone rapidly gave a mixture of two similar products. They were separated with difficulty on preparative scale vapour phase chromatography and identified from their ^{19}F n.m.r. spectra to be the 2- and 4-amino derivatives. Analysis of the original mixture of products by quantitative gas chromatography showed them to be in approximately equal proportions.



(59)

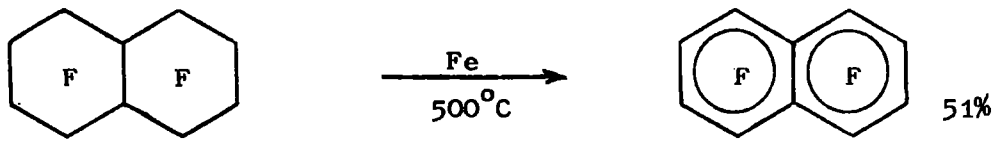
(c) Competative reactions

Reaction between a deficiency of sodium methoxide in methanol and an equimolar solution of heptafluoroquinoline and perfluoro(5,6,7,8-tetrahydroquinoline) in methanol at room temperature and subsequent analysis of the mixture of products by quantitative gas chromatography showed that perfluoro-(5,6,7,8-tetrahydroquinoline) was the more reactive substrate but peak overlap between the products of its methoxylation and heptafluoroquinoline prevented a ratio being calculated.

2. Other reactions

(a) Defluorination

The introduction of unsaturation or the aromatisation of highly fluorinated cyclic compounds has been extensively studied as a route to some perfluoroaromatic compounds.



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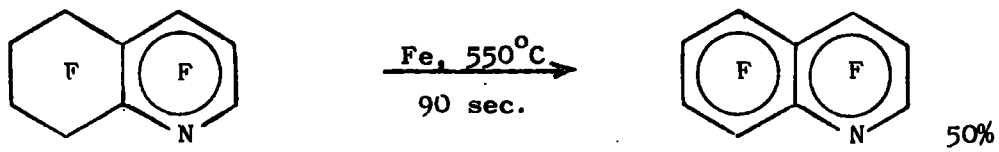
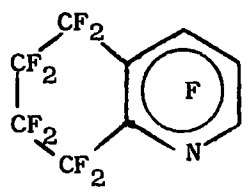
In line with the results of this work perfluoro(5,6,7,8-tetrahydroquinoline) is readily defluorinated by hot iron to give heptafluoroquinoline.



3. Rationalisation of orientation of nucleophilic attack

If perfluoro(5,6,7,8-tetrahydroquinoline) is considered to be a di-alkylated derivative of pentafluoropyridine (64), then the orientation of



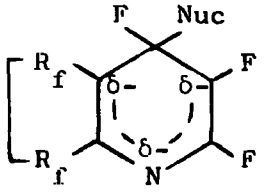
(64)

substitution can be rationalised in terms of the effects of two perfluoroalkyl groups on the substitution in pentafluoropyridine.

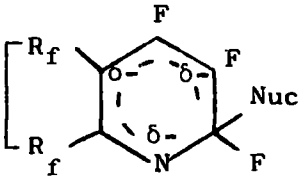
The perfluoroalkyl groups electron-withdrawing capacity will generally activate the system to nucleophilic attack but in particular in the positions para and ortho to the perfluoroalkyl group as found by the increased rate of

attack of methoxide on (64) compared with heptafluoroquinoline which is in turn more reactive than pentafluoropyridine.

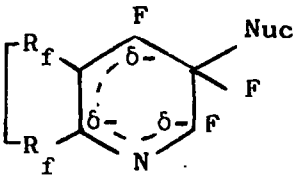
The substitution at the 4-position (65) is largely stabilised by the para aza group but also by the ortho perfluoroalkyl group (5-position). Substitution



(65)



(66)



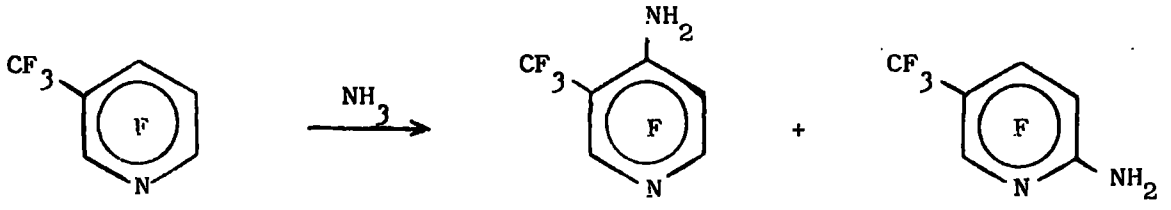
(67)

at the 4-position may also be subject to steric hindrance from the 5-fluorines.

Substitution at the 2-position (66) will be largely stabilised by the para perfluoroalkyl group (5-position) and slightly by the ortho aza centre.

Substitution at the 3-position (67) would be stabilised by the para perfluoroalkyl group at the 6-position but destabilised by two ortho fluorine atoms. Substitution at this position is not observed.

Activation of positions para to a perfluoroalkyl group on pentafluoropyridine has previously been observed in the reaction of 3-trifluoromethyltetrafluoropyridine where attack by ammonia occurs both at the 4- and 6-positions.[119]



119

In the absence of further evidence the formation of proportions of monomethoxylated and monoamine products that are closely similar to the proportions found in the reactions of heptafluoroquinoline must be considered fortuitous.

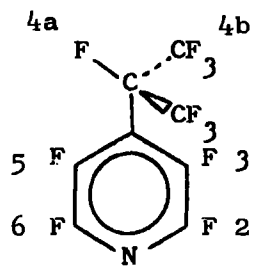
CHAPTER 6

A Rationalisation of the Temperature Dependance of the ^{19}F N.m.r. Spectra of Some Perfluoroalkylheterocyclic Compounds

Introduction

The first attempts at the analysis of the high resolution ^{19}F n.m.r. spectra of some perfluoro-isopropyl- and -sec-butyl-benzenes and -pyridines had shown that the peaks do not have the symmetry expected for the first order coupling within the molecule[104] and there are more ring fluorine resonances than anticipated for the compounds. The spectra were then found to be particularly temperature dependant and it was proposed that there was a large energy barrier to rotation of the perfluoroalkyl group.[40,104,108,109]

The ^{19}F n.m.r. spectrum of perfluoro(4-isopropylpyridine) is temperature dependant. At ambient temperatures the spectrum is broad and poorly resolved but at low temperatures (-30°C) it sharpens and can be explained by restriction of rotation about the alkyl-aryl bond and the freezing out of conformer (68).

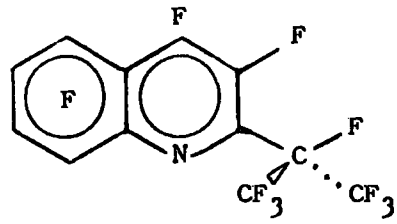


(68)

The ring fluorines are all non-equivalent and the 4a-fluorine couples strongly with the 5-ring fluorine but not with the 3-fluorine. Likewise the 4b-fluorines couple strongly with the 3-fluorine but not with the 5-fluorine. The two CF_3 groups are equivalent and so must be symmetrically placed with respect to the plane of the ring and the reason for this will be discussed later. If

the temperature is raised (ca. 160°C) the spectrum again becomes sharp and is consistent with there being rapid rotation about the alkyl-aryl bond. The 3- and 5-fluorines are equivalent, as are the 2- and 6-fluorines, and the 4a-fluorine couples equally with the 3- and 5-fluorines.

A perfluoroisopropyl group adjacent to a ring nitrogen appears to be in a preferred conformation[109] with the tertiary fluorine adjacent to the ring fluorine e.g. perfluoro(2-isopropylquinoline), (69).



(69)

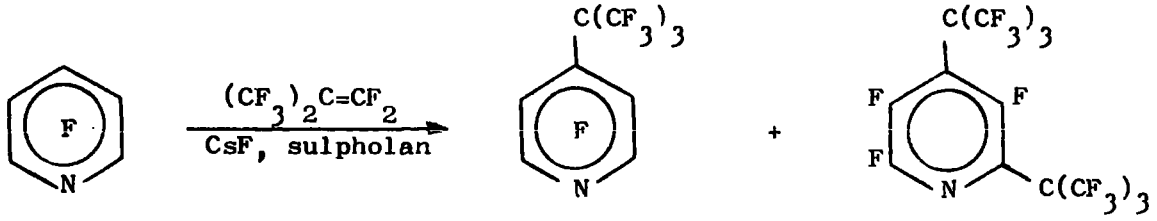
In perfluoro(2,6-di-isopropylquinoline) and some non-symmetrical perfluoro-isopropylpyridines distinguishable conformers are frozen out at low temperature but so far no explanation has been advanced to account for the relative proportions of the conformers.[40]

In order to increase the understanding of the barrier to rotation some perfluoro-t-butyl-pyridines and -quinolines were synthesised and a study made of the variation of their ^{19}F n.m.r. spectra with temperature. In the perfluoroisopropyl compounds the different conformers may have different energies and this additional factor complicates the study of the rotation. With the highly symmetrical perfluoro-t-butyl group the freezing out of the conformers will be indicated by the non-equivalence of the CF_3-groups but the conformers will be identical and so of equal energy. Thus it was envisaged that the study would be only of the barrier to rotation and the factors affecting it.

A. Synthesis of perfluoro-t-butylpyridines

Reaction between perfluoroisobutene, caesium fluoride and pentafluoropyridine in sulpholan at room temperature gave a mixture of compounds. The product in larger amount was separated by preparative scale vapour phase chromatography and readily identified from its ^{19}F n.m.r. spectrum as perfluoro(4-t-butylpyridine). The spectrum consisted of three groups of resonances integrating in the ratio 9:2:2. The perfluoro-t-butyl resonance, readily identified from its intensity, was a sharp triplet indicating coupling to two ortho fluorines. The lowfield resonance (89·6 p.p.m.) of the ring fluorines (assigned to the 2- and 6-fluorines) was complex but well resolved. The higher field resonance (129·8 p.p.m.) of the 3- and 5-ring fluorines, was likewise well resolved but of much greater overall width showing the coupling to the perfluoro-t-butyl group.

A small amount of a second product containing two perfluoro-t-butyl groups was isolated. Although there was insufficient material for all the ring fluorines to be apparent, the ^{19}F n.m.r. spectrum was consistent with the compound being perfluoro(2,4-di-t-butylquinoline). One of the t-butyl resonances was a doublet of doublets i.e. in the 4-position and the other a doublet i.e. ortho to only one ring fluorine in the 2-position. The ring fluorine apparent at the lowfield position (83·5 p.p.m.) was assigned to the 6-fluorine and was a broad doublet of doublets. The other two ring fluorines (3- and 5-) would have been too broad to observe in the weak sample.



B. Variable temperature ^{19}F n.m.r. spectra

1. Perfluoro-t-butyl groups

The insolubility of perfluoro(2,6-di-t-butylquinoline) prevented the temperature dependance of the ^{19}F n.m.r. spectrum from being studied below 40°C. At that temperature the perfluoro-t-butyl group in the 2-position was a sharp doublet and the group in the 6-position a sharp triplet, both consistent with there being little or no hindrance to rotation of the perfluoro-t-butyl groups.

Perfluoro(2-t-butylquinoline) was appreciably soluble in ether and in acetone and the ^{19}F n.m.r. spectrum was recorded from +40°C down to -100°C. Surprisingly, there was no apparent change in the spectrum of the perfluoro-t-butyl group which remain a sharp doublet ($J_{2b,3}$ = 20 Hz.) and there was no significant change in the spectrum of the ring fluorines.

The ^{19}F n.m.r. spectrum of perfluoro(4-t-butylpyridine) was recorded from +40°C to -100°C and the spectrum of perfluoro(2,4-di-t-butylpyridine) recorded between +40° and -80°C and in each case no change in the spectrum of the perfluoro-t-butyl resonances and the observable ring fluorine resonances could be detected. The apparent absence of appreciable barriers to rotation of a perfluoro-t-butyl group when flanked by one or two ring fluorines was a surprising result and is discussed later.

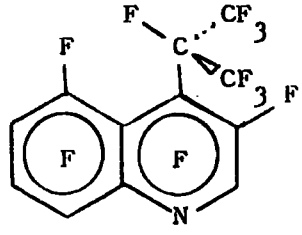
2. Perfluoroethyl groups

Because of the apparent absence of barriers to rotation of the perfluoro-t-butyl groups the variable temperature ^{19}F n.m.r. spectra of some perfluoroethylheterocyclic compounds (with only one bulky $-CF_3$ group in the alkyl moiety) were studied. Perfluoro(4-ethylpyridine), perfluoro(2,4-diethylpyridine), 4-pentafluoroethyl,2-methoxytrifluoropyridine and perfluoro(4-ethylpyridazine) were all studied from +80°C to -100°C either neat (for higher temperatures) or

in acetone (for temperatures below their melting points) but no change in the ^{19}F n.m.r. spectra of either the pentafluoroethyl groups or the aromatic ring fluorines could be detected in any of the compounds studied.

3. Perfluoroisopropyl groups

The greatest contribution to the barrier to rotation of a perfluoroisopropyl group comes from interaction of ring fluorines with the alkyl $-CF_3$ groups. This is further underlined by the orientation assumed by a perfluoroisopropyl group in the 4-position of heptafluoroquinoline, (70).[40] The barrier to rotation is even larger than that experienced by a perfluoroisopropyl group in the 4-position of a pentafluoropyridine derivative and is caused by interaction with the more prominent peri-fluorine and so the CF_3-groups are orientated away from the peri-fluorine and are equivalent.



(70)

C. Rationalisation of spectral changes

1. Spectral changes

Summarising the spectral change in general terms, the perfluoro-t-butyl group appears to experience only a small barrier to rotation both when flanked by two ring fluoring atoms and also when ortho to an aza group and so flanked by only one ring fluorine.

The perfluoroisopropyl group, when flanked by two ring fluorines, appears to experience a barrier to rotation that can be overcome at slightly elevated

temperatures. When the perfluoroisopropyl group is flanked by only one ring fluorine only the conformer with the $-CF_3$ groups away from the ring fluorine is appreciably populated.

No changes in the ^{19}F n.m.r. spectra of pentafluoroethyl substituted compounds could be detected between $+80^{\circ}C$ and $-100^{\circ}C$.

2. Consideration of the relative energies of the energy maxima and minima of rotation

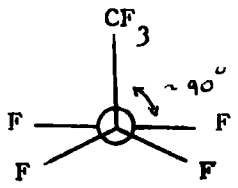
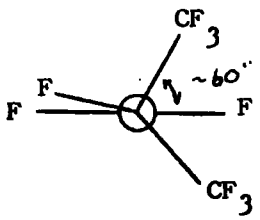
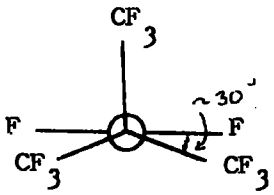
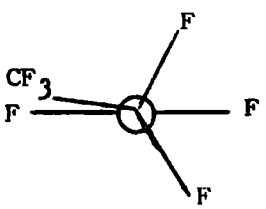
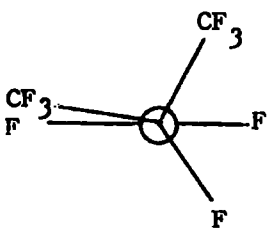
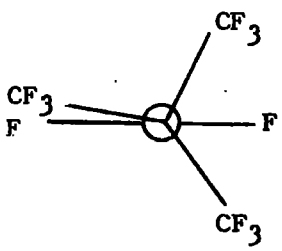
The differences in energy between various maxima and minima arise because of the variation of repulsive energies between the components of the molecule with varying internuclear distance. Over the interatomic distances being considered the internuclear repulsion forces can be assumed to be some inverse function of distance and it is qualitatively apparent that the repulsive energy increases very rapidly with decreasing atomic distance,[133-136] particularly at small separations.

(a) Perfluoroalkyl group with two ortho ring fluorine atoms

The relative energies of the various maxima and minima can now be qualitatively estimated. As the main contribution to the barrier to rotation is interaction between the ring fluorine and the alkyl-CF_3 group with the ring fluorine-tertiary fluorine interaction only of minor importance, then the energy minima are most likely to be the conformations with minimum ring fluorine $-CF_3$ interaction. Similarly the energy maxima are most likely to be the conformations with maximum ring fluorine $-CF_3$ interaction. The conformers are drawn out in Newman projection (Figure 9).

The energy of a particular conformer will be largely controlled by the proximity of the $-CF_3$ groups to the ring fluorines, the nearer the $-CF_3$ group is to the ring fluorine the higher will be energy of that conformation. Thus comparing (71), (72) and (73) the energy of (73) with two $-CF_3$ groups at 30°

FIGURE 9

	Perfluoroethyl group	Perfluoroisopropyl group	Perfluoro-t-butyl group
Energy Minima			
	(71)	(72)	(73)
Energy Maxima			
	(74)	(75)	(76)

to the ring fluorine atoms will be much higher than (72) with the two $-CF_3$ groups at 60° to the ring fluorines and this in turn will be of higher energy than (71) with only one $-CF_3$ group at 90° to both ring fluorine atoms. In the conformations of maximum energy ((74), (75) and (76)) the eclipsing of the CF_3 group and a ring fluorine will be the major source of steric repulsion but there will be significant steric repulsion between the remaining CF_3 groups and the ring fluorines. There are no CF_3 groups at 60° to the ring fluorine atoms in (74), one in (75) and two in (76) and so the increase in steric repulsion will be in that order.

Thus the order of the steric repulsive forces at both the minima and maxima energy conformations is:

perfluoroethyl < perfluoroisopropyl < perfluoro-t-butyl.

(b) Order of barrier heights

The barrier to rotation is clearly the difference between the energy maxima and minima. Assuming that the steric repulsions between the $-CF_3$ groups and the ring fluorines are the most significant forces, the difference in the energy minima of (71) and (73) is that caused by the replacement of two fluorine atoms at 30° with two $-CF_3$ groups. The difference in their energy maxima ((74), (76)) will be much less, being that caused by the replacement of fluorine by $-CF_3$ groups at 60° to the ring fluorines. Thus the difference in energy of maxima and minima will be much smaller for the perfluoro-t-butyl group ((73), (76)) than for the perfluoroethyl group ((71), (74)). The difference between the energy minima of (71) and (72) is not so readily estimated but can be approximated to the energy required to place a $-CF_3$ group at 60° to the ring fluorine plus the energy required to move a $-CF_3$ group from 90° to 60° to the ring fluorine. The change in the energy of the maxima (74) and (75) is caused by the replacement of fluorine by a $-CF_3$ group at 60° to the ring. Hence the difference in energy between (72) and (75) will probably be less than between (71) and (74) but not likely to be as small as between (73) and (76). Hence the order of barrier heights is most likely to be:

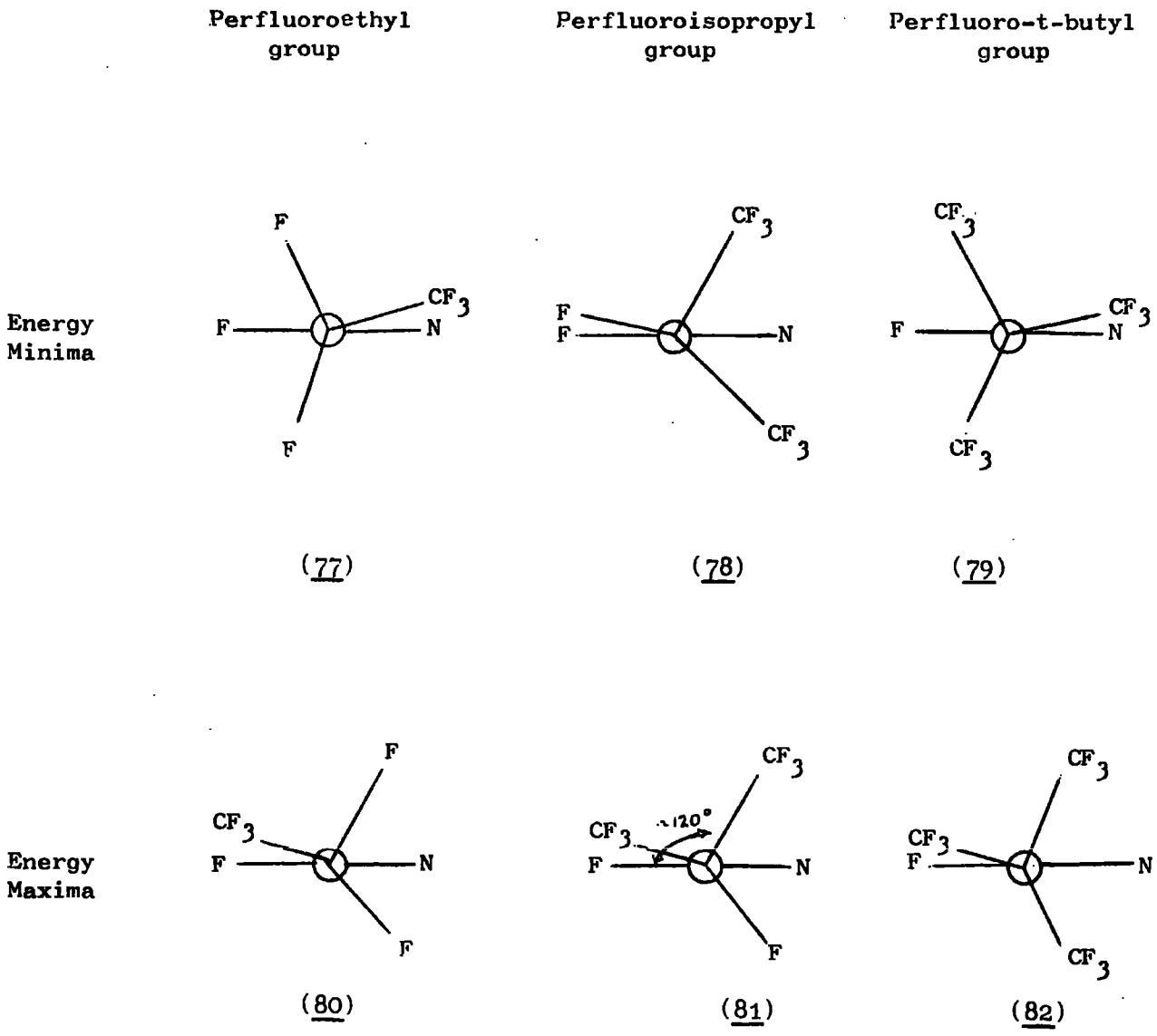
perfluoroethyl > perfluoroisopropyl > perfluoro-t-butyl.

The most bulky group (perfluoro-t-butyl) has the lowest barrier to rotation because of the strong interactions present in the preferred conformation.

(c) Perfluoroalkyl group with one ortho ring fluorine

When a perfluoroalkyl group has only one flanking fluorine (as in the 2-position of perfluoro-pyridine or -quinoline) the conformation adopted by a heptafluoroisopropyl group indicates that to a first approximation steric repulsion by the aza nitrogen is small compared with steric repulsion by a ring fluorine. The energy minima will be the states in which ring fluorine $-CF_3$ repulsions are minimised and likewise the maxima when the repulsions are maximised (Figure 10).

FIGURE 10



Assuming that the energy of the maxima and minima are controlled by the proximity of the $-CF_3$ groups to the ring fluorine atom, it is apparent that the order of energies of the maxima and of the minima is again:

perfluoroethyl < perfluoroisopropyl < perfluoro-t-butyl

(d) Order of barrier heights

Consideration of the differences in the energy maxima and minima leads to an estimate of the order of barrier heights. The difference in the energy of (77) and (78) is essentially that caused by the introduction of two $-CF_3$ groups at 120° to the ring fluorine atom. The difference in the energies of the energy maxima (80) and (81) is less, the introduction of only one $-CF_3$ group at 120° to the ring fluorine. Likewise the difference in energy of (78) and (79), the moving of the two $-CF_3$ groups from 120° to 60° to the ring fluorine may well be much larger than the difference between (81) and (82), the introduction of one $-CF_3$ group at 120° to the ring fluorine, because of the short effective range of the repulsive forces.

Thus the relative order of the barrier heights will probably be:

perfluoroethyl > perfluoroisopropyl > perfluoro-t-butyl

D. Observed behaviour

1. Perfluoroisopropyl group

The observed behaviour of the perfluoroisopropyl group when flanked by two ortho fluorine atoms gives a qualitative idea of the scale of the barriers discussed. This barrier is apparent at ambient temperatures on the n.m.r. timescale and can be overcome rapidly at elevated temperatures.

The fast rotation of a perfluoroisopropyl group at high temperatures and the slow rotation at low temperatures should be considered not as rates of

The barrier to rotation about the marked bond very clearly decreases with increasing size of the group X (Table 23) and this was attributed to the greater hindrance in the preferred conformation and so the smaller energy difference between energy maxima and minima.

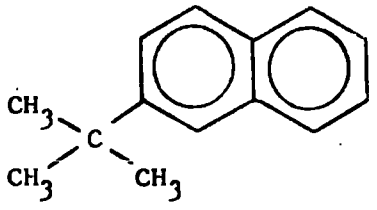
TABLE 23

Barriers to rotation about the sp^2-sp^3 bond of some 9-arylfluorenyl compounds[137]

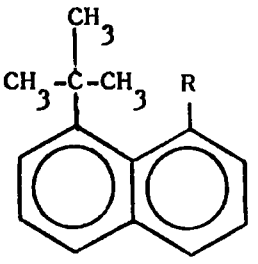
Substituent -X	Compound (87A) $\Delta G^{\ddagger}$	Compound (87B) $\Delta G^{\ddagger}$
H	> 25	20·6
OH	20·2	14·4
Cl	16·2	9·2

$\Delta G^{\ddagger}$ from coalescence data, in Kcal.mole^{-1}

Some recent work on the rotation of t-butyl groups in 1,8-di-t-butyl-naphthalenes[138] has shown that the barrier to rotation of a t-butyl group in environments such as (88) and (89) is too small to be measured by the n.m.r. method at readily available temperatures (down to -150°C).



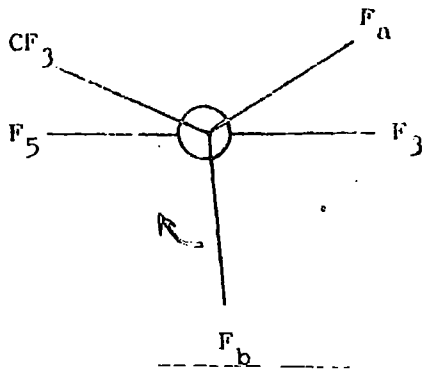
(88)



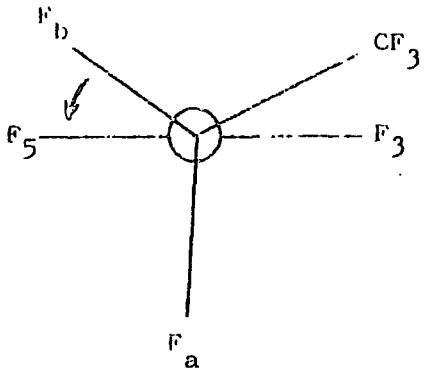
R = CH_3, H

(89)

In contrast the 1,8-diphenylnaphthalenes[138] are observed to have a high



(85)



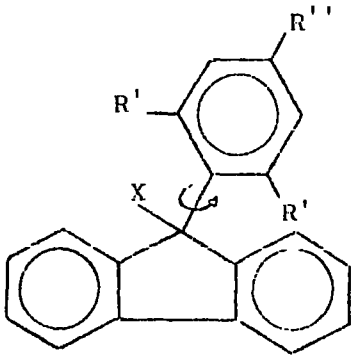
(86)

This means that the change in the ^{19}F n.m.r. spectrum on changing from infrequent to frequent crossing of the barrier may be insignificantly small.

3. Perfluoro-t-butyl group

The barrier to rotation of a perfluoro-t-butyl group is very low and this is a consequence of the steric interactions remaining in the preferred conformation rather than an unusually low maxima of the energy of rotation.

A previous particularly good example of the reduction in the barrier to rotation about an sp^2-sp^3 bond with increase in size of one of the substituents on the sp^3 carbon is shown by some work on various 9-aryl-fluorenyl compounds, (87).[137]



(87)

(87A) R' = CH_3, R'' = CH_3

(87B) R' = OCH_3, R'' = H

X = H, OH, Cl

The barrier to rotation about the marked bond very clearly decreases with increasing size of the group X (Table 23) and this was attributed to the greater hindrance in the preferred conformation and so the smaller energy difference between energy maxima and minima.

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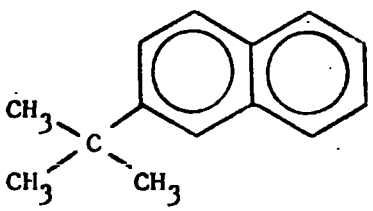

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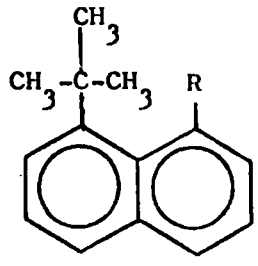


R = CH_3, H

(89)

In contrast the 1,8-diphenylnaphthalenes[138] are observed to have a high

barrier to rotation because the steric repulsions in the preferred conformation are low.

E. Relative proportions of rotational isomers

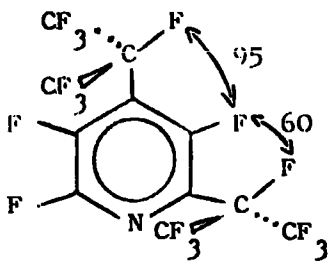
It is proposed that the detailed consideration of the relative energies in the preferred conformation may be extended to account for the relative proportions of conformers frozen out of perfluoro(2,4-di-isopropylpyridine), perfluoro(2,6-di-isopropylquinoline) and perfluoro(2,4,6-tri-isopropylquinoline). The ^{19}F n.m.r. spectrum of perfluoro(2,4,6-tri-sec.butylquinoline) is also discussed.

1. Perfluoro(2,4-di-isopropylpyridine)

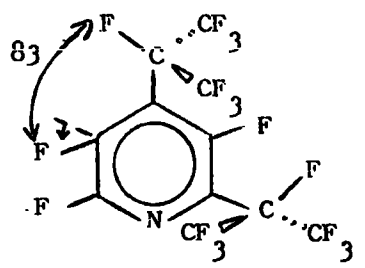
The introduction of a second perfluoroisopropyl group into the 2-position reduces the symmetry of the pyridine ring and accordingly two conformers are frozen out at low temperature in unequal proportions, indicating a difference in ground state energies.

The steric strain in the ground state may well cause a change in the geometry[135c] of the system and in particular a decrease in the angle between the fluorine ortho to the alkyl group and the heterocyclic ring (e.g. (91)) in order to decrease the steric repulsion. This decrease in the bond angle will be hindered by the buttressing effect of an adjacent bulky group. (The rate of racemisation of some diphenyl derivatives is uniformly and considerably decreased by substituents in the meta position).[139]

Consider the two conformers of perfluoro(2,4-di-isopropylpyridine)[109] (90) and (91).



(90)



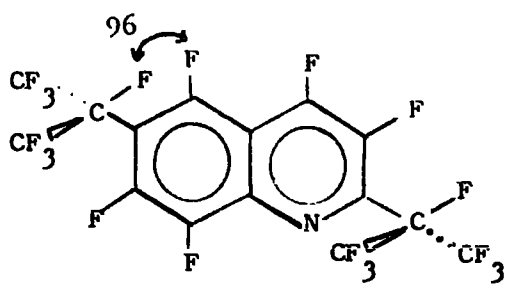
(91)

Coupling values in hertz, ±1 Hz.

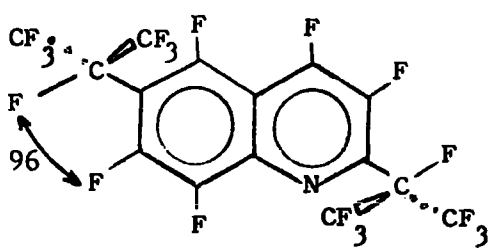
If it is assumed that the strong couplings through many bonds are largely 'through space' couplings and can be equated with close proximity of nucleii, then the significant difference between the coupling of 4a-fluorine to the 3-fluorine in (90) and 4a-fluorine to the 5-fluorine in (91) can be ascribed to the smaller internuclear distance in (90). The buttressing effect of the 2-perfluoroalkyl group prevents the 3-fluorine from moving away from the plane of rotation of the 4-heptafluoroisopropyl group. Thus there will be more steric repulsion between the 4a-fluorine and the 3-fluorine in (90) than between the 4a-fluorine and the 5-fluorine in (91). Because of the greater internuclear distance between the $-CF_3$ groups and the ring fluorine atoms the increase in repulsion between the 4b- and 3-fluorines in (91) compared with the 4b- and 5-fluorines in (90) caused by the buttressing of the 3-fluorine will not be large and so the total steric energy of (90) will be larger than (91). The relative population of rotamers frozen out is approximately 2:1, (91):(90).

2. Perfluoroisopropylquinolines

Consider now perfluoro(2,6-di-isopropylquinoline). At ambient temperatures the 2-group is apparently in fixed conformation[40] as expected but the 6-group is restricted in its rotation and at 0°C two rotamers are frozen out,[40] (92) and (93).



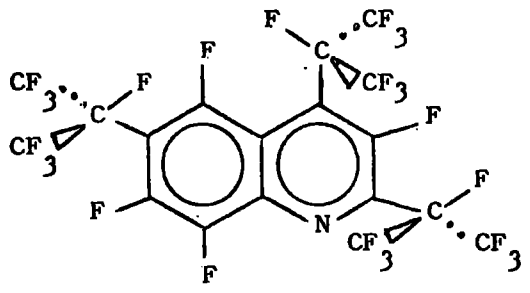
(92)



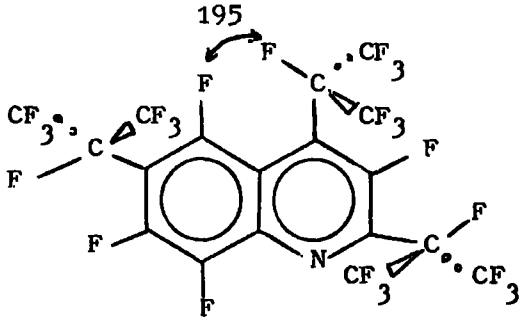
(93)

The coupling between the 6a- and the 5-fluorines in (92) is equal to the coupling between the 6a- and 7-fluorines in (93) so indicating that to a first approximation the internuclear distances are the same. So, as these two ring fluorines are in equivalent positions with respect to the rotation of the perfluoroisopropyl group, the conformers will have very similar repulsive energies and accordingly an approximately equal mixture[40] of the two is frozen out at 0°C

If a third perfluoroisopropyl group is substituted into the ring[40] at the 4-position strong buttressing of the 5-fluorine by the 4a-fluorine takes place, as evidenced by the very large coupling (195 Hz.), hence small internuclear distance. This may well move the 5-fluorine nearer to the plane of rotation of the 6-perfluoroisopropyl group. As the steric repulsive energy of an eclipsed 6a-fluorine and a ring fluorine will be increased more for a small decrease in internuclear distance than the repulsive energy between a more



(94)



(95)

remote CF_3-group and a ring fluorine, conformer (94) will be of higher energy than conformer (95). Accordingly (94) is not observed[40] at ambient temperatures and only at 80°C does the 6-perfluoroisopropyl group show signs of rotation. The increase in the barrier to rotation of (94) and (95) over that of (92) and (93) is in line with the 5-fluorine being forced nearer the plane of rotation or alternatively not being able to move away from a $-CF_3$ group of the perfluoro-

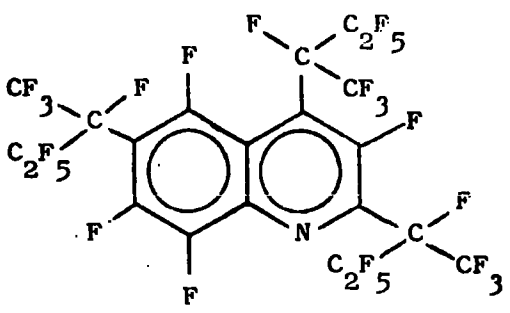
isopropyl group in the maximum energy configuration.

3. Perfluoro-sec-butylquinoline

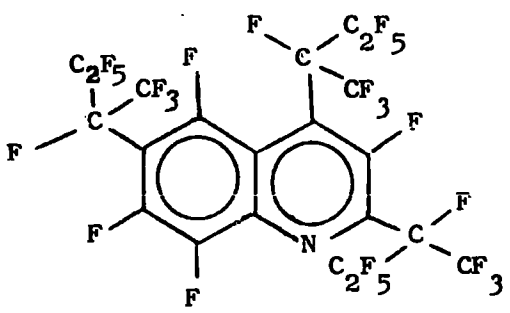
The ^{19}F n.m.r. spectrum of perfluoro(2,4-di-sec-butylquinoline) has been analysed (Chapter 4) and is consistent with the perfluoro-sec-butyl groups being in fixed conformations corresponding to those found for perfluoro(2,4-di-isopropylquinoline). Previous results with perfluoroisopropylbenzene and perfluoro-sec-butylbenzene have shown that the barrier to rotation of the butyl group is larger than that for the isopropyl group in the same environment.[104]

Analysis of the ^{19}F n.m.r. spectrum of the tri-substituted quinoline showed it to be perfluoro(2,4,6-tri-sec-butylquinoline). However, the high resolution spectrum showed there to be weak additional ring fluorine resonances. Integration of each resonance, using the known tertiary fluorine resonances as a standard for the single fluorine, showed that two of the resonances were each split into bands corresponding to 0·7 fluorine atoms and 0·3 fluorine atoms.

The resonance assigned to the 8-fluorine was split into two very similar peaks. Likewise, the 7-fluorine was split into two bands, the first integrating to 0·3 fluorines was very broad and so coupled extensively to the alkyl chains of the perfluoro(6-sec-butyl) group. The other resonance (0·7 fluorine) was a doublet with splitting of 120 Hz. corresponding to the coupling shown in the additional tertiary fluorine resonance. The 5-fluorine was too broad for couplings to be identified.



(96)



(97)

Thus perfluoro(2,4,6-tri-sec-butylquinoline) at room temperature exists as a mixture of two conformers (on the n.m.r. timescale), 30% of (96) and 70% of (97).

F. Determination of the absolute barrier to rotation

Up to the present time only qualitative work has been recorded on the variation of the spectra with temperature and no accurate measurements of the barrier have been made.

An estimate of the barrier to rotation of the 4-heptafluoroisopropyl group of perfluoro(tetraisopropylpyrimidine)[140] is quoted at 82 kJ mole^{-1} (~ 20 Kcal.mole^{-1}). However this was obtained by coalescence data and in view of the large errors inherent in these calculations,[141-143] especially when using the approximation formulae for peaks that are not sharp singlets, the value can be taken only as a very crude estimate of the barrier. The only way to arrive at accurate values of the barrier by n.m.r. techniques is via a full line shape analysis.

An estimate of the energy difference between the various conformers, where they coexist at low temperatures, has shown that the energy difference is around 300 cal.mole^{-1} (~ 70 J.mole^{-1}) for the two conformers of perfluoro(2,4-di-isopropylpyridine) and similarly for 2-methoxyperfluoro(4-isopropylpyridine) as they exist in 2:1 ratio at ca. -20°C.

CHAPTER 7

Experimental

A. General

1. Reagents

Perfluoro-aza aromatic compounds were prepared as in the literature.[2,3,11,16,151] Further experimental details of the preparation of heptafluoroquinoline are given below in Section C. Fluorosulphuric acid was donated by I.C.I. Ltd. and fluorosulphuric acid-antimony pentafluoride mixture purchased from Ozark Mahoning Company. Hexafluoroantimonic acid was prepared by shaking together a slight excess of one molar equivalent of anhydrous hydrogen fluoride with antimony pentafluoride in a polyfluoroethylene bottle.

2. Gases

Tetrafluoroethylene was prepared by pyrolysis of polytetrafluoroethylene flakes (donated by I.C.I. Ltd.) at 600°C to 700°C under high vacuum[144] and was purified by vacuum fractional distillation.

Perfluoroisobutene was first prepared by the atmospheric pressure pyrolysis (600°-800°C) of polytetrafluoroethylene.[145] An alternative technique employed later was the atmospheric pressure pyrolysis of hexafluoropropene[146] discussed in detail in Section C.

3. Solvents

Sulpholan was vacuum distilled and the middle fraction was collected over dried molecular sieves (Type IVA) and stored above room temperature under dry nitrogen.

Tetraglyme was first refluxed over sodium then purified as for sulpholan.

4. Instrumentation

I.r. spectra were recorded on a Grubb-Parsons 'Spectromaster' Spectrometer or a Perkin-Elmer 157 Spectrophotometer. Samples were in the form of a contact

film between potassium bromide plates for liquids or low melting solids, and higher melting solids were pressed into homogeneous plates with potassium bromide.

Proton and fluorine nuclear magnetic resonance spectra were recorded on a Varian A56/60D Spectrometer operating at 56·46 MHz. for fluorine and 60 MHz. for proton. Samples were normally recorded at the ambient temperature of the probe (40°C) but facilities for varying the temperature allowed spectra to be recorded at temperatures different from this.

Mass spectra were recorded on an A.E.I. MS9 Spectrometer and all molecular weights were determined using this machine.

Quantitative vapour phase chromatography (v.p.c.) was carried out on a Griffin and George D6 Gas Density Balance. The ratio of peak areas on this instrument is a known function of the molar proportions in a mixture of known compounds. The columns were either silicone elastomer packed on Celite (Column 'O') or di-n-decylphthalate on Celite (Column 'A'). Further non-quantitative gas chromatography was normally on a Perkin-Elmer 'Fractometer' Model 451 (hot wire detector) or a Pye '104' Chromatography (flame ionisation detector) using the same column packings.

Preparative scale vapour phase chromatography was performed on either a Varian 'Aerograph' or a Perkin-Elmer 'F21' instrument normally on columns packed with silicone elastomer on Celite.

Thin layer elution chromatography was carried out on thin glass plates coated with an even layer of silica (Silic gel/CT, Reeve Angel Scientific Ltd.) containing a fluorescing agent. The presence of compounds on the plate quenched the fluorescence induced by u.v. light.

5. Analysis

Carbon, hydrogen and nitrogen analyses were carried out on a Perkin-Elmer '240' Elemental Analyser. Analysis for halogen was a slightly improved version

of that described in the literature.[146]

Melting points and boiling points were determined at atmospheric pressure unless otherwise stated and are uncorrected.

6. General experimental method

Except for the reactions where water was present in the reactants, all apparatus was oven dried above 130°C prior to use. Extracted ether solutions were dried over anhydrous magnesium sulphate and the ether subsequently removed on a rotary evaporator.

B. Experimental for Chapter 3

1. The preparation of hexafluoroantimonate salts of some polyfluoro-aza aromatic compounds

(a) Tetrafluoropyridazinium hexafluoroantimonate

Into one limb of a dry, double-limbed Schlenk tube, flushed with nitrogen, was condensed sulphur dioxide (ca. 20 ml.). Tetrafluoropyridazine (3·0g., 9·7 m.mole) was dissolved in the sulphur dioxide at about -30°C and the solution was cooled to -70°C. Hexafluoroantimonic acid (2·3g., 9·7 m.mole) was added to the solution and the mixture well stirred and allowed to warm when the sulphur dioxide boiled off leaving light brown crystals in quantitative yield. The salt was recrystallised from sulphur dioxide then completely freed from solvent by pumping under vacuum at room temperature. The apparatus was let down to dry nitrogen and opened in a glove box. The salt was identified from its ^{19}F n.m.r. spectrum as tetrafluoropyridazinium hexafluoroantimonate. ^{19}F n.m.r. peaks in SO_2 at 80·1 and 121·2 p.p.m. of equal intensity, (tetrafluoropyridazine ^{19}F n.m.r. peaks in SO_2 at 90·7 and 144·6 p.p.m. from $CFCl_3$).

(b) Other hexafluoroantimonate salts

The method described above was used for the preparation of the hexafluoroantimonate salts of pentafluoropyridine, 3,5-dichlorotrifluoropyridine and heptafluoroquinoline. The salts were in each case identified by comparison of their ^{19}F n.m.r. spectra with those previously reported.[52]

2. Preparation of n.m.r. samples

(a) First procedure

In a typical case the salt was transferred to an n.m.r. tube in the glove box. The tube was then capped, removed from the box, attached to the vacuum line and quickly evacuated. Sulphur dioxide was condensed onto the salt at -78°C. The solution was then allowed to warm to -23°C, (CCl_4 bath) and stirred until the salt dissolved. The ^{19}F n.m.r. spectrum was then recorded at -30°C.

Small portions of polyfluoro-aza aromatic compounds were then added to the solution at -23°C (from a micro syringe in the case of liquids and directly in the case of solids). The solution was then stirred and left for about ten minutes before the ^{19}F n.m.r. spectrum was re-recorded. Subsequent spectra were recorded after each addition of base, ensuring that all the added base was in solution.

Some typical results obtained from adding 3,5-dichlorotrifluoropyridine to a solution of pentafluoropyridinium hexafluoroantimonate in sulphur dioxide are given below (Table 23).

TABLE 23

Volume of added 3,5-dichlorotrifluoropyridine (see text)	Pentafluoropyridine peaks (p.p.m.) (2,6)	(4)	(3,5)	3,5-Dichlorotrifluoropyridine peaks (p.p.m.) (2,6)	(4)
Starting salt	96·2	108·3	155·7	-	-
+ 15 µl	95·1	114·8	157·5	w	w
+ 5 µl	94·5	117·7	158·3	w	w
+ 15 µl	93·2	122·9	159·4	78·2	69·4
+ 20 µl	92·1	126·9	160·1	77·6	73·1
+ 30 µl	91·7	127·0	160·6	76·8	78·5
+ 35 µl	90·9	131·5	161·9	75·9	82·3
+ 20 µl	90·6	132·0	161·6	75·8	84·0
Salt	97·8	107·1	156·4	79·1	68·1
Base	89·5	135·0	163·5	71·1	96·8

Assignments in parentheses, shifts relative to $CFCl_3$ in a capillary tube (-30°C). Shifts of pure salt and pure base in sulphur dioxide given for comparison.

w = spectrum too weak for peak positions to be measured with certainty.

(b) Second procedure

Approximately equimolar proportions of two bases were dissolved in sulphur dioxide in an n.m.r. tube at -23°C. The ^{19}F n.m.r. spectrum was then recorded at -30°C. To the well stirred solution was added a single drop of either hexafluoroantimonic acid or fluorosulphuric acid-antimony pentafluoride mixture from a fine dropping pipette. The solution was well stirred and left at -23°C for about ten minutes. The ^{19}F n.m.r. spectrum was re-recorded at -30°C and again after each subsequent addition of acid. It was found that although it took a few minutes for a sharp ^{19}F n.m.r. signal to be obtained after each addition of acid, the tubes could subsequently be stored at -78°C for as long as two days with no change in the ^{19}F n.m.r. spectrum.

Some typical results obtained by adding hexafluoroantimonic acid to an approximately equimolar mixture of 3,5-dichlorotrifluoropyridine and tetrafluoropyridazine are given below (Table 24).

TABLE 24

Number of additions of acid ($HSbF_6$) (see text)	3,5-Dichlorotrifluoropyridine peaks (p.p.m.) (4)	(3,5)	Tetrafluoropyridazine peaks (p.p.m.) (3,6)	(4,5)
0	71·2	96·5	90·7	144·3
1	73·8	90·3	81·4	122·7
2	74·5	87·2	80·8	122·2
3	76·3	78·6	80·2	121·5
4	77·0	74·8	80·2	121·5
Salt	79·1	68·1	80·1	121·2
Base	71·1	96·8	90·7	144·6

Assignments in parenthesis. Shifts relative to $CFCl_3$ in a capillary tube. Solvent SO_2 at -30°C. Shifts of pure base and salt given for comparison.

(c) Effect of hexafluoroantimonic acid on the ^{19}F n.m.r. spectrum of tetrafluoropyrazine

Tetrafluoropyrazine was dissolved in sulphur dioxide in an n.m.r. tube at -23°C. The ^{19}F n.m.r. spectrum was then recorded at -30°C. Hexafluoroantimonic acid was then added from a fine dropping pipette. After each drop, the solution was well stirred and left for ten minutes, then the ^{19}F n.m.r. spectrum was recorded at -30° and after each subsequent addition of acid. The signal shifted downfield from the position of the free base in sulphur dioxide (95·9 p.p.m.), beyond the position found for the salt in sulphur dioxide (90·9 p.p.m.) to 89·9 p.p.m. On further addition of acid the signal vanished and no signal attributable to any tetrafluoropyrazine species could be detected. The signal reappeared as a sharp signal to highfield of 89·9 p.p.m. on the addition of further free base.

Corresponding results were observed when fluorosulphuric acid-antimony pentafluoride mixture was used as the acid.

C. Experimental for Chapter 4

1. Preparation of starting materials

(a) Heptafluoroquinoline

The method of preparation of heptafluoroquinoline as outlined previously was essentially via the published route.[3] Some additional experimental observations are given below.

The heptachloroquinoline is prepared by the two step chlorination, firstly by chlorine and aluminium trichloride by the swamping catalyst method and secondly by phosphorus pentachloride. It is normally found to be in a high state of purity (as checked by the melting point or preferably by thin layer elution chromatography on silica eluting with carbon tetrachloride) after the first recrystallisation from benzene. Chloroquinolines are eluted with increasing R_f values apparently associated with increasing numbers of chlorine atoms. The heptachloroquinoline was freed of benzene by vacuum drying at room temperature and stored in an oven at ca. 130°C for at least two days before use.

The products of fluorination as vacuum transferred from the hot autoclave contained amounts of acidic material which were presumed deleterious to the remaining heptafluoroquinoline. Attempted distillation of the crude heptafluoroquinoline caused substantial breakdown of the heptafluoroquinoline and the resultant formation of a black involatile tar and substantial quantities of hydrogen fluoride. To prevent this breakdown, the products of fluorination were taken up in ether, washed with sodium carbonate solution and then water, dried over magnesium sulphate and then evaporated to dryness. The resultant slightly moist yellow solid was pumped under vacuum for a short while to remove the remaining traces of ether and then vacuum transferred from the traces of less volatile material.

Distillation of this material then gave two pure fractions. The first distilling at 160°C was perfluoro(5,6,7,8-tetrahydroquinoline) (5 to 20% yield) and the second distilling at 205° was pure heptafluoroquinoline (15 to 60% yield). The remaining material was retained for refluorination.

(b) Perfluoroisobutene

Perfluoroisobutene is conveniently prepared by the pyrolysis of hexafluoropropene in an unpacked nickel tube at 750°C.

$$4C_3F_6 \xrightarrow[750^\circ C]{\text{Ni tube}} 3C_4F_8$$ [147]

71-95% yield

47-57% conversion

(i) Toxicity

Perfluoroisobutene is an extremely toxic gas[147] (approximate lethal concentration for 4 hr. exposure is 0·5 p.p.m., approximately ten times more toxic than phosgene) and so great care was necessary when preparing, handling or disposing of gases that may have contained perfluoroisobutene. The preparation and use was confined to well ventilated areas and breathing apparatus was worn at all times when handling the gas.

(ii) Disposal

Perfluoroisobutene is rapidly attacked by nucleophilic reagents[140] and so is quickly hydrolysed in aqueous alkaline acetone. Excess perfluoroisobutene from reactions was diluted in a stream of nitrogen and slowly bubbled through such a solution in a well ventilated fumes cupboard. Waste gases from the preparation were either stored in a cylinder for re-use (higher boiling gases only, not containing appreciable quantities of tetrafluoroethylene) or were treated in the same way as above. Care was taken to ensure that the contents of the traps from the vacuum line were similarly treated.

(iii) Preparation

The apparatus consisted essentially of a long unpacked nickel tube (5 cm. x 80 cm.) surrounded by a cylindrical heater controlled by a variable voltage supply and fitted with gas inlet and outlet tubes. The temperature of the tube, as measured by a thermocouple in contact with the exterior of the tube, was set to 750°C. The inlet of the tube was connected to a supply of dry nitrogen and the outlet to two parallel traps immersed in liquid air. The trap outlets were connected together and passed through a flowmeter to measure the nitrogen flow rate and demonstrate a free flow of gas. The outlet led to an efficient extraction system.

The nickel tube was purged with nitrogen and allowed to reach thermal equilibrium. Hexafluoropropene (100g., 0·66 mole) was condensed into a flask equipped with inlet and outlet tubes and inserted in the inlet nitrogen line after the nitrogen flow rate had been adjusted to ca. 200 ml.min^{-1}. The hexafluoropropene was allowed to evaporate and was carried through the nickel tube (contact time ca. 4 mins.) and into the trapping system. The apparatus was purged for at least an hour after the hexafluoropropene had evaporated, then the nitrogen flow was stopped and the whole apparatus slowly evacuated through the traps. The nickel tube was sealed and allowed to cool. The volatile products were vacuum transferred to a fractionation bulb on the vacuum line.

(iv) Fractionation and storage

The products of two pyrolyses were combined and fractionated in the following manner. The condensed gas was surrounded by a solid CO_2-acetone bath (-78°C) and the gas that readily transferred (mainly tetrafluoroethylene) was condensed in liquid air. A high pressure of gas (ca. 60 cm.) was maintained over the material surrounded by the CO_2-acetone bath, by adjusting the interconnecting tap to throttle the gas flow. After the most volatile components had transferred the CO_2-acetone bath was replaced in turn by a

carbon tetrachloride slush bath, an ice-salt bath and finally an ice-water bath. During the final transference the i.r. spectrum of the remaining gas was periodically examined until it showed the gas to be pure perfluoroisobutene.[149] Transference was then stopped and the remaining material (35g., 19%) transferred to a pre-weighed storage cylinder cooled in a solid CO_2-acetone bath.

The boiling points[148] (atmospheric pressure) of the expected contaminants are:

tetrafluoroethylene	=	-76°C
hexafluoropropene	=	-29°C
octafluoro-1-butene	=	+1°C
octafluoro-2-butene	=	0°C
octafluoroisobutene	=	+7°C

2. Reaction of heptafluoroquinoline with nucleophiles

(a) Preparation of 2-N,N-diethylaminohexafluoroquinoline

To a stirred solution of heptafluoroquinoline (1·4g., 5·5 m.mole) in acetone (15 ml.) was added, at room temperature, a solution of diethylamine (1·5 ml., 14·6 m.mole) in acetone (10 ml.) over a period of 10 mins. The solution was stirred for a further 30 mins. then poured into excess water (100 ml.). The aqueous solution was acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The combined ether extracts were washed with water, dried and evaporated under reduced pressure to leave a yellow oil. The oil was vacuum transferred to give 2-N,N-diethylaminohexafluoroquinoline, m.pt. ~18°C, b.pt. > 200°C, (Found: C, 50·49; H, 3·5; F, 36·55%; M, 308. $C_{13}H_{10}F_8N_2$ requires C, 50·6; H, 3·2; F, 37·0%; M, 308). I.r. spectrum no.1, n.m.r. spectrum no.1.

(b) Reaction between ammonia and heptafluoroquinoline in ether

Ammonia (3 ml., 0·880g./ml., ca. 50 m.mole) suspended in ether (10 ml.) was added slowly to a stirred solution of heptafluoroquinoline (0·7g., 2·8 m.mole) in ether (30 ml.) at room temperature. The solution was stirred for a further 30 mins. then poured into excess water (150 ml.). The ether layer was well shaken with the water and the solution acidified (dil. HCl). The ether layer was run off and the aqueous layer extracted with further ether (2 x 50 ml.). The combined ether extracts were dried and evaporated to leave a white solid which was shown, by comparison of the i.r. spectra and the ^{19}F n.m.r. spectra with an authentic sample, to be a mixture of roughly equal proportions of 2-aminohexafluoroquinoline[96] and 4-aminohexafluoroquinoline.[96] Integration of the ^{19}F n.m.r. spectrum showed, from the ratio of the 2-fluorine signal to the 4-fluorine signal, that the mixture comprised 60% of 2-amino-hexafluoroquinoline and 40% 4-aminohexafluoroquinoline (±5%).

(c) Reaction between heptafluoroquinoline and sodium methoxide in t-butanol

Sodium (0·22g., 9·6 mg.-atom) was dissolved in a mixture of dry t-butanol (20 ml.) and dry methanol (1·5 ml., 40 m.mole). This solution was then slowly added to a stirred solution of heptafluoroquinoline (2·4g., 9·4 m.mole) in dry t-butanol (40 ml.) at room temperature under an atmosphere of dry nitrogen. The solution was stirred for 4 hrs. then poured into water (150ml.), the suspension acidified (dil. HCl) and then extracted with ether (3 x 50 ml.), The combined extracts were dried and evaporated under reduced pressure to leave the product which sublimed under vacuum to give a white solid (2·4g., 96%). Analysis by quantitative gas chromatography (Gas Density Balance, Column 'O', 175°C) precalibrated with the expected products, showed the molar composition to be 92% 2-methoxyhexafluoroquinoline[96] with about 6·5% of the 2,4-dimethoxypentafluoroquinoline.[96] No trace of 4-methoxyhexafluoroquinoline could be detected by either that chromatography or by ^{19}F n.m.r. spectroscopy.

A sample was recrystallised from methanol and confirmed to be 2-methoxyhexafluoroquinoline by comparison of i.r. spectrum with an authentic sample. N.m.r. spectrum no.2.

(d) Preparation of 2,4,7-trimethoxytetrafluoroquinoline

Sodium (1g., 43·5 mg.-atom) was dissolved in dry methanol (20 ml.) and added to a solution of heptafluoroquinoline (1·25g., 4·9 m.mole) in dry methanol (60 ml.) under an atmosphere of dry nitrogen. The solution was then refluxed for 3 hrs., cooled and poured into water (100 ml.). The suspension was acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The combined extracts were dried and the solvent evaporated to leave a white solid (1·2g., 84%). Recrystallisation (methanol) afforded pure 2,4,7-trimethoxytetrafluoroquinoline, previously reported[96] as an unidentified trimethoxytetrafluoroquinoline. N.m.r. spectrum no.4.

(e) Preparation of 6-methoxyperfluoro(2,4-di-isopropylquinoline)

To a stirred solution of perfluoro(2,4-di-isopropylquinoline)[40,150] (1·8g., 3·2 m.mole) in dry methanol (40 ml.) at 0°C was added slowly a solution of sodium methoxide (3·5 ml. of 1·0 molar solution in methanol) in additional methanol (2·5 ml.) under an atmosphere of dry nitrogen. After about 4 ml. of the sodium methoxide solution had been added a small sample of the product solution was withdrawn and analysed by gas chromatography (Column 'O', 250°C). It was found to consist mainly of one compound with a little unchanged starting material. The remaining sodium methoxide solution was added dropwise until analysis showed no unchanged starting material. The solution was then poured into water (150 ml.), acidified (dil. HCl) and the suspension extracted with ether (3 x 50 ml.). The combined extracts were dried and the ether removed under reduced pressure to yield, after sublimation (·001 mm., 100°C), a pale yellow solid (1·8g., 99%). Recrystallisation from methanol afforded colourless

crystals of 6-methoxyperfluoro(2,4-di-isopropylquinoline), m.pt. 64°C. (Found: C, 33·7; H, 0·80; N, 2·74; F, 59·89%; M, 567. $C_{16}H_3F_{18}NO$ requires C, 33·86; H, 0·53; N, 2·47; F, 60·32%; M, 567). I.r. spectrum no.3, n.m.r. spectrum no.5.

(f) Preparation of 3,6-dimethoxyperfluoro(2,4-di-isopropylquinoline)

A solution of sodium (0·23g., 10 mg.-atom) in dry methanol (30 ml.) was added slowly to a solution of perfluoro(2,4-di-isopropylquinoline)[150] (3·3g., 5·9 m.mole) in methanol (70 ml.) at room temperature under an atmosphere of dry nitrogen. After about 15 ml. of the sodium methoxide had been added the solution was analysed by v.p.c. as in the previous experiment. The analysis indicated that the solution consisted mainly of a single product with some monomethoxylated product. The remaining sodium methoxide was added slowly until analysis indicated no monomethoxylated product remained. The solution was then poured into water (150 ml.) acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The combined extracts were washed with water (50 ml.) and dried. The ether was removed under reduced pressure to yield, after sublimation (100°C, 0·001 mm.), a yellow paste. Recrystallisation (twice) from petroleum ether (40-60 fraction) yielded colourless crystals of 3,6-dimethoxyperfluoro(2,4-di-isopropylquinoline) (1·2g., 62%), m.pt. 79-80°C. (Found: C, 34·9; H, 0·9; N, 2·3; F, 55·3%; M, 579. $C_{17}H_6F_{17}NO_2$ requires C, 35·2; H, 1·0; N, 2·4; F, 55·8%; M, 579). I.r. spectrum no.4, n.m.r. spectrum no.6.

(g) Polyfluoroalkylation

(i) Apparatus and general procedure

The apparatus consisted of a 50 ml. conical flask with a magnetic stirrer surmounted by a branched adaptor, one arm of which led via a tap to the vacuum line and a supply of dry nitrogen and the other arm led, through a

reflux condenser to a variable volume reservoir (conveniently a football bladder).

The apparatus was baked overnight, assembled and swept with dry nitrogen. The solvent (20 ml.), caesium fluoride and sublimed substrate (if relatively involatile i.e. dimethoxypentafluoroquinoline or heptafluoroquinoline) were added against a countercurrent of nitrogen and the solvent degassed by vigorous pumping for about 15 mins. If the substrate was present in the solvent the apparatus was then let down to an atmosphere of the desired olefin through the vacuum line. If the olefin was the highly toxic perfluoroisobutene the complete evacuated apparatus was transferred to a well ventilated fumes cupboard and the cylinder of perfluoroisobutene attached to the inlet tap via a very short length of rubber tubing and the olefin admitted in this manner.

If the substrate was volatile (i.e. pentafluoropyridine) then after degassing the solvent and the caesium fluoride, the apparatus was let down to dry nitrogen and the substrate (dried over P_2O_5) was added against a countercurrent of dry nitrogen. The solvent and substrate were then frozen in liquid air and the apparatus evacuated, sealed and allowed to warm to room temperature. The olefin was admitted as before.

The conical flask was part immersed in an oil bath and stirred at high speed. After the reaction was complete the normal work up procedure was to pour the mixture into water (200 ml.), acidify (dil. HCl), and extract with ether (3 x 50 ml.). The combined ether extracts were washed thoroughly with water to remove extracted solvent, dried and evaporated to leave the reaction products. If the olefin had been perfluoroisobutene the bladder containing the excess gas was sealed and removed and the whole apparatus inverted, in parts, in a beaker of alkaline water (200 ml.), still in the well ventilated area. After about 1 hr. the aqueous solution was acidified (dil. HCl) and

extracted as above to isolate the products. The excess gas was destroyed in aqueous alkaline acetone as previously described.

(ii) Attempted perfluoroalkylation of 2,4-dimethoxypentafluoroquinoline

Reactions between 2,4-dimethoxypentafluoroquinoline and various olefins with caesium fluoride in either sulpholan or tetraglyme in no case gave more than traces of alkylated product (as indicated by the mass spectra, i.r. spectra and vapour phase chromatography of the recovered material). Recovery of material was normally between 20 and 75%. Olefin was always in excess and normally 3 to 5 m.mole of substrate were admitted. The combinations of olefin, solvent, time and temperature used are given below.

Olefin	Solvent	Time	Temperature °C
Hexafluoropropene	Tetraglyme	20 hrs.	95
Hexafluoropropene	Tetraglyme	12 hrs.	55
Octafluorobut-2-ene	Sulpholan	4 days	100
Octafluoro-isobutene	Sulpholan	6 days	30
Tetrafluoroethylene	Sulpholan	4 days	30

(h) Preparation of 2-n-butylhexafluoroquinoline

(i) In hexane

Butyl-lithium (2·5 ml. of 2·0 molar solution in hexane) in additional dry hexane (10 ml.) was added slowly to a stirred solution of heptafluoroquinoline (1·3g., 5·1 m.mole) in dry hexane (30 ml.) under an atmosphere of dry nitrogen. The solution was stirred at room temperature for 10 mins. then poured carefully into water (100 ml.). The aqueous suspension was acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The combined extracts were washed with water (50 ml.), dried and evaporated

under reduced pressure to leave a pale yellow oil (1·2g., 80%). The oil was vacuum transferred (130°C, ·005 mm.) from a small amount of involatile material. The ^{19}F n.m.r. spectrum showed it to be 2-n-butylhexafluoroquinoline, b.pt. > 200°C. (Found: C, 53·4; H, 3·36; F, 38·7%; M, 293. $C_{13}H_9F_6N$ requires C, 53·24; H, 3·07; F, 38·9%; M, 293). I.r. spectrum no.5, n.m.r. spectrum no.7.

No other component could be detected in the oil by ^{19}F n.m.r. spectroscopy or by v.p.c. (Column 'O', 200°C).

(ii) In ether

Heptafluoroquinoline (1·3g., 5·1 m.mole) was dissolved in dry ether (30 ml.) at room temperature. Butyl-lithium (2·5 ml. of 2·0 molar solution in hexane) in ether (20 ml.) was added slowly to the solution of heptafluoroquinoline under an atmosphere of dry nitrogen. The solution was stirred for a further 10 mins. then poured into water (100 ml.). The solution was acidified (HCl) and extracted with ether (3 x 50 ml.). The combined extracts were washed with water (50 ml.) and dried ($MgSO_4$). The ether was evaporated off under reduced pressure leaving a red oil (1·0g., 67%). Vapour phase chromatography showed it to consist of two similarly retained products, one of which had the same retention time as 2-n-butylhexafluoroquinoline (previous experiment). The i.r. spectrum showed it to be mainly that compound but the ^{19}F n.m.r. spectrum showed the presence of 5% of a material containing a lowfield (i.e. 2-) fluorine.

3. Reactions of heptafluoroquinoline with perfluorocarbanions

(a) From tetrafluoroethylene

This reaction was found to be highly susceptible to traces of moisture in the solvent, caesium fluoride, and heptafluoroquinoline and so every care to exclude moisture was taken. The heptafluoroquinoline was sublimed or vacuum

dried before use. The apparatus and general method were as described previously (this Chapter, Section C.2.g.i).

In a typical experiment heptafluoroquinoline (3·3g., 13·2 m.mole) was reacted with tetrafluoroethylene (ca. 10g., 100 m.mole) in tetraglyme (20 ml.) in the presence of caesium fluoride (ca. 1g.). The solution was stirred rapidly for 26½ hrs. at 80°C and gave, after work up of the solution as previously described, a yellow oil (6·8g.). Analysis by vapour phase chromatography (Column 'O', 200°C; Column 'A', 150°C) showed there to be at least six significant products.

Attempts to reduce the complexity of the mixture by varying the temperature of the reaction (30-115°C), the duration of the reaction (5½ hrs. to 4 days) and the solvent (sulpholan and tetraglyme) did not produce any simplification of the mixture. The mixture could not be separated to yield any pure compounds by vacuum distillation, atmospheric pressure distillation up a short column, elution chromatography, attempted low temperature recrystallisation or by vapour phase chromatography.

(b) From octafluorobut-2-ene

The apparatus was as previously used. In a typical experiment heptafluoroquinoline (2·5g., 9·8 m.mole), tetraglyme (20 ml.) and caesium fluoride (ca. 1g.) were introduced into the conical flask against a countercurrent of dry nitrogen. The solvent was degassed by vigorous pumping then the apparatus was let down to an atmosphere of excess octafluorobut-2-ene (ca. 10g., 50 m.mole). The reaction vessel was sealed and stirred rapidly for 24 hrs. at ambient temperature (30°C). The reaction products were then poured into water (200 ml.), acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The extracts were combined and washed thoroughly with water, dried and evaporated under reduced pressure to leave a yellow oil (6·0g.). Analysis by vapour phase chromatography showed the presence of two components in

approximately equal proportions and only a trace of unchanged heptafluoroquinoline. An increase in the temperature to 80°C or the duration of the reaction did little to alter the proportions of the products to ease the separation.

The products of several reactions were combined and distilled under vacuum through a 20 cm. column packed with glass helices. The first reaction collected (60-65°C) was enriched in the more volatile component and the third fraction enriched in the other. The pure components were isolated from the enriched fractions by preparative scale vapour phase chromatography (Column 'O', 150°C) to yield (first component) perfluoro(2,4,6-tri-sec-butylquinoline), b.pt. 178°C. (Found: C, 29·25; F, 69·2%; M, 855. $C_{21}F_{31}N$ requires C, 29·5; F, 68·9%; M, 855), i.r. spectrum no.6, n.m.r. spectrum no.8 and (second component) perfluoro(2,4-di-sec-butylquinoline) identified by mass spectrum (M, 655), i.r. spectrum and ^{19}F n.m.r. spectrum in comparison with an authentic sample[104], n.m.r. spectrum no.9. The combined yield of crude products was 80%.

(c) From octafluoroisobutene

The apparatus and method have been described previously (this Chapter, Section C.2.g.i). Sublimed heptafluoroquinoline (4·0g., 15·7 m.mole) in sulpholan (35 ml.) with caesium fluoride (ca. 2g.) were reacted with perfluoroisobutene (ca. 9g., 45 m.mole). The flask was stirred vigorously for 2 hrs. at 80°C during which time a white precipitate formed. The bladder was sealed, removed, and the whole apparatus inverted in alkaline water (200 ml.). After leaving for one hour the solution was decanted from the insoluble material and extracted with a large volume of ether (5 x 50 ml.). The water insoluble material was dissolved in the ether and the combined extracts washed thoroughly with water, dried ($MgSO_4$) and evaporated under reduced pressure to

leave a white solid. The solid was sublimed (room temperature, ca. ·005 mm.) and recrystallised (acetone) to give white crystals of perfluoro(2,6-di-t-butylquinoline) (5·0g., 49%), m.pt. 154°C. (Found: C, 31·0; N, 2·14; F, 66·9%; M, 655. $C_{17}F_{23}N$ requires C, 31·14; N, 2·14; F, 66·72%; M, 655). I.r. spectrum no.7, n.m.r. spectrum no.10.

(d) Preparation of perfluoro(2-t-butylquinoline)

Heptafluoroquinoline (4·6g., 18 m.mole), dry tetraglyme (20 ml.) and caesium fluoride (ca. 1g.) were added to the conical flask against a counter-current of dry nitrogen in the apparatus as previously described. The atmosphere above the liquid was evacuated. The apparatus was transferred to a well ventilated fumes cupboard and perfluoroisobutene admitted (ca. 9g., ca. 45 m.mole). The reaction was stirred rapidly for 3 hrs. at room temperature. After this time the bladder was sealed and alkaline water (30 ml.) was poured into the flask and stirred for a further hour to destroy unreacted perfluoroisobutene. The solution was then poured into water (150 ml.) and extracted with ether (3 x 50 ml.). The combined extracts were washed well with water, dried and evaporated under reduced pressure to leave a yellow oil (3·5g., ca. 40% crude). The oil was purified by vacuum transfer at ambient temperature and attempts to remove the traces of heptafluoroquinoline by preparative scale vapour phase chromatography (Column 'O', 75°-150°C) were not successful. Satisfactory analyses could not be obtained but the ^{19}F n.m.r. spectrum and the mass spectrum were consistent with it being perfluoro-(2-t-butylquinoline) (M, 455. $C_{13}F_{15}N$ requires M, 455). A sample free of heptafluoroquinoline could not be obtained from repeated experiments. N.m.r. spectrum no.11.

4. Attempted preparation of derivatives of heptafluoroquinoline via organolithium compounds

(a) From 2-bromohexafluoroquinoline

(i) Attempted preparation of 2-hydrohexafluoroquinoline

A solution of 2-bromohexafluoroquinoline[52] (1·5g., 4·7 m.mole) in a mixture of dry ether (40 ml.) and dry hexane (30 ml.) was cooled to -78°C (acetone-solid CO_2) in a dry nitrogen swept flask. Butyl-lithium (2·0 ml. of 2·0 molar solution in hexane) was added slowly to the stirred solution which darkened rapidly. About 2 mins. after all the butyl-lithium had been added a current of hydrogen chloride gas, diluted with nitrogen, was passed into the solution whilst the solution was allowed to warm to room temperature over a period of 2 hrs. The solution was poured onto ice, washed and extracted with further ether (2 x 50 ml.). The combined extracts were dried and evaporated under reduced pressure to leave a dark paste (0·4g.).

Attempted sublimation of the paste afforded n-butylbromide (identified by comparison of i.r. spectrum with an authentic sample) and a small amount (ca. 250 mg.) of yellow paste. Analysis by vapour phase chromatography (Column 'O', 175°C) indicated that the paste was a complex mixture of products.

The experiment was repeated using in turn pure ether and pure hexane as solvents but in each case a complex mixture of products was formed in low yield.

(ii) Attempted preparation of other derivatives

Similar experiments to form the carboxylic acid derivative from solid carbondioxide and the mercury chloride derivative from mercuric chloride were likewise unsuccessful.

(b) From 2,4-dibromopentafluoroquinoline

2,4-Dibromopentafluoroquinoline[52] (2·1g., 5·6 m.mole) was dissolved in dry ether (50 ml.) and the solution cooled to -78°C under an atmosphere of dry nitrogen. A solution of butyl-lithium (2·5 ml. of 2·0 molar solution in

hexane) in dry ether (20 ml.) was added slowly. Immediately after the butyl-lithium had been added a stream of hydrogen chloride gas, diluted with nitrogen was passed into the dark solution which was allowed to warm to room temperature. The solution was then poured into water (100 ml.) and extracted further with ether (2 x 50 ml.). The combined extracts were dried and evaporated under reduced pressure to leave a dark paste (0·6g.). This paste partly sublimed (150°C, 0·001 mm.) to a yellow paste containing n-butyl-bromide (v.p.c. Column 'O', 150°C) with a small amount of a second unidentified compound.

Repeated reactions in ether and in hexane and the attempted formation of trimethylchlorosilane and carboxylic acid derivatives in all cases resulted in considerable tar formation and low yields of unidentified products.

5. Attempted preparation of a Grignard derivative of 2,4-dibromopentafluoro-quinoline

Dry ether (100 ml.), dry magnesium (0·2g., 8·3 mg.-atom) and a few drops of methyl iodide as initiator were introduced into a nitrogen purged flask with reflux condenser. A solution of 2,4-dibromopentafluoroquinoline (1·85g., 4·9 m.mole) in dry ether (20 ml.) was slowly run into the stirred ether at room temperature. The contents of the flask turned black almost immediately and after hydrolysis with water the extracted ether solution was dried and evaporated to leave a dark tar which was not investigated further.

6. Reactions between dihalopentafluoroquinolines* and sodium methoxide

(a) 2,4-Dichloropentafluoroquinoline

Sodium methoxide (1·5 ml. of 1·0 molar solution) in additional methanol (5 ml.) was slowly added to a stirred solution of 2,4-dichloropentafluoro-quinoline[52] (0·38g., 1·3 m.mole) in methanol (20 ml.) at room temperature under

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* Halo denotes chloro, bromo or iodo only

an atmosphere of dry nitrogen. The solution was stirred for a further 5 mins. then poured into water (100 ml.). The suspension was acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The combined extracts were washed with water, dried and evaporated under reduced pressure to leave a yellow low melting solid which sublimed (100°C, 0·001 mm.) to yield a mixture of two isomers of methoxychloropentafluoroquinoline (0·2g., ca. 54%). (Found: C, 42·31; H, 1·20; N, 4·74; Cl, 13·07; F, 32·9%; M, 283 and 285. $C_{10}H_3ClF_5NO$ requires C, 42·33; H, 1·06; N, 4·94; Cl, 12·52; F, 33·5%; M, 283 (^{35}Cl) and 285 (^{37}Cl)). High resolution ^{19}F n.m.r. spectroscopy showed the major component (>90%) to be 2-methoxy,4-chloropentafluoroquinoline. N.m.r. spectrum no.12.

(b) 2,4-Dibromopentafluoroquinoline

By exactly the same method as above, 2,4-dibromopentafluoroquinoline[52] (2·0g., 5·3 m.mole) in dry methanol (30 ml.) was reacted with sodium methoxide (5·5 ml. of 1·0 molar solution) in additional methanol (15 ml.) at room temperature to give, after extraction and sublimation (100°C, 0·001 mm.) a mixture of two isomeric methoxybromopentafluoroquinolines. (Found: C, 36·89; H, 0·89; N, 4·02; Br, 24·8; F, 28·2%; M, 327 and 329. $C_{10}H_3BrF_5NO$ requires C, 36·59; H, 0·91; N, 4·27; Br, 24·39; F, 28·9%; M, 327 (^{79}Br) and 329 (^{81}Br)). High resolution ^{19}F n.m.r. spectroscopy showed the major component (~75%) to be 2-methoxy,4-bromopentafluoroquinoline. N.m.r. spectrum no.13.

(c) 2,4-Di-iodopentafluoroquinoline

Likewise 2,4-di-iodopentafluoroquinoline[52] (0·47g., 1 m.mole), dissolved in dry methanol (10 ml.), reacted with sodium methoxide (1·0 ml. of 1·0 molar solution) in additional methanol (5 ml.) to give, after sublimation (100°C, 0·005 mm.), a mixture of two isomeric methoxyiodopentafluoroquinolines (0·2g., 50%). (Found: C, 31·68; H, 0·91; N, 3·69; I, 33·3; F, 25·8%; M, 375.

$C_{10}H_3F_5INO$ requires C, 32·0; H, 0·80; N, 3·73; I, 33·87; F, 25·33%; M, 375). High resolution ^{19}F n.m.r. spectroscopy showed the major component (~80%) to be 2-methoxy,4-iodopentafluoroquinoline. N.m.r. spectrum no.14.

7. Preparation of trifluoromethyl derivatives of heptafluoroquinoline

A nickel lined autoclave (150 ml.) was thoroughly cleaned and baked dry. Heptafluoroquinoline (5g., 20 m.mole) and oven dried (130°C) polytetrafluoroethylene flakes (10g., 200 m.mole of $:CF_2$) were sealed into the evacuated autoclave which was heated to 550°C for a total of 10 hrs. The volatile products of the reaction were vacuum transferred from the hot autoclave into a trap cooled in liquid air. Volatile material that boiled off on warming to room temperature and that boiled readily under vacuum was allowed to escape leaving a yellow oil (3·4g.). Analysis of the oil by vapour phase chromatography (Column 'O', 220°C and Column 'A', 150°C) showed the presence of at least eight significant components.

A repeat of the experiment at 520°C showed no marked simplification of the mixture and so separation was not attempted.

8. Pyrolysis of heptafluoroquinoline

The pyrolysis apparatus consisted of a silica tube packed with silica wool and surrounded by a cylindrical heater controlled by a variac. The temperature of the tube was measured by a thermocouple in contact with the tube at the centre of the heater. Heptafluoroquinoline was vapourized in a small flask at one end of the tube and passed into the pyrolysis region by a current of dry nitrogen. The products were collected at the other end of the tube in a trap surrounded by solid carbon dioxide.

With a contact time of ca. 15 secs. the following weights of solid products were obtained.

Temperature °C	720	760	800	820	840	880	920	950
Weight (%) of solid product	85	87	60	50	20	<5	0	0

Above 800°C an increasing amount of volatile material, identified from its i.r. spectrum as mainly silicon tetrafluoride, was formed. Analysis of the products obtained above 800° by vapour phase chromatography (Column 'A', 150°) showed a small fraction of material with the same retention time as heptafluoroisoquinoline but no pure material could be isolated.

9. Attempted formation of an N-oxide of heptafluoroquinoline

(a) Acetic acid and sulphuric acid as mixed

Heptafluoroquinoline (1g., 3·9 m.mole), hydrogen peroxide (2 ml. of 90% solution), glacial acetic acid (10 ml.) and sulphuric acid (10 ml. of 100% acid) were mixed in a 50 ml. conical flask fitted with dry nitrogen inlet, drying tube and magnetic stirrer. The mixture was stirred for 48 hrs. at room temperature under an atmosphere of dry nitrogen then cautiously poured onto ice. The white precipitate was filtered off, recrystallised from methylated spirits and shown, by comparison of its i.r. spectrum with an authentic sample to be 2-hydroxyhexafluoroquinoline (0·8g., 80%). Thin layer elution chromatography (eluent chloroform) showed the presence of only one compound.

(b) Polyphosphoric acid as solvent

In the same apparatus as above, heptafluoroquinoline (1g., 3·9 m.mole) was dissolved in polyphosphoric acid (30 ml.) at 35°C (to keep the acid fluid). Hydrogen peroxide (2 ml. of 90% solution) was very cautiously added to the mixture which was subsequently stirred at 35°C for 36 hrs. The solution was then cautiously poured onto ice, the white precipitate filtered off and identified (as above) as pure 2-hydroxyhexafluoroquinoline (200 mg., 20%).

D. Experimental for Chapter 5

1. Preparation of perfluoro(5,6,7,8-tetrahydroquinoline)

Reaction between heptachloroquinoline and potassium fluoride

(a) At 470°C

An intimate mixture of heptachloroquinoline (25g., 0·1 mole) and potassium fluoride (75g., 1·3 mole) were charged into a nickel lined autoclave (150 ml.) and the autoclave evacuated and sealed. After heating to 470° for a total of 17½ hrs., the volatile products were vacuum transferred from the hot autoclave into a trap cooled in liquid air. Analysis of the products (12g.) by quantitative gas chromatography (Column 'O', 250°C) showed there to be mainly three components, a volatile product (ca. 5%), heptafluoroquinoline (80%) and monochlorohexafluoroquinolines (ca. 15%).

(b) At 550°C

The autoclave was loaded as above and heated to 550° for a total of 17½ hrs. The volatile products (6g.) were vacuum transferred from the hot autoclave into a trap cooled in liquid air and shown by vapour phase chromatography (Column 'O', 250°) to comprise mainly of the volatile component found in low yield in the previous experiment. Vacuum transference of the liquid product followed by atmospheric distillation of the combined products of several reactions through a 20 cm. column packed with glass helices afforded perfluoro(5,6,7,8-tetrahydroquinoline) in ca. 15% yield (based on the heptachloroquinoline introduced), b.pt. 160°C. (Found: C, 32·39; N, 4·52; F, 62·80%; M, 331. $C_9F_{11}N$ requires C, 32·63; N, 4·23; F, 63·14%; M, 331). I.r. spectrum no.8, n.m.r. spectrum no.15.

2. An investigation of the preparative route to perfluoro(5,6,7,8-tetrahydroquinoline)

(a) Addition of chlorine to the reaction of heptachloroquinoline with potassium fluoride

Chlorine (1 litre at atmospheric temperature and pressure, 40 m.mole) was sealed into a small glass ampoule and charged into a nickel lined autoclave (150 ml.) with an intimate mixture of heptachloroquinoline (7·1g., 19·1 m.mole) and anhydrous potassium fluoride (ca. 25g., 450 m.mole). The autoclave was cautiously evacuated, sealed and heated to 470°C for a total of 17 hrs. No volatile products could be vacuum transferred from the hot autoclave into a trap cooled in liquid air.

(b) Addition of chlorine to heptafluoroquinoline

Chlorine (1 litre, 40 m.mole) and sublimed heptafluoroquinoline (5·0g., 19·6 m.mole) were sealed into an evacuated pyrex Carius tube (ca. 25 cm. x 3 cm.). The tube was irradiated for 24 hrs. by u.v. light (1 kw. high pressure mercury lamp), frozen in liquid air, opened and the viscous oil washed out with dry ether (150 ml.). The ether was washed with water (2 x 25 ml.) dried and evaporated under reduced pressure. The remaining oil was transferred under high vacuum (100°C, ·001 mm.) to give (6·8g., 87%) 5,6,7,8-tetrachloroheptafluoroquinoline, b.pt. >200°C at atmospheric pressure. (Found: C, 27·27; N, 3·74; F, 33·9; Cl, 36·2%; M, 397 (for 4 x ^{35}Cl). $C_9Cl_4F_7N$ requires C, 27·2; N, 3·53; F, 33·5; Cl, 35·8%; M, 397 (4 x ^{35}Cl)). I.r. spectrum no.9, n.m.r. spectrum no.16.

(c) Attempted addition of chlorine to heptachloroquinoline

(i) No solvent

Chlorine (1 litre, 40 m.mole) and heptachloroquinoline (7·1g., 19·1 m.mole) were sealed in a pyrex Carius tube and irradiated by u.v. light for

24 hrs. as above. The tube was frozen in liquid air, opened, the chlorine allowed to escape and the solid shaken from the tube. Thin layer chromatography (silica eluted with chloroform) and the i.r. spectrum demonstrated a quantitative return of unchanged starting material.

(ii) With solvent

Chlorine (1 litre, 40 m.mole), heptachloroquinoline (6g., 16 m.mole) and dry carbon tetrachloride (50 ml.) were sealed in a Carius tube as above and irradiated for 24 hrs. by u.v. light. The tube was frozen, opened, the chlorine allowed to escape and the mixture shaken from the tube. The carbon tetrachloride was allowed to evaporate and the heptachloroquinoline was quantitatively recovered unchanged (identified by i.r. spectrum, pure by thin layer elution chromatography, silica eluted with chloroform).

(d) Reaction between 5,6,7,8-tetrachloroheptafluoroquinoline and potassium fluoride

(i) At 470°C

5,6,7,8-Tetrachloroheptafluoroquinoline (5g., 12·6 m.mole) and potassium fluoride (10g., 170 m.mole) were sealed in an evacuated nickel lined autoclave (150 ml.) and heated to 470°C for a total of 17 hrs. The autoclave was vented into a liquid air cooled trap and vapour phase chromatography (Column 'O', 250°C) showed the product (1·4g.) to be mainly heptafluoroquinoline (ca. 44%). An i.r. spectrum confirmed the identification.

(ii) At 400°C

5,6,7,8-Tetrachloroheptafluoroquinoline (5·1g., 12·8 m.mole) and potassium fluoride (10g., 170 m.mole) were sealed into an evacuated nickel lined autoclave (150 ml.) and heated to 400°C for 3 hrs. The autoclave was pumped out into a liquid air cooled trap and analysis of the product (2·5g.) by vapour phase chromatography (Column 'O', 250°C) showed it to be largely

heptafluoroquinoline but also contained some material (ca. 15%) of the same retention time as perfluoro(5,6,7,8-tetrahydroquinoline).

3. Nucleophilic substitution in perfluoro(5,6,7,8-tetrahydroquinoline)

(a) Ammonia

Perfluoro(5,6,7,8-tetrahydroquinoline) (3·3g., 10 m.mole) was dissolved in acetone (30 ml.). Ammonia (1·7 ml. of 0·880 g./ml., 31·4 m.mole) was dissolved in acetone (10 ml.) and added slowly to the stirred solution of substrate over 5 mins. The solution was stirred at room temperature for 30 mins. then poured into excess water (100 ml.). The aqueous suspension was extracted with ether (3 x 50 ml.), the combined extracts dried and evaporated under reduced pressure. Quantitative vapour phase chromatography (Column 'O', 150°C) showed the product (3·2g., 97%) to be a mixture of two components of similar retention time. The components were separated by preparative scale vapour phase chromatography (Column 'O', 125-140°C) and gave after recrystallisation (60-80 petroleum ether), 4-aminoperfluoro(5,6,7,8-tetrahydroquinoline), m.pt. 124°C. (Found: C, 32·64; H, 0·61; N, 8·30; F, 57·4%; M, 328. $C_9H_2F_{10}N_2$ requires C, 32·93; H, 0·61; N, 8·54; F, 57·93%; M, 328). I.r. spectrum no.10, n.m.r. spectrum no.17 and the less volatile component after recrystallisation (60-80 petroleum ether) was identified as 2-aminoperfluoro(5,6,7,8-tetrahydroquinoline), m.pt. 111°C. (Found: C, 32·99; H, 0·77; N, 8·36; F, 57·33%; M, 328. $C_9H_2F_{10}N_2$ requires C, 32·93; H, 0·61; N, 8·54; F, 57·93%; M, 328). I.r. spectrum no.11, n.m.r. spectrum no.18.

(b) Sodium methoxide

(i) One molar equivalent

Perfluoro(5,6,7,8-tetrahydroquinoline) (5g., 15·1 m.mole) was dissolved in dry methanol (30 ml.) in a nitrogen flushed flask fitted with a dropping funnel. Sodium methoxide (15 ml. of 1·0 molar solution in methanol)

was added slowly at room temperature over a period of 5 mins. The solution was stirred for a further 5 mins. then poured into water (100 ml.). The aqueous mixture was acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The combined extracts were dried and evaporated under reduced pressure to leave a clear liquid (4·9g., ca. 95%). Quantitative gas chromatography (Column 'O', 150°C) showed it to be mainly (> 85%) two isomeric monomethoxylated products in the ratio of 2·3:1 and small amounts of a dimethoxylated product and unchanged starting material. Separation of the two isomers by preparative scale vapour phase chromatography (Column 'O', 120°C) afforded as the more volatile component and in greater amount 2-methoxyperfluoro(5,6,7,8-tetrahydroquinoline), m.pt. ca. 18°C, b.pt. 168°C. (Found: C, 35·29; H, 0·90; N, 3·89; F, 55·1%; M, 343. $C_{10}H_3F_{10}NO$ requires C, 34·98; H, 0·87; N, 4·08; F, 55·39%; M, 343). I.r. spectrum no.12, n.m.r. spectrum no.19.

The second component was identified from its ^{19}F n.m.r. spectrum as 4-methoxyperfluoro(5,6,7,8-tetrahydroquinoline), b.pt. 193°C. (Found: C, 34·68; H, 1·01; N, 3·79; F, 54·96%; M, 343. $C_{10}H_3F_{10}NO$ requires C, 34·98; H, 0·87; N, 4·08; F, 55·39%; M, 343). I.r. spectrum no.13, n.m.r. spectrum no.20.

(ii) Two molar equivalents

Sodium methoxide (6·1 ml. of 1·0 molar solution in methanol) was added slowly to a stirred solution of perfluoro(5,6,7,8-tetrahydroquinoline) (1·0g., 3·0 m.mole) in methanol (20 ml.) at room temperature under an atmosphere of dry nitrogen. After stirring for 15 mins. the solution was poured into water (100 ml.). The aqueous suspension was acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The combined extracts were dried and evaporated under reduced pressure to leave a white solid (1·5g.). The solid was recrystallised from methanol giving (70%) 2,4-dimethoxyperfluoro(5,6,7,8-

tetrahydroquinoline), m.pt. 48°C. (Found: C, 36·85; H, 1·99; N, 3·86; F, 47·88%; M, 355. $C_{11}H_6F_9NO_2$ requires C, 37·18; H, 1·69; N, 3·94; F, 48·16%; M, 355). I.r. spectrum no.14, n.m.r. spectrum no.21.

4. Defluorination of perfluoro(5,6,7,8-tetrahydroquinoline)

The defluorination apparatus consisted essentially of a nitrogen swept silica tube (ca. 75 cm. x 1 cm.) packed with steel wool and surrounded by a cylindrical heater. The temperature of the tube was controlled by a variable voltage input and stabilised by thermal equilibrium. A thermocouple measured the temperature at the centre of the heater.

Perfluoro(5,6,7,8-tetrahydroquinoline) (1·5g., 4·5 m.mole) was entrained in a stream of nitrogen (ca. 6 l./hr.) and passed through the defluorination tube (estimated contact time 1½ mins.). The products were collected in a trap cooled by solid carbon dioxide. Analysis of the product (0·75g.) by vapour phase chromatography (Column 'O', 200°C) showed it to be entirely one product with the same retention time as heptafluoroquinoline (64%). Thin layer elution chromatography (silica eluted with hexane) showed the presence of only one compound and the i.r. spectrum confirmed the identification. No attempt to maximise the yield by varying temperature or flow rate was made.

5. Relative reactivities of heptafluoroquinoline and perfluoro(5,6,7,8-tetrahydroquinoline) towards sodium methoxide

To a stirred solution of heptafluoroquinoline (0·25g., 1·0 m.mole) and perfluoro(5,6,7,8-tetrahydroquinoline) (0·33g., 1·0 m.mole) in dry methanol (20 ml.) under an atmosphere of dry nitrogen was slowly added sodium methoxide (1·0 ml. of 1·0 molar solution) in additional methanol (6 ml.) at room temperature. The solution was stirred for 15 mins. then poured into water (100 ml.), acidified (dil HCl) and extracted with ether (3 x 50 ml.). The combined extracts were dried and evaporated cautiously under reduced pressure

until little ether remained. Analysis of the mixture by quantitative gas chromatography (Column 'O', 150°, precalibrated with the expected products) showed qualitatively that a larger portion of the perfluoro(5,6,7,8-tetrahydroquinoline) had reacted. Peak overlap between unchanged heptafluoroquinoline and 4-methoxyperfluoro(5,6,7,8-tetrahydroquinoline) prevented a quantitative reactivity ratio from being calculated.

E. Experimental for Chapter 6

1. Preparation of perfluoro(4-t-butylpyridine)

The apparatus and method have been previously described in this Chapter (Section C.2.g.i). Pentafluoropyridine (2g., 11·8 m.mole, dried over P_2O_5) in sulpholan (20 ml.) with caesium fluoride (ca. 1g.) was reacted with perfluoroisobutene (ca. 5g., 25 m.mole) at ambient temperature (30°C) for 4 hrs. The products were extracted in the normal way to yield a pale yellow liquid (2·2g., ca. 40%). The liquid was vacuum transferred and analysis by vapour phase chromatography (Column 'O', 78°C; Column 'A', 100°C) showed it to be mainly (ca. 90%) one product with a small amount of a second component. The component in larger proportion was separated by preparative scale vapour phase chromatography (Column 'O', 100°C) and found to be perfluoro(4-t-butylpyridine)[152], b.pt. 135°C. (Found: F, 66·6%; M, 369. $C_9F_{13}N$ requires F, 66·39%; M, 369). I.r. spectrum no.15, n.m.r. spectrum no.22.

The minor component could not be obtained uncontaminated by perfluoro(4-t-butylpyridine) but the mass spectrum and ^{19}F n.m.r. of the compound were consistent with it being perfluoro(2,4-di-t-butylpyridine). (Found: M, 569. $C_{13}F_{21}N$ requires M, 569). N.m.r. spectrum no.23.

2. Preparation of 2-methoxyperfluoro(4-ethylpyridine)

Sodium methoxide (8·5 ml. of a 1·0 molar solution in methanol) was added slowly to a stirred solution of perfluoro(4-ethylpyridine)[50] (2·3g., 8·5 m.mole) in methanol (40 ml.) at room temperature under an atmosphere of dry nitrogen. The solution was stirred for a further 15 mins. then poured into water (200 ml.). The aqueous suspension was acidified (dil. HCl) and extracted with ether (3 x 50 ml.). The combined extracts were dried and evaporated under reduced pressure to leave a white solid which sublimed under vacuum (100°C, ·005 mm.) to give 2-methoxyperfluoro(4-ethylpyridine) (2g., 83%) identified by comparison

of the i.r. spectrum and the ^{19}F n.m.r. spectrum with an authentic sample.

3. Other samples

Samples of perfluoro(4-ethylpyridazine) and perfluoro(4-ethylpyridine) were kindly donated by Dr. M.Y. Gribble.

APPENDIX 1

^{19}F and ^{1}H n.m.r. spectra

A. Index to n.m.r. spectra

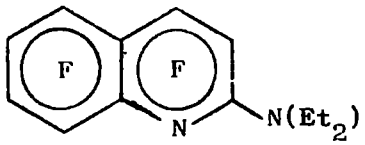
1. 2-N,N-diethylaminohexafluoroquinoline*
2. 2-methoxyhexafluoroquinoline*
3. 2,4-dimethoxypentafluoroquinoline*
4. 2,4,7-trimethoxytetrafluoroquinoline*
5. 6-methoxy,perfluoro(2,4,-di-isopropylquinoline)*
6. 3,6-dimethoxy,perfluoro(2,4-di-isopropylquinoline)*
7. 2-n-butylhexafluoroquinoline
8. perfluoro(2,4,6-tri-sec-butylquinoline)*
9. perfluoro(2,4-di-sec-butylquinoline)*
10. perfluoro(2,6-di-t-butylquinoline)*
11. perfluoro(2-t-butylquinoline)
12. 2-methoxy,4-chloropentafluoroquinoline*
13. 2-methoxy,4-bromopentafluoroquinoline*
14. 2-methoxy,4-iodopentafluoroquinoline*
15. perfluoro(5,6,7,8-tetrahydroquinoline)
16. 5,6,7,8-tetrachloroheptafluoroquinoline
17. 4-amino,perfluoro(5,6,7,8-tetrahydroquinoline)
18. 2-amino,perfluoro(5,6,7,8-tetrahydroquinoline)
19. 2-methoxy,perfluoro(5,6,7,8-tetrahydroquinoline)
20. 4-methoxy,perfluoro(5,6,7,8-tetrahydroquinoline)
21. 2,4-dimethoxy,perfluoro(5,6,7,8-tetrahydroquinoline)
22. perfluoro(4-t-butylpyridine)
23. perfluoro(2,4-di-t-butylpyridine)

Compounds marked * are included in the table of coupling constants following the spectra.

All spectra, unless otherwise stated were run as solutions in acetone at 40°C. Shifts in p.p.m., relative to external $CFCl_3$ and $Si(Me)_4$ (0·0 p.p.m.).

Tentative assignments in parentheses.

1. 2-N,N-diethylaminohexafluoroquinoline*

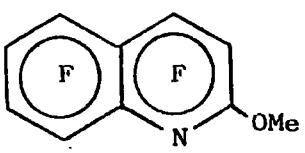


	Shift	Assignment
^{19}F	137·6	4
	150·3	5
	154·9	6
	157·4	7
	157·8	3
	166·4	8
^{1}H	1·3	$-CH_3$
	3·6	$-CH_2-$

$J_{CH_2-CH_3}$ = 7 Hz.

Spectrum recorded at 40°C as a melt with external $CFCl_3$ and $Si(CH_3)_4$

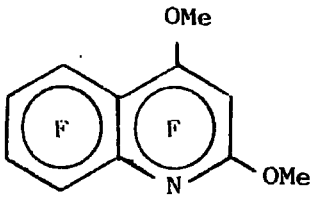
2. 2-methoxyhexafluoroquinoline*



	Shift	Assignment
^{19}F	134·6	4
	148·5	5
	151·9	6
	155·1	7
	160·8	8
	161·5	3
^{1}H	4·3	$2-OCH_3$

$J_{2-OMe-3F}$ = 0·0 Hz.

3. 2,4-dimethoxypentafluoroquinoline*

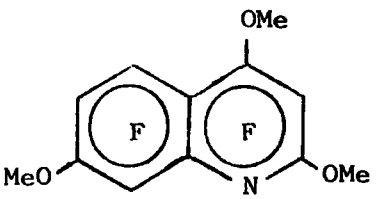


	Shift	Assignment
^{19}F	146·7	5
	153·2	6
	158·1	7
	159·2	3
	163·5	8
^{1}H	4·75	2-OCH_3
	4·9	4-OCH_3

$J_{2\text{-MeO-3F}}$ = 0·0 Hz.

$J_{4\text{-MeO-3F}}$ = 4·6 Hz.

4. 2,4,7-trimethoxytetrafluoroquinoline*

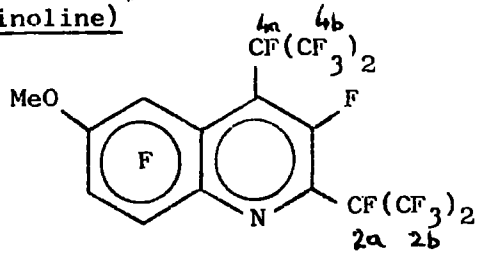


	Shift	Assignment
^{19}F	146·6	6
	147·9	5
	156·9	3
^{1}H	3·8	2-OMe
	4·0	7-OMe
	4·2	4-OMe

$J_{2\text{-OMe-3F}}$ = 0·0 Hz. $J_{4\text{-OMe-3F}}$ = 4·4 Hz.

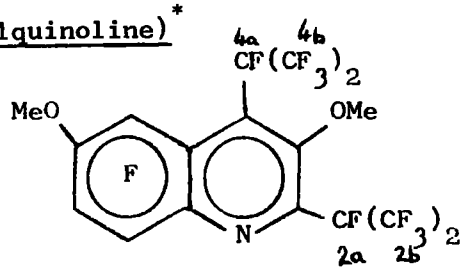
$J_{7\text{-OMe-6F}}$ = 1·8 Hz. $J_{7\text{-OMe-8F}}$ = 0·9 Hz.

5. 6-methoxy,perfluoro(2,4-di-isopropylquinoline)*



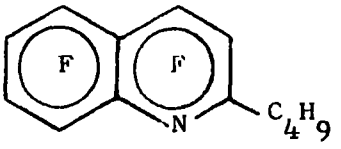
	Shift	Assignment
^{19}F	74·6	4b
	75·7	2b
	113·0	3
	125·6	5
	149·1	7 and 8
	169·9	4a
	184·7	2a
^{1}H	4·0 (broad)	6-OMe

6. 3,6-dimethoxy,perfluoro(2,4-di-isopropylquinoline)*



	Shift	Assignment
^{19}F	69·8	4b
	73·5	2b
	127·1	5
	148·4	7
	149·0	8
	159·2	4a
	183·7	2a
^{1}H	3·8 (multiplet)	(3-MeO)
	4·0 (broad)	(6-MeO)

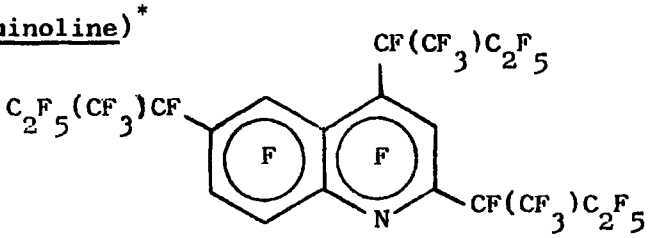
7. 2-n-butylhexafluoroquinoline



	Shift	Assignment
^{19}F	136	4
	149	5
	150	(6 or 3)
	152	(3 or 6)
	156	(7)
	158	(8)

Spectrum recorded as neat liquid

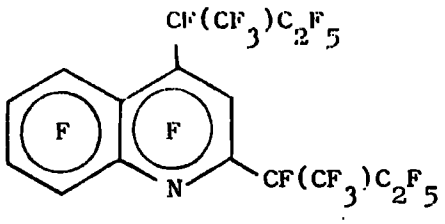
8. perfluoro(2,4,6-tri-sec-butylquinoline)*



	Shift	Assignment
^{19}F	75·5	3 x $-CF_3$
	83·6	3 x $-CF_3$
	ca. 90	5
	108·9	3
	117·9	$-CF_2-$
	121·8	2 x $-CF_2-$
	129·9 + 135·3	7
	147·9 + 149·6	8
	173·7	4a
	182·4	6a
	187·0	2a

Spectrum recorded as neat liquid

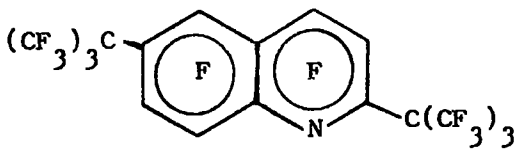
9. perfluoro(2,4-di-sec-butylquinoline)*



	Shift	Assignment
^{19}F	72·5	2 x CF_3
	80·6	2 x CF_3
	110·3	3
	116·3	$-CF_2-$
	119·2	$-CF_2-$
	128·1	5
	143·6	6
	145·4	(8)
	151·5	(7)
	170·0	4a
	184·7	2a

Spectrum recorded as neat liquid

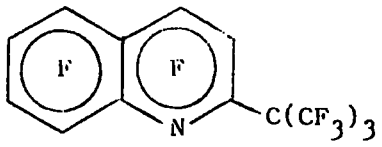
10. perfluoro(2,6-di-t-butylquinoline)*



	Shift	Assignment
^{19}F	60·9	6b
	61·7	2b
	101·8	5
	122·4	4
	124·8	7
	141·2	3
	149·4	8

Spectrum recorded as a saturated solution in acetone at 55°C

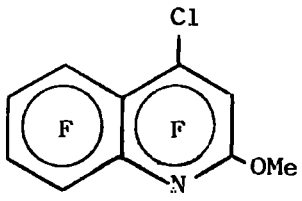
11. perfluoro(2-t-butylquinoline)



	Shift	Assignment
^{19}F	63·3	2b
	129·4	4
	141·9	(3)
	148·2	(6)
	148·6	(5)
	152·5	(7)
	153·7	(8)

Spectrum recorded as neat liquid contaminated with heptafluoroquinoline

12. 2-methoxy,4-chloropentafluoroquinoline*



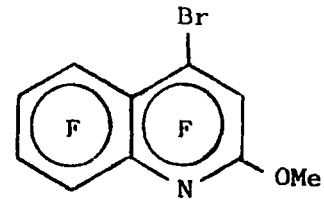
	Shift	Assignment
^{19}F	134·7	3
	147·2	5
	151·0	6
	155·6	7
	160·2	8
^{1}H	3·91	2-OMe

J_{OMe-F} = 0·0 Hz.

Spectrum recorded at 60°C as a melt with external $CFCl_3$ and $Si(Me)_4$.

Mixture with 2-chloro,4-methoxypentafluoroquinoline

13. 2-methoxy,4-bromopentafluoroquinoline*



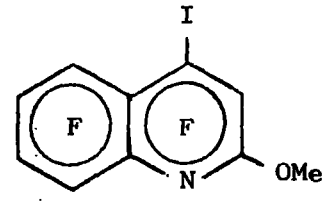
	Shift	Assignment
^{19}F	123·7	3
	145·5	5
	150·0	6
	154·9	7
	159·3	8
^{1}H	4·33	2-OMe

J_{OMe-F} = 0·0 Hz.

Spectrum recorded as a melt at 60°C with external $CFCl_3$ and $Si(Me)_4$.

Mixture with 2-bromo,4-methoxypentafluoroquinoline.

14. 2-methoxy,4-iodopentafluoroquinoline*



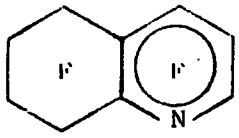
	Shift	Assignment
^{19}F	105·9	3
	126·4	5
	149·0	6
	154·6	7
	158·6	8
^{1}H	4·41	2-OMe

J_{OMe-F} = 0·0 Hz.

Spectrum recorded as a melt at 60°C with external $CFCl_3$ and $Si(Me)_4$.

Mixture with 2-iodo,4-methoxypentafluoroquinoline.

15. perfluoro(5,6,7,8-tetrahydroquinoline)



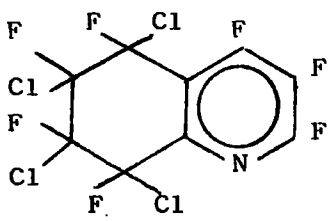
	Shift	Assignment
^{19}F	72·9	2
	108·8	CF_2
	113·1	CF_2
	118·2	4
	136·2	CF_2
	137·0	CF_2
	155·8	3

$J_{2,3}$ = 23 Hz. $J_{2,4}$ = 30·5 Hz. $J_{3,4}$ = 16 Hz.

$J_{4\text{-}CF_2}$ = 17 Hz. $J_{3\text{-}CF_2}$ = 3 Hz.

Spectrum recorded as neat liquid.

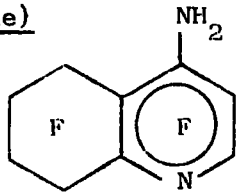
16. 5,6,7,8-tetrachloropentafluoroquinoline



	Shift	Assignment
^{19}F	75·2	2
	85·5 - 101	2 carbocyclic ring fluorines
	109 - 125·5	2 carbocyclic ring fluorines and 4
	156·2	3

Spectrum recorded as neat liquid

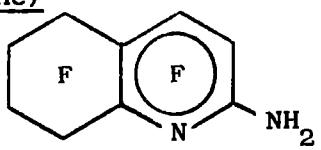
17. 4-amino,perfluoro(5,6,7,8-tetrahydroquinoline)



	Shift	Assignment
^{19}F	86·6	2
	109·9	CF_2
	111·7	CF_2
	135·1	CF_2
	136·2	CF_2
	161·2	3
^{1}H	6·3 (broad)	4-NH_2

$J_{2,3}$ = 23 Hz.

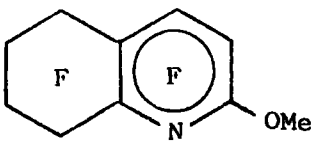
18. 2-amino,perfluoro(5,6,7,8-tetrahydroquinoline)



	Shift	Assignment
^{19}F	105·1	CF_2
	112·4	CF_2
	132·2	4
	134·9	CF_2
	135·6	CF_2
	160·0	3
^{1}H	6·8 (broad)	2-NH_2

$J_{3,4}$ = 16 Hz. $J_{4\text{-}CF_2}$ = ~16 Hz.

19. 2-methoxy,perfluoro(5,6,7,8-tetrahydroquinoline)

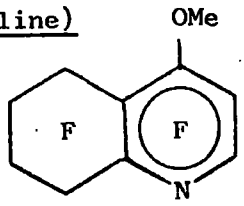


	Shift	Assignment
^{19}F	107·2	CF_2
	112·3	CF_2
	127·3	4
	135·2	CF_2
	136·1	CF_2
	157·6	3
^{1}H	3·94	2-OMe

$J_{3,4}$ = 15·5 Hz. $J_{3\text{-}CF_2}$ = 3 Hz. $J_{4\text{-}CF_2}$ = 16·5 Hz. $J_{OMe\text{-}F}$ = 0·0 Hz.

Spectrum recorded as neat liquid

20. 4-methoxy,perfluoro(5,6,7,8-tetrahydroquinoline)

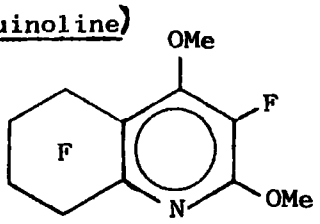


	Shift	Assignment
^{19}F	80·0	2
	111·4	CF_2
	113·9	CF_2
	136·7	CF_2
	138·1	CF_2
	155·9	3
^{1}H	4·1	4-OMe

$J_{OMe\text{-}3F}$ = 6 Hz. $J_{2,3}$ = 23 Hz.

Spectrum recorded as neat liquid

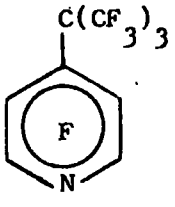
21. 2,4-dimethoxy,perfluoro(5,6,7,8-tetrahydroquinoline)



	Shift	Assignment
^{19}F	106·3	CF_2
	111·8	CF_2
	134·0	CF_2
	135·2	CF_2
	153·8	3
^{1}H	3·9	2-OMe
	4·0	4-OMe

$J_{2\text{-OMe-F}}$ = 0·0 Hz. $J_{4\text{-OMe-F}}$ = ~4 Hz. $J_{3\text{-}CF_2}$ = 4 Hz.

22. perfluoro(4-t-butylpyridine)

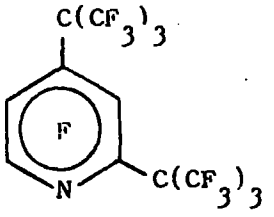


	Shift	Assignment
^{19}F	62·9	4b
	89·6	2,6
	129·9	3,5

$J_{4b\text{-}3,5}$ = 25·0 Hz.

Recorded as neat liquid, external $CFCl_3$

12. perfluoro(2,4-di-t-butylpyridine)



	Shift	Assignment
^{19}F	62·3	4b
	63·5	2b
	83·5	6

J_{4b-5}, J_{4b-3} = 24 and 27 Hz.

J_{2b-3} = 23 Hz.

J_{6-5}, $J_{6,3}$ = 23 and 30 Hz.

Spectrum recorded as impure liquid (containing perfluoro-4-t-butylpyridine) in a capillary tube.

B. Table of fluorine coupling constants of some derivatives of heptafluoroquinoline

Compound No. / Coupling	1	2	3	4	5	6	8	9	10	12	13	14
2a,2b	-	-	-	-	6·6	5·5	c	c	-	-	-	-
2a,3	-	-	-	-	60	-	70	65	-	-	-	-
2b,3	-	-	-	-	7·6	-	c	c	20	-	-	-
3,4	13·2	12·6	-	-	-	-	-	-	12·5	-	-	-
3,4b	-	-	-	-	29·2	-	c	c	-	-	-	-
3,5	7·2	7·4	6·8	6·3	c	-	c	c	c	9	11·5	14·5
3,6	3·6	3·6	3·2	3·0	-	-	-	(~ 4)	-	4	3·5	3·5
3,7	7·8	7·6	6·8	-	c	-	c	(6·5)	c	7·5	7·5	7·5
3,8	1·4	1·5	1·7	1·2	n	-	c	(~ 3)	(1·5)	n	0·5	n
4a,4b	-	-	-	-	3·8	2·8	c	c	-	-	-	-
4a,5	-	-	-	-	197	160	210	210	-	-	-	-
4b,5	-	-	-	-	15·2	17·8	c	c	-	-	-	-
4,5	47·4	47·8	-	-	-	-	-	-	75	-	-	-
4,6	1·8	1·6	-	-	-	-	-	-	-	-	-	-
4,7	3·2	3·4	-	-	-	-	-	-	(1·7)	-	-	-
4,8	3·3	3·4	-	-	-	-	-	-	(4)	-	-	-
5,6	14·2	14·8	14·2	14·7	-	-	-	(14·5)	-	14·5	14·5	14·5
5,7	1·2	1·4	1·8	-	c	c	c	(~ 5)	c	2	2	2
5,8	18·4	18·4	18·8	17·8	c	13·8	15	(14)	(11·8)	17	17·5	18
6a,7	-	-	-	-	-	-	120	-	26·5	-	-	-
6,7	17·4	17·0	18·8	-	-	-	-	(18)	-	18	18	18·5
6,8	0·8	1·5	n	2·8	-	-	-	(5)	-	n	n	n
7,8	19·6	18·5	20·2	-	c	18·2	14	(19)	(16·8)	19·5	19	19·5

Legend for Table

Coupling constants in Hz. ($\pm$ 1 Hz.).

n = Coupling constant not measured, too small.

c = Coupling constant not measured, resonance too broad or complex.

Coupling constants in parentheses are tentative assignments.

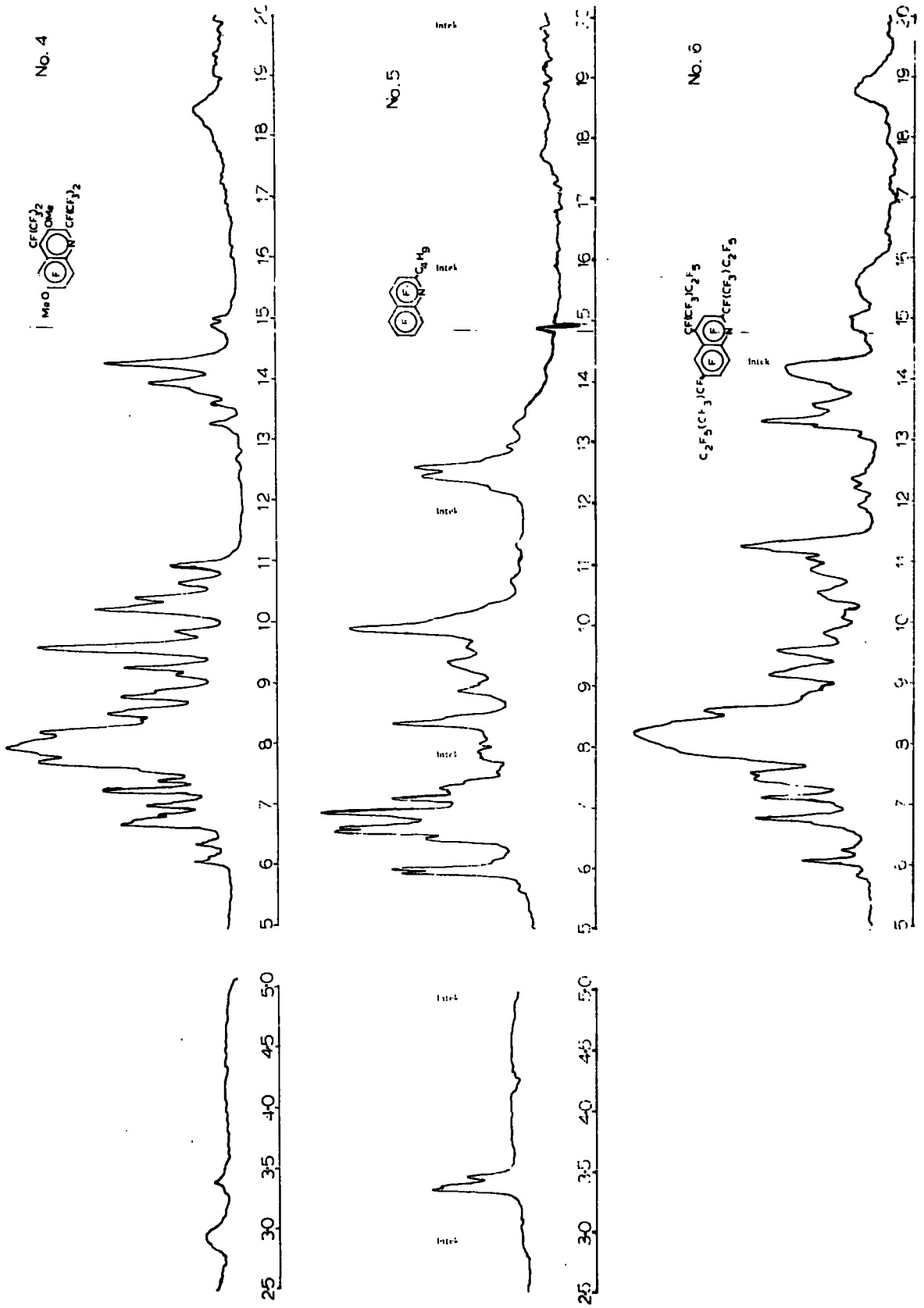
APPENDIX 2

Infra-red spectra

Spectrum No.	Compound	
1	2-N,N-diethylaminohexafluoroquinoline	(l)
2	2,4,7-trimethoxytetrafluoroquinoline	(s)
3	6-methoxy,perfluoro(2,4-di-isopropylquinoline)	(s)
4	3,6-dimethoxy,perfluoro(2,4-di-isopropylquinoline)	(s)
5	2-n-butylhexafluoroquinoline	(l)
6	perfluoro(2,4,6-tri-sec-butylquinoline)	(l)
7	perfluoro(2,6-di-t-butylquinoline)	(s)
8	perfluoro(5,6,7,8-tetrahydroquinoline)	(l)
9	5,6,7,8-tetrachloroheptafluoroquinoline	(l)
10	4-amino,perfluoro(5,6,7,8-tetrahydroquinoline)	(s)
11	2-amino,perfluoro(5,6,7,8-tetrahydroquinoline)	(s)
12	2-methoxy,perfluoro(5,6,7,8-tetrahydroquinoline)	(l)
13	4-methoxy,perfluoro(5,6,7,8-tetrahydroquinoline)	(l)
14	2,4-dimethoxy,perfluoro(5,6,7,8-tetrahydroquinoline)	(l)
15	perfluoro(4-t-butylpyridine)	(l)

(l) - sample as contact film between potassium bromide discs.

(s) - sample compressed to thin disc with potassium bromide.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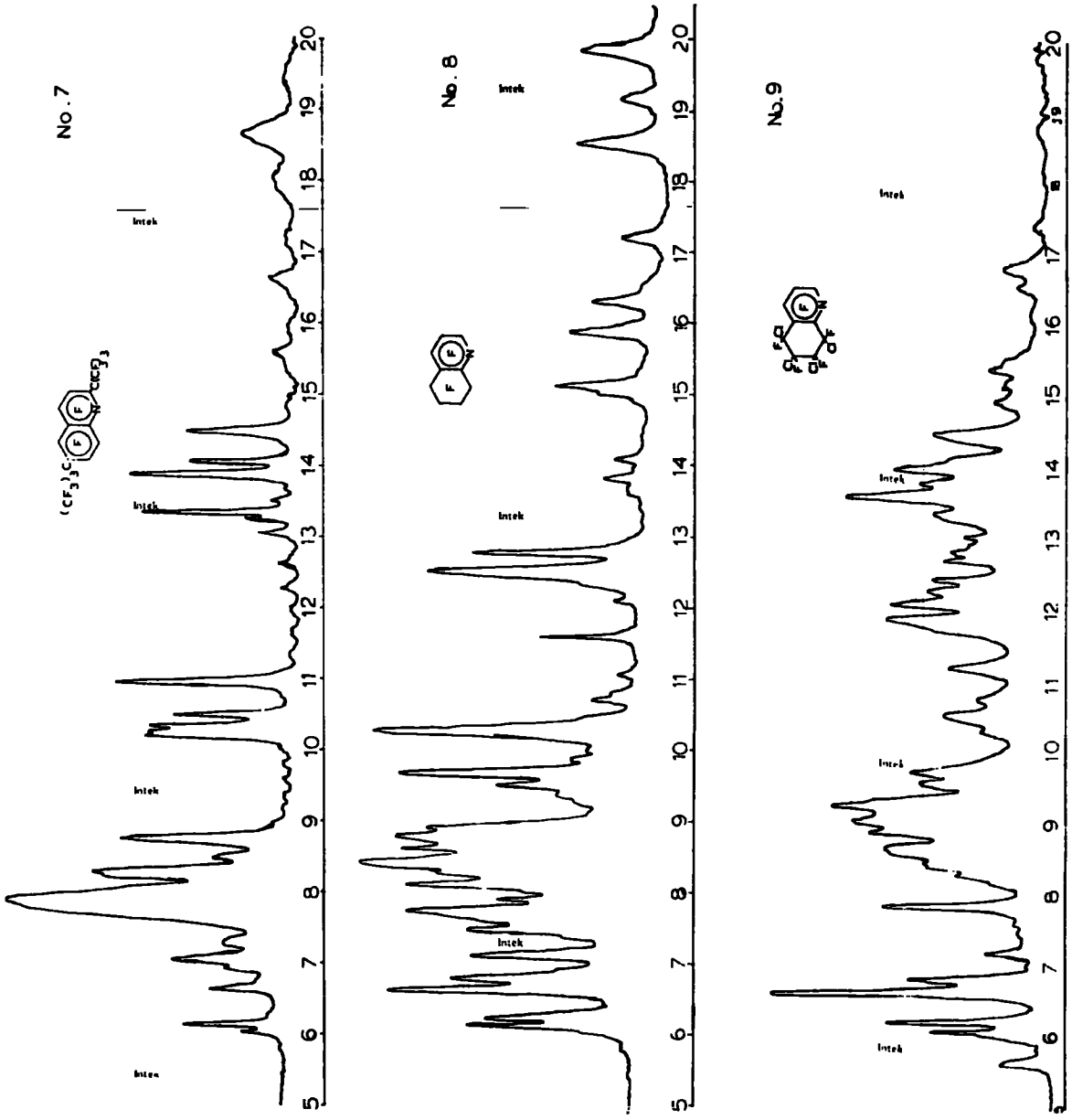
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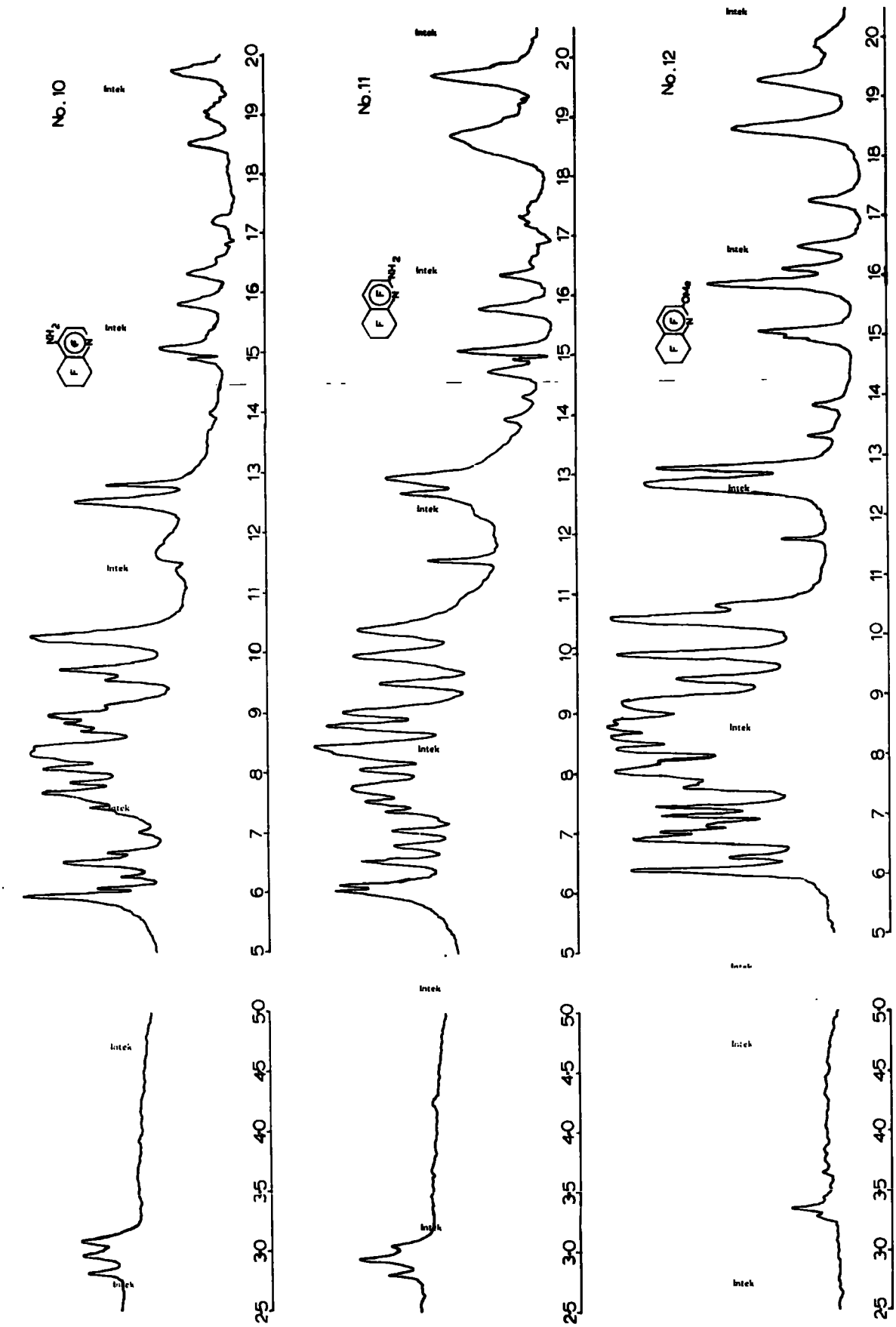
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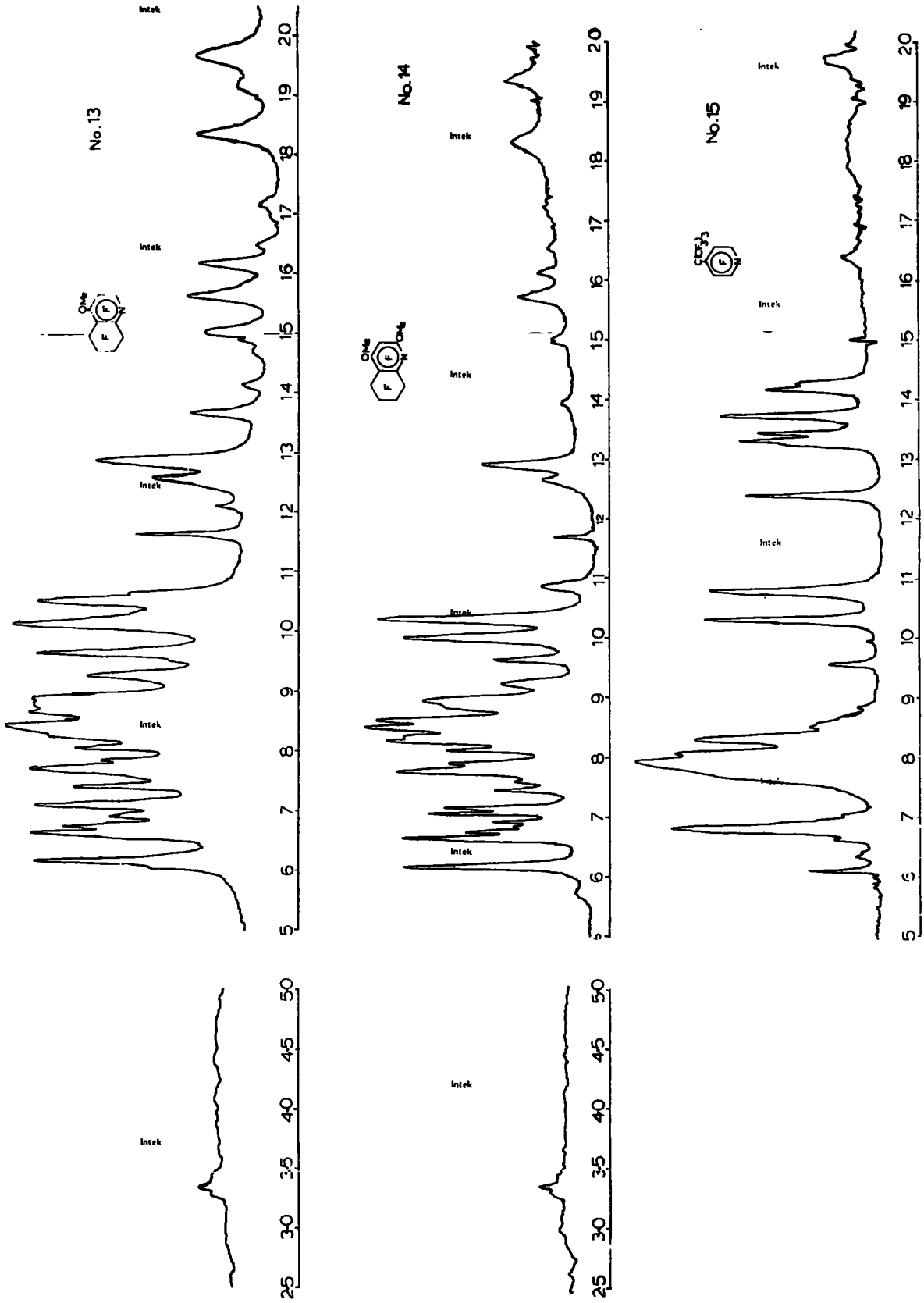
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