Some fluoride ion-initiated reactions of fluoroethylenes

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A THESIS

entitled

SOME FLUORIDE ION-INITIATED REACTIONS OF FLUOROETHYLENES

submitted by

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Finally, thanks are due to the Science Research Council for a maintenance grant.

TO

PAM AND MY PARENTS

MEMORANDUM

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

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

R.D. Chambers, R.P. Corbally, M.Y. Gribble, and W.K.R. Musgrave, J. Chem. Soc. (D), 1971, 1345.

SUMMARY

Some Fluoride Ion-Initiated Reactions of Fluoroethylenes.

Development of an atmospheric pressure system suitable for fluoride ion-initiated reactions of some fluoro-olefins with perfluoro-N-hetero-aromatic compounds has minimised some of the problems encountered in analogous autoclave reactions. From the observed results it is concluded that polyfluoroalkylation of perfluoro-pyridine and -pyridazine is possible under relatively mild conditions.

In the presence of caesium fluoride and tetraglyme, tetrafluoro-ethylene and pentafluoropyridine afforded five products in low to moderate yields, identified as the 4-, 2,4-di-, 2,4,5-tri-, tetrakis and pentakis-(pentafluoroethyl) derivatives. Defluorination of perfluoro-(4-ethyl-pyridine) and perfluoro-(4-isopropylpyridine) over heated iron filings gave perfluoro-(4-vinylpyridine) and 2-(2',3',5',6'-tetrafluoropyridyl)-pentafluoropropene respectively. Treatment of perfluoro-(4-ethylpyridine) with sodium methoxide in methanol gave the 2-methoxy derivative and similar reactions with perfluoro-(2,4-di-ethylpyridine) and perfluoro-(2,4-di-isopropylpyridine) gave the corresponding 5-methoxy derivatives. Fluoride ion-initiated rearrangement of perfluoro-(2,4,5-tri-ethylpyridine) to the 2,4,6-isomer was not observed at elevated temperatures.

Analogous perfluoroethylations of tetrafluoropyridazine gave low yields of the 4-, 4,5-di- and 3,4,5-tri-(pentafluoroethyl) derivatives. Treatment of perfluoro-(4-ethylpyridazine) with sodium methoxide in methanol gave the 5-methoxy derivative. Fluoride ion-initiated rearrangement of perfluoro-(4,5-di-ethylpyridazine) to the 3,5-isomer was not observed at elevated temperatures.

Excess perfluoroisobutene, in the presence of caesium fluoride and sulpholan, reacted with perfluoro-pyridine and -pyridazine to give perfluoro-(2,4,6-tri-t-butylpyridine) and perfluoro-(3,6-di-t-butyl-pyridazine) respectively. The unique substitution pattern of the latter was deduced from a correlation of the observed and calculated ^{19}F n.m.r. spectra, and from results of hydrolysis reactions under acidic and basic conditions.

In conjunction with previously reported results for analogous perfluoroisopropylation reactions, it is concluded that a clear cut variation from kinetic to thermodynamic control of products is observed for polyfluoroalkylation reactions of $CF_3CF_2^-$, $(CF_3)_2CF^-$, and $(CF_3)_3C^-$ with pentafluoropyridine and tetrafluoropyridazine.

Fluoride ion-initiated reactions of chlorotrifluoroethylene with pentafluoropyridine gave 1-chloro-(2',3',5',6'-tetrafluoropyridyl)-tetrafluoroethane, 4-chlorotetrafluoropyridine and the previously characterised mono-, di- and tri-perfluoroethylpyridines. The relative ratios of products formed were observed to be strongly solvent dependent. Analogous reactions with tetrafluoropyridazine afforded the previously characterised mono-, di- and tri-perfluoroethylpyridazines; no chlorine-containing polyfluoroalkyl derivatives were detected.

In comparable reactions of bromotrifluoroethylene and pentafluoro-pyridine, halogen exchange between $CF_2{=}CFBr$ and $CF_3\bar{C}FBr$ occurred in preference to polyfluoroalkylation, giving 1,1-dibromotetrafluoroethane. A polyfluoropyridine derivative, 1,1-bis(2',3',5',6'-tetrafluoropyridyl)-tetrafluoroethane, was also isolated and perfluoro-(4-vinylpyridine) was shown to be an intermediate in its formation. No bromine-containing

polyfluoroalkylpyridines were detected. Similar reactions with tetrafluoropyridazine resulted in polyfluoroalkylation rather than halogen exchange, however, the products isolated were the known mono-, di- and tri-(pentafluoroethyl) derivatives and tetrakis(pentafluoroethyl)-pyridazine. No bromopolyfluoroalkyl derivatives were detected.

Loss of chlorine and bromine in these reactions was shown to occur after polyfluoroalkylation and it was concluded that either a benzylic-type or a pseudo-S_N2'-type displacement mechanism was operating.

A fluoride ion-initiated reaction of trifluoroethylene with pentafluoropyridine gave a low yield of 1,1-bis(2',3',5',6'-tetrafluoropyridyl)-tetrafluoroethane, however, a similar reaction with tetrafluoropyridazine gave no tractable products.

Preparation of several 2,4,5-tri-substituted perfluoroalkylpyridines, containing both CF_3CF_2- and $(CF_3)_2CF$- groups, and their reactions with fluoride ion at elevated temperatures, indicated the factors which affect the ease of rearrangement to the 2,4,6-isomer. It is tentatively concluded that the migratory aptitude of the 5-substituent is the major factor, with steric interactions and the effect of the 2-substituent of lesser importance.

^{19}F N.m.r. studies have been carried out on the prepared fluorinated compounds.

CONTENTS

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EXPERIMENTAL

General Introduction

Research into synthetic fluorocarbon chemistry, principally conducted during the last thirty years, has become of considerable academic and industrial importance. This arises from the unique ability of fluorine to extensively or completely replace hydrogen, in a hydrocarbon system, without serious distortion of the geometry of the system. Consequently the differences in properties between fluorocarbons and hydrocarbons are not, despite the slightly larger size of the fluorine atom, significantly affected by stereochemical considerations. Clearly, therefore, a whole branch of synthetic organic chemistry primarily founded on carbon and fluorine rather than carbon and hydrogen is feasible.

The differences in the properties of fluorocarbons compared to their hydrocarbon analogues can be attributed to the variation in the electronic environment on the functional groups in the molecule. Such variations originate from the difference in electronegativity between hydrogen and fluorine; extensive replacement of hydrogen by fluorine leads to functional groups which are relatively electron deficient. Thus the chemistry of unsaturated fluorocarbons is complementary to that of their hydrocarbon analogues since the former undergo predominantly nucleophilic attack whereas the latter undergo predominantly electrophilic attack. Clearly, therefore, the fluoride ion in fluorocarbon systems has a parallel chemistry to the proton in hydrocarbon systems and the resultant fluorocarbanions are equivalent to the well-studied carbonium ions. Confirmation of accepted theories in hydrocarbon chemistry and illuminating information about mechanisms and reaction processes in fluorocarbon chemistry can be acquired on studying reactions involving such fluorocarbanion intermediates.

The enhanced thermal and chemical stability of fluorocarbons compared to hydrocarbons derives from a high carbon-fluorine bond strength and increased shielding of the carbon skeleton due to the higher electron density and marginally larger size of the fluorine atom. Commercial exploitation of these advantageous characteristics is at present limited to aliphatic fluorocarbons, notably for inert polymers, lubricants, coolants and sealants, aerosol sprays and refrigerants, however, possible applications of aromatic fluorocarbons are being continuously investigated.

The work described in this thesis is concerned with two types of fluoride-ion initiated reactions of fluorocarbons. The first is attack by fluoride-ion on some fluoro-olefins to produce a carbanion which subsequently displaces fluoride ion from a perfluorinated N-heterocyclic system, and the second is a novel fluoride ion catalysed rearrangement of some perfluoroalkyl-N-heterocyclic compounds.

INTRODUCTION

CHAPTER 1

Nucleophilic Substitution in Polyfluoroaromatic Compounds

In general, highly fluorinated aromatic compounds undergo nucleophilic substitution by a process analogous to electrophilic substitution in aromatic hydrocarbon chemistry. The orientation of substitution in polyfluorobenzenoid compounds can be predicted largely on the basis of a controlling I_π effect, except in certain instances where steric or specific interactions are important. In contrast, the orientation of substitution in polyfluoro-aromatic nitrogen heterocyclic compounds is dominated largely by the hetero-atom, with a relatively minor contribution from the I_π effect.

1.1. Polyfluorobenzenoid compounds.

Nucleophilic substitution in hexafluorobenzene is effected quite readily with a variety of suitable reagents including $^-OCH_3$,[1] ^-OH,[2,3] ^-SH,[4] NH_3,[5] $N_2H_4.H_2O$,[5b] CH_3NH_2,[5b] $^-CH_3$,[6] $^-C_6H_5$,[7] $^-HN.C_6H_5$,[8] $^-N(C_6H_5)_2$,[8] $^-O\text{-}CH_2\text{-}CH_2\text{-}OH$[9] and $^-HN\text{-}CH_2\text{-}CH_2\text{-}OH$[9] to give reasonable yields of the corresponding pentafluorophenyl derivatives. Further nucleophilic substitution of these pentafluorophenyl compounds, C_6F_5X, was reported extensively by Tatlow, Burdon and co-workers[7,8,10-20] who showed quite clearly the interesting possibility of positional isomerism. The orientation of substitution in C_6F_5X compounds was investigated with a series of nucleophiles and it was observed that attack occurred predominantly at the para position[10] when X = H, CH_3, C_6H_5, CF_3, C_6F_5, SCH_3, $N(CH_3)_2$, SO_2CH_3, Hg and halogen. In contrast, when X = O^- or NH_2 meta attack predominated,[14] and when X = OCH_3 or $NHCH_3$ similar yields of meta and para products were observed.[15] Anomalously high ortho replacement when X = COO^-,[16] NO,[19] NO_2[20] or when X = NO_2 and Nuc. = NH_3,

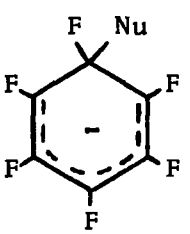
NHR_2[11,21] were attributed to solvent effects and specific nucleophile-substituent interactions respectively.

1.1.1. Rationalisation of the observed results[1-21] of nucleophilic substitution.

The observed orientation and relative reactivity in nucleophilic substitution reactions of polyhaloaromatic compounds were rationalised[22] in terms of the stability of the ground and transition states involved.

Thermodynamic evidence suggested[22] that, qualitatively, electron withdrawing substituents destabilised and electron donating substituents stabilised the ground states of pentafluorophenyl compounds relative to hexafluorobenzene.

Wheland intermediates of the type 1 usually provided a good guide to the transition states in nucleophilic aromatic substitution reactions and of the two resonance hybrids, 2 and 3, the former para quinoid structure was assumed to be the major contributor to this intermediate,



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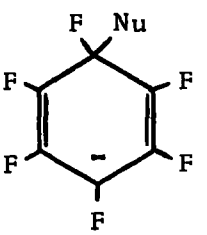

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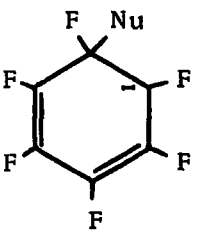


3

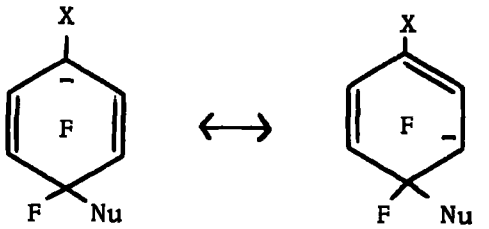
Nu. = nucleophile

with 3 of only minor importance. This assumption was substantiated by molecular orbital calculations[23] and experimental evidence.[24]

The effect of substituents in pentafluorophenyl compounds, C_6F_5X, on the stability of the transition state in nucleophilic substitution reactions was derived from a consideration of all the possible intermediates, 4 to 6, especially 4(a), 5(a) and 6(a), and the effect of

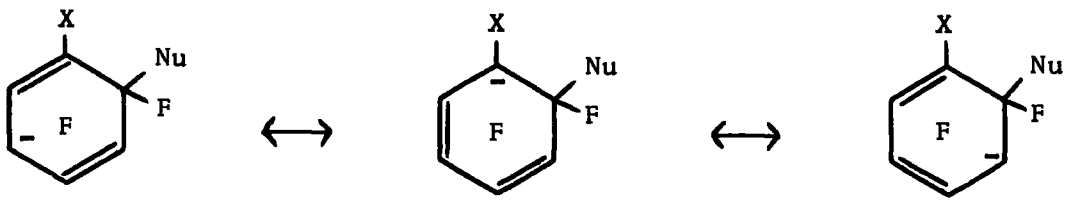
the substituent on the stability of the localised negative charge.

Clearly, if X stabilised the negative charge more than fluorine the



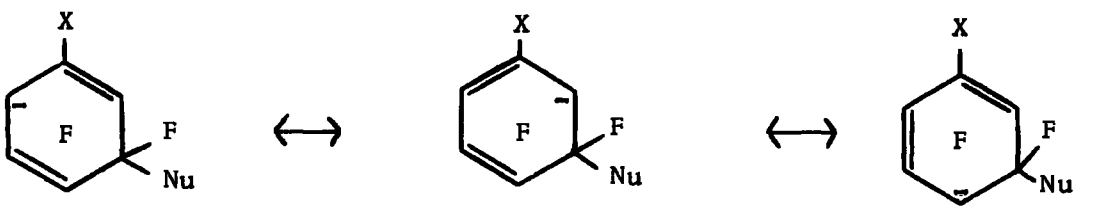
(a) (b)

4



(a) (b) (c)

5



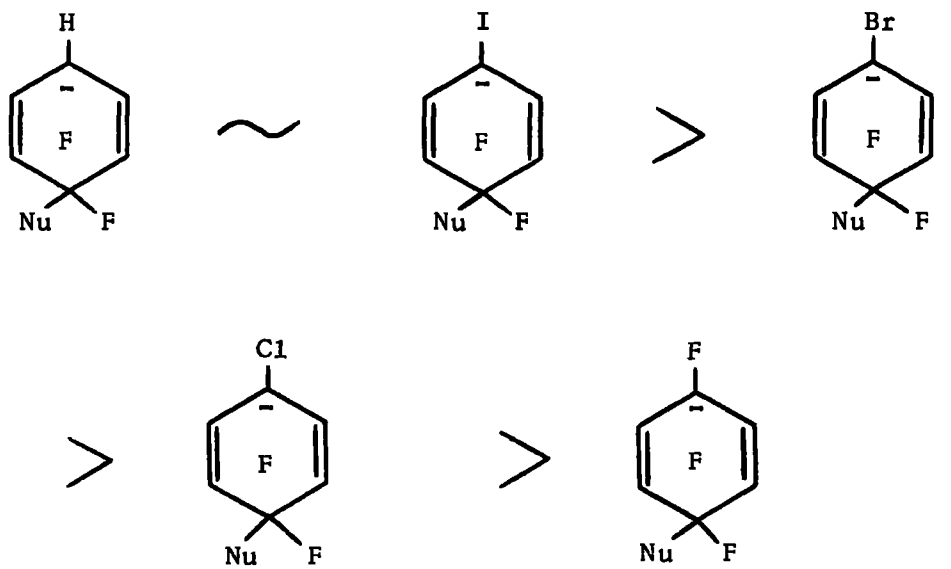
(a) (b) (c)

6

intermediate stabilities would be 4 > 5 > 6, due to major and minor contributions from 4(a) and 5(b). Nucleophilic attack would therefore occur para, and to a lesser extent ortho, to the substituent. Conversely, if X destabilised the negative charge then the intermediate stabilities would be reversed and meta attack would predominate. However, if X and fluorine had an identical effect upon the stability of the negative charge, a statistical ratio of 1:2:2 for para:ortho:meta substitution would be predicted.

Effect of substituents.

In general, the nitro and perfluoroalkyl groups stabilised the negative charge whereas the halogens destabilised it in the order F > Cl > Br > I ~ H[22] due to I_{π} repulsion.[25] This repulsion arises from Coulombic interaction between the p-electrons of the halogen and the ring π-electrons on the neighbouring carbon atom and is maximised in nucleophilic aromatic substitution due to the enforced planar geometry. Hence, the order of stability of hybrids of the type 2 for C_6F_5X (X = H or halogen) is:-



Quantitative I_{π} repulsive effects were not similarly derivable for nitrogen and oxygen but were assumed to be N > O > F which received some justification from observed data.[14]

In certain cases, the observed low percentage ortho replacement was attributed[5b,14,15,26] to steric interaction between the substituent and the nucleophile, or the ortho fluorines. Conversely, the observed high percentage ortho replacement of $C_6F_5NO_2$ with NH_3 or CH_3NH_2 was attributed[11,21] primarily to hydrogen bonding between the nucleophile and the substituent. Further work indicated[20] that substitution of $C_6F_5NO_2$ by other nucleophiles e.g. CH_3O^- depended upon the polarity of the solvent.

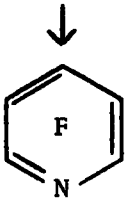
1.2. Polyfluoroheterocyclic compounds.

Extension of nucleophilic substitution reactions to polyfluoro-heterocyclic compounds has been concerned primarily with polyfluoro-aromatic nitrogen heterocyclic compounds, although similar replacement reactions of heterocyclic compounds based on sulphur have been reported recently.

1.2.1. Polyfluoro-aromatic nitrogen heterocyclic compounds.

(a) Basic conditions.

Nucleophilic substitution of perfluoro-pyridine[27-33] (7), -quinoline[34,35] (8), -isoquinoline[34,35] (9), -pyridazine[36-41] (10), -pyrimidine[42-44] (11) and -pyrazine[45,46] (12) under moderate conditions with a variety of nucleophiles, gave mono-substituted compounds predominantly at the positions indicated.



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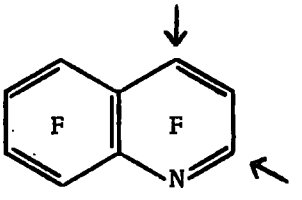

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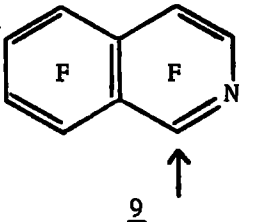

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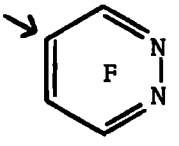

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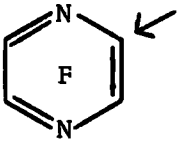
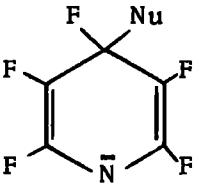


12

Chambers, Musgrave and co-workers[37] proposed, on the basis of the observed results, that the orientation of nucleophilic substitution in polyfluoro-aromatic nitrogen heterocyclic compounds is controlled, in contrast to the polyfluorobenzene systems, by the influence of the ring nitrogen atom(s), rather than the effect of I_{π} repulsion, on the stability of the transition state. Clearly the latter effect must be

considered but a high electron density on nitrogen in the transition state, as in 13 and 14, reduced the electron density on the carbon atoms, compared with substitution in polyfluorobenzenes, and consequently the relative importance of the I_{π} destabilisation. This was consistent with



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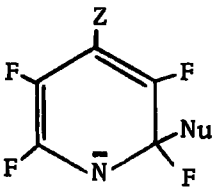
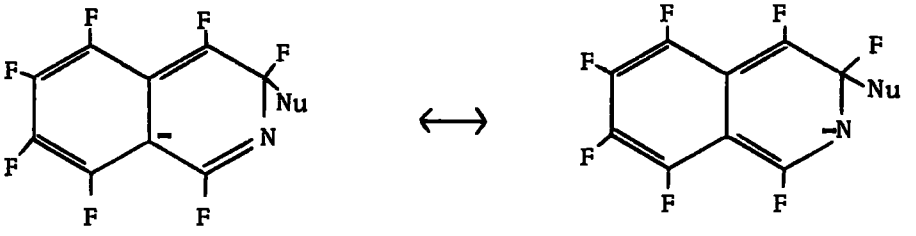


14

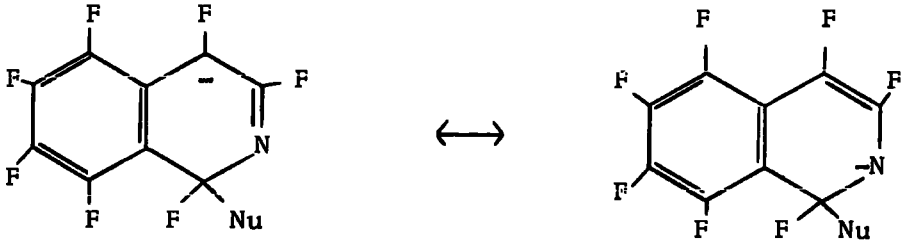
the observed order of reactivity, hexafluorobenzene < pentafluoropyridine < heptafluoro-quinoline and -isoquinoline < tetrafluoropyridazine.

The predicted position of nucleophilic attack para to the nitrogen atom in 7, 8, 10 and 11 was identical with the nitrogen or the I_{π} repulsive effect as the controlling factor. However, for heptafluoroisoquinoline (9) the I_{π} effect predicted 3-substitution, via hybrid 15 analogous to octafluoronaphthalene,[47] whereas 1-replacement was observed via hybrid 16 which indicated control of orientation by the nitrogen.



(a) (b)

15



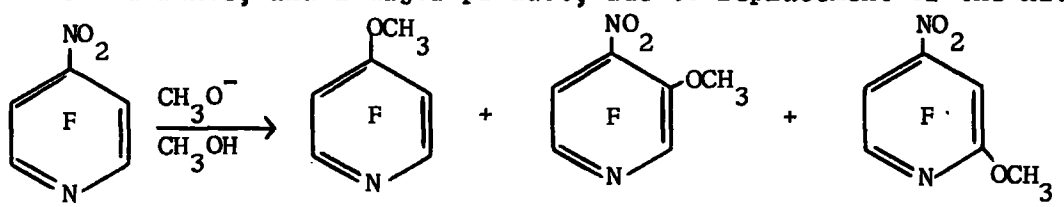
(a) (b)

16

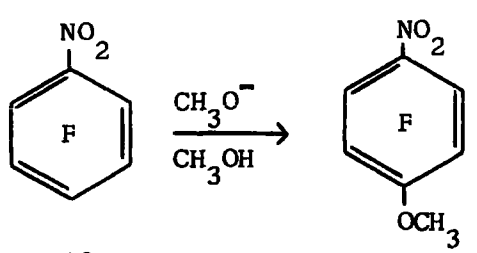
The transition state preceding the intermediate 16 is therefore more stable than that preceding intermediate 15, despite the unfavourable I_π effect in 16(a), due to the influence of the ring nitrogen. Simplified M.O. calculations of the localisation energies[48] for nucleophilic substitution in heptafluoroisoquinoline indicated[49] quite clearly that 1-substitution was preferred.

In general, 4-substituted tetrafluoropyridines reacted with suitable nucleophiles[28,30] to replace the 2-fluorine; further reaction of the 2,4-dimethoxy derivative with methoxide ion[28] afforded 2,4,6-trimethoxy-3,5-difluoropyridine. Some evidence for a two step mechanism in nucleophilic aromatic substitution was obtained[30] from the replacement of the 2-fluorine, and not the 4-bromine, by methoxide ion in 4-bromo-tetrafluoropyridine.

In contrast, the reaction of 4-nitrotetrafluoropyridine (17) with methoxide ion[50] afforded two minor products, due to replacement of the 2- and 3-fluorines, and a major product, due to replacement of the nitro-group.



17 70% 7% 23%



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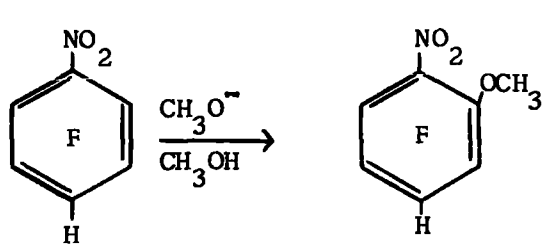
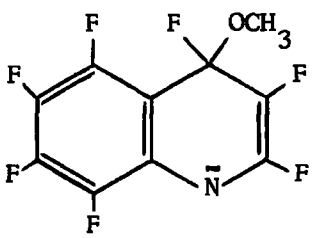


19

Methoxylation of pentafluoronitrobenzene[11] (18) and 1,2,4,5-tetrafluoro-3-nitrobenzene[37] (19) occurred para and ortho to the nitro-group respectively. However, on the basis of a controlling I_{π} effect it was predicted that, for the latter, replacement of the nitro-group would be preferred. The different behaviour of the nitropyridine (17), and the hydro-compound (19) was attributed[37] to extreme stabilisation of a transition state in which high electron density was localised on a ring-nitrogen, or a nitro group, and not to unfavourable I repulsive effects.

Reaction of heptafluoroquinoline (8) with methoxide ion[34] afforded a mixture of 2-methoxy and 4-methoxyhexafluoroquinoline in the ratio of 3·4:1, which was predicted[37] qualitatively from the similar stability of the hybrids 20 and 21.



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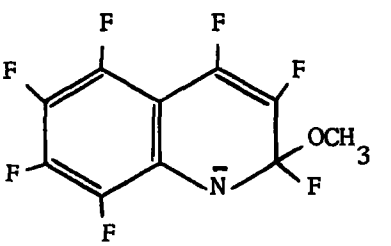
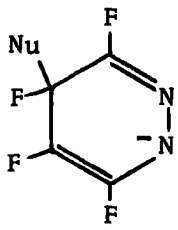


21

The higher reactivity of tetrafluoropyridazine[37-41] (10) and -pyrimidine[42-44] (11) compared with tetrafluoropyrazine[45,46] (12) towards a variety of nucleophiles, and the observed orientation of substitution were rationalised in terms of the stability of the transition states, assuming similar ground state stabilities. Type 2 Wheland intermediates, with the negative charge localised on the ring-nitrogen, were possible for tetrafluoro-pyridazine (22) and -pyrimidine (23). However, for tetrafluoropyrazine, which was not subject to orientation complications, only a less stable type 3 hybrid (24) was possible.



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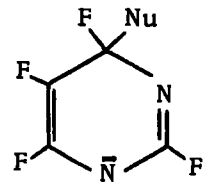

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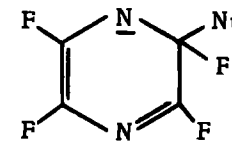
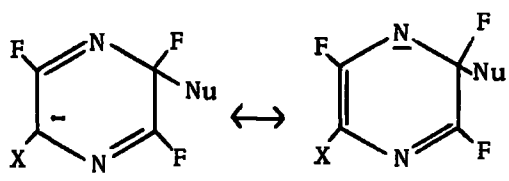


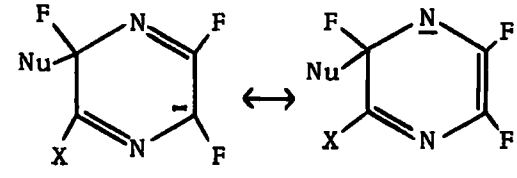
24

Further nucleophilic substitution of the trifluoro-pyridazine[37] and -pyrimidine[43] derivatives occurred, as expected, para to the second ring-nitrogen, however the orientation of disubstitution in tetrafluoropyrazine depended upon the initial substituent. The observed results were rationalised[46] from a consideration of the stability of the possible type 2 Wheland intermediates, 25 - 27.



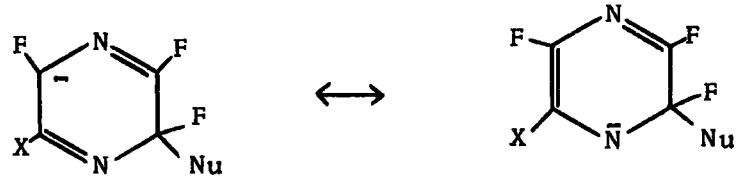
(a) (b)

25



(a) (b)

26



(a) (b)

27

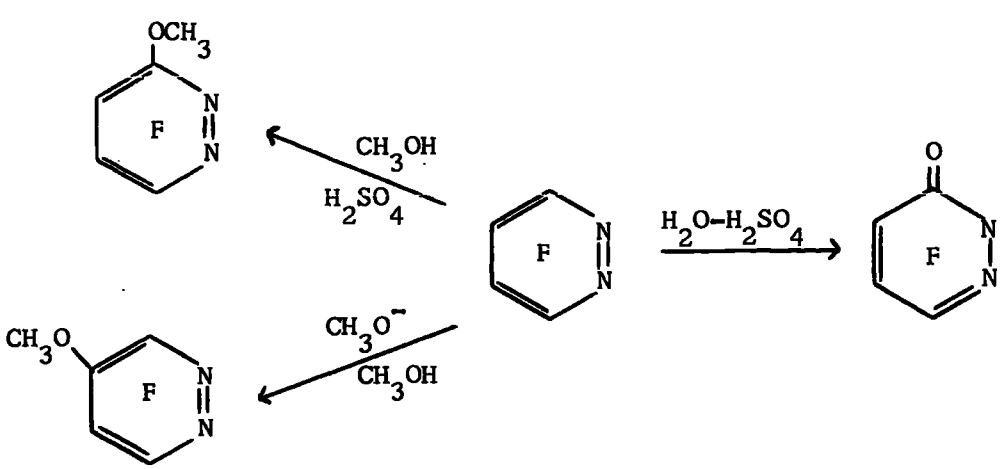
The stability of hybrid 25 relative to 26 and 27, was increased if X was alkyl or chlorine, due to reduced $I_{\eta\gamma}$ repulsion, and decreased if X was alkoxy, due to enlarged $I_{\eta\gamma}$ repulsion. Para replacement was predicted, and observed, for the former substituents while ortho or meta replacement was predicted for alkoxy substituents; only ortho substitution was

observed. The proposed rationalization was that the fluorine atom adjacent to the localised negative charge on the ring-nitrogen in 26(b) stabilised the transition state more than the alkoxy-group in the corresponding intermediate 27(b). Analogous carbanion stabilisation by β-fluorine atoms has been reported previously.[51]

(b) Acidic conditions.

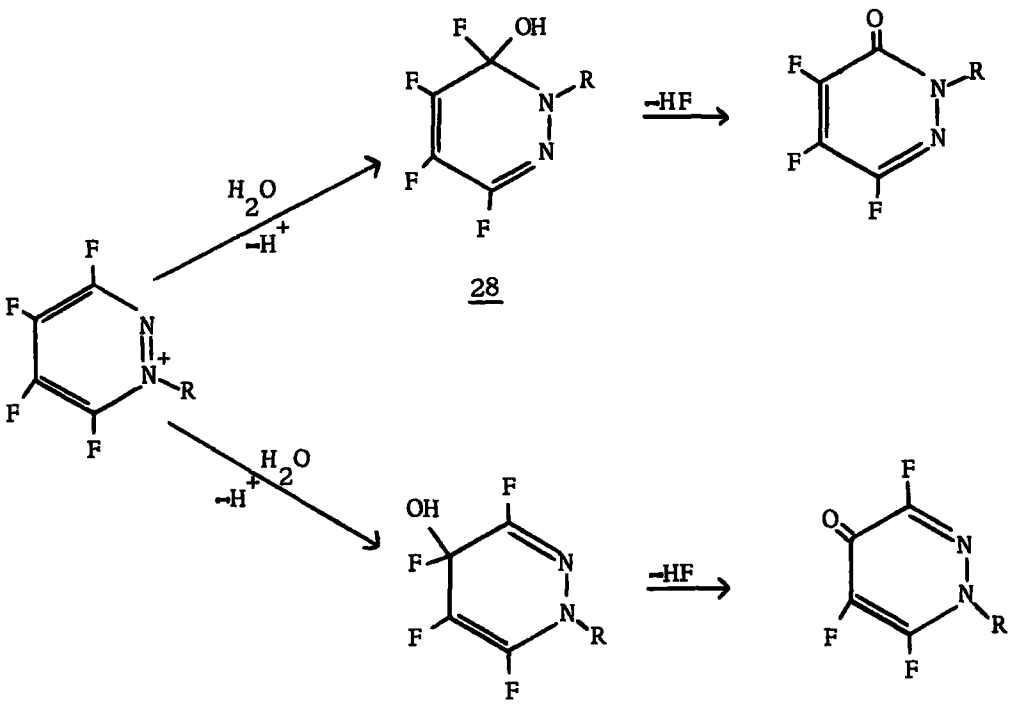
Acid-induced nucleophilic substitution of polyfluoro-aromatic nitrogen heterocyclic compounds, in contrast to the preceding discussion on replacement reactions under basic conditions, were reported recently.[52,53,46] Rapid or slow dilution of concentrated sulphuric acid solutions of perfluoro-pyridine and -isoquinoline gave[52] unchanged starting material, however with heptafluoroquinoline under identical conditions, hexafluoro-2-hydroxyquinoline was obtained exclusively in trace and large amounts respectively. Addition of methanol, followed by water, to an acidic solution of heptafluoroquinoline afforded[52] substantial amounts of the 2-methoxy and 2-hydroxy derivatives.

The orientation of nucleophilic substitution in tetrafluoropyridazine was reversed under acidic conditions compared with the previously reported results[37-41] under basic conditions. Slow dilution of a concentrated sulphuric acid solution of tetrafluoropyridazine with water or methanol afforded[53] the 6-hydroxy and 6-methoxy derivatives respectively; the former compound was shown to exist as the pyridazinone tautomer. Reaction of tetrafluoropyrazine with methanol under acidic conditions[46] gave the



6-methoxy and 5,6-dimethoxy derivatives. The orientation of substitution of tetrafluoropyrazine, unlike tetrafluoropyridazine, was identical to that observed under basic conditions.

Chambers, Musgrave and co-workers[53] showed that these contrasting orientations did not arise from kinetic versus thermodynamic control of reaction products. The observed 6- rather than 4-replacement was attributed[53] to the relative stabilities of the transition states, being higher for formation of uncharged intermediate 28 than 29; elimination of hydrogen fluoride from 28 and 29 was equally probable and unlikely to be the rate- or product-determining step.

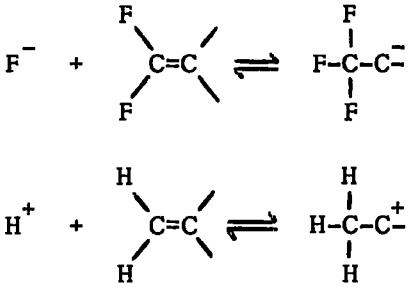


R = H, CH_3, C_2H_5.

CHAPTER 2

Fluoride Ion-Initiated Reactions of Fluoro-olefins

Evidence for the complementary nature of the chemistry of hydrocarbon and fluorocarbon olefinic and aromatic systems increases continually, however, the fundamental analogy between the proton and fluoride ion towards their respective unsaturated systems was emphasized some years ago by Miller and co-workers.[54,55] They showed that fluoro-olefins were susceptible to nucleophilic attack and that addition of fluoride ion afforded a polyfluorocarbanion in contrast to hydrocarbon olefins which were predominantly susceptible to electrophilic addition, forming carbonium ions with protons.



The high basicity of such polyfluorocarbanions necessitated the development of suitable experimental conditions which subsequently afforded important advances in preparative and mechanistic fluorocarbon chemistry.

A discussion of these experimental conditions, the factors governing the stability of polyfluorocarbanions, the formation and reactions of polyfluorocarbanions from fluoro-olefins and fluoride ion, and associated fluoride ion-induced rearrangements is presented; fluoride ion-initiated reactions of other types of unsaturated fluorocarbons, e.g. acetylenes and carbonyls, are also briefly discussed.

2.1. Experimental conditions.

Reversible addition of fluoride ion to perfluoro-olefins under suitable conditions has been known for a considerable time. Alkali metal fluorides

with low lattice energies, particularly those of potassium and caesium, are the most frequently reported sources of fluoride ion, however, the similar tetraethylammonium,[55-57] silver[58-60] and mercuric fluorides[61] have also been utilised. The observed[62,63] order of reactivity of the alkali metal fluorides is CsF > RbF > KF > NaF > LiF, the reverse order of their lattice energies.[64] This order of reactivity was further confirmed by exchange reactions of labelled alkali metal fluorides (MF^{18}) and hexafluoropropene.[65]

$$CF_3\text{-}CF{=}CF_2 \;+\; MF^{18} \rightleftharpoons C_3F_6{}^{18} \;+\; MF$$

Possible reaction media are hydroxylic or dipolar aprotic solvents. The former dissolve significant amounts of alkali metal fluorides but are too acidic to co-exist with polyfluorocarbanions and therefore afford, by proton abstraction from the solvent, polyfluorocarbon hydrides. Conversely, the solubility of alkali metal fluorides in the latter, from which proton abstraction is considerably reduced owing to the absence of labile hydrogen atoms, is extremely limited. Anhydrous solvents of this type include acetone, chloroform, acetonitrile, dimethylformamide, sulpholan, di-, tri- and tetraglyme. In general, cations are strongly solvated in such solvents which usually possess a high electron density localised on an exposed oxygen atom allowing strong ionic interactions with the cation.[66] In contrast, anions are less efficiently solvated owing to the relatively dispersed positive end of the dipole; solvation decreases with decreasing anionic size in the order:-[67]

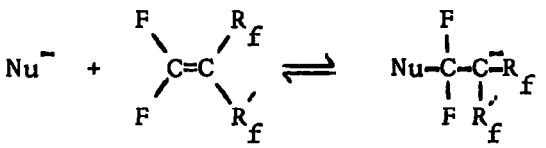
$$I^- > SCN^- > Br^- > N_3^-,\ Cl^- \gg F^-$$

Reactions in the absence of a solvent[68] have avoided the inherent complications, however, the system is clearly less reactive and requires more forcing conditions than the moderate temperatures (20° - 180°) and

pressures (1 - 25 atm.) employed with a solvent.

2.2. Polyfluorocarbanions.

Since polyfluorocarbanions have been cited[62,69] as reaction intermediates in fluorocarbon chemistry it is essential to consider the effects of substituents upon their stability. Such carbanions are formed on addition of a nucleophile[69] (Nu^-) to polyfluoro-olefins, however, the majority of the

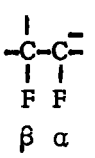


quantitative results related to their stabilities were obtained from measurements of relative acidities of fluorocarbon hydrides,[51a] when proton abstraction by a suitable base (B) afforded the polyfluorocarbanion. However, the conclusions made are equally applicable to carbanions

produced by the former, or any other route.

2.2.1. Substituent effects.

The stability of polyfluorocarbanions was shown, from the results discussed in the following sections, to depend on the inductive (I_σ and I_η), hybridisation (sp^2 - sp^3), mesomeric and 2p - 3d orbital overlap effects for α-substituents while only inductive effects are important for β-substituents. The most commonly used nomenclature for the position of substituents in polyfluorocarbanions is as shown. The order of ability

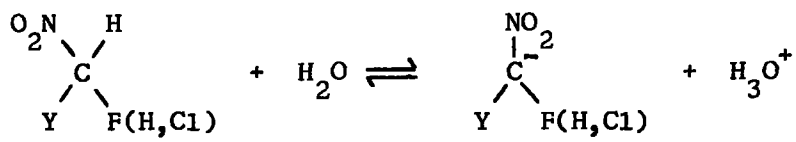


of fluorine to stabilise a carbanion was found to be β-F > α-F (on sp^3-C) > (α-H) > α-F (on sp^2-C).

(a) α-Substituents.

Kinetic measurements of the base-catalysed deuterium exchange of a series of haloforms,[70] substituted methanes[71] (CHX_3; X = OEt, perfluoroalkyl) and substituted ethanes[72] (CF_3CHXY; X, Y = Cl, Br, I) indicated that α-substituents facilitated carbanion formation in the order: I > Br > Cl > F > OEt, which was subsequently confirmed by results for alkoxide attack on 1,2-dihaloperfluorocyclic-olefins.[73]

Hine,[74,75] Adolph and Kamlet,[76] and more recently Kaplan and Pickard[77] have shown that the effect of α-substituents, especially fluorine, on carbanion stability depends upon the conformation and electronic configuration of the carbanionic carbon. The measured pKa values[76] for a series of nitromethanes (30) depended upon the substituent Y, which determined the hybridisation of the central carbon; the observed carbanion stabilisation



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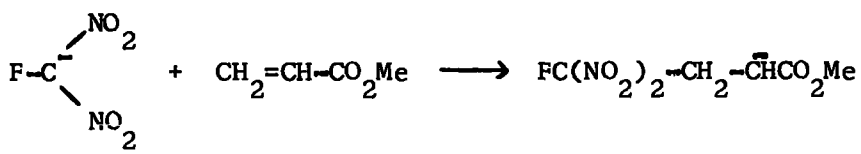
Y = COOEt, $CONH_2$, Cl, NO_2

was Cl > H > F for a given Y group (except for Y = NO_2, where Cl ≃ H). The "α-fluorine effect" was demonstrated[77] by the greatly increased nucleophilicity of fluorodinitromethide ion (31) towards methyl acrylate, due only to destabilisation of 31, compared to methyl-, ethyl-, and chloro-dinitromethide ions.



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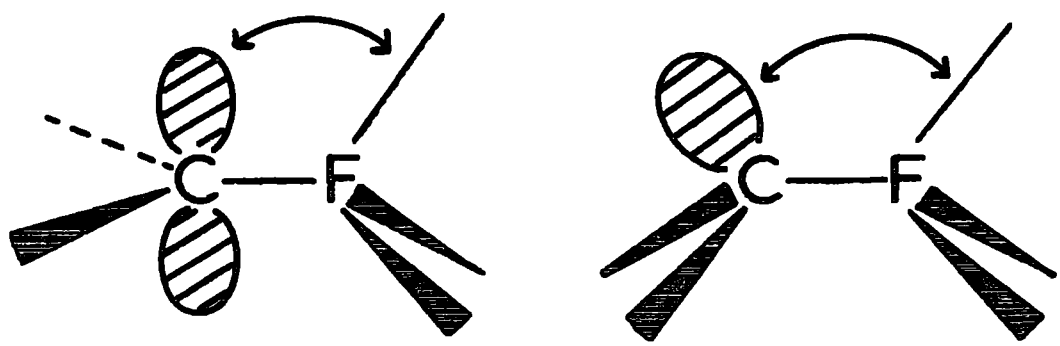
The destabilising effect of α-fluorine on a planar (sp^2) carbanion, relative to hydrogen in contrast to a stabilising effect on a tetrahedral (sp^3) carbanion, was

rationalised by Hine[75] as a weakening of the carbon-halogen σ bond resulting from the increased electronegativity of an sp^2-hybridised carbon relative to an sp^3-hybridised carbon, being more pronounced for fluorine than chlorine, bromine or iodine. An alternative explanation based on the $I_{\eta\eta}$ effect[25] was also proposed.[76] Coulombic repulsion, between the non-bonding electrons on fluorine and the non-bonding electron pair on carbon, is maximised for a planar (sp^2) carbanion (32) and minimised for a tetrahedral (sp^3) carbanion (33). The magnitude of $I_{\eta\eta}$ repulsion effects was shown to be F > Cl > Br > I[25] and therefore this effect is less important for chlorine, bromine and



32 33

iodine than fluorine, and non-existent for hydrogen.

Electrostatic polarisation of the halogen,[76] which increases F < Cl < Br ~ I, and carbon 2p-substituent 3d orbital overlap[78] were also postulated to account for the observed effects of α-substituents on carbanion stability.

(b) β-Substituents.

A systematic study of the effect of β-substituents on carbanion stability has only been reported for fluorine. Andreades[51a] measured the rates of base catalysed hydrogen-deuterium exchange for a series of monohydrofluorocarbons (Table 1, 34 - 37), from which it was deduced that the order of carbanion stability was tertiary > secondary > primary. Polarographic data on electrochemical reduction of a series of compounds,

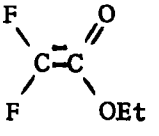
Table 1

	Compound	Relative Reactivity	pKa Value I[a]	pKa Value II[b]
34	CF_3H	1	28	25•5
35	$CF_3(CF_2)_5CF_2H$	6	27	-
36	$(CF_3)_2CFH$	2×10^5	18	22•5
37	$(CF_3)_3CH$	10^9	11	7

[a] Streitweiser scale - Ref. 78, page 70

[b] by polarography - Ref. 79

$(R_f)_2Hg$, afforded[79] estimated pKa values of the corresponding hydrides, R_fH, which were in reasonable agreement with those reported previously. Estimated pKa values[79] for 38 and 39 of 25 and 14 respectively demonstrated the superior stabilising effect of β-fluorine, compared to α-fluorine, on carbanions.



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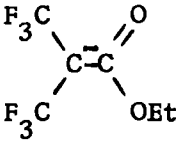

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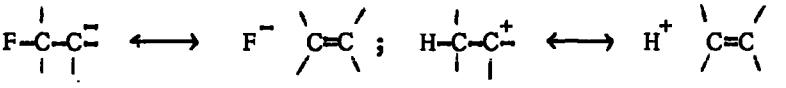
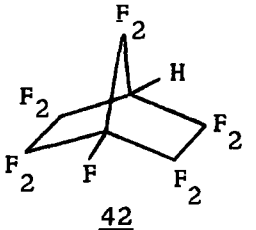
Andreades[51a] attributed this stabilisation of a carbanion by β-fluorine to a negative hyperconjugation effect (40) analogous to the stabilising hyperconjugation for carbonium ions (41). To establish the significance of



40 41

this effect Streitweiser[51b] investigated the relative rates of base-catalysed hydrogen-tritium exchange for 1-H-undecafluorobicyclo[2.2.1]-heptane (42) and (tristrifluoromethyl)methane (43). Since the intermediate



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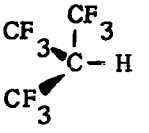


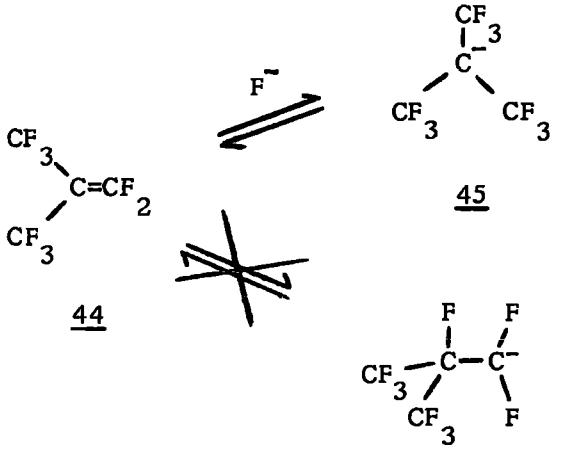
43

carbanion from 42 is forced to remain pyramidal the possibility of stabilisation by negative hyperconjugation is remote compared to 43 and hence, on this basis, the predicted rate of exchange was 43 >> 42. The reverse order was observed with k_{42}/k_{43} = 5, which Streitweiser rationalised[51b] in terms of increased stabilisation of the intermediate carbanion from 42 by enhanced inductive effects.

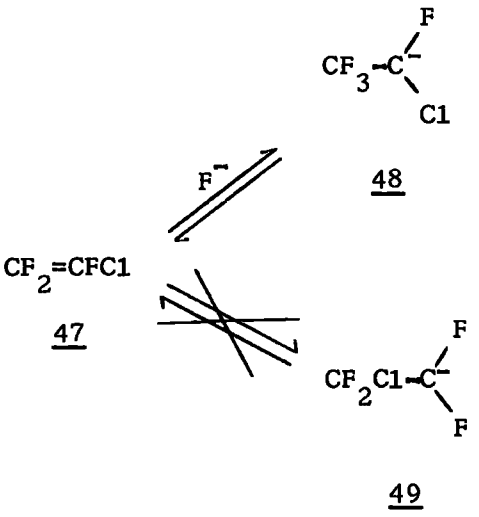
The exchange reactions of m-dihalobenzenes[80] indicated that β-fluorine may be more effective than β-chlorine at stabilising a carbanion although evidence to support the reverse has been reported.[72]

2.3. Orientation of addition of fluoride ion to fluoro-olefins.

In general, nucleophilic addition to fluoro-olefins proceeds via the intermediate carbanion which is most stabilised by the particular substituents. For example, addition of fluoride ion to 44 and 47 occurred exclusively at the difluoromethylene group[69] to afford 45 and 48 respectively, with more stabilising β-fluorines and fewer destabilising α-fluorines compared to the alternative carbanions 46 and 49 respectively.



44 45 46



2.4. Relative reactivities of fluoro-olefins.

The absence of data relevant to nucleophilic attack on a series of fluoro-olefins under identical conditions has prohibited a quantitative comparison of their relative reactivities. For such reactions, however, a possible energy profile can be represented schematically as in Fig. 1 and clearly the relative reactivities of fluoro-olefins depend upon the effect of the substituents on the stabilities of the ground and transition states.[69] Substituent effects in the former have not yet been reported, whereas substituent effects in the latter are approximated to those in the intermediate carbanion (C), which have been discussed previously (See 2.2.1). Recent work indicated[81] that, for nucleophilic attack by ethoxide on polyfluoro-olefins, the formation of B is the rate determining step, however,

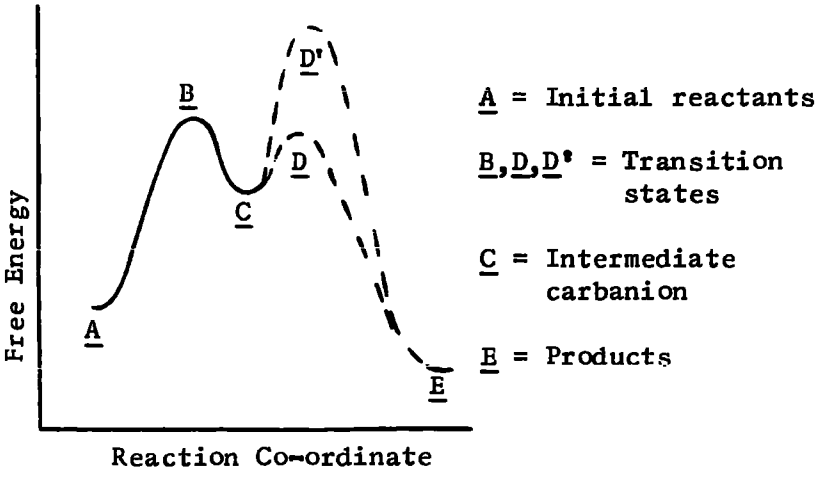


Fig. 1

in the discussion the author has shown that, for fluoride ion-initiated reactions of fluoro-olefins, this is certainly not always the case and that much more complex energy profiles are observed.

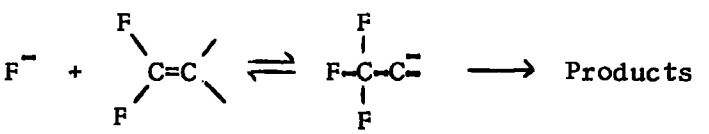
In general, it was concluded[69,82] that an olefin containing a difluoromethylene group is the most reactive to nucleophiles and that reactivity increases along the series:

$CF_2=CF_2 < CF_2=CFCF_3 < CF_2=C(CF_3)_2$ Ref. 69

$CF_2=CF_2 < CF_2=CFCl < CF_2=CFBr$ Ref. 82

2.5. Products formed in fluoride ion-initiated reactions of fluoro-olefins.

Carbanions, formed by nucleophilic addition to fluoro-olefins, were shown[81] to be intermediates and subsequent reactions of them have been extensively reported.[62,69] In general, the following discussion is limited to a review of fluoride ion-initiated reactions of fluoro-olefins (50), analogous to proton induced reactions of hydrocarbons (51), and the



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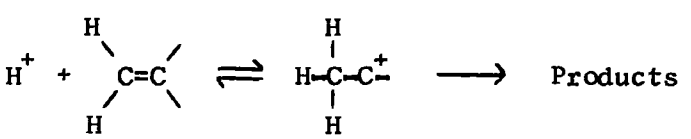

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possible modes of reaction observed for the polyfluorocarbanion intermediates.

Several different processes are known to occur under suitable conditions and these are conveniently considered in sections on proton abstraction, substitution reactions, reaction with activated systems and olefinic and aromatic rearrangements. Reactions of carbanions formed on addition of fluoride ion to other types of unsaturated fluorocarbons are also briefly mentioned.

2.5.1. Proton abstraction.

Miller and co-workers[55] reported the formation of hydrogen fluoride adducts in fluoride ion-initiated reactions of fluoro-olefins due to proton abstraction from the solvent, formamide (See Table 2). Resultant

$$F^- + \diagdown C{=}C \diagup \rightleftharpoons F\text{-}\overset{|}{C}\text{-}\overset{|}{C}^- \xrightarrow{\text{solvent}} F\text{-}\overset{|}{C}\text{-}\overset{|}{C}\text{-}H + \text{solvent anion}$$

competition between the solvent and fluoride anions for the olefin adversely affected the yields of hydrogen fluoride adducts and afforded complex side

Table 2*

Olefin	Temp. °C	Reaction Time (hr.)	Product	Yield %
$CF_2{=}CFCl$	55	30	CF_3CHFCl	72
$CF_2{=}CFCF_3$	25	5	CF_3CHFCF_3	60
$CF_2{=}CClCF_3$	25	6	$CF_3CHClCF_3$	61
$CF_3CF{=}CFCF_3$	81	24	$C_2F_5CHFCF_3$	35

* Ref. 55

products. Graham[83,84] showed that secondary reactions with the solvent clearly depended upon the reactivity of the intermediate polyfluoro-carbanion since the stable tristrifluoromethyl anion,[84] although protonated by dry gaseous hydrogen chloride, was not reactive enough to form diglyme anions by proton abstraction. However, in similar reactions with tetrafluoroethylene,[83] a substantial proportion (50%) of the olefin reacted with diglyme anions which were readily produced on deprotonation by the much more reactive pentafluoroethyl anion.

2.5.2. Substitution reactions.

Nucleophilic substitutions in fluoro-olefins, which predominated over proton abstraction for internal, branched and cyclic olefins, were classified[54] as either vinylic or allylic replacements. Two mechanistic

interpretations of these reactions were proposed by Miller[54] and Park,[85] based on a concerted process (S_N2')[54] and discrete carbanion formation[85] respectively. Both mechanisms are considered, however, recent evidence[81] indicated that the latter was more probable.

(a) Vinylic substitution.

Examples of vinylic substitution in fluoride ion attack on acyclic fluoro-olefins are limited owing to the relatively low reactivity[55] of the =CFX group (X = Cl, Br, I, OR, H) compared to the difluoromethylene group. However, direct vinylic displacement of chloride by fluoride from 1,2-dichlorotetrafluoropropene (52) in formamide, and subsequent hydrogen fluoride addition to the 2-chloropentafluoropropene (53) was proposed by Miller et al.[55] to account for the observed 2-chloro-1,1,1,3,3,3-hexa-

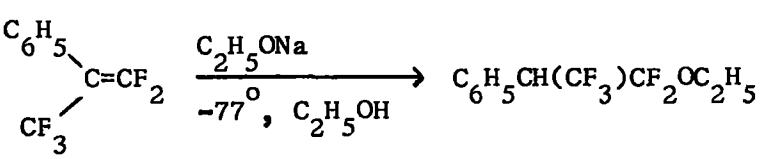
$$CClF{=}CClCF_3 + F^- \longrightarrow CF_2{=}CClCF_3 + Cl^-$$

52 53

$$CF_2{=}CClCF_3 + F^- \xrightarrow{H^+} CF_3{-}CHClCF_3$$

54

fluoropropane (54). Nucleophilic attack by ethoxide on 2-phenylpenta-fluoropropene (55) afforded[81] the saturated ether (56) (15%) and the vinyl ethers (57) (76%) and (58) (9%).



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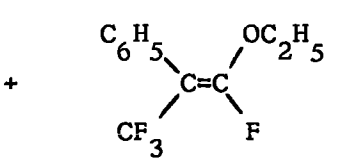
$$\xrightarrow[-77^\circ,\ C_2H_5OH]{C_2H_5ONa} C_6H_5CH(CF_3)CF_2OC_2H_5$$

56



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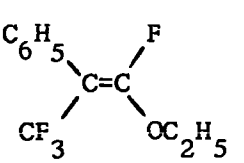

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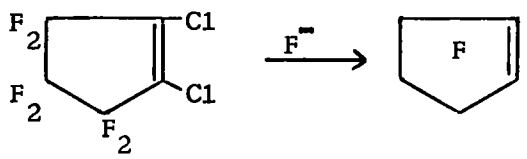
Reaction of polyfluorocyclic-olefins (59) and (60) with potassium fluoride in N-methyl-2-pyrrolidone afforded[86] good yields of the perfluorocyclic-olefins (61) and (62) respectively, via vinylic substitution of chloride by fluoride ion.



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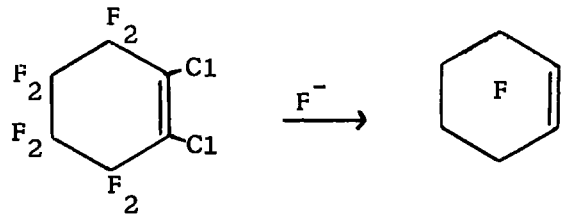


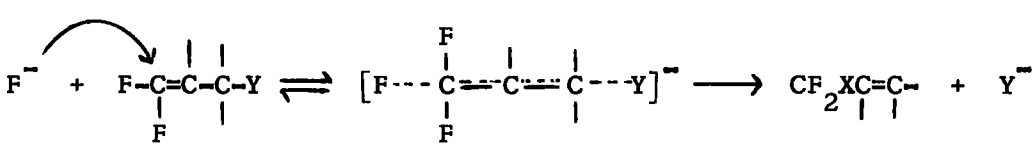
60 62

Alkoxide attack on polyfluorocyclic-olefins, extensively reported by Park and co-workers,[73,85] resulted in vinylic and allylic (See 2.5.2.(b)) substitution. The observed orientation of substitution was attributed[85] to the stability of the intermediate carbanion, determined by the substituents, and the order of leaving groups for carbanions:[85a,87]

$$I > Br > Cl > F > OR > H$$

(b) Allylic substitution.

Nucleophilic attack by halide ions on polyfluoroallyl systems[54,55,88,89] of the type $CF_2=CXCYRR'$ (X,R,R' = halogen, H, perfluoroalkyl; Y = Cl, Br, I) afforded replacement of Y, the allylic halogen. Miller and co-workers[54,55,88,89] proposed a concerted mechanism (S_N2') with initial attack at the difluoromethylene group (63) accompanied by rearrangement and loss of allylic halide ion, Y^-. Involvement of the difluoromethylene group, rather than direct S_N2



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displacement of Y, was confirmed by the inertness, under equivalent conditions, of $C_6H_5CF_2Cl$, $CFCl=CFCF_2Cl$ and $CCl_2=CClCF_2Cl$, and also the observed[54] order of reactivity of attacking halide ions was $F^- \gg Cl^- > Br^- > I^-$, the reverse of that observed for S_N2 reactions.[90]

Reaction of fluoride ion with 3,3-dichloro-1,1,3-trifluoropropene (64) and 3,3-dichlorotetrafluoropropene (65) further confirmed[54] the mechanism involved in allylic substitution. Structurally different products were predicted for S_N2 and S_N2' mechanisms, however only those from the latter were observed.

$$CF_2=CHCF_2Cl \xleftarrow[F^-]{S_N2} CF_2=CHCFCl_2 \xrightarrow[F^-]{S_N2'} CF_3CH=CFCl$$

64

$$CF_2=CFCF_2Cl \xleftarrow[F^-]{S_N2} CF_2=CFCFCl_2 \xrightarrow[F^-]{S_N2'} CF_3CF=CFCl$$

65

Park and co-workers[74,85] observed similar allylic substitutions in reactions of ethoxide with halogenated cyclobutenes. The orientation of substitution was rationalised,[85] as for vinylic substitution (See 2.5.2.(a)), on the basis of the stability of the intermediate carbanion and the order of leaving groups for carbanions:[85a,87]

$$I > Br > Cl > F > OR > H$$

2.5.3. Reactions with activated compounds.

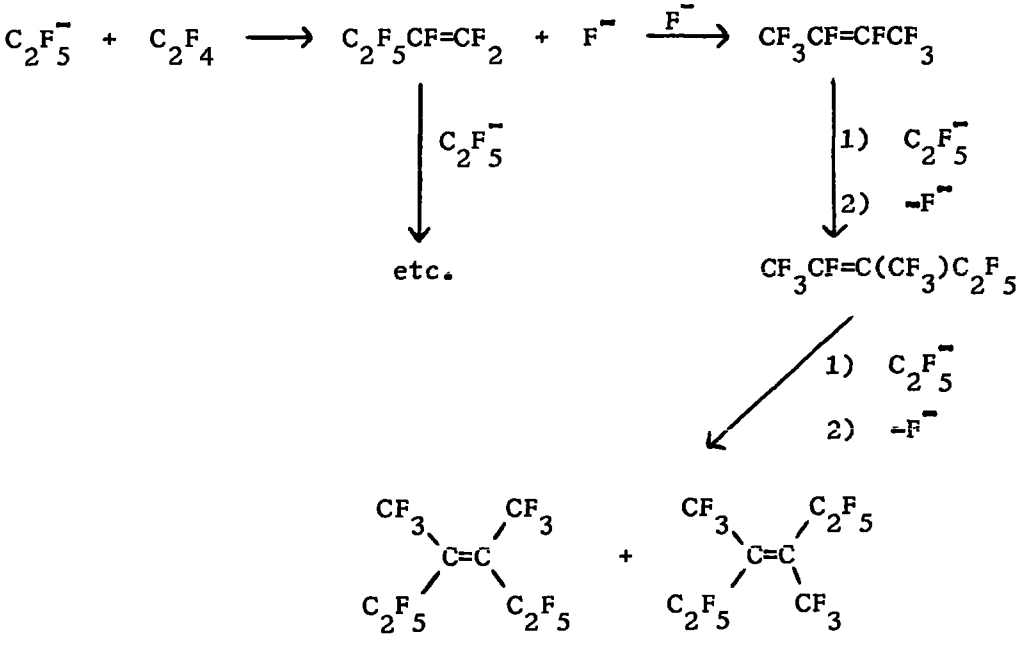
Polyfluorocarbanions are themselves nucleophiles and therefore capable of attack at electron deficient centres, especially on carbon. Fluoride ion-initiated reactions of fluoro-olefins with activated systems have been extensively reported[62] and are, for discussion, divided into reactions of polyfluoroalkyl carbanions with fluoro-olefins, polyfluoro-aromatic compounds, polyfluorocarbonyl compounds, and halogen, sulphur and nitrogen compounds.

(a) Fluoro-olefins.

In general, fluoride ion-initiated polymerisation of fluoro-olefins, although theoretically possible, has not afforded suitable high molecular weight products for several reasons. Double bond migration, rather than propagation, was the observed effect[62] of fluoride ion on fluoro-olefins which contained in excess of three linear carbon atoms (See 2.5.6.(a)), while for fluoro-olefins in which this was not structurally possible, proton abstraction from the solvent, formation of low molecular weight highly branched unsaturated oligomers or simply non self-condensation was observed.[62]

(i) Acyclic.

Oligomerisation of tetrafluoroethylene by caesium fluoride in di-, tri- and tetraglyme under moderate conditions was reported by Graham[83,91] to yield complex mixtures of highly branched internally unsaturated products of general formula $(C_2F_4)_n$ in which n was 4,5,6 and 7. The mechanism proposed,[83] as shown, involved nucleophilic addition of pentafluoroethyl anion to tetrafluoroethylene, elimination of fluoride ion, possibly with rearrangement, to form an olefin which reacted further



66 67

with pentafluoroethyl anion. Identification of tetramers (66) and (67) substantiated this mechanism. Product yields were reduced[83] owing to consumption of the olefin in side reactions involving the solvent, however the reaction rate was increased with increased quantities of caesium fluoride and change of solvent in the order monoglyme < diglyme < triglyme < tetraglyme. Similar results were obtained[68b] independently using a greater variety of solvents and initiators under more forcing conditions.

In contrast, under moderate conditions in the presence of alkali metal fluorides hexafluoropropene only di- and tri-merised,[68a,83,92-94] with or without a solvent. The reaction mechanism shown was proposed by Haszeldine and co-workers,[93] who identified two dimers, (68) and (69) and three trimers, (70), (71) and (73), of hexafluoropropene and observed,

$$CF_3CF{=}CF_2 \overset{F^-}{\rightleftharpoons} (CF_3)_2CF^- \xrightarrow[2)\ -F^-]{1)\ C_3F_6} (CF_3)_2CFCF{=}CFCF_3$$

$$(CF_3)_2CFCF{=}CFCF_3 \overset{68}{\rightleftharpoons} (CF_3)_2C{=}CFC_2F_5 \quad (69)$$

$$69 \xrightarrow[2)\ -F^-]{1)\ (CF_3)_2CF^-} (CF_3)_2C{=}C(C_2F_5)\cdot CF(CF_3)_2 \quad (70) \overset{F^-}{\rightleftharpoons} ((CF_3)_2CF)_2C{=}CFCF_3 \quad (71)$$

$$70 \overset{F^-}{\rightleftharpoons} (CF_3)_2C{=}CFC_2F_5 + (CF_3)_2CF^-$$

$$69 \xrightarrow{F^-}$$

$$F^- + n\text{-}C_3F_7(CF_3)C{=}CF_2 \quad (72) \xrightarrow[2)\ -F^-]{1)\ (CF_3)_2CF^-} n\text{-}C_3F_7(CF_3)C{=}CFCF(CF_3)_2 \quad (73)$$

in the presence of fluoride ion under suitable conditions, the conversion of 68 into 69, the equilibrium between 70 and 71, the formation of the

thermodynamically stable trimer (73) from 70 and 71, but not the dimer (72). The formation of terminal olefin (74) from 69 and ethoxide at -80° substantiated the postulation of 72 as a reaction intermediate.

$$\underset{69}{(CF_3)_2C{=}CFC_2F_5} \xrightarrow{\bar{O}Et} \underset{74}{CF_2{=}C(CF_3)CF(OEt)C_2F_5} + F^-$$

Only dimerisation of perfluoroisobutene was observed[83,95] with caesium or rubidium fluoride in an inert solvent at -50° to -20°, possibly due to the low reactivity of the tristrifluoromethyl anion.[69] Graham[83] reported a mixture of perfluoro-olefins (75) and (76), however, a recent patent[95]

$$(CF_3)_2C{=}CF_2 \rightleftharpoons (CF_3)_3C^- \xrightarrow{i\text{-}C_4F_8} (CF_3)_3CCF_2\bar{C}(CF_3)_2$$

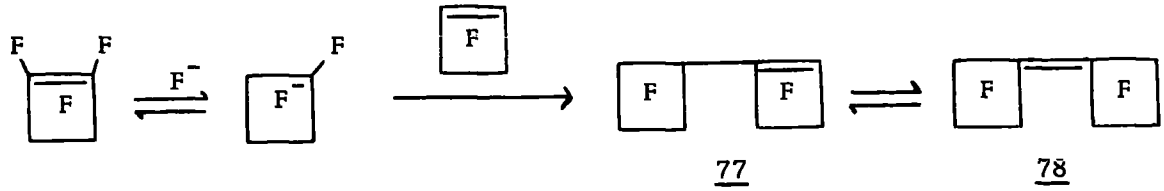
$$(CF_3)_2C{=}CF_2 \rightleftharpoons (CF_3)_3C^- \xrightarrow{i\text{-}C_4F_8} (CF_3)_3CCF_2\bar{C}(CF_3)_2 \xrightarrow{-F^-} \underset{75}{(CF_3)_3CCF{=}C(CF_3)_2}$$

$$(CF_3)_2C{=}CF_2 \rightleftharpoons (CF_3)_3C^- \xrightarrow{i\text{-}C_4F_8} (CF_3)_3CCF_2\bar{C}(CF_3)_2 \xrightarrow{-F^-} \underset{76}{(CF_3)_3CCF_2C(CF_3){=}CF_2}$$

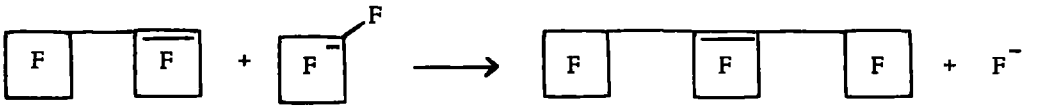
claimed that a single product, identified as 75, was obtained.

(ii) Cyclic.

Certain polyfluorocyclic-olefins were also found to oligomerise with caesium fluoride in dipolar aprotic solvents. Pruett and co-workers[96] reported the anionic di- and tri-merisation of perfluorocyclobutene in the presence of pyridine, however a fluoride ion-catalysed reaction has been described subsequently.[94,97] Caesium fluoride and perfluorocyclobutene in dimethylformamide[94] rapidly afforded two dimers, (77) and (78) and trimers, predominantly a single isomer (79), via the proposed mechanism.

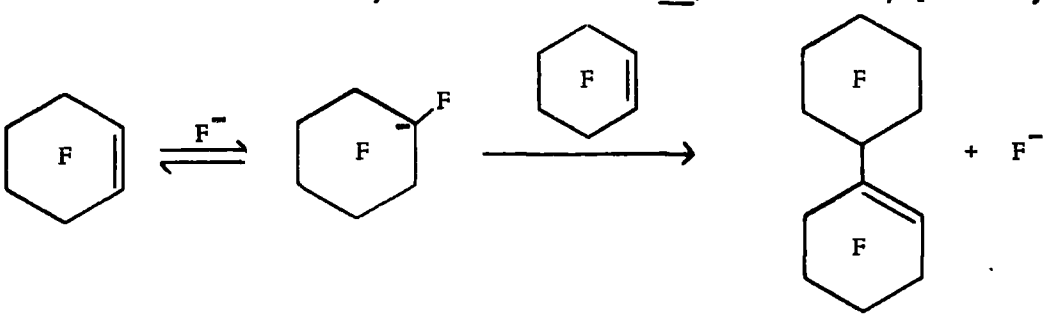


77 78



87 79

Only dimerisation of perfluorocyclo-hexene and -pentene was observed,[97] requiring more vigorous conditions than similar reactions for perfluorocyclobutene. The proposed mechanism[97] for perfluorocyclohexene involved vinylic substitution of fluorine by perfluorocyclohexyl carbanion to form the observed perfluoro(1-cyclohexylcyclohexene) (80), however, perfluorocyclopentene afforded[97] the symmetrical dimer (81) as the only product, via



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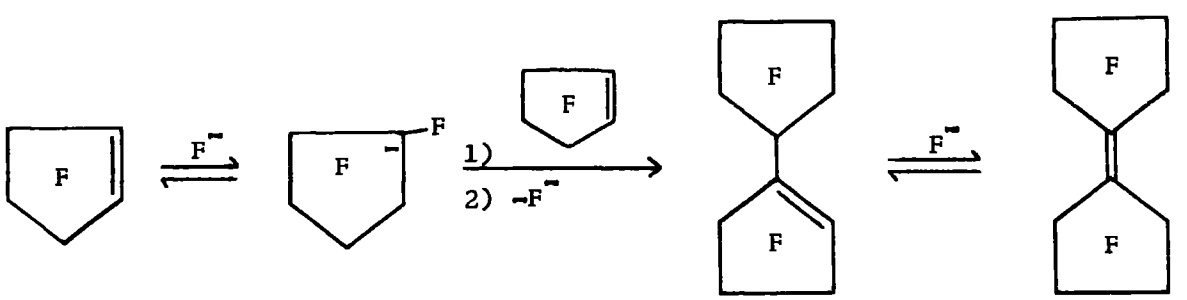
initial vinylic substitution accompanied by a fluoride ion-induced



81

rearrangement to 81, the thermodynamically most stable isomer.

(iii) Co-dimerisation.

An extension of fluoride ion-induced oligomerisation to co-dimerisation of a mixture of fluoro-olefins[62,94] proved successful. However, the products obtained depended upon the reactivity of each olefin towards

fluoride ion and also towards the individual perfluorocarbanions formed from both olefins. Consequently dimers of each olefin as well as co-dimers were also expected.

In the absence of solvent the major process for several pairs of olefins was found to be the independent reaction of one or both olefins with fluoride ion,[62] but co-dimers were obtained with pairs of olefins which were individually reactive towards caesium fluoride.

An investigation[94] into fluoride ion-catalysed co-dimerisation of fluoro-olefins in solution indicated a strong solvent dependance for the observed products. In dimethylformamide perfluoro-propene and -but-2-ene afforded a co-dimer (82) as the major product, while in tetrahydrofuran

$$CF_3CF{=}CF_2 \rightleftharpoons (CF_3)_2CF^- \xrightarrow{C_3F_6} \text{dimer} + F^-$$

$$(CF_3)_2CF^- \xrightarrow{CF_3CF{=}CFCF_3} F^- + (CF_3)_2CFC(CF_3){=}CFCF_3 \xrightarrow{F^-} (CF_3)_2C{=}C(CF_3)C_2F_5$$

82

the dimer of the former was obtained preferentially. Similar results were observed[94] for the co-dimerisation of perfluoro-propene and -cyclobutene.

(b) Polyfluoroaromatic compounds.

Nucleophilic displacement of fluoride ion from highly fluorinated aromatic compounds by a polyfluoroalkyl carbanion, analogous to Friedel-Crafts reactions in hydrocarbon chemistry, was reported originally by

$$F^- + CF_2{=}C\!\!\rightleftharpoons CF_3{-}C^- \xrightarrow{ArF} CF_3{-}C(Ar){-}F^-$$

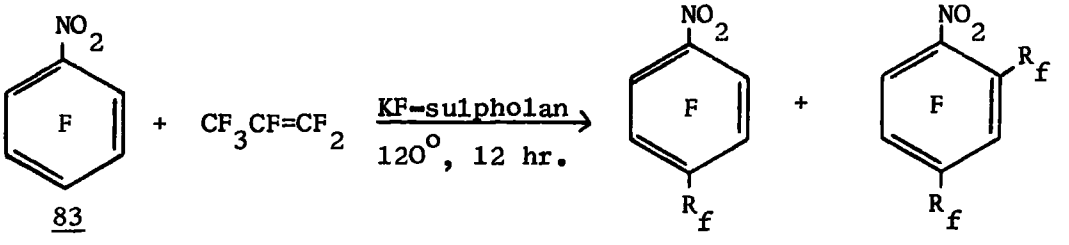
$$H^+ + CH_2{=}C\!\!\rightleftharpoons CH_3{-}C^+ \xrightarrow{ArH} CH_3{-}C(Ar'){-}H^+$$

Chambers, Musgrave and co-workers.[32,33] Subsequent investigations have confirmed polyfluoroalkylation as a general synthetic method in this field

and have also afforded some interesting mechanistic and orientation effects, some of which are discussed in Chapters 3, 4 and 5.

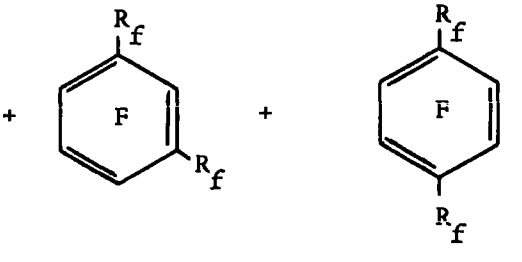
Perfluoroalkylation of hexafluorobenzene[98,99] under moderately severe conditions (up to 75 atm. and 150°) with $CF_2=CF_2$, $CF_3CF=CF_2$ or $(CF_3)_2C=CF_2$ and caesium or tetraethylammonium fluoride in a dipolar aprotic solvent afforded perfluoroalkylbenzenes of the general formula $C_6F_{6-n}(R_fF)_n$, where R_f = perfluoro-olefin and n = 1 to 6. Similar results were reported[98] for perfluoro-toluene, -biphenyl, -naphthalene and -anthracene; for chloro-fluorobenzenes, eventual loss of chlorine poisoned the catalyst.

Using moderate conditions, the expected 4-substituted derivatives were obtained[33] from both octafluorotoluene and methylpentafluorobenzoate with hexafluoropropene, whereas hexafluorobenzene, bromopentafluorobenzene and 1,3,5-trichlorotrifluorobenzene were inert.[33,100] Heptafluoroisopropylation of pentafluoronitrobenzene (83) with potassium fluoride and hexafluoro-propene in sulpholan at 120° gave, in addition to the 4-isopropyl- and 2,4-di-isopropyl-derivatives (84) and (85), products 86 and 87 from displacement of the nitro-group.



83 84 85

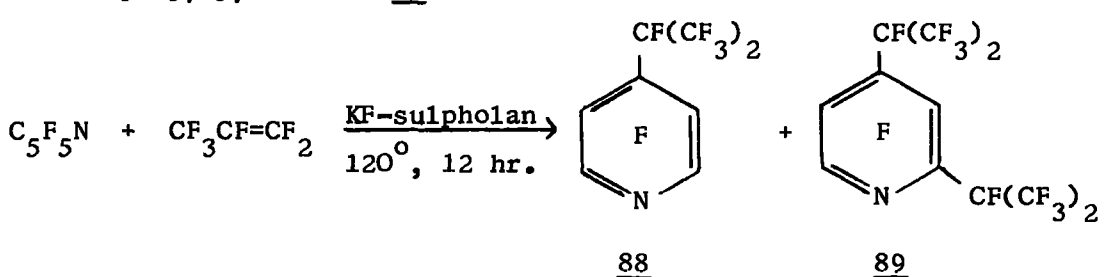
R_f = $(CF_3)_2CF$



86 87

A similar reaction with pentafluorobenzonitrile was carried out at 20°, being uncontrollable at higher temperatures, to give perfluoro-4-isopropyl-benzonitrile.

Polyfluoroalkylation of pentafluoropyridine, which is of comparable reactivity to pentafluoronitrobenzene towards nucleophiles, has been extensively studied by Chambers, Musgrave and co-workers.[49,97,102,103] When pentafluoropyridine, hexafluoropropene, potassium fluoride and sulpholan were heated[32,33] in a sealed tube at 120°, a ca. 90% yield of perfluoro-(4-isopropylpyridine) (88) was obtained together with a trace of perfluoro-(2,4-di-isopropylpyridine) (89). An evaluation[33,49] of solvents and

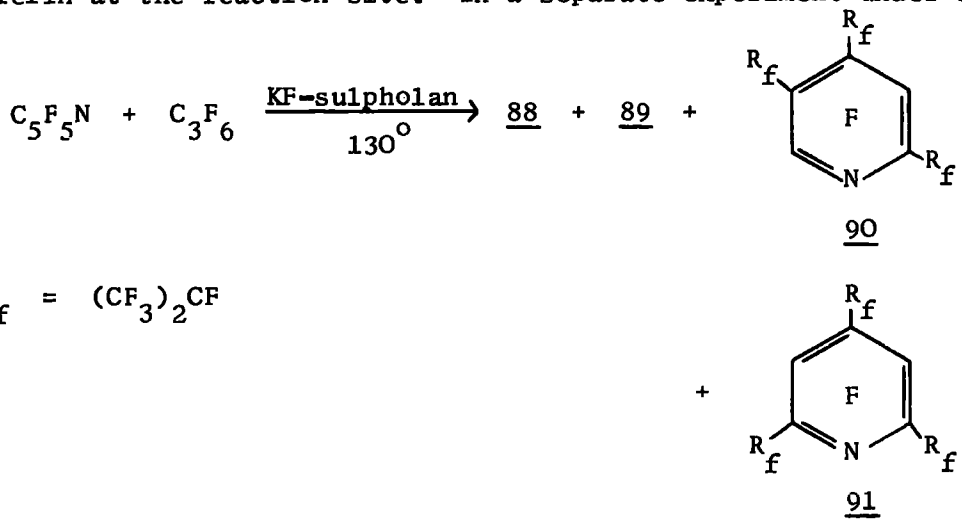


88 89

initiators for this reaction concluded that sulpholan was superior to dimethylformamide, di- and tri-glyme as solvent, and caesium fluoride was a more effective initiator than potassium fluoride; the latter observation was in agreement with previous results from fluorination reactions.[103] However, for other systems different solvents were shown to be more effective, as for example in the polyfluoroalkylation of octafluoro-naphthalene[101] using tetraglyme in preference to sulpholan.

Despite the use of excess hexafluoropropene, further substitution in 88 was very limited[33] owing to the preferential formation of dimers and trimers. However, reaction in an autoclave at elevated temperatures and higher pressure (ca. 30 atm.) afforded[102] 4-, 2,4-bis- and a mixture of 2,4,5- and 2,4,6-tris-(heptafluoroisopropyl) derivatives, (88), (89), (90)

and (91) respectively, probably due to an increased concentration of the olefin at the reaction site. In a separate experiment under similar

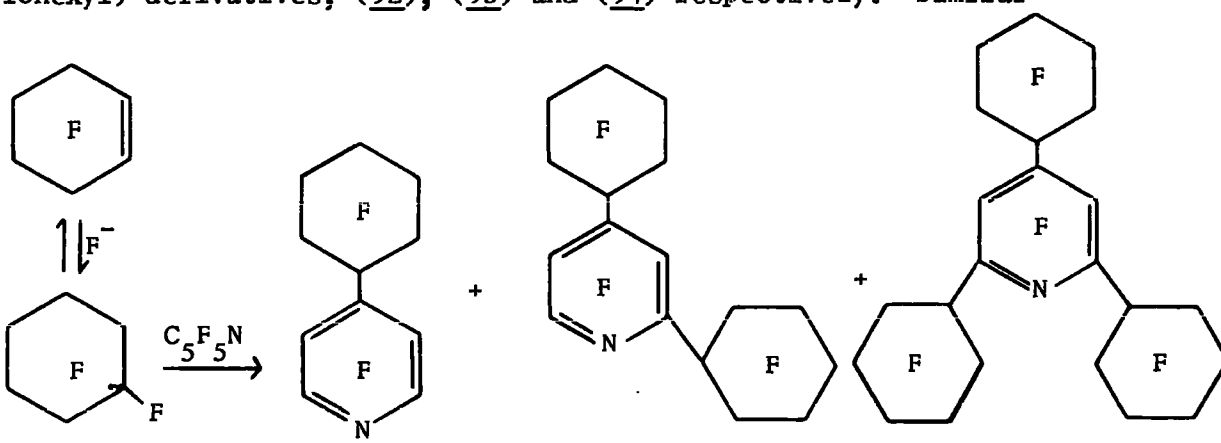


$R_f = (CF_3)_2CF$

conditions it was shown[102] that 90 rearranged to 91 in the presence of fluoride ion.

Reaction of tetrafluoroethylene and pentafluoropyridine with caesium fluoride in sulpholan at an elevated temperature in an autoclave[33] gave a mixture of perfluoroethylpyridines of general formula $C_5F_{5-n}N(C_2F_5)_n$ for n = 1 to 5. Similar polyfluoroalkylation reactions of pentafluoropyridine[39,104,105] and chlorofluoropyridines[104] have also been reported recently.

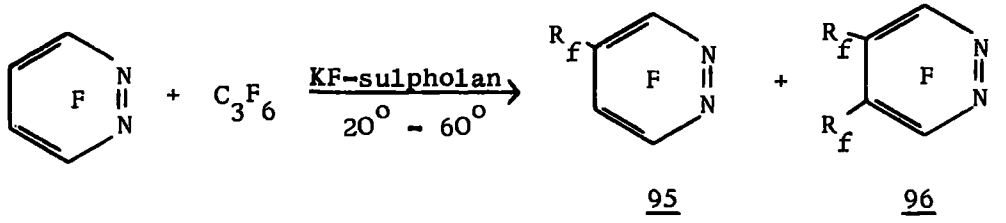
Perfluorocyclic-olefins were also shown[97] to be suitable for the polyfluoroalkylation of pentafluoropyridine. Under autogenous conditions perfluorocyclohexene afforded 4-, 2,4-bis- and 2,4,6-tris-(undecafluorocyclohexyl) derivatives, (92), (93) and (94) respectively. Similar



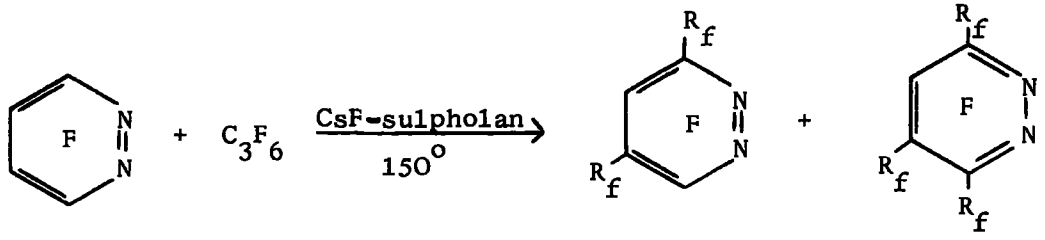
92 93 94

reactions with perfluorocyclo-pentene and -butene gave[97] only the 4-substituted compounds.

More recently, heptafluoroisopropylation of tetrafluoropyridazine[39-41] under mild conditions gave a mixture of 4- and 4,5-bis-(heptafluoroisopropyl) derivatives, (95) and (96) respectively, while more vigorous conditions afforded the 4,6-bis- and 3,5,6-tris-(heptafluoroisopropyl) compounds (97) and (98) respectively. Conversion of the 4,5-disubstituted compound (96) into the 4,6-isomer (97) was effected at elevated temperatures



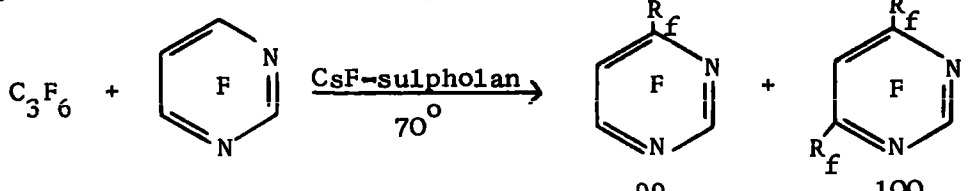
95 96



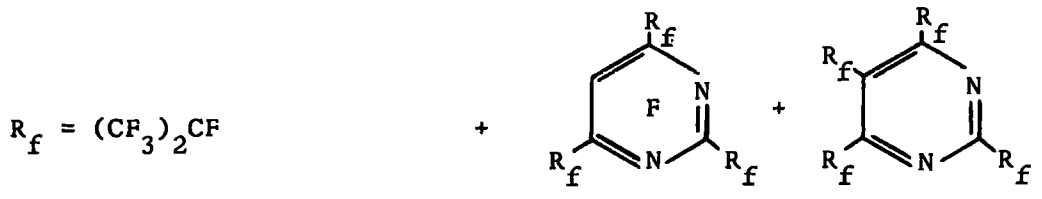
97 98

with potassium fluoride in sulpholan, giving substantial disproportionation to the mono- and tris-substituted compounds, (95) and (98) respectively.

Reaction of hexafluoropropene and tetrafluoropyrimidine with caesium fluoride in sulpholan at 70° afforded[106] 4-, 4,6-bis-, 2,4,6-tris- and tetra-(heptafluoroisopropyl) derivatives, (99) - (102) respectively, in agreement with the previously observed orientation for nucleophilic



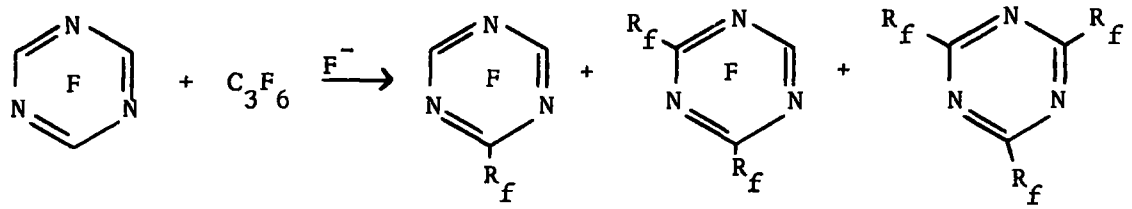
99 100



101 102

substitution.[43] Interconversion of 101 and 102 was observed in the presence of fluoride ion and a dipolar aprotic solvent.

Formation of perfluoroalkyl-substituted s-triazines was reported[100,107,108] from fluoride ion-catalysed reactions of fluoro-olefins with cyanuric fluoride (2,4,6-trifluoro-1,3,5-triazine). In the absence of a solvent under autogenous conditions,[100,107] hexafluoropropene and caesium fluoride at 100° gave a mixture of mono-, bis- and tris-(heptafluoroisopropyl) derivatives, (103), (104) and (105) respectively. Variation of reactant



$R_f = (CF_3)_2CF$ 103 104 105

ratios afforded preferential formation of any one of the observed products. Similar results were observed[108] for perfluoro-ethylene, -propene and -butenes with alkali metal fluorides in dipolar aprotic solvents at moderate temperatures and pressures.

(c) Polyfluorocarbonyl compounds.

The susceptibility of polyfluorocarbonyl compounds to nucleophilic displacement by polyfluoroalkylcarbanions was demonstrated[56] by the fluoride ion-catalysed reaction of a number of fluoro-olefins with carbonyl fluoride in a dipolar aprotic solvent. Hexafluoropropene, carbonyl fluoride and potassium fluoride in acetonitrile at 100° afforded hepta-fluoroisobutyryl fluoride (106) in high yield, and subsequent reports[57,109] showed that such polyfluoroacyl fluorides reacted further with polyfluoro-

$$CF_3CF{=}CF_2 + F^- \rightleftharpoons (CF_3)_2CF^- + COF_2 \longrightarrow (CF_3)_2CFCOF + F^-$$

106

alkyl carbanions to give disubstituted ketones, e.g. (107) in moderate yields.

$$(CF_3)_2CFCOF + (CF_3)_2CF^- \longrightarrow ((CF_3)_2CF)_2CO + F^-$$

106 107

Caesium perfluoroalkoxides and tetrafluoroethylene in diglyme at 100° afforded,[110] on acidification, a perfluoro tertiary alcohol (108) and not an ether, which indicated that nucleophilic attack by $C_2F_5^-$ upon the

$$CF_2{=}CF_2 \overset{F^-}{\rightleftharpoons} C_2F_5^- + \begin{matrix} R_f \\ \diagdown \\ C{=}O \\ \diagup \\ R_f' \end{matrix} \xrightarrow{H^+} C_2F_5{-}\overset{R_f}{\underset{R_f'}{C}}{-}OH$$

108

equilibrium concentration of the ketone was favoured.

A reversible fluoride ion-initiated reaction between tetrafluoroethylene, hexafluoropropene or chlorotrifluoroethylene and carbon dioxide in triglyme gave,[84] on acidification, the corresponding polyfluoro-carboxylic acid (109). A similar reaction with perfluoroisobutene was unsuccessful.

$$CF_2{=}CFY + F^- \rightleftharpoons CF_3CFY^- + CO_2 \overset{H^+}{\rightleftharpoons} CF_3CFYCO_2H$$

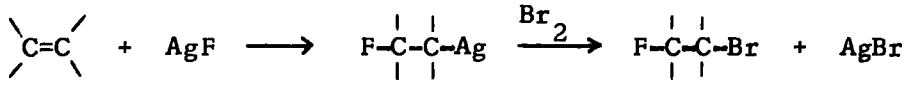
Y = F, Cl, CF_3 109

(d) Halogen, nitrogen and sulphur compounds.

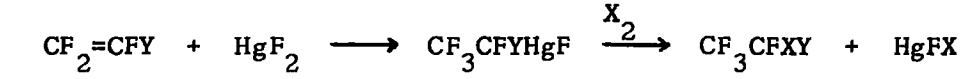
(i) Halogen compounds.

Krespan[111] observed that the addition of iodine to a variety of fluoro-olefins in the presence of potassium fluoride and a dipolar aprotic solvent afforded perfluoroalkyl iodides. The proposed mechanism involved displacement of iodide ion from iodine by a polyfluorocarbanion, generated by addition of fluoride ion to the fluoro-olefin, and the formation of isomeric products from terminal olefins was due to fluoride ion-catalysed rearrangement to the internal olefin and subsequent addition of IF. Similar results were obtained[58] in reactions of perfluoroalkylsilver compounds,

formed from silver fluoride and fluoro-olefins in a dipolar aprotic solvent, with hydrogen chloride and bromine. Displacement of chloride and bromide ions respectively resulted in overall addition of HF and BrF to the olefin.



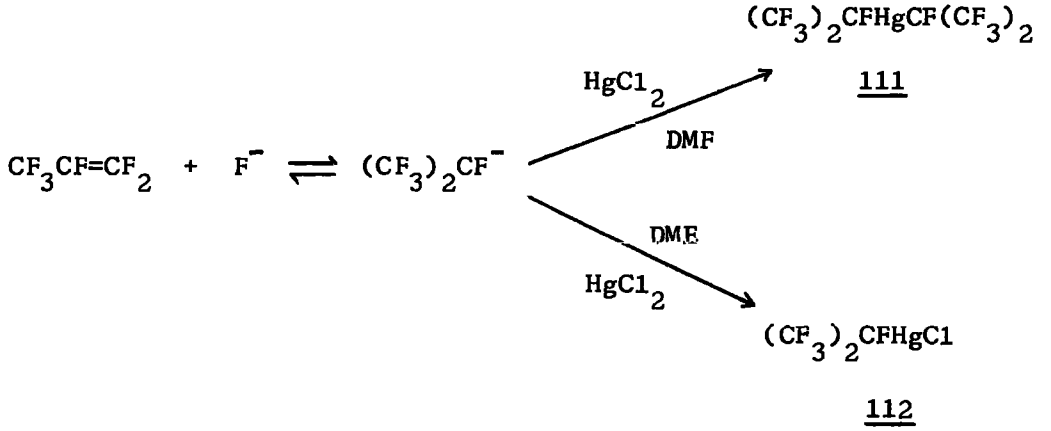
Reaction of mercuric fluoride with fluoro-olefins gave[61] polyfluoroalkylmercuric fluorides (110) via a proposed ionic mechanism involving initial nucleophilic attack by fluoride ion on the fluoro-olefin. Subsequent



Y = F, Cl; X = Cl, I 110

reaction of 110 with chlorine or iodine displaced chloride and iodide ions and effectively gave addition of chlorine- and iodine-monofluorides respectively to the fluoro-olefins. However, this ionic mechanism has been disputed[112,113] recently since the absence of a suitable catalyst and solvent is not conducive to nucleophilic displacements.

Knunyants and co-workers[112,113] have reported the displacement reaction of polyfluoroalkyl carbanions, from alkali metal fluorides and fluoro-olefins in an inert solvent, with mercuric fluoride and chloride. At 40° in dimethylformamide (DMF) and 1,2-dimethoxyethane (DME) perfluoropropene, potassium fluoride and mercuric chloride afforded bis-perfluoroisopropyl mercury (111) and perfluoroisopropylmercury chloride (112) respectively. Similar results were observed with perfluoro-isobutene and -cyclobutene.

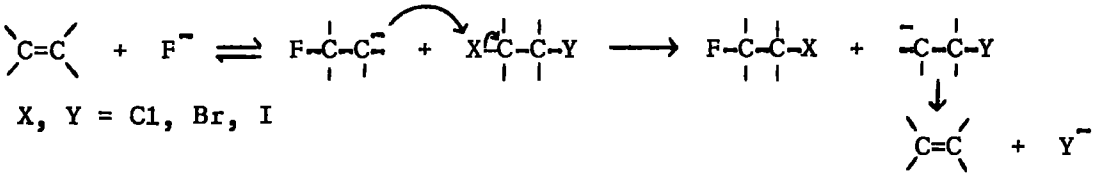


111

112

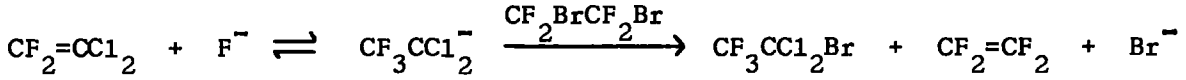
A related investigation[114] into the reactions of the stable bisperfluoroalkyl mercurials showed an increased lability of the substituents in the presence of alkali metal fluorides and are therefore a convenient source of perfluoroalkyl carbanions.

Miller et al.[115] recently reported the preferential nucleophilic displacement of carbon from halogen in perhaloalkanes by fluoroperhalocarbanions, generated from fluoride ion and fluoro-olefins, rather than addition of the carbanion to the sterically hindered parent olefin.



X, Y = Cl, Br, I

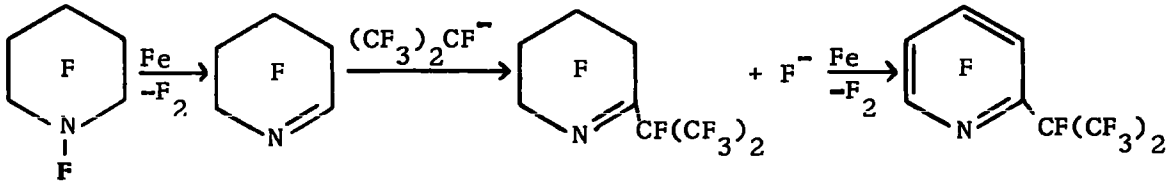
In general the products formed were a different perhaloalkane, an olefin and an halide ion as, for example with 1,1-dichlorodifluoroethylene, potassium or caesium fluoride and 1,2-dibromotetrafluoroethane which gave 1-bromo-1,1-dichlorotrifluoroethane (113), tetrafluoroethylene and bromide ion.



113

(ii) Nitrogen compounds.

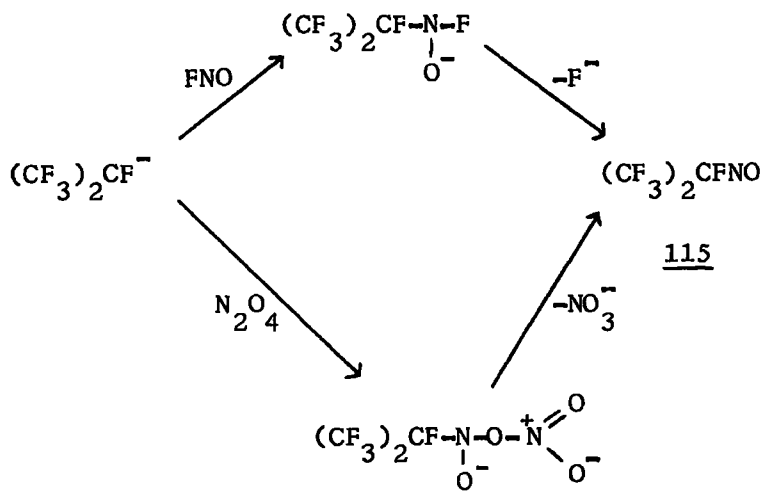
Only a few examples of nucleophilic displacement at nitrogen by polyfluoroalkyl carbanions have been reported in the literature. Heptafluoroisopropylation of perfluoropiperidine afforded[68a] a product which was originally identified as the N-substituted derivative, however, a more recent investigation[116] of the reaction gave the same product which was correctly characterised as perfluoro-(2-isopropylpyridine) (114).



114

Formation of 114 was rationalised as shown, with catalytic defluorination by the autoclave.

Knunyants and co-workers[117,118] demonstrated the fluoride ion-catalysed addition of fluoro-olefins to nitrosyl fluoride and dinitrogen tetroxide in sulpholan to give, in both cases, nitrosoperfluoroalkanes. Hexafluoropropene, potassium fluoride and nitrosyl fluoride[117] or dinitrogen tetroxide[118] at 30° afforded 2-nitrosoperfluoropropane (115). Similar results were obtained with perfluoro-isobutene and -cyclobutene.



(iii) Sulphur compounds.

Fluoride ion-catalysed addition of hexafluoropropene to sulphur tetrafluoride at 150° in the absence of a solvent afforded[119] a mixture of mono- and bis-(heptafluoroisopropyl) derivatives, (116) and (117) respectively. Hexafluoropropene, caesium fluoride and CF_3SF_3 gave the mixed disubstituted compound (118).

$$CF_3CF{=}CF_2 + F^- \rightleftharpoons (CF_3)_2CF^- \xrightarrow{SF_4} (CF_3)_2CFSF_3 + ((CF_3)_2CF)_2SF_2 + F^-$$

116 117

$$(CF_3)_2CF^- \xrightarrow{CF_3SF_3} (CF_3)_2CFSF_2CF_3 + F^-$$

118

Heptafluoroisopropylation of a series of N-perfluoroalkyl imino-sulphur difluorides ($R_fN{=}SF_2$) at 80° without a solvent produced[120] the corresponding S-heptafluoroisopropyl derivative (119) in fair yields. Similar reactions between perfluoro-ethyl or -isopropyl carbanions and

$$CF_3CF{=}CF_2 + F^- \rightleftharpoons (CF_3)_2CF^- \xrightarrow{R_fN{=}SF_2} R_fN{=}SFCF(CF_3)_2$$

$R_f = CF_3,\ C_2F_5,\ (CF_3)_2CF$ 119

sulphuryl fluoride afforded[121] perfluorodiethyl sulphone (120) and heptafluoro-2-propanesulphonyl fluoride (121) respectively. Attempted

$$CF_2{=}CF_2 + F^- \rightleftharpoons C_2F_5^- \xrightarrow{SO_2F_2} (C_2F_5)_2SO_2 + F^-$$

120

$$CF_3CF{=}CF_2 + F^- \rightleftharpoons (CF_3)_2CF^- \xrightarrow{SO_2F_2} (CF_3)_2CFSO_2F + F^-$$

121

preparations of the perfluoro-di-isopropyl- and ethylisopropyl-sulphones were unsuccessful.

2.5.4. Olefinic and aromatic rearrangements.

(a) Fluoro-olefins.

A special example of allylic substitution[54,55] (See 2.5.2.(b)) is fluoride ion-catalysed rearrangement of fluoro-olefins in which equilibration between isomers occurs. It was shown that internal olefins required much more vigorous conditions than terminal olefins[62] which contained the reactive difluoromethylene group,[54] however, extended reaction times generally afforded the thermodynamically most stable isomer. The operation of a concerted mechanism (S_N2') or formation of a discrete carbanion for such rearrangement reactions is still uncertain.

$$F^- + CF_2{=}\overset{\displaystyle R_f}{\underset{|}{C}}{-}CF_2{-}R_f^s \rightleftharpoons CF_3{-}\overset{\displaystyle R_f}{\underset{|}{C}}{-}CF_2{-}R_f^s \rightleftharpoons R_f{-}\overset{\displaystyle R'_f}{\underset{\displaystyle CF_3}{\overset{|}{C}}}{=}CF + F^-$$

Polyfluoro-1-heptene was isomerised[55] to a mixture of cis and trans perfluoro-2- and -3-heptenes, (122) and (123) respectively, by tetraethylammonium fluoride in chloroform at room temperature. Increased concentration

$$n\text{-}C_5F_{11}CF{=}CF_2 \xrightleftharpoons{F^-} n\text{-}C_4F_9CF{=}CFCF_3 \xrightleftharpoons{F^-} n\text{-}C_3F_7CF{=}CFC_2F_5$$

122 123

of catalyst and a longer reaction time favoured higher conversion and formation of 123. Oligomerisation of hexafluoropropene[68a,92,93] (See 2.5.3.(a)(i)) gave isomeric unsaturated dimers and trimers, the formation of which was rationalised in terms of fluoride ion-induced rearrangements to give the thermodynamically most stable product.

Similar results were reported by Burton and Herbes[63] who developed a Wittig-type synthesis of β-substituted perfluoro-olefins from triphenylphosphine, sodium chlorodifluoroacetate and polyfluorinated ketones. Using 1-phenylpentafluoropropanone in diglyme at 100° they obtained not only the desired 2-phenylheptafluoro-1-butene (124) but also the more stable isomeric cis and trans 2-phenylheptafluoro-2-butene (125).

$$(C_6H_5)_3P + ClCF_2CO_2Na + C_6H_5COC_2F_5 \xrightarrow[100^\circ]{\text{diglyme}} C_6H_5C(C_2F_5){=}CF_2$$

124

$$+ \; C_6H_5C(CF_3){=}CFCF_3$$

cis and trans

125

Treatment of pure 124 with caesium and rubidium fluoride indicated that rearrangement of 124 afforded cis and trans isomers of 125.

$$C_6H_5C(C_2F_5){=}CF_2 \xrightleftharpoons{F^-} \underset{\text{cis}}{\overset{C_6H_5}{\overset{CF_3}{\diagdown}}\!\!C{=}C\!\!\overset{F}{\diagup}\!\!\underset{CF_3}{\diagdown}} + \underset{\text{trans}}{\overset{C_6H_5}{\overset{F}{\diagdown}}\!\!C{=}C\!\!\overset{CF_3}{\diagup}\!\!\underset{CF_3}{\diagdown}}$$

124

125

Fluoride ion-catalysed rearrangements of perfluorodienes and perfluoroallenes have also been reported. When perfluoro-1,3-butadiene was heated[122] with caesium fluoride at 150° in the absence of a solvent hexafluorobut-2-yne (126) was formed. A similar reaction with perfluoro-1,4-pentadiene at 250° afforded[122] perfluoropent-2-yne (127), however,

$$CF_2{=}CFCF{=}CF_2 \overset{F^-}{\rightleftharpoons} CF_3C{\equiv}CCF_3$$

126

in the liquid phase at 45° two intermediate dienes (128) and (129) were isolated which confirmed the reaction mechanism as a series of fluoride ion-initiated S_N2' substitutions.

$$CF_2{=}CFCF_2CF{=}CF_2 \overset{F^-}{\rightleftharpoons} CF_3\bar{C}FCF_2CF{=}CF_2 \rightleftharpoons CF_3CF{=}CFCF{=}CF_2 + F^-$$

128

$$\downarrow F^- \qquad\qquad \uparrow\downarrow F^-$$

$$CF_3C{\equiv}CC_2F_5 \overset{F^-}{\rightleftharpoons} F^- + CF_3CF{=}C{=}CFCF_3 \rightleftharpoons CF_3CF{=}CF\bar{C}FCF_3$$

127 129

Recently Haszeldine and co-workers[123-125] reported similar results in fluoride ion-induced isomerisations of perfluoroallenes. On passing perfluoropenta-1,2-diene vapour over caesium fluoride at 100° perfluoropent-2-yne (127) was formed,[123] however perfluoro-(3-methylbuta-1,2-diene)

$$C_2F_5CF{=}C{=}CF_2 \rightleftharpoons C_2F_5C{\equiv}CCF_3$$

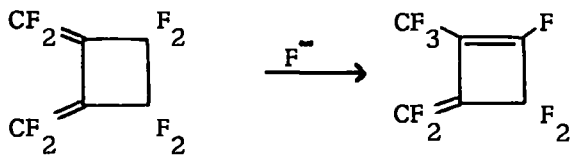
127

at 205° gave[124] only partial isomerisation to perfluoroisoprene (130) via perfluorocarbanion (131). When perfluoro-(1,2-dimethylenecyclobutane) (132),

$$(CF_3)_2C{=}C{=}CF_2 \overset{F^-}{\rightleftharpoons} [F\cdots CF_2{=}C(CF_3){-}\bar{C}{=}CF_2] \overset{F^-}{\rightleftharpoons} CF_2{=}C(CF_3){-}C{=}CF_2$$

131 130

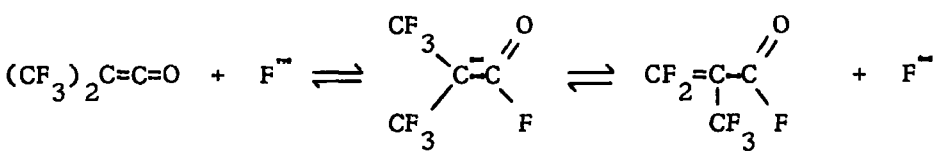
the dimer of tetrafluoroallene, was heated[125] with caesium fluoride at 100° perfluoro-(2-methyl-3-methylenecyclobutene) (133) was obtained



132 133

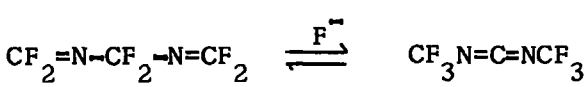
quantitatively via an S_N2' process. Attempts to isomerise 133 further under more forcing conditions were unsuccessful.

Similar fluoride ion-catalysed isomerisations have been reported for perfluoro-ketenes and -α-ω-bisazomethines. Passage of bis(trifluoromethyl)-ketene (134) vapour over sodium fluoride at 300° afforded[126] an equilibrium mixture of 134 and pentafluoromethyl acryloyl fluoride (135). In the



134 135

presence of caesium fluoride, perfluoro-2,4-diazapenta-1,4-diene (136) isomerised[127] rapidly at room temperature to bis(trifluoromethyl)carbodi-imide (137) and was shown to be a typical example of a series of such rearrangements.



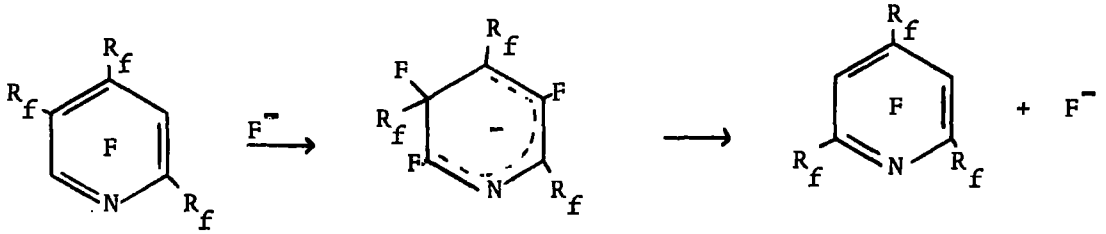
136 137

(b) Perfluoroaromatic compounds.

Acid induced rearrangements of alkylbenzenes[128] in hydrocarbon chemistry have been extensively investigated, however, the analogous fluoride ion-induced rearrangements in fluorocarbon chemistry were reported only recently.[102]

(i) Perfluoroalkylpyridines.

Nucleophilic substitution in pentafluoropyridine with methoxide ion afforded 4-methoxy-,[27,28] 2,4-dimethoxy-[28] and 2,4,6-trimethoxy-[28] derivatives, however, with heptafluoroisopropyl carbanion[33] (See 2.5.3.(b)) a mixture of 4-, 2,4-bis-, 2,4,5- and 2,4,6-tris-(heptafluoroisopropyl) derivatives was obtained. Fluoride ion-catalysed rearrangement of the 2,4,5-isomer (90) to the 2,4,6-isomer (91), via Wheland intermediate (138) and under more vigorous conditions than for their preparation,[129] was reported by Chambers, Musgrave and co-workers[102] who postulated that 90

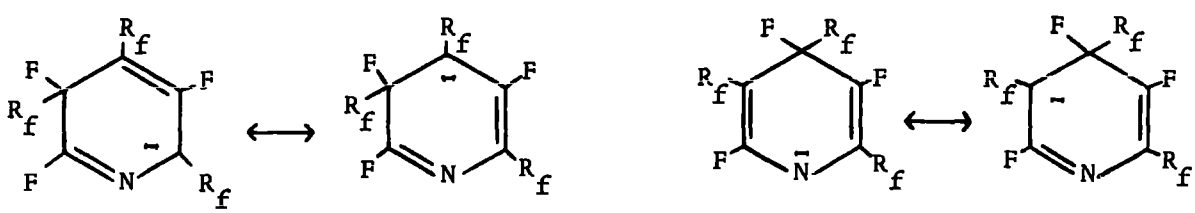


90 138 91

R_f = $(CF_3)_2CF$

and 91 were the products of kinetic and thermodynamic control respectively.

Replacement of the 5-fluorine atom of perfluoro-(2,4-di-isopropyl-pyridine) by a heptafluoroisopropyl carbanion, despite adverse steric interactions, was attributed[39] to the much larger stabilising effect of an α-perfluoroalkyl substituent, compared to an α-fluorine, on the intermediate carbanion (139). Further investigation of the fluoride ion-induced rearrangement of the 2,4,5-isomer indicated that loss of the 4- and 5-substituents occurred via carbanionic intermediates (139) and (140) respectively. This result was attributed to the comparable stabilities of



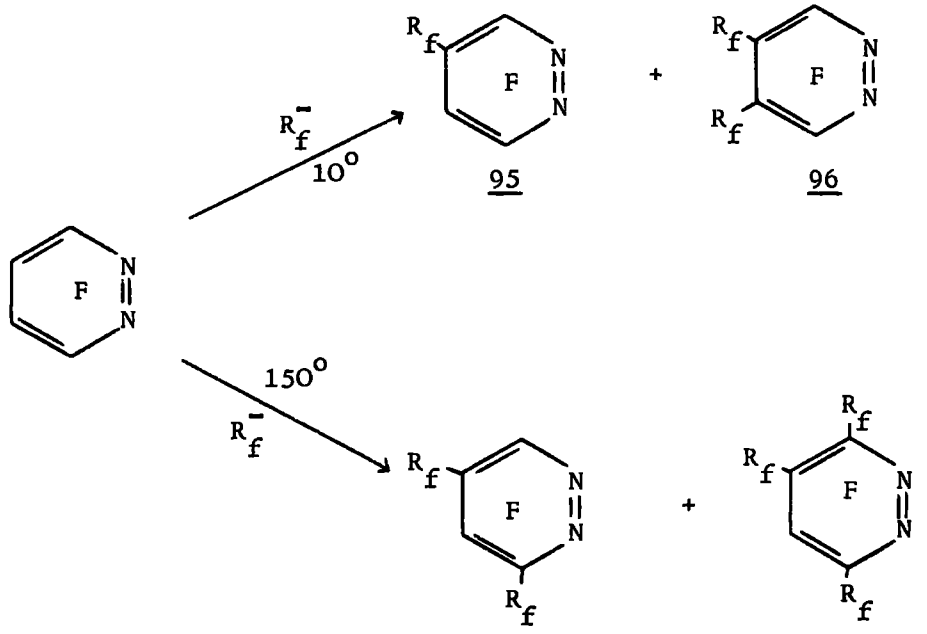
(a) (b) (a) (b)

139 140

139 and 140.

(ii) Perfluoroalkylpyridazines.

Perfluoroisopropylation of tetrafluoropyridazine[38,40,41] under mild conditions afforded perfluoro-(4-isopropylpyridazine) (95) and perfluoro-(4,5-di-isopropylpyridazine) (96) while under more vigorous conditions perfluoro-(4,6-di-isopropylpyridazine) (97) and perfluoro-(3,4,6-tri-isopropylpyridazine) (98) were obtained. Similar results were reported[39]

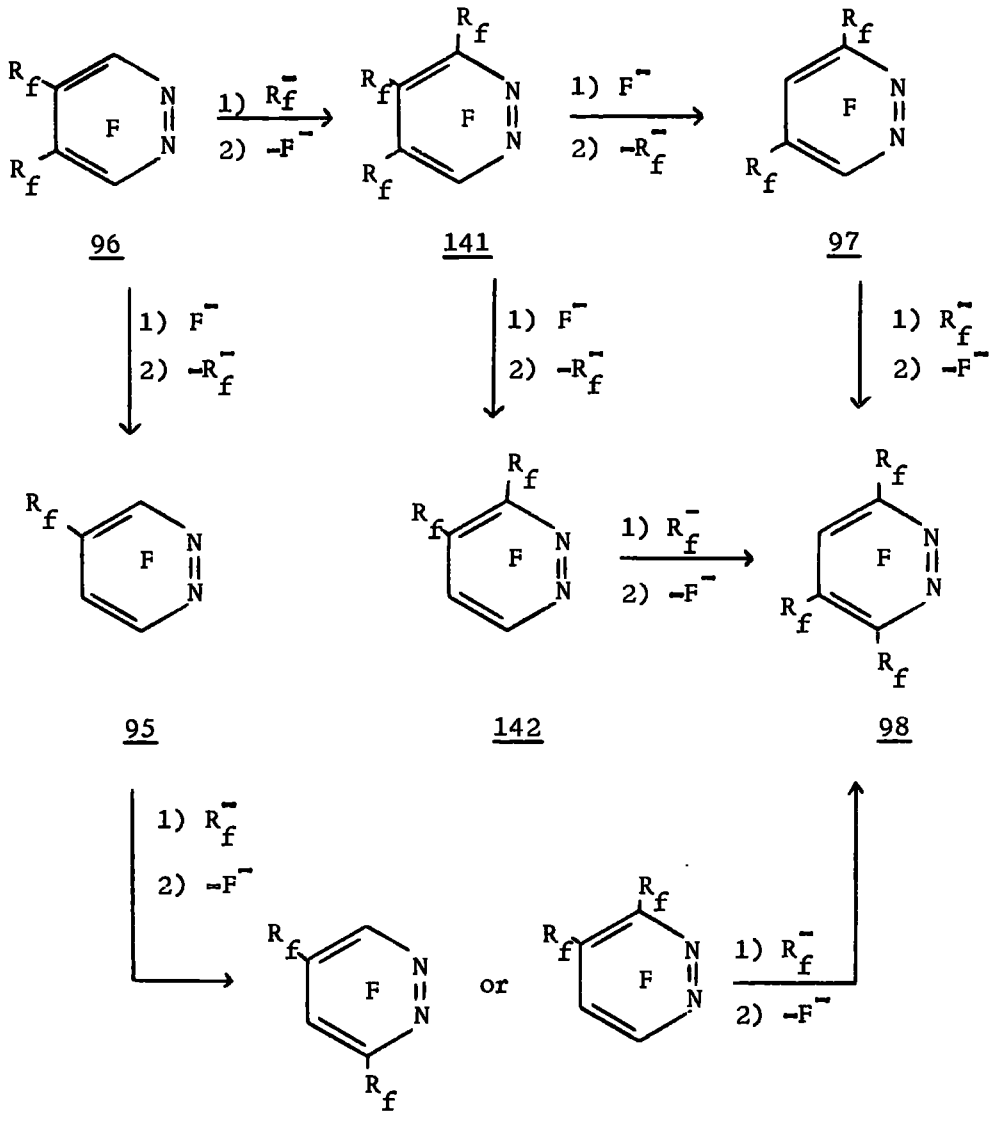


R_f = $(CF_3)_2CF$ 97 98

under moderate conditions (i.e. 70°) and clearly the products isolated depended on whether kinetic or thermodynamic control operated.

Attempted fluoride ion-induced rearrangement of 96 at 150° [40,41] gave a mixture which contained approximately equal amounts of 95, 97 and 98. Further reaction of 96 with $(CF_3)_2CF^-$ produced[39] the 3,4,6-tri-substituted compound (98). The observed results were rationalised, as shown, by either[40] initial rearrangement of the 4,5-isomer (96) to the 4,6-isomer (97), via the mono-substituted derivative (95), with

subsequent attack of $(CF_3)_2CF^-$ at the 3-position of 97 to form 98, or alternatively,[39] initial formation of the 3,4,5-tri-substituted derivative (141) which rearranged to the isolated 3,4,6-isomer (98). The relief of steric interactions in 96 or 141 would facilitate rearrangement.



$R_f = (CF_3)_2CF$

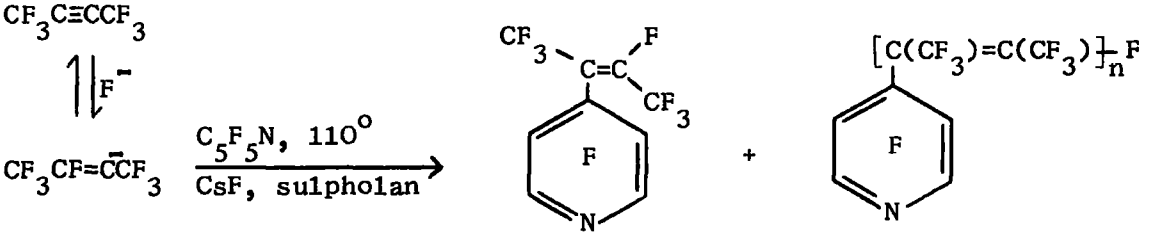
2.6. Fluoride ion-initiated reactions of non-olefinic unsaturated fluorocarbons.

The formation of polyfluorocarbanions on addition of fluoride ion to unsaturated fluorocarbons, other than fluoro-olefins, has been extensively reported, especially in the patent literature. Fluoro-acetylenes,

-carbonyl compounds, -epoxides and polyfluorocarbon-nitrogen compounds have afforded carbanions with fluoride ion, under suitable conditions, which subsequently reacted with activated substrates in an analogous manner to carbanions derived from fluoro-olefins.

2.6.1. Perfluoroacetylenes.

Hexafluorobut-2-yne and caesium fluoride in a dipolar aprotic solvent gave[130,131] perfluorovinyl- and, on dimerisation, perfluoro-alkadienyl carbanions which effected nucleophilic displacement either in the acetylene giving a polymer eventually or in an activated polyfluoro-aromatic compound such as perfluoro-benzonitrile,[130] -pyridine[131] or pyridazine.[131] Pentafluoropyridine afforded low yields of compounds 143, 144 and 145, the latter two of which were not formed[131,132] by extension of the side-chain in 143.



143 144 n = 2 145 n = 3

Miller and co-workers[59] have prepared perfluoro-1-methylpropenyl-silver (146) from silver fluoride and hexafluorobut-2-yne in acetonitrile at 35°. Reaction of 146 with water or hydrogen chloride and bromine

$$AgF + CF_3C{\equiv}CCF_3 \longrightarrow CF_3CF{=}CCF_3Ag$$

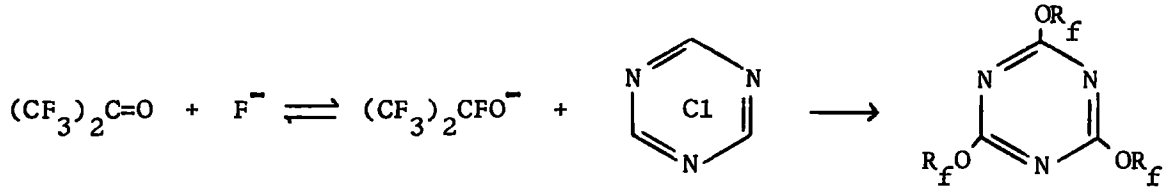
146

gave exclusive trans addition of HF and BrF respectively.

2.6.2. Fluorocarbonyl compounds.

Caesium, potassium, silver or tetraethylammonium fluorides and

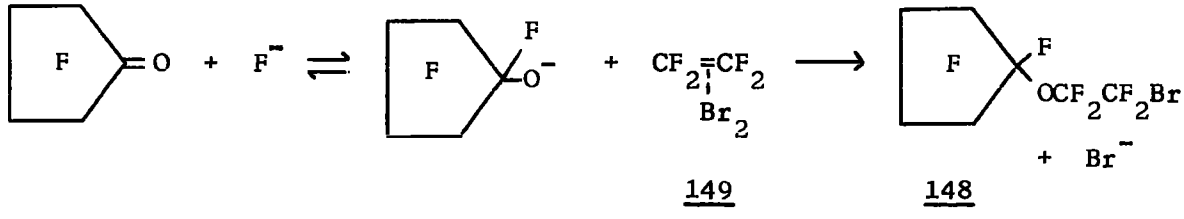
polyfluoroketones in dipolar aprotic solvents afforded[133] polyfluorocarbanions which effected nucleophilic displacement in activated substrates. Hexafluoroacetone and potassium fluoride reacted[134] with cyanuric chloride (2,4,6-trichloro-1,3,5-triazine) to give 2,4,6-tri-perfluoroisopropoxy-1,3,5-triazine (147); variation of the reactant ratio gave the mono- and di-substituted derivatives also. Similar



$R_f = (CF_3)_2CF$ 147

reactions with carbonyl fluoride resulted in the formation of the chloroperfluoromethoxy derivatives.[134]

Previous reactions between caesium fluoride, perfluoroketones and tetrafluoroethylene in diglyme afforded[110] only perfluoro tertiary alcohols from nucleophilic attack by $C_2F_5^-$ on the ketone. However, under similar conditions in the presence of a halogen an ether was formed exclusively.[135] Perfluorocyclopentanone, caesium fluoride, tetrafluoroethylene and bromine gave perfluorocyclopentyl-2'-bromotetrafluoroethyl ether (148) and in general, the proposed mechanism involved



149 148

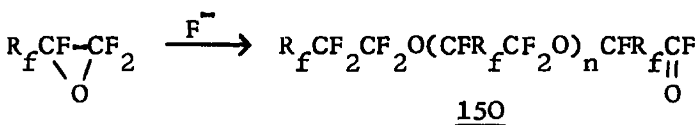
an "olefin-halogen complex" (149) with subsequent nucleophilic attack by perfluoroalkoxide and elimination of an halide ion.

The metal fluoride catalysed addition of ClF and F_2 to perfluorinated

carbonyl compounds, to form hypochlorites[136] and fluoroxyperfluoroalkyl derivatives[137] respectively, involved a perfluoroalkoxide carbanion which displaced fluoride ion from chlorine monofluoride and fluorine.

2.6.3. Perfluoroepoxides.

Fluoride ion-catalysed polymerisation of perfluoroepoxides afforded[138] fluorinated polyethers under suitable conditions and the products obtained were inert high boiling liquids of general formula (150).



150

R_f = F, CF_3, C_2F_5

2.6.4. Polyfluorocarbon-nitrogen compounds.

Investigation of fluoride ion-induced reactions of unsaturated carbon-nitrogen compounds has been mainly concerned with polyfluoroazomethines ($R_fN{=}CF_2$), however, a few similar reactions of nitriles ($R_fC{\equiv}N$) and terminal N-fluoroimines ($R_fCF{=}NF$) have been reported.

Perfluorodimethylaminocarbanion (152), from perfluoro-2-azapropene (151) and fluoride ion, reacted[62] with activated substrates including 151, cyanuric fluoride, nitrosyl fluoride and fluoro-olefins. Self-condensation afforded a dimer (153).

$$\underset{151}{CF_3N{=}CF_2} + F^- \rightleftharpoons \underset{152}{(CF_3)_2N^-} \xrightarrow{CF_3N=CF_2} \underset{153}{(CF_3)_2NCF{=}NCF_3}$$

Ruff[139] has reported the catalytic fluorination of perfluoroacetonitrile and -propionitrile at -78° with elemental fluorine in the presence of caesium fluoride to give perfluoroalkyldifluoroamines (154) and (155) respectively.

$$CF_3C{\equiv}N + 2F_2 \xrightarrow{CsF} CF_3CF_2NF_2$$

154

$$C_2F_5C{\equiv}N + 2F_2 \xrightarrow{CsF} n\text{-}C_3F_7NF_2$$

155

The reported[140] fluoride ion-initiated co-polymerisation of perfluoroguanidine (156) and formaldehyde illustrated the susceptibility of a terminal N-fluoroimine group to nucleophilic attack, giving a polymer of general formula (157).

$$(NF_2)_2C{=}NF + F^- \rightleftharpoons (NF_2)_2\bar{C}F\bar{N}F \xrightarrow{CH_2O} [(NF_2)_2CNF(CH_2O)]_n$$

156 157

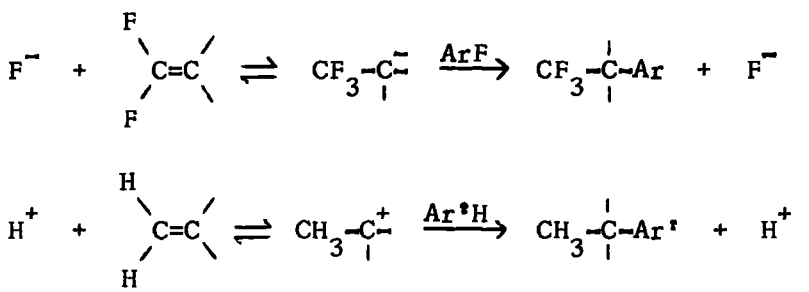
DISCUSSION OF EXPERIMENTAL

CHAPTER 3

Polyfluoroalkylation with Perfluoro-olefins

Introduction.

Nucleophilic substitution in activated fluoroaromatic compounds with polyfluoroalkylanions, generated from fluoride ion and fluoro-olefins, was shown previously in Chapter 2 to be widely applicable to the preparation of polyfluoroalkylaryl compounds. Originally described by Chambers, Musgrave and co-workers,[32] polyfluoroalkylation afforded numerous highly fluorinated aromatic compounds which are complementary to



alkylaryl hydrocarbons prepared in Friedel Crafts reactions. Earlier work in these laboratories employed autoclaves and it was originally thought that elevated temperatures were also essential. In this and related work[129,132] we have shown that apparatus operating at atmospheric pressure can be used with obvious advantages in convenience, as well as other advantages, described later. Considerable effort has been made to develop the best experimental procedures, which vary with the system; the relative merits of these processes are described first.

3.1. Development of experimental procedures.

Previous investigations of fluoride ion-initiated reactions of polyfluoro-olefins with highly fluorinated aromatic compounds in autoclaves indicated their complex nature as well as their potential

synthetic usefulness[49,102] and, therefore, the following discussion outlines the complexity and difficulties encountered in such reactions. Some of the more obvious equilibria which exist in such reaction mixtures are summarised in Equations (A) - (H) and demonstrate some of the problems which are involved in polyfluoroalkylation reactions.

Initiation:

$$MF\ (solid) \rightleftharpoons M^+\ (solv.)\ F^- \qquad (A)$$

$$MF\ (solid) + \underset{}{\overset{F}{\diagdown}}C{=}C\underset{}{\overset{}{\diagup}} \xrightleftharpoons{solvent} R_f^- + M^+\ (solv.) \qquad (B)$$

$$M^+\ (solv.)\ F^- + \underset{}{\overset{F}{\diagdown}}C{=}C\underset{}{\overset{}{\diagup}} \rightleftharpoons R_f^- + M^+\ (solv.) \qquad (C)$$

Polyfluoroalkylation:

$$R_f^- + ArF \rightleftharpoons R_f\text{-}Ar + F^- \qquad (D)$$

$$R_f\text{-}Ar + F^- \rightleftharpoons \text{rearranged } (R_f\text{-}Ar) + F^- \qquad (E)$$

Side-reactions:

$$R_f^- + \underset{}{\overset{F}{\diagdown}}C{=}C\underset{}{\overset{}{\diagup}} \rightleftharpoons R_f^{\prime -} \longrightarrow R''_{f\,|}C{=}C\underset{}{\overset{}{\diagup}} + F^- \qquad (F)$$

$$R_f^- + solvent \rightleftharpoons R_fH + (solvent)^- \qquad (G)$$

$$(solvent)^- + \underset{}{\overset{F}{\diagdown}}C{=}C\underset{}{\overset{}{\diagup}} \rightleftharpoons \text{involatile products} \qquad (H)$$

3.1.1. Metal fluoride-solvent.

Previously, Storey[49] and Jackson[101] observed that potassium fluoride, despite its economic advantages, is a less efficient initiator than caesium fluoride, however, the choice of solvent was much less clear cut. For some polyfluoroalkylations, sulpholan was superior to the glymes,[49] and for others tetraglyme was better than sulpholan,[101] however, reactions at elevated temperatures (ca. > 150°) were usually better in sulpholan than tetraglyme because the by-products of tetraglyme

decomposition cause more difficulties in the work-up stage.[101] In general, therefore, it appears difficult to deduce any correlation between the solvent employed and the reactivity of the system. A possible exception was indicated by Graham[83] who reported that a combination of caesium fluoride and tetraglyme is the most effective system for initiating reactions of tetrafluoroethylene, which was confirmed by preliminary perfluoroethylations of pentafluoropyridine.

Formation of polyfluoroalkylanions from fluoro-olefins and fluoride ion theoretically only requires catalytic quantities of alkali metal fluoride, however, previous reports not only indicated their relative effectiveness as CsF > KF > NaF but also demonstrated a dependence of reaction rate upon the quantity of initiator present, which suggested that a surface effect must be involved.[83,101]

3.1.2. Reaction temperature.

Carbanion formation, from fluoride ion and a fluoro-olefin, is temperature dependent as expected and, although polyfluoroalkylanions can be formed at room temperature,[83,143] their rates of formation are increased at higher temperatures.[83] Subsequent nucleophilic substitution by polyfluoroalkylanions in perfluoro-N-heteroaromatic compounds is also temperature dependent, varying from ca. 20^{o} to ca. > 150^{o} with the reactivity of the substrate and the carbanion involved.

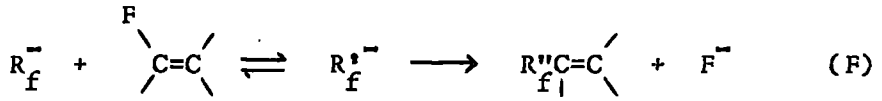
3.1.3. Reaction conditions.

Previously, polyfluoroalkylation was thought to proceed only in autoclaves at elevated temperatures (ca. > 120^{o}),[102] however, under these conditions, the unwanted competing reactions outlined previously are apparent. Therefore, the reaction conditions are invariably critical

in determining which of the possible reactions occurs preferentially, as shown in the discussion of the atmospheric pressure reactions. The common side-reactions in autoclaves are discussed below.

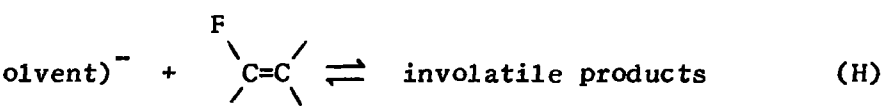
(a) Oligomerisation.

Self-condensation, as in Equation (F) is particularly pronounced with



(F)

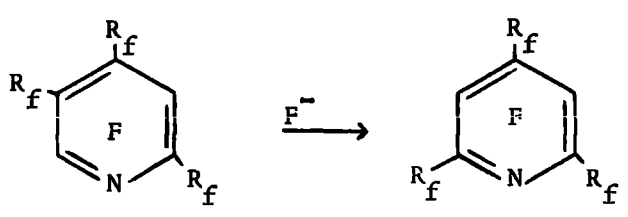
perfluoro-propene[101] and -cyclobutene[97] to give their respective dimers and trimers; for hexafluorobut-2-yne the sole product obtained was a polymer of the acetylene, with no polyfluorovinylation of pentafluoropyridine being observed.[132] Although tetrafluoroethylene is known to oligomerise under these conditions,[68b,83] no mention was made of this on formation of perfluoroethylpyridines,[101,104] however, the major side-reaction in this system was reaction between the solvent and the olefin, as shown in Equation (H), to give highly involatile products.[83,101]



(H)

(b) Rearrangement of products.

Another complication is the variability of isomer ratio with reaction conditions. Tri-substitution in pentafluoropyridine by heptafluoroisopropylanions was achieved previously only in an autoclave at ca. 150°, but ^{19}F n.m.r. spectroscopy indicated that a mixture of 2,4,5- and 2,4,6-isomers, (158) and (159) respectively, was formed.[33] Further treatment of the mixture with caesium fluoride at ca. 180° afforded[102] the pure,



158 159

(E)

R_f = $(CF_3)_2CF$

thermodynamically stable 2,4,6-isomer (159) as in Equation (E), however, it was not possible to obtain the pure, kinetically controlled 2,4,5-isomer from autoclave reactions.

3.1.4. Work-up of the mixture.

Recovery of products from autoclave reactions by vacuum distillation and ether extraction of an aqueous solution of the involatile reaction mixture varied from excellent to moderate.[49,101] Heptafluoroisopropylations invariably afforded almost quantitative yields of products whereas reactions with polyfluoroethylenes appeared to be much more complex,[101] giving varying quantities of intractable tarry residues. No comprehensive theory has been proposed previously, however, these results do correlate with observations by Graham, who found that decreased stability of the carbanion gave reduced recovery and yields.[83] Miller and co-workers[55] reported the formation of water soluble products from fluoride ion-initiated reactions of some polyfluoroethylenes, therefore, reduced yields may possibly be attributed to loss of products in the work-up of the involatile reaction mixture which was dissolved in water and ether extracted.

3.2. Reactions at atmospheric pressure.

The use of atmospheric pressure systems for reactions originally carried out in autoclaves has avoided or, more often, minimised some of the difficulties discussed previously, however, others appear to be inherently part of polyfluoroalkylation reactions. Development of systems suitable for polyfluoroalkylation has led to essentially two procedures with additional modifications in some cases.

3.2.1. Flow system.

It was observed that on bubbling gaseous polyfluoro-olefins through a heated and stirred reaction mixture consisting of caesium fluoride and pentafluoropyridine in sulpholan under dry nitrogen, limited polyfluoroalkylation occurred. Extension of this crude method to a closed apparatus containing an atmosphere of fluoro-olefin, which was circulated with a pump through the stirred reaction mixture, gave an automated system (Fig. 2) and, in some cases, efficient polyfluoroalkylation.

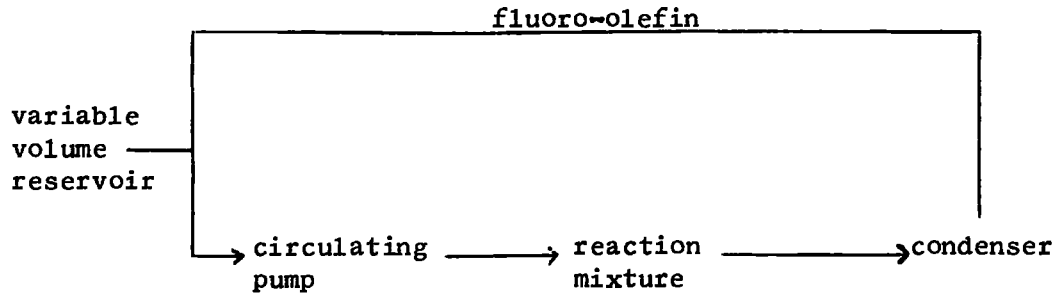
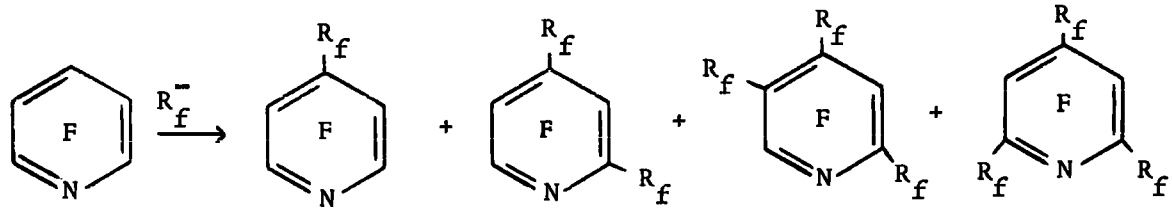


Fig. 2

Heptafluoroisopropylations of pentafluoropyridine in sulpholan at ca. 70° - 135° in a flow process gives[129] comparable yields of substituted derivatives, (160) - (163), to those reported for autoclave reactions at higher temperatures. However, self-condensation of



$R_f = (CF_3)_2CF$ 160 161 162 163

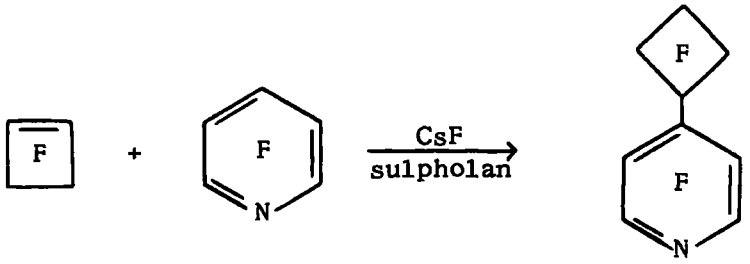
hexafluoropropene to oligomers was substantially reduced owing to a lower concentration of olefin than perfluoroaromatic compound in the reaction mixture, which results in less competition for the heptafluoro-

isopropylanions than in an autoclave and hence preferential nucleophilic aromatic substitution. With this method it is also possible to obtain virtually a single tri-substituted product, the kinetically controlled 2,4,5-isomer (162) in ca. > 90% purity, and an excellent recovery of materials.[129]

In contrast, similar reactions with substituted polyfluoroethylenes, CF_2=CFX (X = F, Cl, Br, H), gives poor recovery of tractable material and low yields of substituted pyridines. Intractable tar formation is attributed to the relative reactivity of intermediate carbanions, once formed, and the lack of nucleophilic substitution to loss of pentafluoropyridine from the reaction flask, past the condensers, in the outflow of hot circulating olefin. This latter effect results from the relatively slow formation of less volatile substituted products, compared to heptafluoroisopropylations,[129] due to either the slow rate of formation or low reactivity of carbanions from these olefins. Marginal improvements obtained on modification of the apparatus to incorporate an acetone-Drikold condenser and a very slow flow rate were not sufficient to persevere with this system for polyfluoroalkylations using these substituted polyfluoroethylenes.

Fluoro-olefins and -acetylenes which primarily self-condense during fluoride ion-initiated reactions with polyfluoroaromatic compounds in autoclaves, giving negligible nucleophilic aromatic substitution, gave similar results in a standard flow process.[97,132] Therefore, the fluoro-olefin or -acetylene is competing much more effectively for the carbanion than the fluoroaromatic compound, hence a reduction in the concentration in solution of the former is essential for preferential aromatic substitution. This was effected by dilution of the gaseous substrate with a large amount of dry nitrogen which, particularly in reactions of

perfluoro-cyclobutene[97] and -but-2-yne[131,132] with pentafluoropyridine, either suppressed oligomerisation or minimised polymerisation to give the substituted products (164) - (166) as shown.



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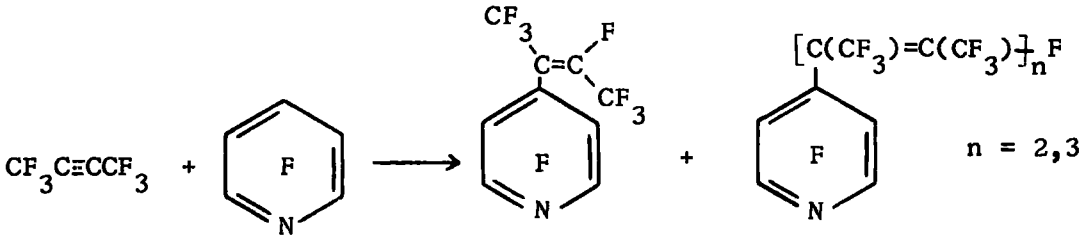


165 166

3.2.2. Static system.

Development of a static system suitable for polyfluoroalkylation with substituted polyfluoroethylenes, CF_2=CFX (X = F, Cl, Br, H), which avoided the difficulties encountered in the flow system due to the circulation of the fluoro-olefin, simply consists of a reaction flask, condenser and variable volume reservoir (See Fig. 9 , page 142). Moderate yields and reasonable conversions are obtained in most cases; consequently this method was used extensively for polyfluoroalkylation reactions and is described fully in the Experimental Section (page 141).

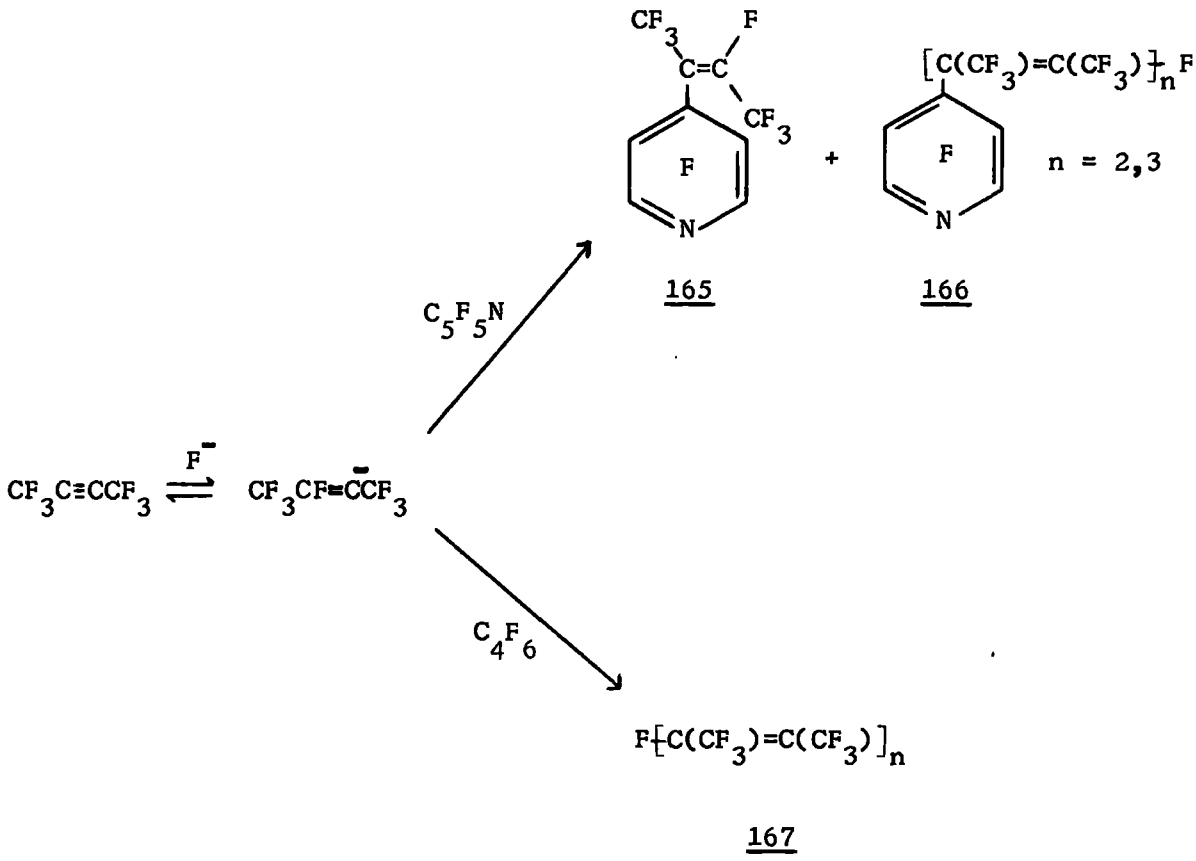
The system was found to be useful over a large temperature range (ca. 20^{o} - 150^{o}), minimising self condensation of the fluoro-olefin and permitting the preparation of unrearranged products at moderate temperatures. Intractable tar formation is still observed but varies considerably with the reactants, however, it does appear to be less than equivalent reactions in autoclaves at elevated temperatures. A visible estimation of the extent of reaction at any instance is possible

from the relative volume of the collapsable reservoir, therefore, for polysubstitution in fluorinated aromatic substrates it is possible to judge approximately when to terminate a reaction in order to obtain a required ratio of products.

Since the reaction most probably occurs in solution, polyfluoroalkylation depends upon dissolution of the fluoro-olefin in the reaction mixture; the factors which control this, excluding temperature, are thought to be two-fold, although no quantitative results were measured. Firstly, variation in the rate of magnetic stirring of the reaction mixture alters the surface area of solvent in contact with the gaseous fluoro-olefin and hence faster stirring appears to give a faster rate of reaction. Secondly, it was observed that vigorous degassing of the solvent prior to admitting the fluoro-olefin also seemed to facilitate its dissolution in the reaction medium. It had previously been noted that dry solvent appeared to dissolve a considerable volume of dry nitrogen while stored under it, which was removed under high vacuum. Similarly, addition of fluoro-olefin to thoroughly degassed solvent followed by immediate removal under high vacuum, again indicated that a substantial amount of gas had dissolved in the solvent.

A modified technique was developed for polyfluoroalkylations with gaseous substrates which polymerise rapidly in the presence of fluoride ion similar to that discussed previously for flow reactions. Reactions are carried out under dry nitrogen at slightly less than atmospheric pressure (ca. 65 cms. Hg) with small controlled additions of the substrate e.g. hexafluorobut-2-yne, from the collapsable reservoir.[131,132] The concentration of the fluoro-olefin or -acetylene in the reaction mixture therefore is small compared to the polyfluoroaromatic compound, which favours nucleophilic substitution in the latter by the intermediate

carbanion to give e.g. 165 and 166 rather than self condensation with the former to give a polymer (167).



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3.3. Structure determination.

The structures of products prepared in reactions using the atmospheric pressure systems described previously were proposed on the basis of information from several sources. Application of substituent chemical shifts (s.c.s.) to the known chemical shifts of ring fluorine atoms in perfluoro-pyridine and -pyridazine can be useful in assigning the orientation of nucleophilic substitution in these substrates, when correlated with the experimental data obtained.[141,142] This procedure is only valid because of the large differences in chemical shifts of the various non-equivalent fluorine atoms in the heterocyclic compound and, even though s.c.s. are neither expected nor found to be always constant, the differences in calculated shifts for different substitution

patterns are so large as to make the assignments often quite unambiguous.[141,142] Ortho, and to a lesser extent para, s.c.s. for polyfluoroalkyl groups are larger than for other substituents[141,142] giving quite distinctive results, however, where possible confirmatory evidence has been obtained, particularly from additional chemistry such as, for example, the preparation of methoxyl derivatives.

Final support for the proposed substitution pattern was obtained from the self-consistent ^{19}F n.m.r. results. This data is listed comprehensively in Chapter 9, including calculated chemical shifts from s.c.s. values, however, where a structural determination is less clear cut it is also incorporated in the discussion.

3.4. Reactions with tetrafluoroethylene.

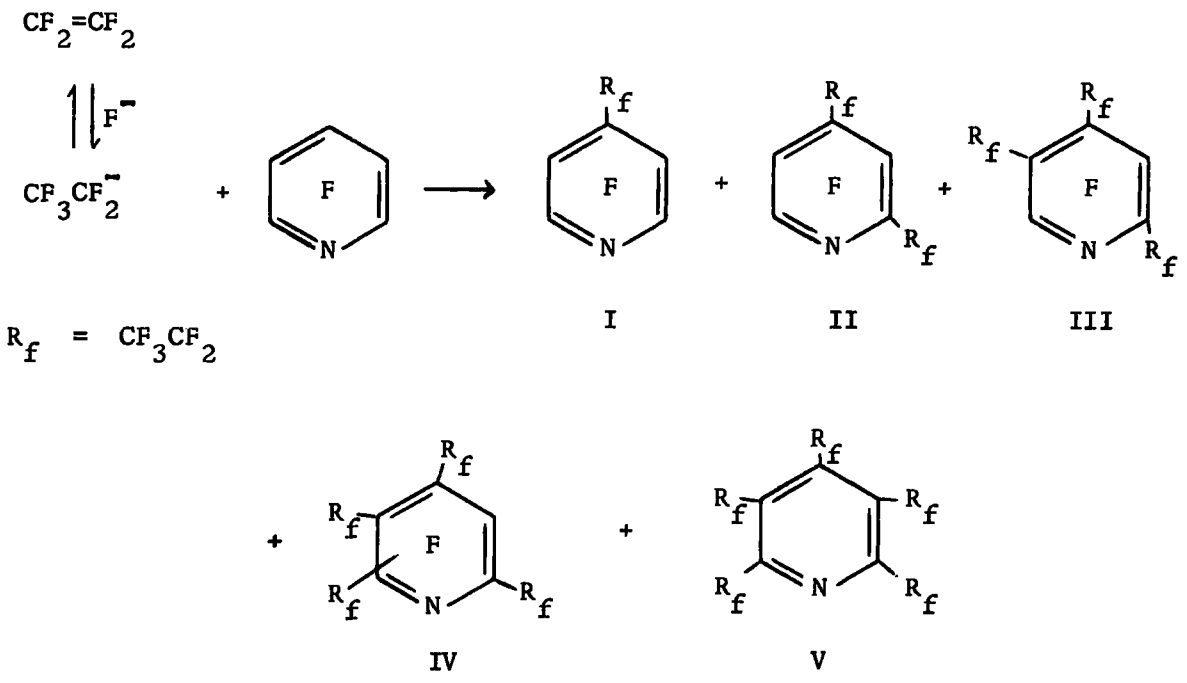
Since it was shown that a combination of caesium fluoride and tetraglyme is the most effective system for initiating reactions of tetrafluoroethylene,[83] all of the reactions described here involve these reagents. The results are discussed under the heading of the perfluoro-N-heteroaromatic compound used.

3.4.1. Pentafluoropyridine.

(a) Conditions and products.

Previously reported perfluoroethylations of pentafluoropyridine were carried out in autoclaves at elevated temperatures and afforded five products,[33,101,104] of which only the tetra- (IV) and penta-substituted (V) derivatives have been characterised in the literature.[33,101] Atmospheric pressure reactions, using a static system, were investigated at ca. 80° to obtain the fastest rate of reaction with the maximum concentration of pentafluoropyridine (b.pt. 83·5°). Unreacted tetra-

Scheme 1



fluoroethylene, identified by i.r. spectroscopy, and a colourless liquid were recovered after the reaction was terminated. The latter contained unreacted pentafluoropyridine and up to five products (See Scheme 1) which were separated by preparative scale v.p.c. and identified as perfluoro-(4-ethylpyridine) (I); perfluoro-(2,4-di-ethylpyridine) (II); perfluoro-(2,4,5-triethylpyridine) (III); perfluoro-(tetra-ethylpyridine) (IV); and pentakis(pentafluoroethyl)pyridine (V) in order of their increasing retention time. Of the latter two products, V was identified by comparison of its i.r. spectrum with that of an authentic sample obtained previously in an autoclave reaction[101] and IV, which was difficult to obtain pure in reasonable quantities, was identified by mass spectrometry only. The remaining products were, however, fully characterised. Product yields under these conditions, for short reaction times are summarised in Table 3, and clearly increased reaction time gives a higher conversion and more extensive substitution.

Table 3

Reaction Time (hrs.)	Products: Percentage Yields (%)*					Conversion %
	C_7F_9N I	$C_9F_{13}N$ II	$C_{11}F_{17}N$ III	$C_{13}F_{21}N$ IV	$C_{15}F_{25}N$ V	
1	76	-	-	-	-	16
2	49	13	4	-	-	53
3	46	17	10	-	-	62
4	41	18	10	-	-	63
5	38	19	12	1•5	-	68
6	37	15	13	3	-	72
7	36	16	30	3	5	76
8	27	20	32	6•5	5•5	79

* Based on the weight of C_5F_5N consumed.

Attempts to improve the percentage yield of pentakis(pentafluoroethyl)pyridine (V) using a longer reaction time (ca. 7 days) at ca. 80° and 120° afforded a colourless liquid and a white crystalline solid. The latter was identified as V by comparison of the i.r. spectrum with that of an authentic sample[101] and chromatographic analysis of the former indicated a complex mixture of products including III, IV, V and a product of almost identical retention time with IV. The yields obtained for III and V are shown in Table 4; the reaction at ca. 80° giving a significantly increased yield of V compared to much shorter reaction times whereas at ca. 120° the reaction is more complicated and less satisfactory.

Attempted separation of the unidentified product in the mixture by preparative scale v.p.c. afforded a small amount of colourless liquid

Table 4

Temp. °C	Estimated Yields* (%) after 7 days		Percentage Yields after 8 hrs.†	
	III	V	III	V
80	8	20	32	5•5
120	7	12	-	-

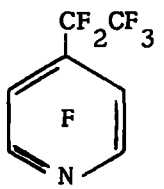
* Based on 100% conversion.

† See Table 3.

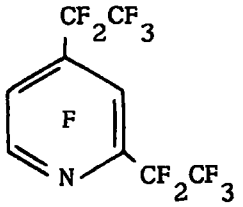
whose mass spectrum had a similar breakdown pattern to known perfluoroalkylpyridines and $^{m}/e$ = 769. Since the maximum molecular weight for perfluoroethyl substituents in pyridine is 669, it is suggested that this product arises from oligomerisation of the tetrafluoroethylene and subsequent reaction of the anions with either pentafluoropyridine or perfluoroethylpyridines. Because of the practical difficulties involved in separation, no further investigation of this compound was undertaken. Extraction of the involatile reaction mixtures afforded large amounts of intractable tars which were not investigated further.

(b) Structure.

Correlation of calculated chemical shifts from s.c.s. data for mono- and di-substitution at the 4- and 2,4-positions by perfluoroalkylanions in pentafluoropyridine[141] with the observed ^{19}F n.m.r. shifts for I and II respectively confirmed the expected substitution pattern based on similar heptafluoroisopropylation products.[33,141] The proposed structures for I and II were further substantiated by methoxylation of pentafluoro-

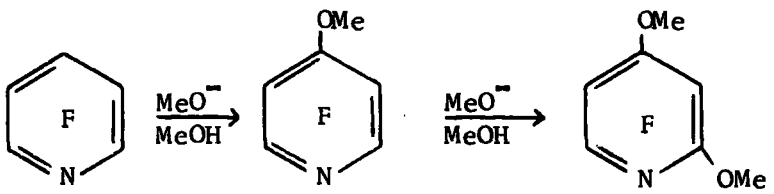


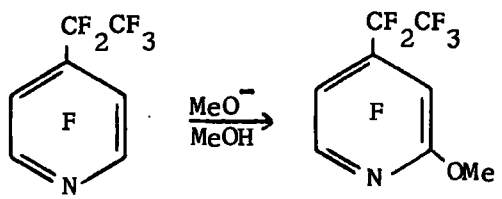
I



II

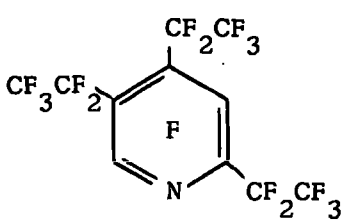
pyridine,[27,28] 4-methoxytetrafluoropyridine[28] and perfluoro-(4-ethyl-pyridine) (I) to give 4-, 2- and 2-substitution respectively as shown.





I XXVII

However, the recently proposed structure of perfluoro-(tri-ethyl-pyridine) as the 2,4,6-isomer,[104] analogous to tri-substitution in pentafluoropyridine with methoxide,[28] is totally incompatible with the observed ^{19}F n.m.r. results for III. These results correlate with calculated values, from s.c.s. data, for 2,4,5-substitution as shown,

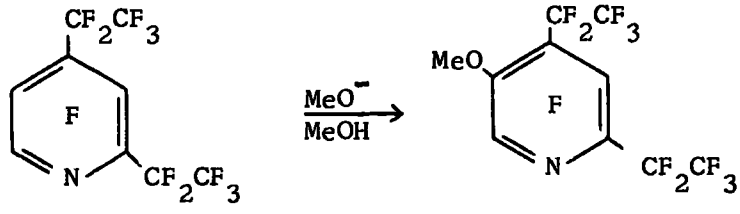


Chemical shifts for ring fluorines in III

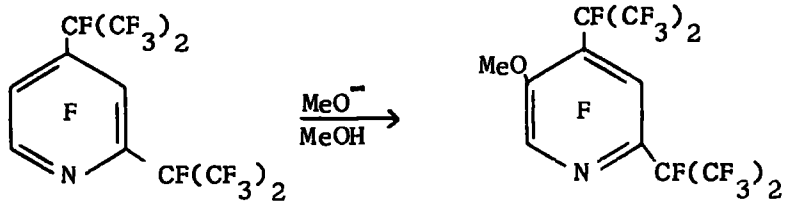
	3	6
Obs.	115·7	55·5
Calc. using I	119	61
Calc. using II	113	62

but are significantly different from those for 2,4,6-substitution. Heptafluoroisopropylation of pentafluoropyridine similarly affords, under suitable conditions, the 2,4,5-isomer. Formation of perfluoro-(2,4,6-tri-ethylpyridine), as reported previously,[104] is extremely doubtful because, although the reported preparative conditions were not repeated exactly i.e. ca. 110° and 20 atm., it was found that only the 2,4,5-isomer was formed at ca. 120° and atmospheric pressure, and III does not rearrange to the 2,4,6-isomer in the presence of fluoride ion even at ca. 190°, unlike perfluoro-(2,4,5-tri-isopropylpyridine) which readily isomerises to the 2,4,6-derivative at ca. 160°.[129]

Reactions of perfluoro-(2,4-di-ethylpyridine) (II) and -(2,4-di-isopropylpyridine) with methoxide at ca. 20° and 70 - 85° to give the 5-methoxy derivatives, (XXVIII) and (XXIX) respectively, substantiated the proposed structure for III. The products were identified by correlation



II XXVIII



XXIX

of the observed ^{19}F n.m.r. data with calculated chemical shifts, derived from s.c.s. values for 4-heptafluoroisopropyl-2-methoxy-3,5,6-trifluoro-pyridine,[33] as shown. In reactions of perfluoroalkylpyridines with methoxide there is no evidence to date for replacement of alkyl, rather than aromatic, fluorine atoms analogous to that reported by Kobayashi

Chemical shifts for ring fluorines in XXVIII

	3	5	6
Obs.	123·2	-	77·8
Calc.	123	-	83
Calc.	129	126	-

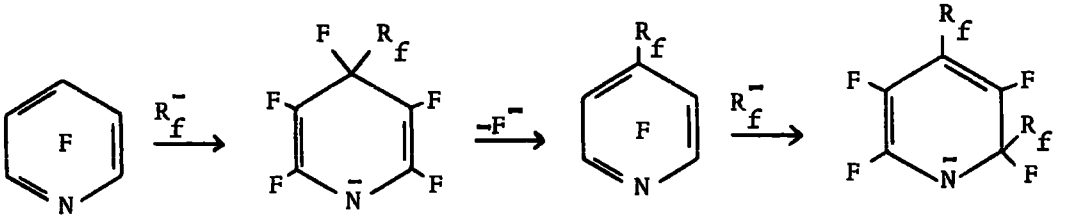
Chemical shifts for ring fluorines in XXIX

	3	5	6
Obs.	120·2	-	78·7
Calc.	119	-	83
Calc.	125	124	

and co-workers[144,145] in reactions of trifluoromethylquinolines with MeO^- and NH_2^-. The mechanism proposed for these novel reactions is discussed fully in Chapter 4 in connection with observed fluorine-halogen exchange.

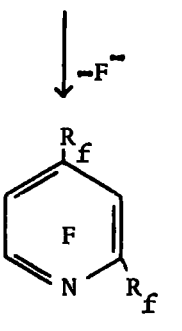
(c) Mechanism.

Recently, the orientation of nucleophilic substitution in perfluoro-N-heteroaromatic compounds has been rationalised from a consideration of the stability of the intermediate carbanions.[37] It was concluded that stabilisation due to localisation of a negative charge on a ring nitrogen atom was more important than avoiding destabilising L_{ff} repulsions in such intermediate carbanions.[37] With pentafluoropyridine, therefore, mono- and di-substitution by $CF_3CF_2^-$ are expected, and observed, at the 4- and 2,4-positions via the most stable intermediate carbanions (168) and (169) to give I and II respectively.



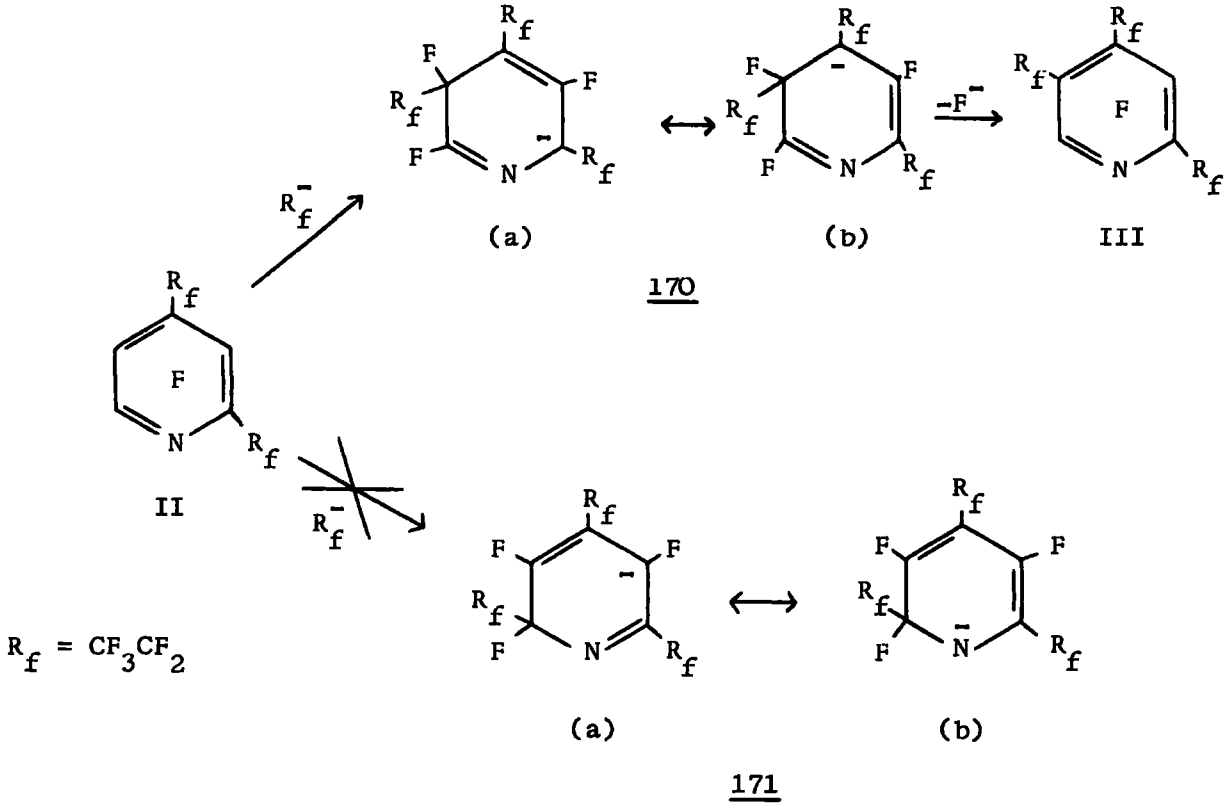
168 I 169

$R_f = CF_3CF_2$



II

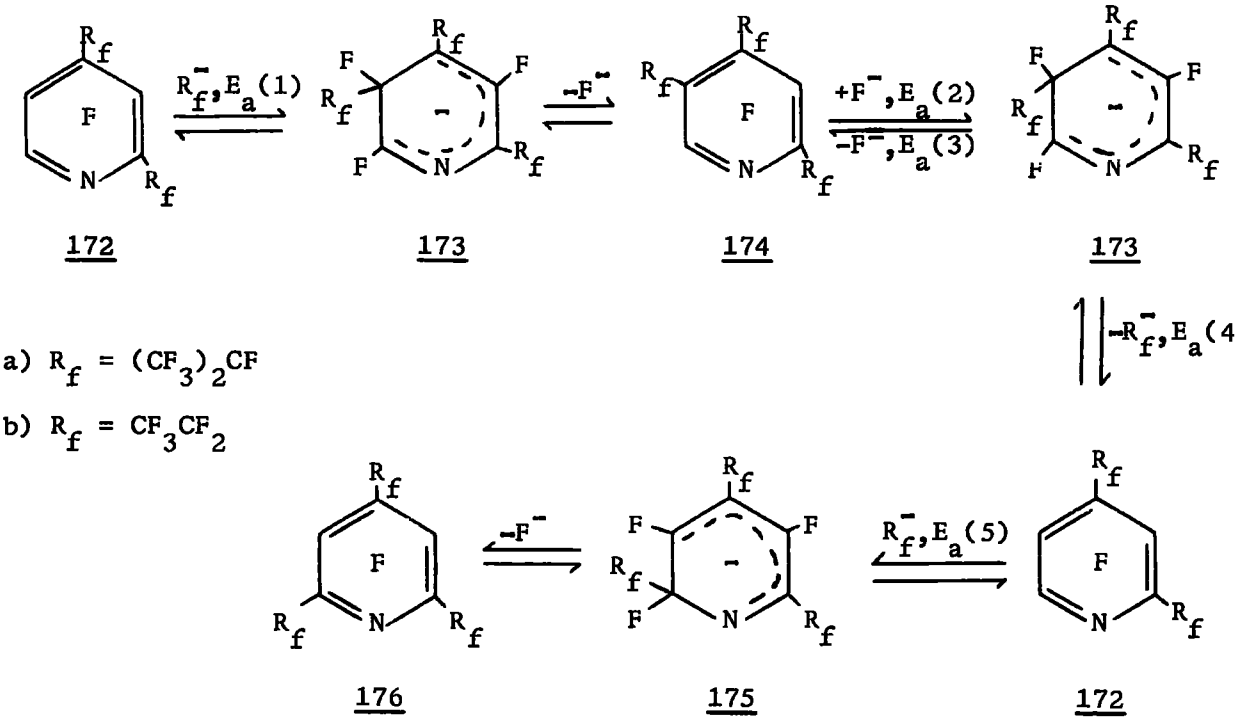
Further substitution in II by $CF_3CF_2^-$ is expected at the 6-position from the preceding argument and by analogy with most other anionic attack on pentafluoropyridine, however, only replacement of the 5-ring fluorine atom is observed to give perfluoro-(2,4,5-tri-ethylpyridine) (III). The observed orientation of substitution in II can be attributed, from a consideration of the intermediate carbanions (170) and (171) for 5- and 6-substitution respectively, to the strongly stabilising effect of an α-



pentafluoroethyl group on the localised negative charge in 170 compared to the destabilising I_{π} repulsive effect of α-fluorine in 171. A somewhat similar situation has been reported for heptafluoroisopropylation of pentafluoropyridine, with mainly perfluoro-(2,4,5-tri-isopropylpyridine) formed at moderate temperatures due to kinetic control of the products, however, at elevated temperatures (ca. > 135°) the thermodynamically-stable 2,4,6-isomer was obtained;[39,102] no analogous isomer of perfluoro-

(tri-ethylpyridine) was observed, even at ca. 190°.

These observed differences between perfluoro-ethylation and -iso-propylation of pentafluoropyridine can be rationalised from a consideration of a qualitative representation of the relevant general energy profile for each system (See Fig. 3), which is intrinsically very complex, giving an insight into the factors controlling the reaction products.



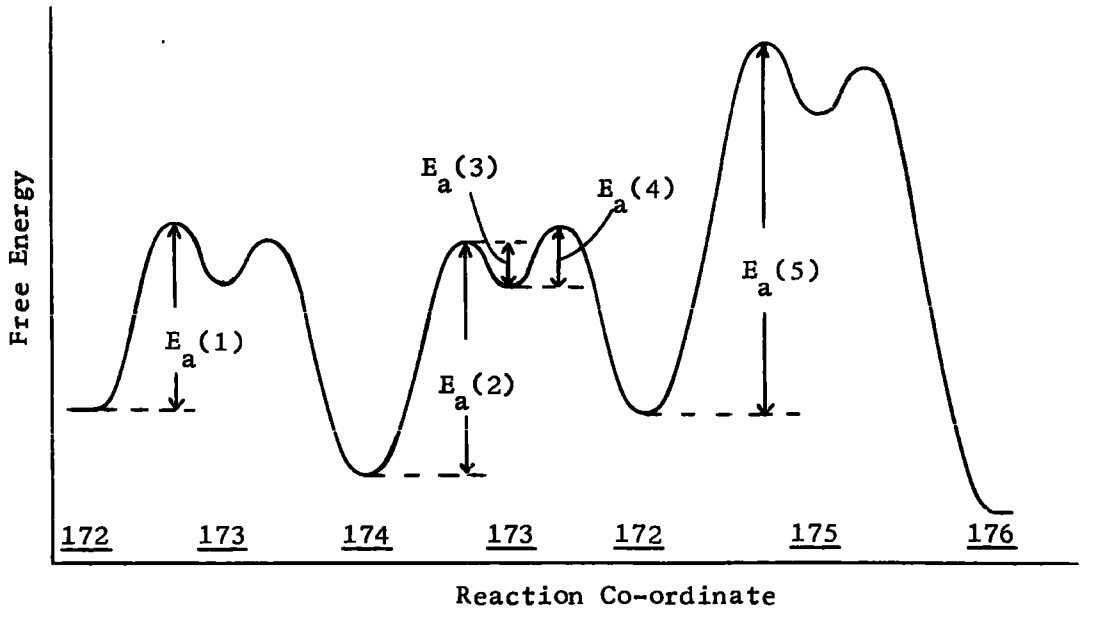
172 173 174 173

(a) $R_f = (CF_3)_2CF$

(b) $R_f = CF_3CF_2$

176 175 172

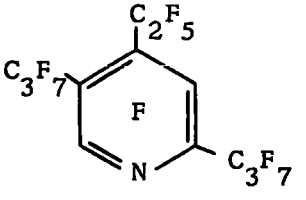
Fig. 3



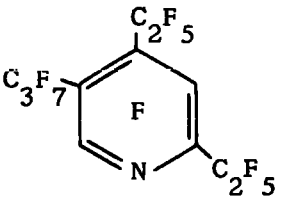
The activation energy for addition of R_f^- to the di-substituted compound (172) to form the intermediate carbanion (173) is $E_a(1)$, which is always larger than $E_a(4)$, the activation energy for loss of R_f^- from 173. Therefore, if further substitution by R_f^- in 172 is energetically possible then, theoretically, loss of R_f^- from 173 is also possible. However, fluoride ion-initiated reaction of the 2,4,5-isomers, (174(a)) and (174(b)), at elevated temperatures in the presence of heptafluoroquinoline, which readily reacts with carbanions, clearly indicated that, under these conditions, addition of $(CF_3)_2CF^-$ to 172(a) is reversible[102] whereas addition of $CF_3CF_2^-$ to 172(b) is not reversible.

From a consideration of Fig. 3, two explanations of the different behaviour of the two systems are possible. Either $E_a(2)$, the activation energy for formation of 173 from 174, is significantly increased for $R_f = CF_3CF_2$ compared to $R_f = (CF_3)_2CF$ or alternatively, $E_a(3)$ and $E_a(4)$, the activation energies for the two modes of decomposition of 173, are very different for $R_f = CF_3CF_2$ but similar for $R_f = (CF_3)_2CF$. This effectively gives only a single mode of decomposition in the former case in contrast to the possibility of both types in the latter.

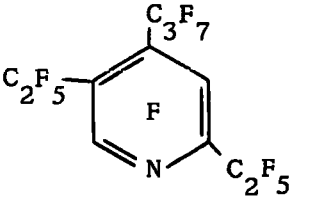
The former reason is highly unlikely from steric considerations and furthermore, results obtained from rearrangement reactions of XVIII, XIX and XXI, as discussed in Chapter 5, indicated reasonably conclusively that



XVIII



XIX

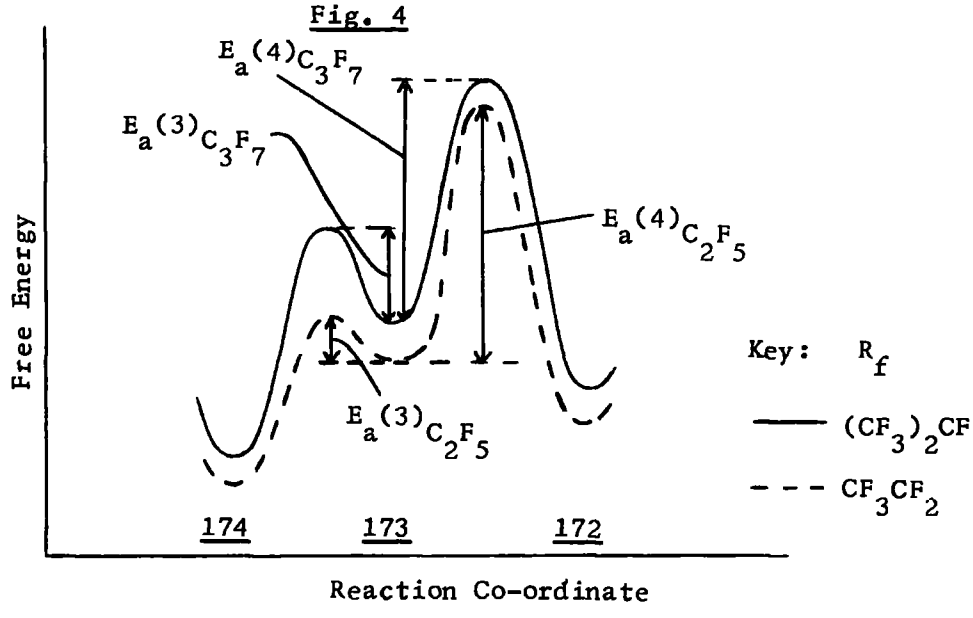


XXI

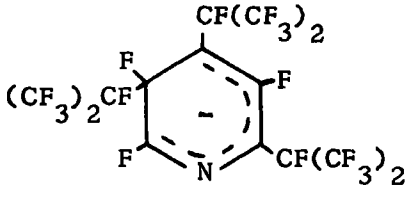
this is not the controlling factor. It is concluded, therefore, that the latter reason is the important one and can be represented schematically

for the two systems as in Fig. 4. Clearly, the rate of loss of fluoride

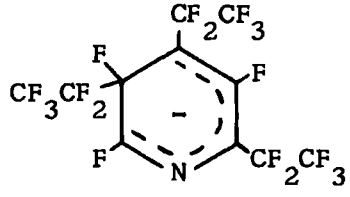
Fig. 4



ion and $(CF_3)_2CF^-$ from 173(a) are similar whereas the rate of loss of fluoride ion from 173(b) is much faster than the rate of loss of $CF_3CF_2^-$.



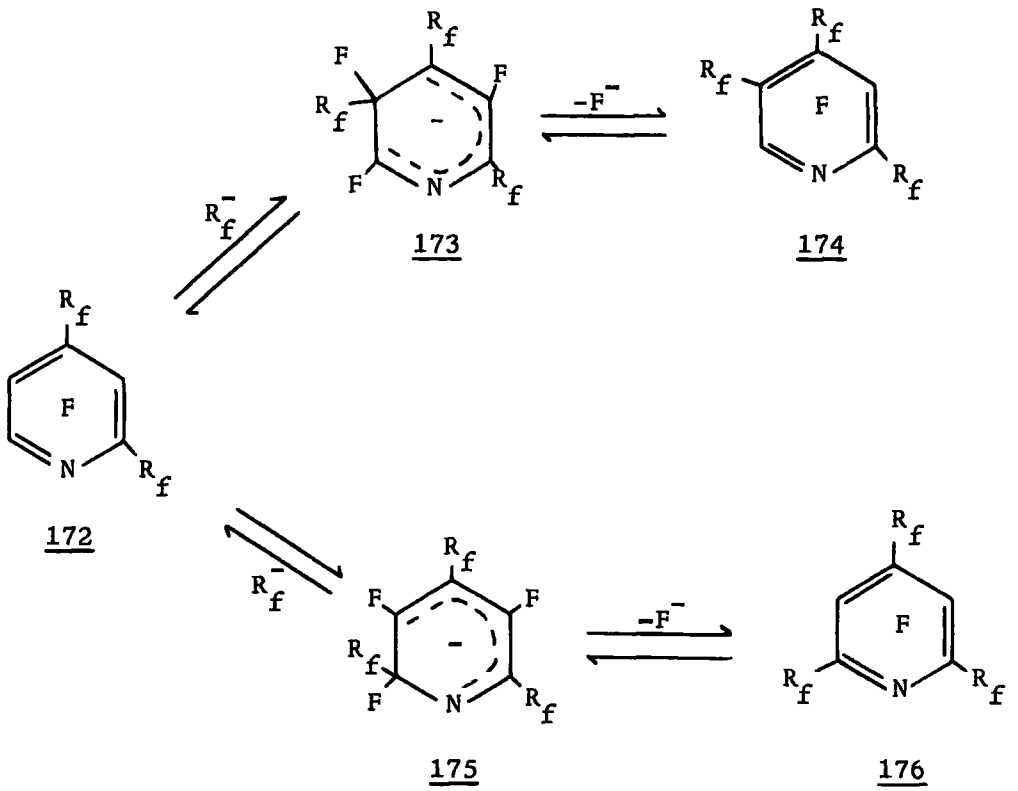
173(a)



173(b)

The activation energy, $E_a(5)$, for nucleophilic substitution at the 6-position in the di-substituted compound (172) must necessarily be greater than $E_a(1)$, for analogous substitution at the 5-position. Clearly, since some 2,4,6-isomer is formed on heptafluoroisopropylation of pentafluoropyridine at ca. 100°, $E_a(5)$ and $E_a(1)$ are fairly similar, however, since pentafluoroethylation at ca. 120° and atmospheric pressure gives only the 2,4,5-isomer, there is obviously a substantial difference between $E_a(5)$ and $E_a(1)$ in this system.

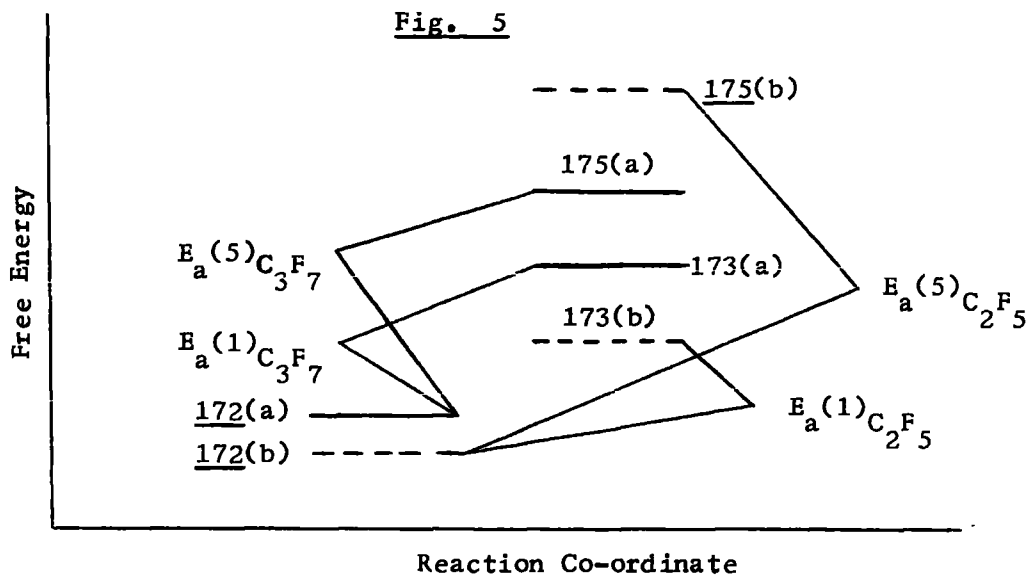
The relative difference between $E_a(5)$ and $E_a(1)$ for the two systems may result from a reduction in $E_a(1)$ or an increase in $E_a(5)$ for perfluoroethylation compared to perfluoroisopropylation. A combination of both of these effects is the most likely and is shown schematically in Fig. 5. The reduction in $E_a(1)$ for $R_f = CF_3CF_2$ compared to $R_f = (CF_3)_2CF$



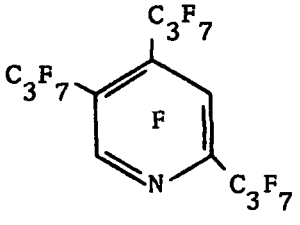
(a) $R_f = (CF_3)_2CF$

(b) $R_f = CF_3CF_2$

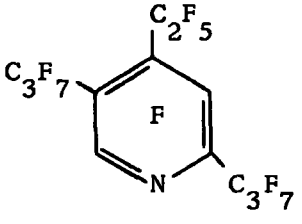
Fig. 5



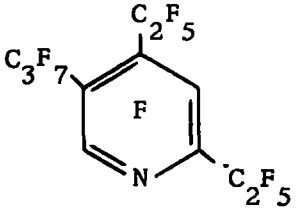
probably arises from decreases in the transition- (173(b)) and ground-state (172(b)) energies, relative to 173(a) and 172(a) respectively, due to diminished crowding between the perfluoroethyl substituents. An increase in $E_a(5)$ for $R_f = CF_3CF_2$ can be attributed to the lower ground state energy of 172(b) and possibly a higher transition state energy for 175(b). Results obtained from attempted fluoride ion-initiated rearrangements of 177, XVIII, XIX, XXI and III have indicated, as discussed fully in Chapter 5, that $E_a(5)$ varies with the perfluoroalkyl substituents, however, a lot more results are required before any definite correlation can be drawn.



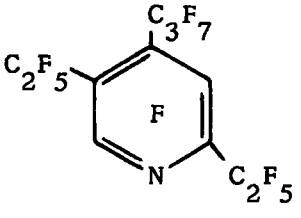
177



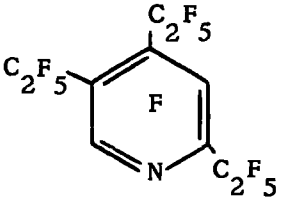
XVIII



XIX



XXI



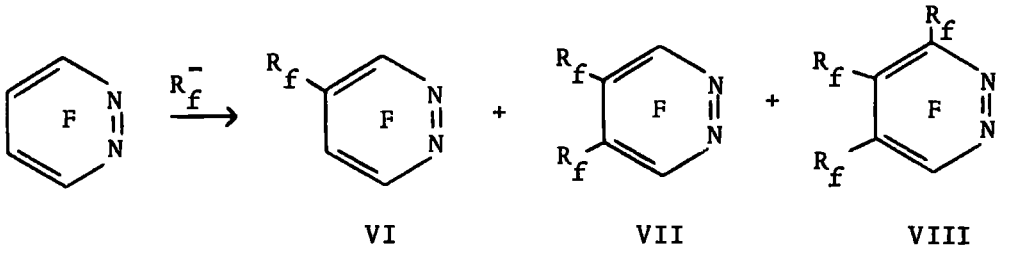
III

3.4.2. Tetrafluoropyridazine.

(a) Conditions and products.

Using a static system, nucleophilic substitution in tetrafluoropyridazine with $CF_3CF_2^-$, generated in tetraglyme at ca. 80° from caesium fluoride and tetrafluoroethylene comparable to previously discussed perfluoroethylations of pentafluoropyridine, afforded low yields of 4-, 4,5-bis- and 3,4,5-tris-(pentafluoroethyl) derivatives, (VI) - (VIII)

respectively (See Scheme 2), and large amounts of intractable tarry



VI VII VIII

$R_f = CF_3CF_2$

Scheme 2

residues. No evidence for the formation of a tetra-substituted derivative was obtained. Reaction times in excess of five hours were not investigated owing to the low yields of products recovered; the results obtained are summarised in Table 5.

Table 5

Reaction Time (hrs.)	Products: Percentage Yields* (%)			Conversion %
	$C_6F_8N_2$ VI	$C_8F_{12}N_2$ VII	$C_{10}F_{16}N_2$ VIII	
1	37	7	-	45
2	21	11	2	94
3	13	8	3	100
4	9	6	5	100
5	4	3	4	100

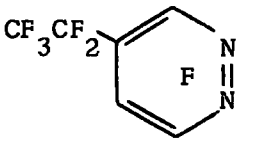
* Based on the weight of $C_4F_4N_2$ consumed.

The surprisingly low yields of identifiable products observed with such a reactive substrate as tetrafluoropyridazine are difficult to rationalise, however, it may simply be that, since the system is highly moisture sensitive, the solvent is not adequately dried giving mainly polymeric hydrolysis products. Whatever the reason, this system

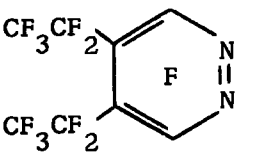
obviously merits further investigation, possibly with different solvents and initiators over a large temperature range.

(b) Structure.

As mentioned previously, correlation of calculated chemical shifts, determined from s.c.s. data,[41] and observed chemical shifts is a valid procedure in structure determination of substitution products from tetrafluoropyridazine due to the large difference in chemical shifts of the 3,6 and 4,5 ring fluorines, making assignments often quite unambiguous. Such correlations indicated that mono- and di-substitution in tetrafluoropyridazine on nucleophilic attack of $CF_3CF_2^-$ occurs, as expected, at the 4- followed by the 5-positions, para to the ring nitrogen atoms, to give VI and VII respectively. This is in agreement with

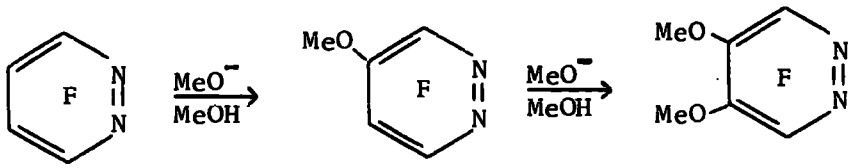


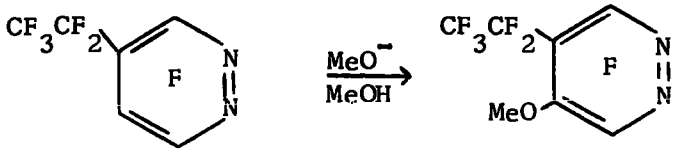
VI



VII

heptafluoroisopropylation of tetrafluoropyridazine at ca. 60°[41] and confirmed by reaction of tetrafluoropyridazine,[37] 4-methoxytrifluoropyridazine[37] and VI with methoxide to give 4-, 5- and 5-replacement respectively as shown.

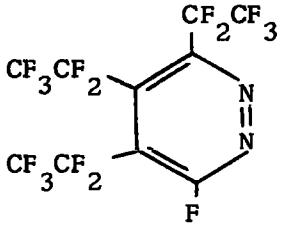




VI XXX

However heptafluoroisopropylation of tetrafluoropyridazine at ca. 150° afforded an isomeric 3,5-di-substituted derivative which was also formed by fluoride ion-catalysed rearrangement of the 4,5-isomer at ca. 150°.[40,41] An attempted fluoride ion-catalysed rearrangement of perfluoro-(4,5-di-ethylpyridazine) (VII) at ca. 150° gave only recovered starting material. Initial investigations of VII had shown certain inconsistencies in the relative intensities of several absorptions in the i.r. spectrum which were thought to be due to a mixture of isomers. However, ^{19}F n.m.r. spectroscopy indicated quite clearly that only the 4,5-isomer (VII) was present and further investigation of the i.r. spectrum revealed that a marked change in intensity of several absorptions occurred with a change of phase of the contact film from liquid to solid (see Appendix 2, Spectra 29(a) and (b)). This interesting phenomenon may possibly be due to rotational isomerism of the perfluoroethyl substituents similar to that reported previously in ^{19}F n.m.r. studies of related systems.[141]

From a correlation of the calculated and observed chemical shifts, tri-substitution by $CF_3CF_2^-$ in tetrafluoropyridazine to give perfluoro-(3,4,5-tri-ethylpyridazine) (VIII) is indicated, which is in agreement



VIII

Chemical shifts for ring fluorines in VIII

	3	4
Obs.	70·2	-
Calc.*	75	-
Calc.†	-	107

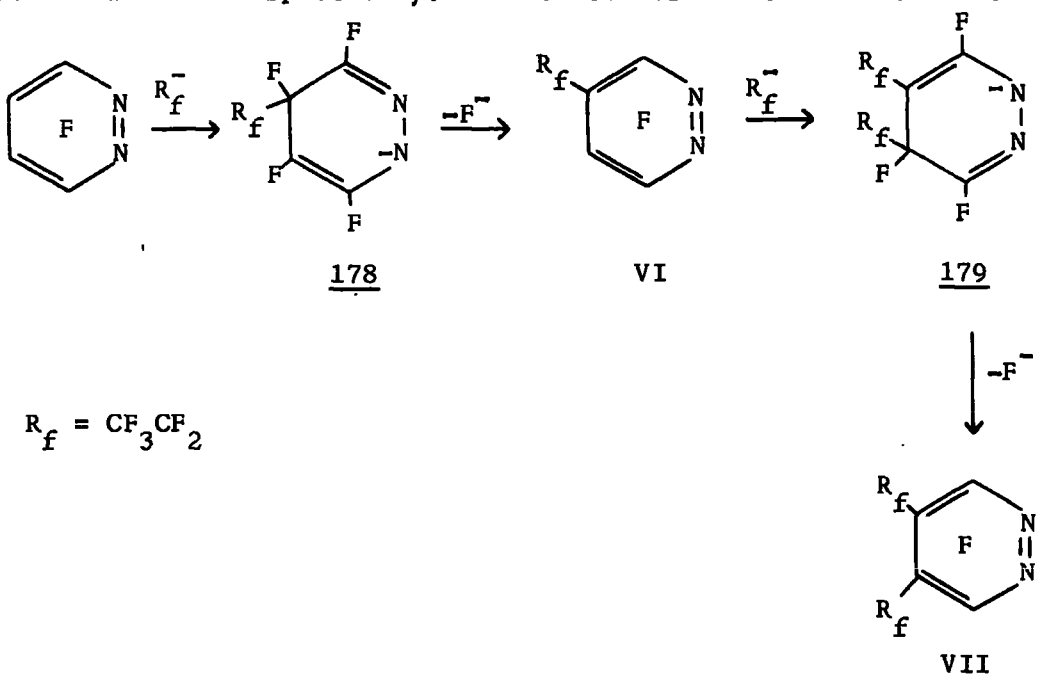
* From VII and s.c.s. of $(CF_3)_2CF$ group in perfluoro-(3,5-di-isopropylpyridazine).[41]

† From VI and s.c.s. of $(CF_3)_2CF$ group in 4,5- and 3,5-isomers of perfluoro-(di-isopropylpyridazine).[41]

with the reported substitution pattern for the tri-methoxy derivative[37] but contrasts with the reported identification of a 3,4,6-isomer only on heptafluoroisopropylation.[39-41] However, formation of perfluoro-(3,4,6-tri-isopropylpyridazine) was suggested to proceed via the thermodynamically-stable 3,5-di-substituted compound and therefore, on this basis, formation of perfluoro-(3,4,6-triethylpyridazine) is not expected since perfluoro-(4,5-di-ethylpyridazine) (VII) is not catalytically rearranged to the 3,5-isomer.

(c) Mechanism.

The effect of the ring nitrogen on the stability of the intermediate carbanion was shown previously to be the major factor controlling the orientation of nucleophilic substitution in perfluoro-N-heteroaromatic compounds.[37] On this basis, mono- and di-substitution by $CF_3CF_2^-$ in tetrafluoropyridazine are expected, and observed, at the 4- and 4,5-positions via the most stable intermediate carbanions, (178) and (179), to give VI and VII respectively. These results are similar to those reported



$R_f = CF_3CF_2$

previously for heptafluoroisopropylation of tetrafluoropyridazine at up to ca. 60°,[40,41] however, unlike perfluoro-(4,5-di-isopropylpyridazine),[39-41]

VII is not rearranged to the 3,5-isomer by fluoride ion at elevated temperatures (ca. 150°).

Clearly the energy profiles for the two systems differ considerably and, since two possible mechanisms have been proposed previously,[39-41] two qualitative schematic representations are possible. Rearrangement of 180 via the mono-substituted compound (181) is considered in Route 1 and Fig. 6, and via the tri-substituted derivative (186) is shown in Route 2 and Fig. 7.

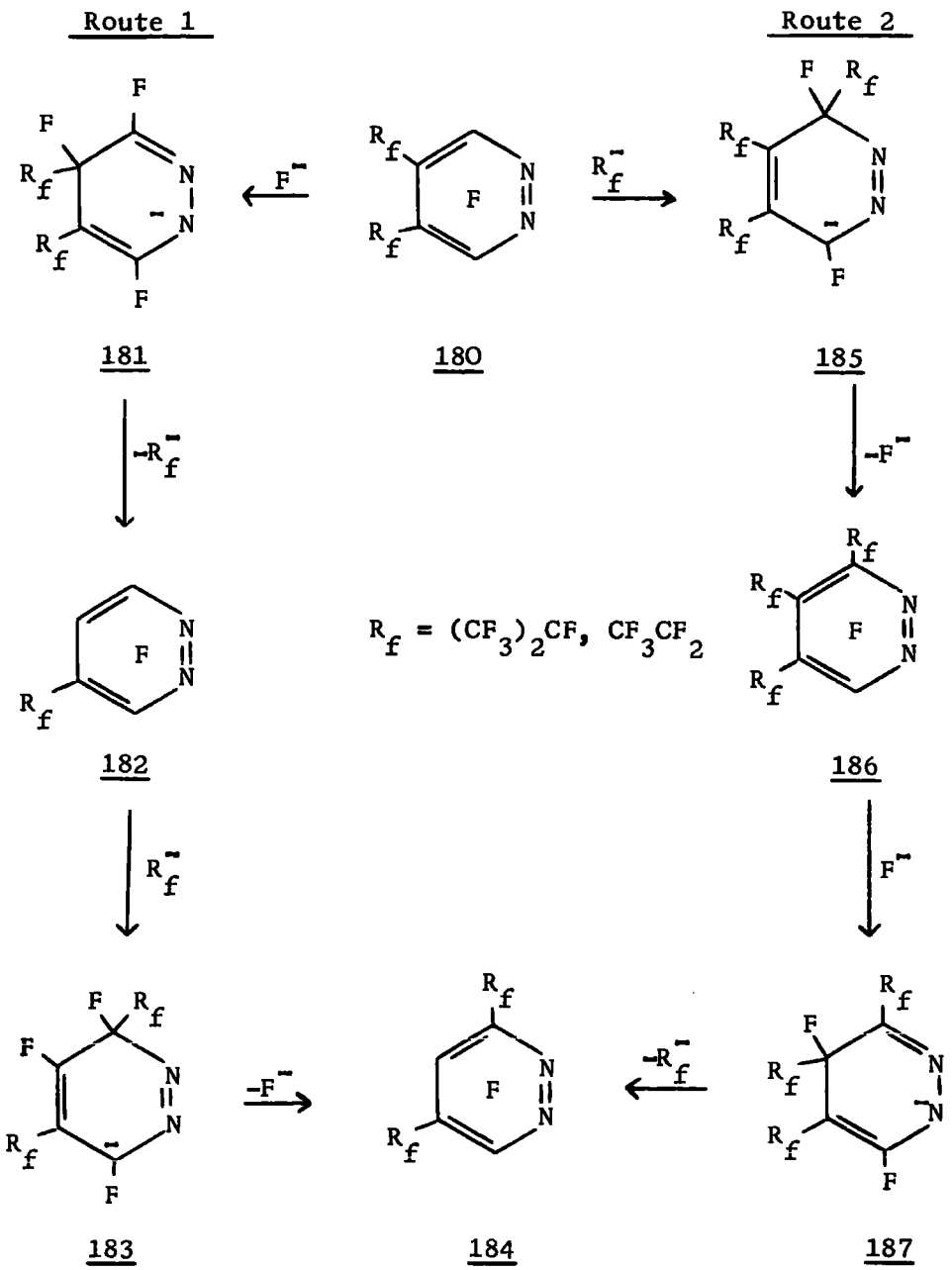


Fig. 6

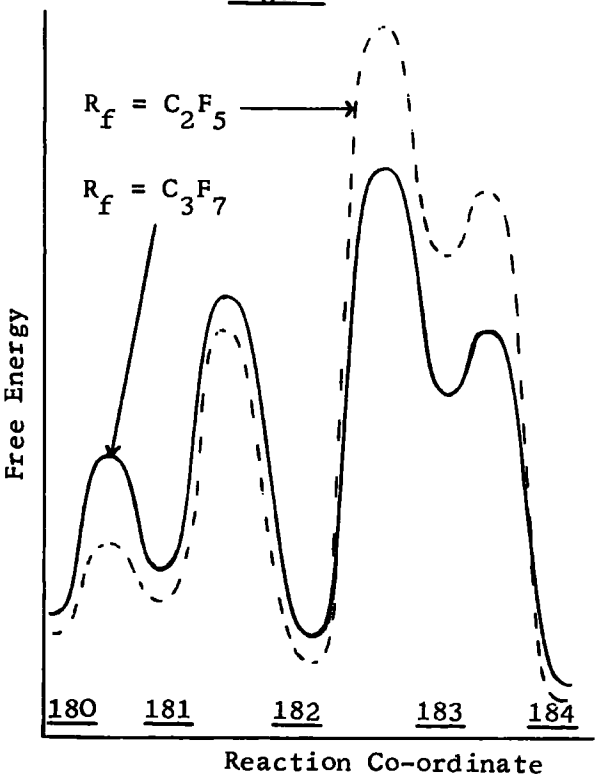
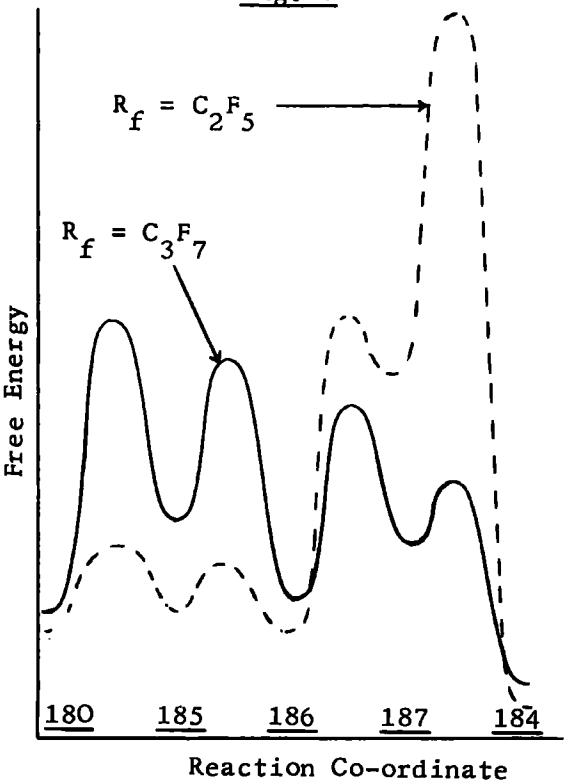
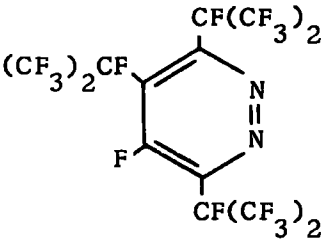


Fig. 7

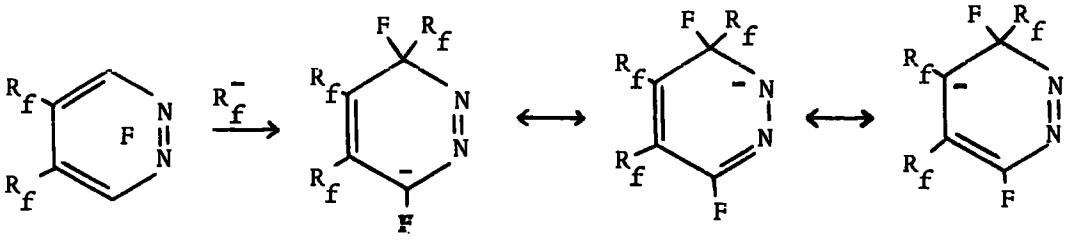


Pentafluoroethylation of tetrafluoropyridazine afforded a single tri-substituted derivative which was identified as the 3,4,5-isomer (VIII), in contrast to the formation of only the 3,4,6-isomer (188) on heptafluoroisopropylation, presumably formed via intermediate



188

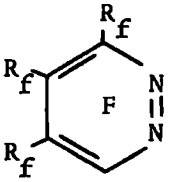
carbanion (186) on substitution by $CF_3CF_2^-$ in VII. Formation of VIII is



186

$-F^-$

$R_f = CF_3CF_2$



VIII

expected since, unlike the formation of 188 which involves rearrangement to relieve steric interactions between adjacent substituents, rearrangement of VII is not observed and steric effects appear less important for pentafluoroethyl than heptafluoroisopropyl substituents, as surmised from the pentafluoropyridine system.

3.5. Reactions with perfluoroisobutene.

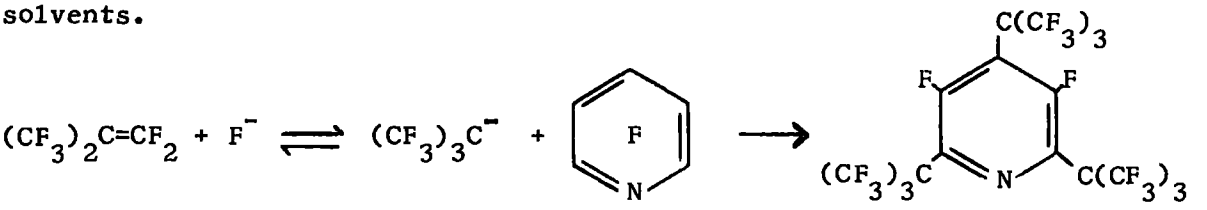
Nucleophilic substitution in perfluoro-N-heteroaromatic compounds by perfluoro-t-butylanions, generated by reaction of fluoride ion and perfluoroisobutene, are of interest for several reasons. The products from such reactions are an integral part of a series which include perfluoro-ethyl and -isopropyl derivatives and, from a consideration of all of the results, it has been possible to make certain conclusions relating to kinetic and thermodynamic control of reaction products[146] (see Section 3.6.). Due to the high degree of symmetry of a perfluoro-t-butyl group it may be possible to measure rotational energy barriers in certain cases from ^{19}F n.m.r. data. An estimate of the steric requirements of this very bulky substituent may also be possible from the preparation of suitable compounds.

Only reactions involving excess perfluoroisobutene were investigated by the author, thus introducing the maximum number of perfluoro-t-butyl groups into pentafluoropyridine and tetrafluoropyridazine, however, more selective reactions with the former substrate have been investigated subsequently.[143] The high toxicity of perfluoroisobutene necessitated minor modifications to the static system described previously to ensure maximum safety; the procedure is fully described in Section 6.3.1.

3.5.1. Pentafluoropyridine.

(a) Conditions and products.

Excess perfluoroisobutene, caesium fluoride and pentafluoropyridine reacted smoothly and quickly in a static system at ca. 80° with sulpholan as solvent. Recovery of material after reaction was excellent and the products obtained consisted of small quantities of dimers of the olefin,[83] identified by mass spectrometry, and a white crystalline solid. The latter separated on vacuum transfer of the products and was identified as perfluoro-(2,4,6-tri-t-butylpyridine) (XXXI) in high yield (ca. 85%). XXXI was a high melting solid which was insoluble in common organic solvents.

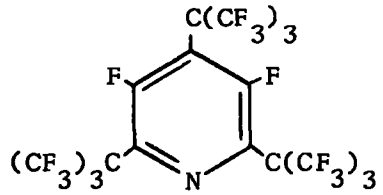


XXXI

Under these conditions no mono- or di-substituted derivatives were observed, however, since perfluoro-t-butylanions are readily formed at room temperature,[84] it is feasible that more selective polyfluoro-alkylation is possible at lower temperatures. Subsequently, reaction at room temperature afforded perfluoro-(4-t-butylpyridine) as the major product.[143] No evidence for a 2,4,5-tri-substituted isomer was found at ca. 20°[143] or 80°.

(b) Structure.

Correlation of the calculated chemical shifts for tri-substitution by $(CF_3)_3C^-$ in pentafluoropyridine, derived from s.c.s. data for perfluoro-(4-t-butylpyridine)[143] and perfluoro-(2,4-di-isopropylpyridine),[33] with the observed ^{19}F n.m.r. chemical shifts for XXXI indicates quite clearly that 2,4,6-substitution occurs. This is expected on the basis



XXXI

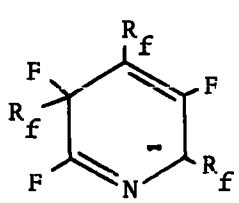
Chemical shifts for ring fluorines in XXXI

	3	5	6
Obs.	87·3	87·3	-
Calc.	84	84	-
Calc.	91	-	51

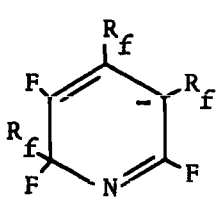
of the previously discussed progression from the 2,4,5-isomer exclusively with $CF_3CF_2^-$ to a mixture of the 2,4,5- and 2,4,6-isomers with $(CF_3)_2CF^-$.[102] Analysis of the uncomplicated ^{19}F n.m.r. spectrum, which contained two overlapping resonances at 60·7 and 61·8 due to twenty seven fluorine atoms and a broad resonance at 87·3 due to two fluorine atoms, further substantiate a symmetrical 2,4,6-substitution pattern.

(c) Mechanism.

The usual pattern of nucleophilic substitution in pentafluoropyridine at position 4 followed by 2 then 6 has been rationalised in terms of increased stability of transition states in which the negative charge is localised on the ring nitrogen compared to a carbon carrying an α-fluorine.[37] Therefore, mono- and di-substitution by $(CF_3)_3C^-$ are expected at the 4- and 2,4-positions, analogous to perfluoroisopropylation reactions,[102] and this has been confirmed recently.[143] However, nucleophilic substitution in perfluoro-(2,4-di-isopropylpyridine) at moderate temperatures occurred at position 5, and not 6, despite adverse steric interactions. This was attributed to the powerful stabilising effect of an α-perfluoroalkyl group compared to an α-fluorine in the intermediate carbanions (189(a)) and (190(a)) respectively. In contrast, similar stabilisation of the intermediate



189



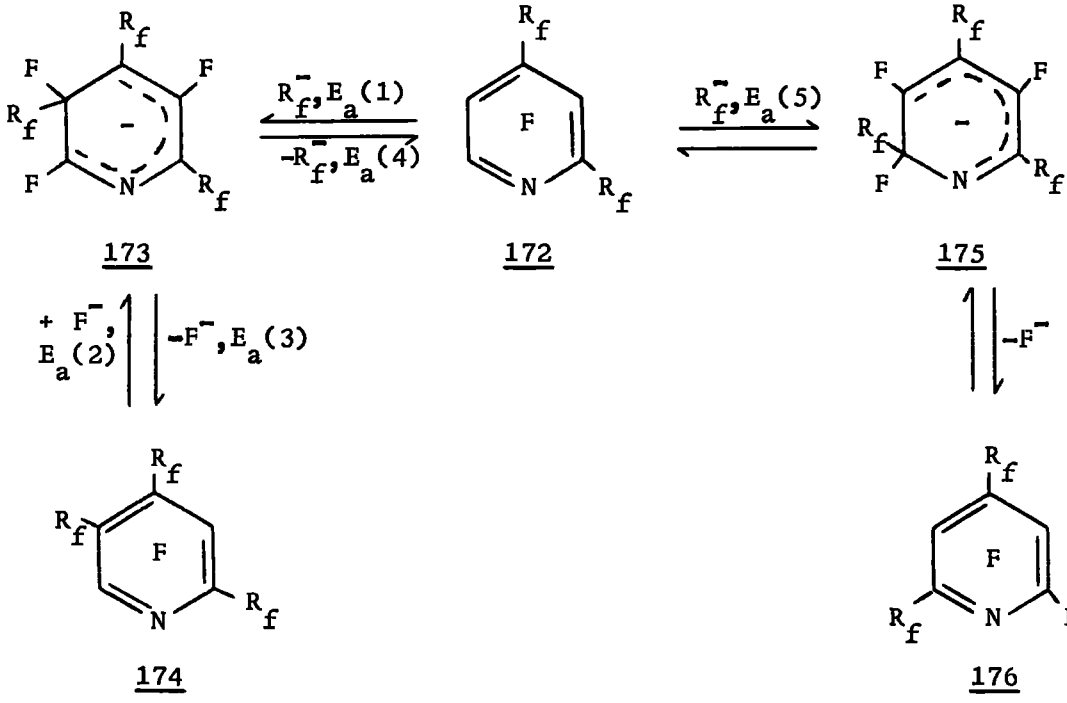
190

(a) $R_f = (CF_3)_2CF$

(b) $R_f = (CF_3)_3C$

carbanion (189(b)) for nucleophilic substitution in perfluoro-(2,4-di-t-butylpyridine) at the 5-position does not compensate for the much increased steric interactions, hence formation of the 2,4,6-isomer (XXXI) is favoured via the most stable carbanion (190(b)).

From a consideration of a qualitative representation of the general energy profile, postulated previously in connection with analogous perfluoro-isopropylation and -ethylation reactions (see Fig. 3, page 70), an insight into the factors controlling the reaction products is possible. The ground state energies of 172 and 174 are increased and, more important,



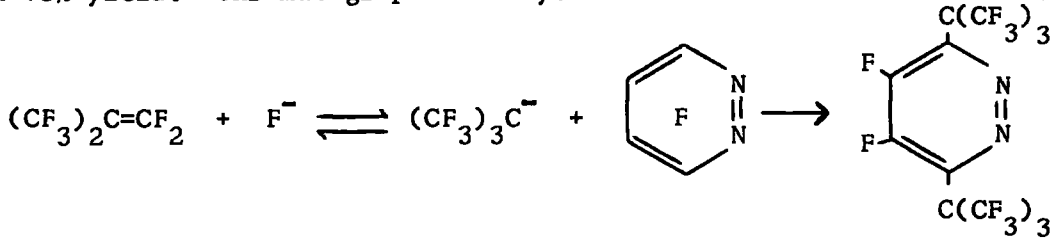
$R_f = (CF_3)_3C$

$E_a(2)$ and $E_a(4)$ are significantly decreased, especially the latter with respect to $E_a(3)$, and although position 5 is kinetically preferred, loss of $(CF_3)_3C^-$ from 174 is extremely facile. Since the ground state energy of 172 is increased, $E_a(5)$ is decreased, favouring the formation of the thermodynamically-stable 2,4,6-isomer (176).

3.5.2. Tetrafluoropyridazine.

(a) Conditions and products.

Excess perfluoroisobutene, caesium fluoride and tetrafluoropyridazine reacted smoothly and quickly in a static system at ca. 80° with sulpholan as solvent. Recovery of material after reaction was good and it consisted of a white solid and a colourless liquid. The former was recrystallised from acetone and identified as perfluoro-(3,6-di-t-butylpyridazine) (XXXII) in 75% yield. Chromatographic analysis of the latter showed dimers of the

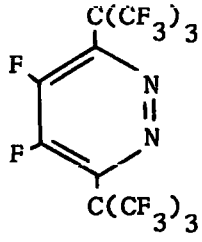


XXXII

olefin,[83] a minor product (< 3%) which was not identified, and large amounts of dissolved XXXII. No isomeric di-substituted products were observed under these conditions.

(b) Structure.

Correlation of calculated chemical shifts for di-substitution by $(CF_3)_3C^-$ in tetrafluoropyridazine, derived from s.c.s. data for perfluoroisopropylpyridazines,[41] with the observed ^{19}F n.m.r. chemical shifts for XXXII clearly shows that 3,6-replacement occurs, which



XXXII

Chemical shifts for ring fluorines in XXXII

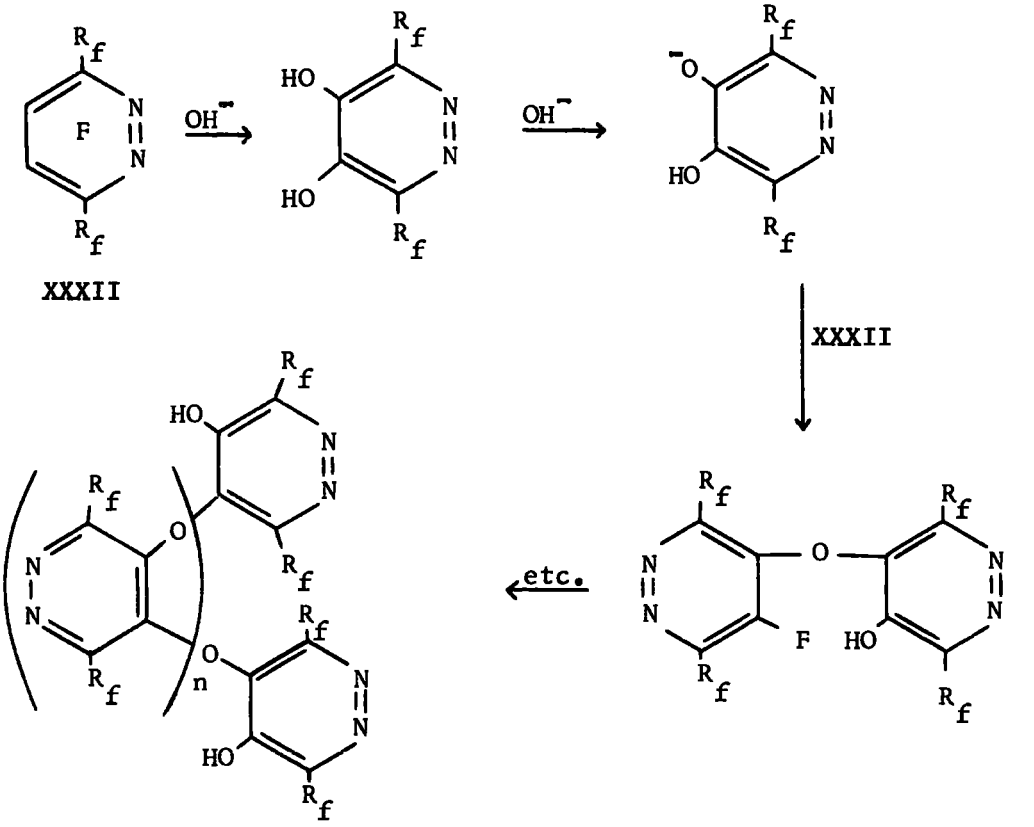
	4,5
Obs.	129·2
Calc.	133

is quite distinct from any previously reported polyfluoroalkylation reactions of this substrate.[39-41] Analysis of the ^{19}F n.m.r. spectrum, which contained only two resonances at 62•4 and 129•2 due to eighteen and two fluorine atoms respectively, further substantiated the symmetrical substitution pattern.

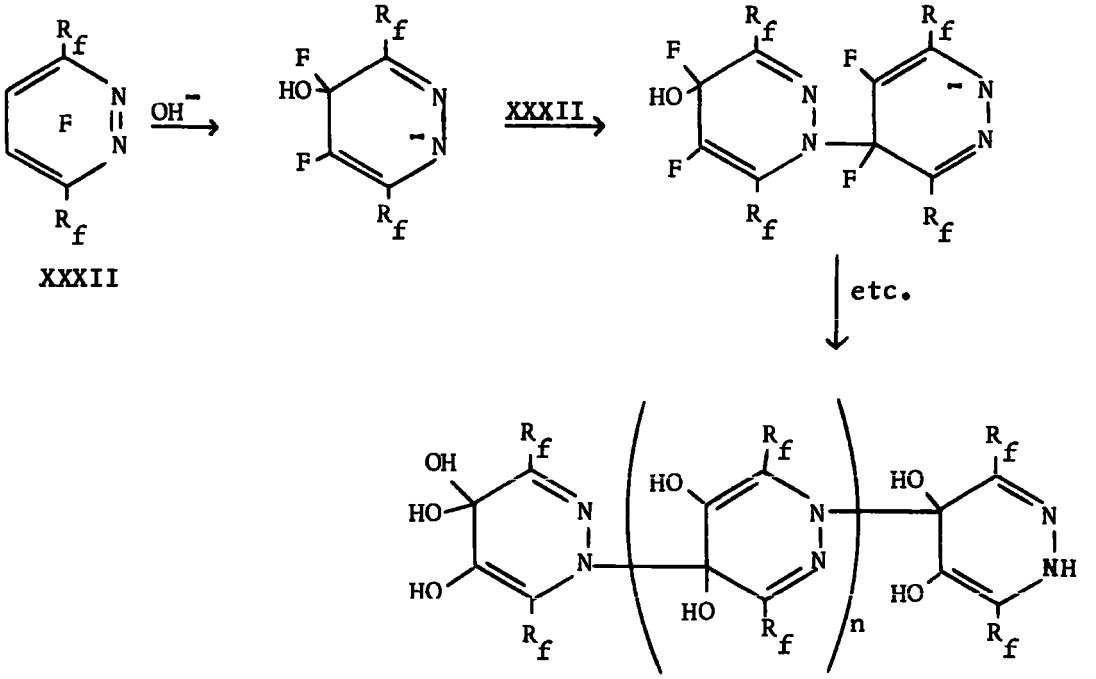
Structure confirmation from chemical evidence was obtained from hydrolysis reactions under basic and acidic conditions. It was demonstrated recently that in reactions of tetrafluoropyridazine with nucleophiles, the 4,5 fluorine atoms are the most reactive under basic conditions,[37] while the 3,6 fluorine atoms, adjacent to the ring nitrogen atoms, are replaced[53] preferentially under acidic conditions. Consequently, in contrast to perfluoro-(4,5-di-isopropylpyridazine), perfluoro-(3,6-di-t-butylpyridazine) (XXXII) should be readily hydrolysed under basic conditions, due to the presence of the highly reactive 4,5 ring fluorine atoms, but relatively inert to hydrolysis under acidic conditions.

Reaction of perfluoro-(3,6-di-t-butylpyridazine) (XXXII) with potassium hydroxide in t-butanol at ca. 70° and 25° readily afforded a quantitative yield of highly involatile solid. In contrast, XXXII was stable to and virtually insoluble in concentrated sulphuric acid at ca. 80°, giving quantitative recovery of starting material, however, at ca. 160° for 45 hours, only a 30% recovery of starting material was obtained along with an involatile solid similar to that formed so readily under basic conditions. The involatile solid from these reactions contained carbon, nitrogen and fluorine, was stable at ca. 350° for several hours and was too involatile to obtain a mass spectrum. ^{19}F N.m.r. spectroscopy indicated the presence of perfluoro-t-butyl groups but no evidence was found for ring fluorine atoms.

These results suggest that the involatile solid is polymeric in nature, possibly formed by base-catalysed self-condensation of XXXII to give a polyether-type structure as shown:



Alternatively, loss of aromaticity may occur, allowing nitrogen-carbon bond formation in the polymerisation step:

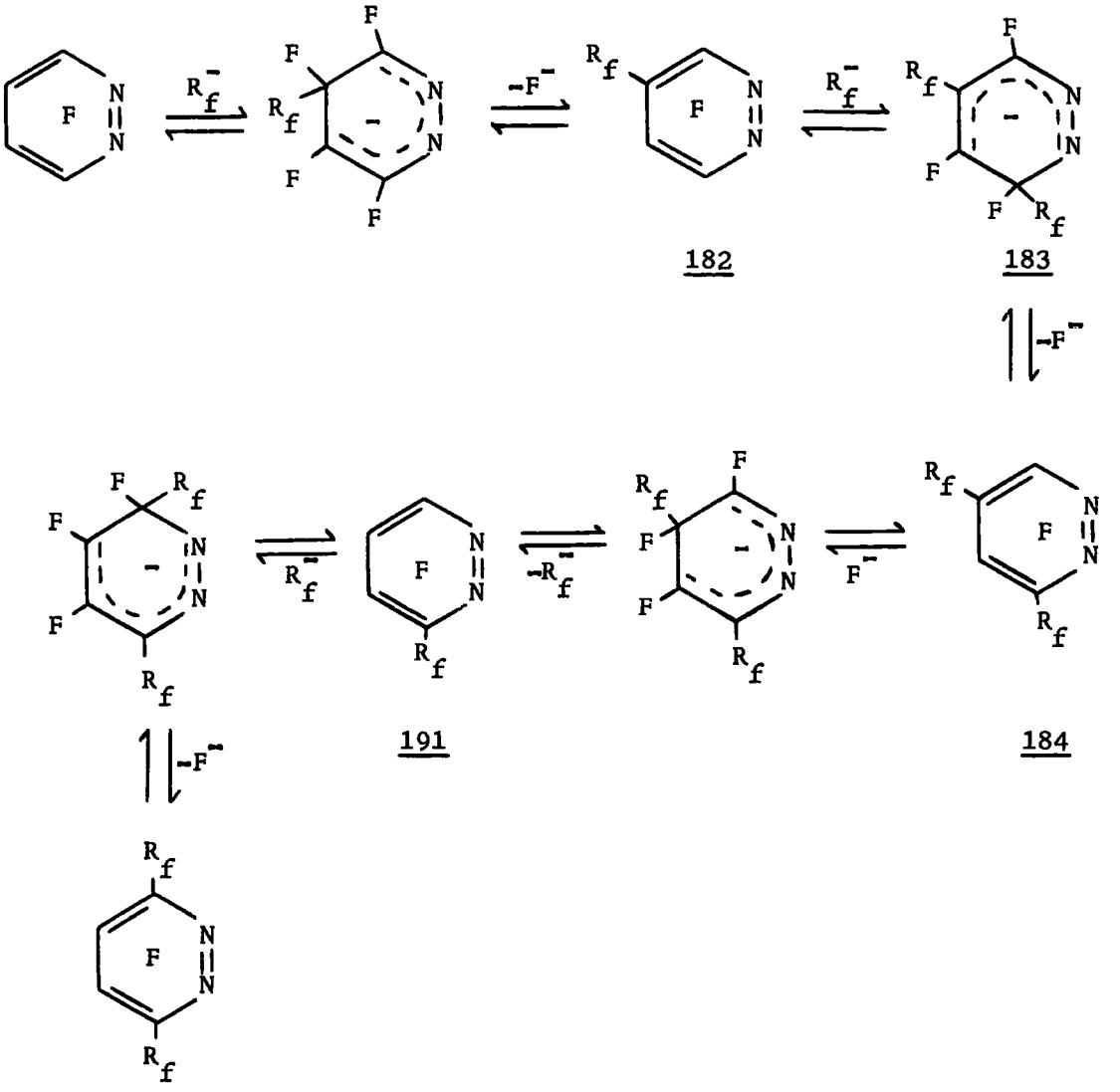


Whatever the mechanism of the reaction and the structure of the product, the susceptibility of XXXII to nucleophilic attack under basic conditions confirms the presence of the 4 and 5 ring fluorines and, therefore, the perfluoro-t-butyl substituents at the 3 and 6-positions.

(c) Mechanism.

The usual pattern for nucleophilic attack on tetrafluoropyridazine is position 4 followed by 5, due to increased stability of transition states in which the negative charge is localised on the ring nitrogen atom compared to a carbon carrying an α-fluorine. Di-substitution by $(CF_3)_3C^-$ at ca. 80° is therefore expected at the 4,5-positions, as found for perfluoro-ethylation and -isopropylation[39-41] under similar conditions, or possibly at the 3,5-positions, analogous to heptafluoroisopropylation at elevated temperatures (ca. 150°),[40,41] to reduce the steric interactions between the substituents. However, the only product isolated was perfluoro-(3,6-di-t-butylpyridazine) (XXXII).

Rationalisation of the formation of XXXII can be postulated from a consideration of a qualitative schematic representation of the general energy profile which was outlined previously for perfluoro-isopropylation and -ethylation reactions of tetrafluoropyridazine (see Route 1 and Fig. 6, page 80). Nucleophilic attack at the 4 position by $(CF_3)_3C^-$ to give 182 should be possible since the steric interactions are comparable to those for the observed 4-substitution by $(CF_3)_3C^-$ in pentafluoro-pyridine. The higher ground state energy of 182 will facilitate further substitution at the 6 position to give 184 and not at the kinetically preferred 5 position, from which loss of $(CF_3)_3C^-$ would be very easy. The 4,6-isomer, once formed, will rapidly rearrange in the presence of fluoride ion to the thermodynamically more stable 3,6 isomer (XXXII), the observed product, via 191.



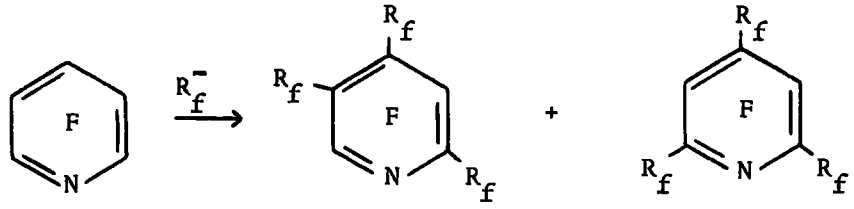
XXXII $R_f = (CF_3)_3C$

3.6. Kinetic vs. thermodynamic control of products in polyfluoroalkylation of pentafluoropyridine and tetrafluoropyridazine.

A clear cut variation from kinetic to thermodynamic control of reaction products is observed for polyfluoroalkylation reactions of $CF_3CF_2^-$, $(CF_3)_2CF^-$ and $(CF_3)_3C^-$ with pentafluoropyridine and tetrafluoropyridazine.[146] It has been reported previously that reaction of $(CF_3)_2CF^-$ with pentafluoropyridine or tetrafluoropyridazine could result in kinetic or thermodynamic control of reaction products, depending on the conditions.[39,41,102] A comparison of these results with those discussed above from corresponding reactions of $CF_3CF_2^-$ and $(CF_3)_3C^-$ provides one

of the most striking examples available of the interplay of kinetic vs. thermodynamic control in aromatic substitution reactions.

3.6.1. Pentafluoropyridine.

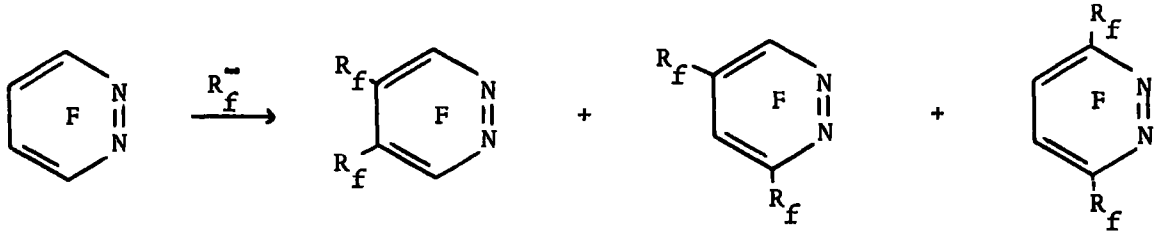


tri-substituted derivatives

R_f =		
CF_3CF_2	192	
$(CF_3)_2CF$	193	194
$(CF_3)_3C$		195

Considering only the tri-substituted products from pentafluoropyridine at 80°: with $CF_3CF_2^-$, isomer 192 is obtained exclusively, which is not rearranged when heated with fluoride ion even to 190°; with $(CF_3)_2CF$, mainly isomer 193 is obtained which is rearranged,[102] on heating with fluoride ion at 180°, to give a mixture of 194 and side products; while with $(CF_3)_3C^-$, only 195 is obtained directly. Therefore, across this series there is a complete transition from kinetic control, in reactions with $CF_3CF_2^-$, to thermodynamic control of products with the bulky $(CF_3)_3C$.

3.6.2. Tetrafluoropyridazine.



di-substituted derivatives

R_f =			
CF_3CF_2	196		
$(CF_3)_2CF$	197	198	
$(CF_3)_3C$			199

The situation is even more striking with tetrafluoropyridazine, here considering only di-substituted derivatives formed at 80°. From CF_3CF_2, isomer 196 was formed exclusively and was not rearranged by fluoride ion even up to 150°; $(CF_3)_2CF$ gave 197 which afforded a mixture of 197 and 198 on heating with fluoride ion;[41] while $(CF_3)_3C$ gave only 199. This is quite distinct from the other products described and clearly steric interactions are minimised with both of the bulky $(CF_3)_3C$ groups adjacent to a ring nitrogen, rather than being flanked by fluorine atoms attached to the ring.

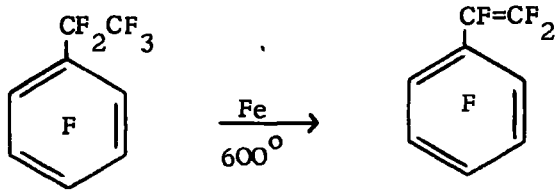
3.7. Reactions of perfluoroalkylpyridines.

Perfluoroalkylpyridines, prepared in fluoride ion-initiated reactions of perfluoro-olefins and pentafluoropyridine, were subjected to further reactions to introduce either a vinyl or a methoxyl group. Products derived from the latter reactions have been discussed earlier in connection with structure determination of perfluoroalkylpyridines; the former reactions were effected by defluorination of the perfluoroalkyl substituent as discussed below.

3.7.1. Defluorination reactions.

The introduction of unsaturation into highly fluorinated compounds by catalytic removal of fluorine has been extensively studied by Tatlow and co-workers,[147-150] who observed that passage of perfluoroalicyclic compounds over iron or nickel at ca. 400° - 650° afforded perfluoroaromatic derivatives. More recently, defluorination was effected by zinc under relatively mild conditions (ca. 230°).[97]

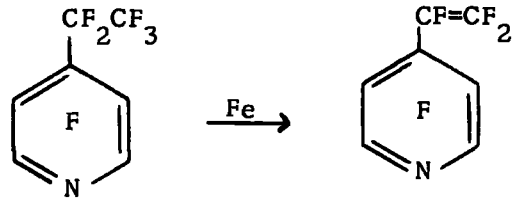
Perfluoroethylbenzene (200), prepared in 15% yield on defluorination of perfluoroethylcyclohexane,[147] was further defluorinated over steel Dixon gauzes at ca. 600° to give a 15% yield of perfluorostyrene (201). Extension of this technique to perfluoroalkylpyridines similarly afforded vinyl



200 201

derivatives, however, the yields were only moderate, in accord with previous results.[147-150]

Perfluoro-(4-ethylpyridine) (I) was passed over heated iron filings to give a mixture of I and perfluoro-(4-vinylpyridine) (IX), which was separated by preparative scale v.p.c.; the results obtained at various temperatures are summarised in Table 6. Attempted defluorination of



I IX

Table 6

Temp. °C	Percentage Yield* of IX (%)	Conversion %
410	50	35
420	40	60
450	25	95

* Based on weight of I consumed.

I over zinc was found not to be a feasible route to IX due to low yields and conversions, as shown in Table 7.

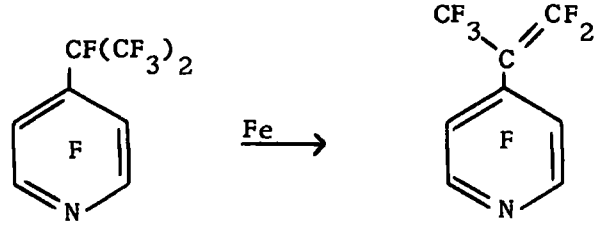
Spectral information obtained for perfluoro-(4-vinylpyridine) (IX) was in agreement with that reported for perfluorostyrene (201).[150,151] The ^{19}F n.m.r. spectrum of IX was analysed by analogy with 201 and confirmed the

Table 7

Temp. °C	Wt. of I used	Products
280	1·0 g.	0·8 g. unchanged I
320	0·6 g.	0·55 g. " "
380	0·7 g.	0·2 g. mixture of I and IX

expected structure.

Perfluoro-(4-isopropylpyridine)[152] was similarly defluorinated on passage over heated iron filings, however, for this substrate it was possible to obtain a moderate yield of product, 2-(2',3',5',6'-tetrafluoropyridyl)-pentafluoropropene (X), with a 100% conversion (see Table 8). Spectral data obtained for X confirmed the expected structure.



X

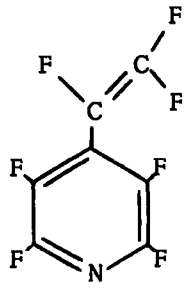
Table 8

Temp. °C	Percentage Yield* of X (%)	Conversion %
350	45	85
420	45	100
450	Only gaseous material recovered	

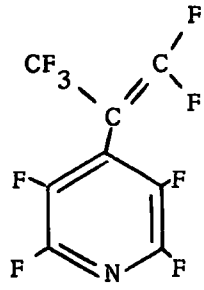
* Based on weight of $C_8F_{11}N$ consumed.

Attempted rationalisation of an unexpected medium intensity absorption at 6·08μ in the i.r. spectrum of IX in addition to the expected strong C=C absorption at 5·64μ revealed, on further investigation, a possible

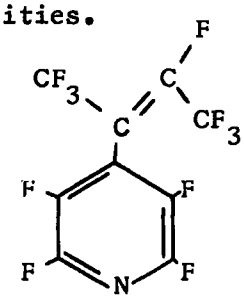
correlation between steric interactions and relative intensities.



IX



X



165

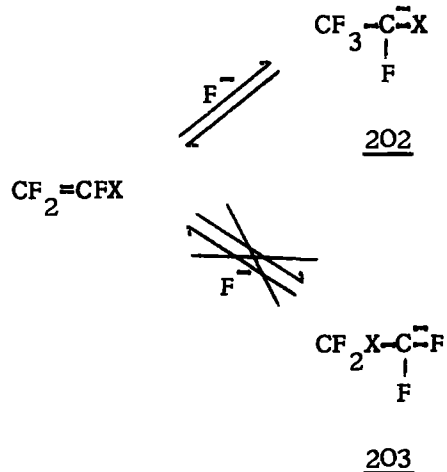
Similar absorptions have been reported previously for conjugated vinyl-aromatic systems and were assigned to the carbon-carbon double bond. The corresponding absorptions in X and 165[132] were significantly weaker, from which it is tentatively postulated that increased steric interactions decrease the extent of conjugation between the vinyl and aromatic systems, however, many more examples are required before anything definite can be formulated.

CHAPTER 4

Polyfluoroalkylation with Substituted Polyfluoro-olefins

Introduction.

In general, fluoride ion-initiated reactions of substituted polyfluoro-olefins CF_2=CFX (X = Cl, Br, H) result in attack at the difluoromethylene group to give 202, the more stable intermediate carbanion, rather than at the CFX = group to give 203. The relative reactivity of these olefins



towards fluoride ion is increased compared to CF_2=CF_2 owing to the incorporation of the substituent X, however, the reactivity of the resultant polyfluoroalkylanion (202) is reduced compared to $CF_3CF_2^-$ owing to diminished importance of I_{π} repulsions, with a consequent relative stabilising effect for the substituent X.

4.1. Reaction conditions.

The majority of the experimental problems associated with fluoride ion-initiated reactions were extensively discussed in Chapter 3 and are equally applicable to reactions involving substituted polyfluoro-olefins (CF_2=CFX) with perfluoro-N-heteroaromatic compounds. In general, better yields are obtained using a static system rather than a flow system, however, the yields are still only moderate due to side-reactions. Sulpholan

and tetraglyme are suitable solvents and, in one instance discussed later, a pronounced dependence of the product distribution on the solvent used is observed. Potassium and caesium fluorides are suitable initiators, however, in contrast to previously discussed polyfluoroalkylations, observed displacement of X implies that, theoretically, equimolar quantities of initiator are required. In practice, the yields obtained in reactions with equimolar amounts of initiator were similar to those with substantially less initiator.

4.2. Type of products formed.

Identification of the products clearly indicates that these reactions are much more complex than those discussed previously. In all, three types of substituted products have been identified from a series of fluoride ion-initiated reactions of substituted polyfluoro-olefins, CF_2=CFX (X = Cl, Br, H), with perfluoro-N-heteroaromatic compounds. These are firstly, substitution in Ar-F by polyfluoroalkylanions, $CF_3\bar{C}FX$, to give CF_3CFX-Ar; secondly, the formation of perfluoroalkyl-N-heteroaromatic derivatives, CF_3CF_2-Ar, which requires the replacement of X (X = Cl and Br only) with fluorine at some stage; and thirdly, formation of a perfluoro-1,1-bis-arylethane, $(Ar)_2CFCF_3$, which similarly involves loss of X, and a perhaloalkane, CF_3CFX_2.

Clearly several different competing processes are possible, as indicated in the following discussion, and the type of product obtained depends upon the relative rates of these various processes for particular reactants.

4.3. Possible reaction processes.

A general review of the possible processes in which polyfluoro-olefins

(CF_2=CFX) and polyfluoroalkylanions ($CF_3\overline{C}FX$) may be involved, and also in which displacement of X may occur, subsequently facilitates discussion of specific reactions. Therefore, in fluoride ion-initiated reactions of polyfluoro-olefins with perfluoro-N-heteroaromatic compounds the feasible processes are considered to be: oligomerisation of CF_2=CFX; vinylic displacement of X from CF_2=CFX; α-elimination of X^- from $CF_3\overline{C}FX$; halogen exchange between $CF_3\overline{C}FX$ and CF_2=CFX; polyfluoroalkylation of Ar-F; and displacement of X from CF_3CFX-Ar.

4.3.1. Oligomerisation of CF_2=CFX.

Fluoride ion-initiated oligomerisation of CF_2=CFX, analogous to the previously discussed oligomerisation of CF_2=CF_2 and CF_2=$CFCF_3$, is theoretically feasible as shown. In practice, no oligomers are obtained for X = Cl or H, however, for X = Br an involatile polymeric material containing bromine may

$$CF_2{=}CFX + F^- \rightleftharpoons CF_3\overline{C}FX + CF_2{=}CFX \longrightarrow CF_3{-}(CFXCF_2)_nCF{=}CFX$$

possibly be due to such an oligomerisation as shown.

4.3.2. Vinylic displacement.

The formation of tetrafluoroethylene, on direct displacement of X^- from the polyfluoro-olefin CF_2=CFX by fluoride ion, is also a possible process for loss of the substituent X. Subsequent fluoride ion-initiated reactions of CF_2=CF_2 with Ar-F would give the observed products, as shown previously in Chapter 3.

$$F^- \curvearrowright X{-}\underset{F}{C}{=}CF_2 \rightleftharpoons CF_2{=}CF_2 + X^-$$

$$\downarrow F^-$$

$$CF_3\overline{C}F_2 \xrightarrow{Ar\text{-}F} CF_3CF_2\text{-}Ar + F^-$$

4.3.3. α-Elimination of X^- from $CF_3\overline{C}FX$.

An α-elimination of X^- from a polyfluoroalkylanion to give a

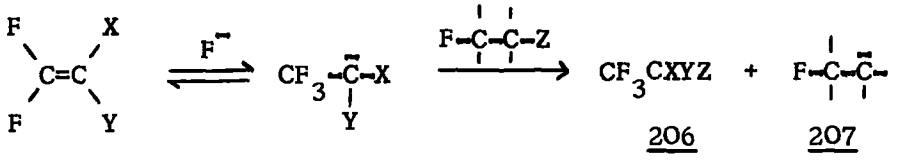
perfluorocarbene (204) is a plausible process for loss of X. Subsequent addition of fluoride ion to 204 would give a pentafluoroethylanion (205) which would react rapidly with an activated perfluoroaromatic substrate

$$CF_2{=}CFX \xrightleftharpoons{F^-} CF_3\bar{C}FX \xrightleftharpoons{-X^-} \underset{204}{CF_3CF:} \xrightleftharpoons{F^-} \underset{205}{CF_3CF_2^-} \xrightarrow{Ar\text{-}F} CF_3CF_2\text{-}Ar + F^-$$

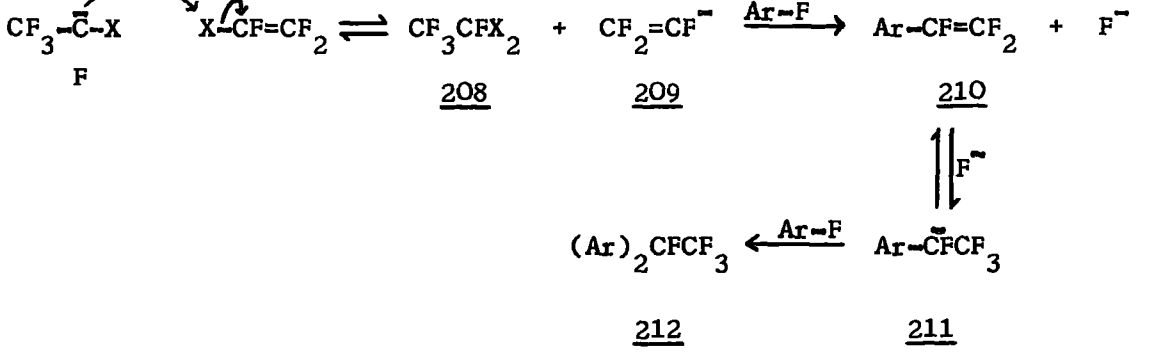
(Ar-F) to give a perfluoroethyl derivative.

4.3.4. Halogen exchange between $CF_3\bar{C}FX$ and CF_2=CFX.

Nucleophilic attack by polyfluoroalkylanions on halogen, other than fluorine, in perhaloalkanes to displace the carbon-halogen bonding electrons has been reported previously to give a different perhaloalkane (206) and a different polyfluoroalkylanion (207).[115]



Therefore, in addition to the possibility of nucleophilic attack of $CF_3\bar{C}FX$ on carbon in CF_2=CFX to produce oligomers, attack on X would give a perhaloalkane (208) and a highly reactive trifluorovinylanion (209). Rapid reaction of 209 with Ar-F would give the perfluorovinyl derivative (210) which, in the presence of fluoride ion, would give 211. Subsequent



substitution in excess Ar-F by 211 would give a perfluoro-1,1-bis-arylethane (212).

4.3.5. Polyfluoroalkylation of Ar-F.

Nucleophilic substitution in perfluoro-N-heteroaromatic compounds by polyfluoroalkylanions ($CF_3\bar{C}FX$) to give polyfluoroalkyl derivatives (213) would be expected by analogy with previously discussed reactions using perfluoro-olefins (See Chapter 3).

$$CF_2{=}CFX \rightleftharpoons CF_3\bar{C}FX \xrightarrow{Ar\text{-}F} CF_3CFX\text{-}Ar + F^-$$

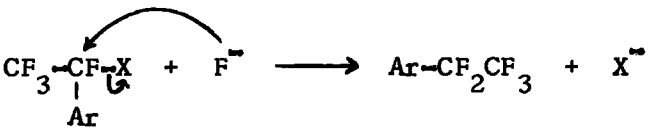
213

4.3.6. Displacement of X from CF_3CFX-Ar.

Displacement of X after polyfluoroalkylation by $CF_3\bar{C}FX$ would also give perfluoroalkyl derivatives, however, more than one process is feasible for such a reaction. Three possible processes are proposed and they are considered in the following sections.

(a) Direct benzylic-type displacement.

Nucleophilic attack by fluoride ion on the α-carbon atom of CF_3CFX-Ar (213) would give a direct benzylic-type displacement of X^- from the side-chain and would result in the formation of a perfluoroalkyl derivative.

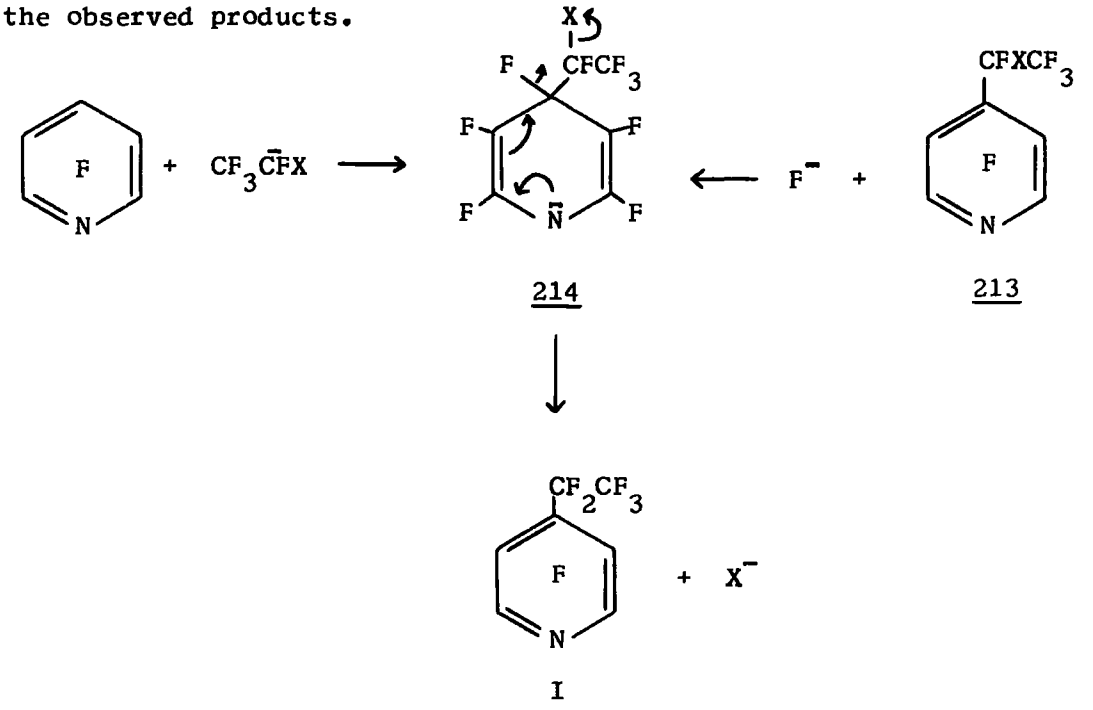


213

(b) Concerted benzylic-type displacement.

Nucleophilic substitution by $CF_3\bar{C}FX$ in a perfluoro-N-heteroaromatic compound, e.g. pentafluoropyridine, proceeds via a σ-complex (214) which is also formed on addition of fluoride ion to the polyfluoroalkyl derivative (213). On the breakdown of such a complex, it is possible that the leaving fluoride ion attacks the α-carbon, displacing X^- in a concerted benzylic-type process involving the aromatic nucleus, to give

the observed products.

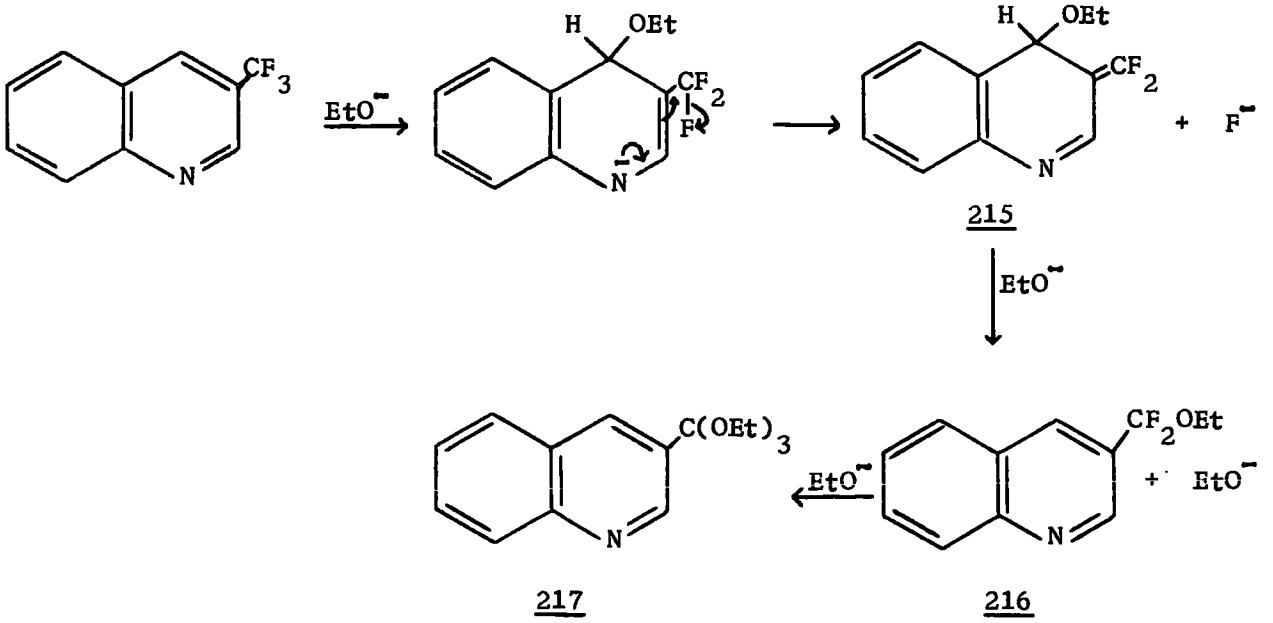


214 213

I

(c) 'Pseudo-allylic' displacement.

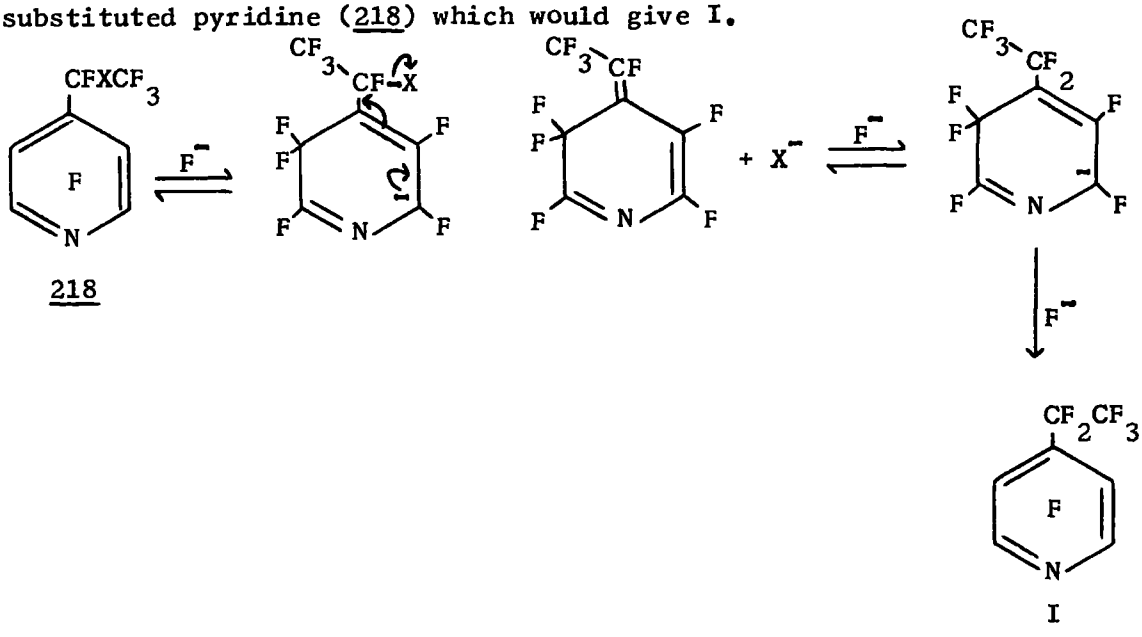
Kobayashi and co-workers[144,145] recently proposed that the replacement of the first fluorine substituent in 3-trifluoromethylquinoline by ethoxide involved a 'pseudo-allylic' or pseudo-S_N2' process as shown to give 216 via 215. Subsequent displacement of fluorine from 216 to give 217 occurred via benzylic-type displacements owing to their increased lability.



215

217 216

Extension of this type of process to the displacement of X from CF_3CFX-Ar (213) is also feasible as shown with, for example, a 4-substituted pyridine (218) which would give I.



218

4.4. Reactions with chlorotrifluoroethylene.

Atmospheric pressure fluoride ion-initiated reactions of chlorotrifluoroethylene are conveniently discussed under the heading of the perfluoro-N-heteroaromatic compound used. Since the formation of perfluoroalkyl derivatives is a predominant feature of both these reactions and the analogous reactions of bromotrifluoroethylene, the main conclusions about the mechanism for loss of halide ion are drawn after a discussion of the results obtained for reactions of the latter.

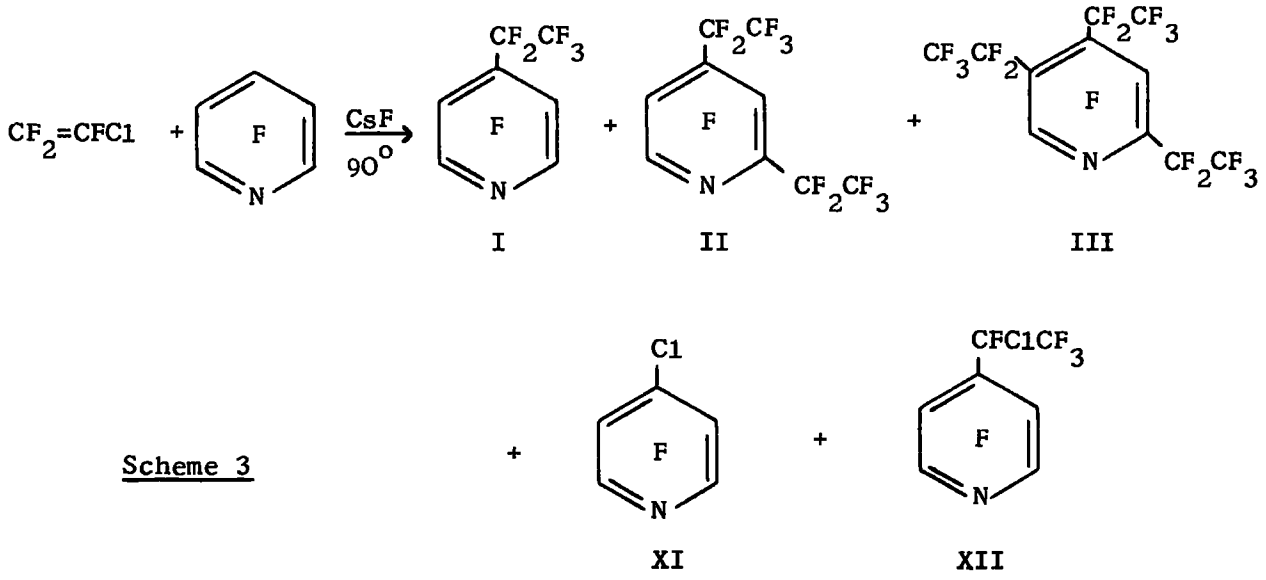
4.4.1. Pentafluoropyridine.

(a) Conditions and products.

Previously reported fluoride ion-initiated reactions of chlorotrifluoroethylene and pentafluoropyridine were carried out in autoclaves at elevated temperatures (ca. 190°).[32,49,101] Unreacted starting materials and five products were obtained, three of which were identified as

perfluoro-(4-ethylpyridine) (I), 4-chlorotetrafluoropyridine (XI) and 1-chloro-1-(2′,3′,5′,6′-tetrafluoropyridyl)tetrafluoroethane (XII).[49,101]

Atmospheric pressure reactions with a combination of caesium fluoride and sulpholan or tetraglyme at ca. 90°, using a static system, gave unreacted CF_2=CFCl, identified by i.r. spectroscopy, and a colourless liquid. Chromatographic analysis of the latter indicated unreacted pentafluoropyridine and five products, which were identified as perfluoro-(4-ethylpyridine) (I), perfluoro-(2,4-di-ethylpyridine) (II), perfluoro-(2,4,5-tri-ethylpyridine) (III), 4-chlorotetrafluoropyridine (XI) and 1-chloro-1-(2′,3′,5′,6′-tetrafluoropyridyl)tetrafluoroethane (XII) as shown in Scheme 3.



Scheme 3

However, the relative ratios of the products were observed to be extremely solvent dependent, while yields and conversions were only marginally increased with longer reaction times as shown in Table 9. In contrast to reactions in sulpholan, which give low yields of all five products, analogous reactions in tetraglyme give moderate yields of XII as the major product, low yields of II, III and XI, and negligible amounts of I. Under no circumstances were any derivatives containing two or more

chlorine atoms isolated which, in connection with the halogen displacement mechanism, is extremely important.

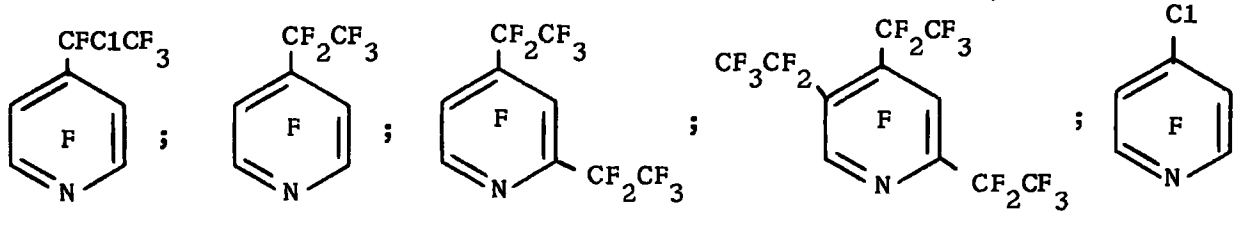
Table 9

Solvent	Reaction Time (hrs.)	Percentage Yields (%)*					Conversion %
		I	II	III	XI	XII	
Sulpholan	4	15	4	3	4	15	78
Sulpholan	24	19	8	8	5	17	82
Tetraglyme	4	-	6	4	8	46	67
Tetraglyme	24	-	5	8	9	40	76

*Based on the weight of C_5F_5N consumed.

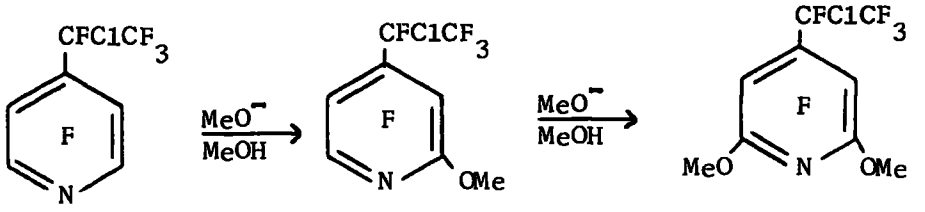
(b) Structure.

Correlation of the calculated chemical shifts, derived from s.c.s. data for 4-substitution by polyfluoroalkylanions in pentafluoropyridine, with the observed ^{19}F n.m.r. shifts for XII confirmed the expected and previously reported structure.[32,49] Formation of the 2-methoxy (XIII)



XII I II III XI

and 2,6-dimethoxy (XIV) derivatives of XII on reaction with methoxide, identified by correlation of the calculated chemical shifts, determined from s.c.s. data for 4-heptafluoroisopropyl-2-methoxy-3,5,6-trifluoropyridine,[33] with the observed ^{19}F n.m.r. chemical shifts further substantiated the proposed substitution pattern for XII.



XII XIII XIV

Chemical shifts of ring fluorines for XIII

	3	5	6
Obs.	137·2	150·0	93·4
Calc.	137	148	93

Chemical shifts of ring fluorines for XIV

	3	5	6
Obs.	148·3	148·3	-
Calc.	150	149	-
Calc.*	141	-	93

* assuming a 2,4,5-substituted derivative formed.

The structures of products I, II and III were discussed previously in Section 3.4.1.(b) and the structure of XI has been reported previously.[154]

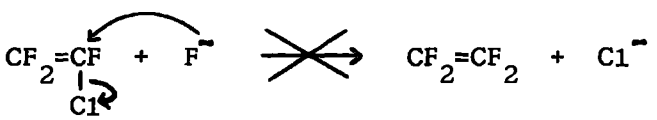
(c) Mechanism.

Suitable mechanisms for the formation of I, II, III, XI and XII in fluoride ion-initiated reactions of chlorotrifluoroethylene and pentafluoropyridine are clearly more complex than the previously discussed perfluoroalkylation mechanisms of Chapter 3. Initially it is essential to establish whether loss of chlorine occurs before or after nucleophilic aromatic substitution, since it is then possible to decide if both $CF_3\bar{C}FCl$ and $CF_3CF_2^-$ or only the former are substituting in pentafluoropyridine. Of the previously proposed processes for loss of the substituent X (See Section 4.1.2.(b)), vinylic displacement and α-elimination occur prior to substitution in contrast to direct benzylic-, concerted benzylic- and pseudo- S_N2^*-type displacements which occur after substitution. A consideration of the results of several experiments

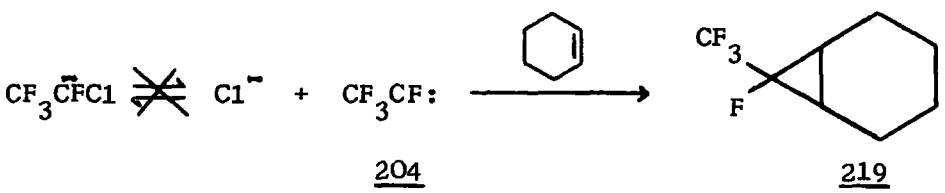
enables the two possibilities to be differentiated.

(i) Chlorine displacement.

Loss of chlorine by vinylic displacement is discounted because no evidence has been obtained for the formation of tetrafluoroethylene in previously reported fluoride ion-initiated reactions of chlorotrifluoroethylene.[55,101] Similarly, no tetrafluoroethylene was observed, by i.r. or mass spectroscopy, in the gaseous residues from reactions of chlorotrifluoroethylene with pentafluoropyridine in which perfluoroethylpyridines were formed. Qualitatively, the rate of formation of perfluoroethylpyridines in reactions with $CF_2=CFCl$ is significantly faster than similar reactions with $CF_2=CF_2$, indicating that the intermediacy of the latter is highly unlikely.



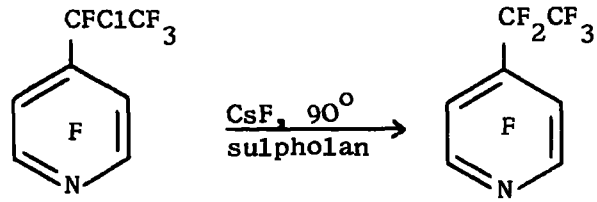
An α-elimination of chloride from $CF_3\bar{C}FCl$ would give a perfluorocarbene (204) which, if formed, should be trapped by a suitably activated substrate such as cyclohexene to give a cyclopropane derivative (219). A fluoride ion-initiated reaction of chlorotrifluoroethylene and



cyclohexene resulted in quantitative recovery of the latter, which indicates that 204 is not formed and that chlorine is not lost via this type of process.

Consequently, from these results it is concluded that displacement of chlorine must occur after aromatic substitution, in which only $CF_3\bar{C}FCl$ attacks pentafluoropyridine. This was confirmed since XII was completely

converted to perfluoro-(4-ethylpyridine) (I) in 60% yield in the presence of fluoride ion and under identical conditions to its preparation.



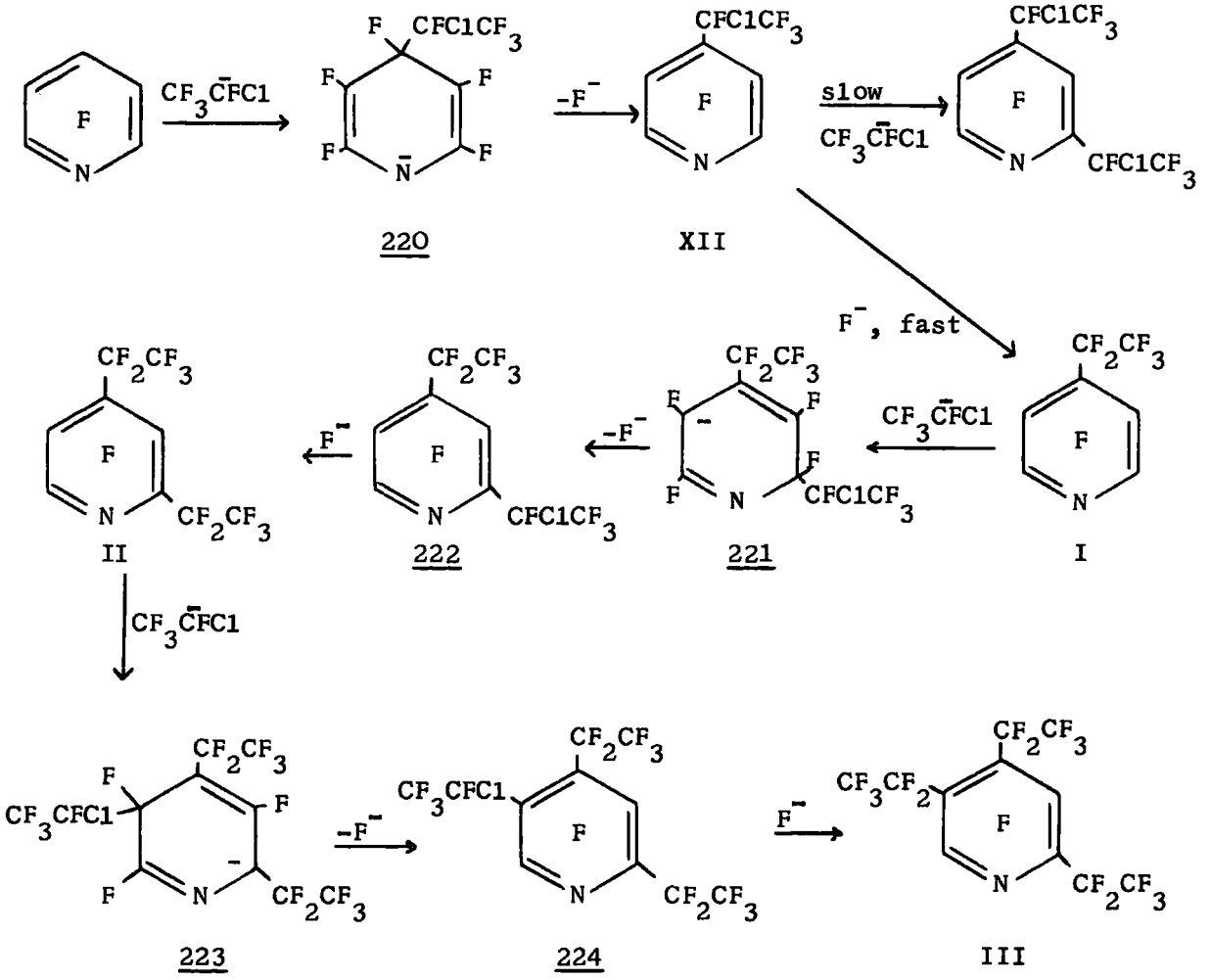
XII I

However, a discussion concerned with the differentiation of the previously proposed mechanisms for displacement after substitution is deferred until after discussion of the results for analogous reactions of CF_2=CFCl with tetrafluoropyridazine and CF_2=CFBr with perfluoro-pyridine and -pyridazine.

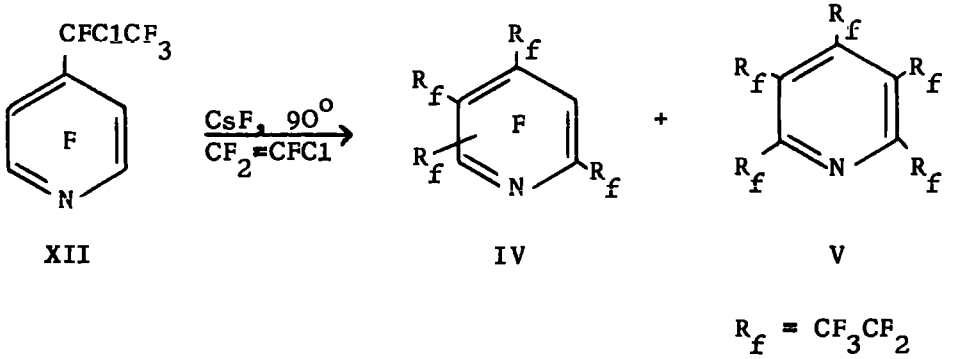
(ii) Nucleophilic aromatic substitution.

The major factor controlling the orientation of nucleophilic substitution in perfluoro-N-heteroaromatic compounds was shown recently to be the effect of the ring nitrogen on the stability of the localised negative charge in the transition state.[37] Therefore, on this basis mono-substitution by $CF_3\bar{C}FCl$ in pentafluoropyridine is expected, and observed, at the 4-position to give XII via the most stable intermediate carbanion (220). Since no other chloropolyfluoroalkylpyridines have been observed, it is concluded that the rate of displacement of chloride from XII to give I must be much faster than the rate of further substitution by $CF_3\bar{C}FCl$ in XII.

Further substitution in I by CF_3CFCl^- is expected at the 2-position, as discussed previously (See Section 3.4.1.(c)), via 221 and, since 222 is not isolated, displacement of chloride from 222 by fluoride to give II must be rapid. Substitution by $CF_3\bar{C}FCl$ in II is expected at the 5-position via 223 to give the kinetically preferred product (224), analogous to previously discussed perfluoroethylation reactions, followed by rapid displacement of chloride from 224 to give III, the observed product.



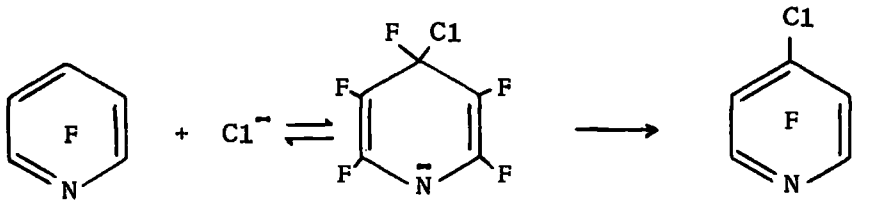
Further evidence for this type of mechanism was obtained from fluoride ion-initiated reactions of chlorotrifluoroethylene with XII at ca. 90°, from which the only tractable products recovered were perfluoro-(tetraethylpyridine) (IV) and pentakis(pentafluoroethyl)pyridine (V) in low yields, even after a one hour reaction.



XII IV V

$R_f = CF_3CF_2$

Displacement of chloride ion by fluoride ion during these reactions introduces a further nucleophile into the reaction mixture which is expected to attack the 4-position in pentafluoropyridine to give XI via 225. Reaction of chloride ion with C_5F_5N under similar conditions has been reported previously to give 4-chlorotetrafluoropyridine (XI).[101,154]



225 XI

The different product distribution observed for reactions in tetraglyme, compared to analogous reactions in sulpholan, can be attributed to a substantial difference in the rate of displacement of chloride from XII, since the rates of formation of XII in both solvents, estimated from the observed yields of XII and the products derived from XII, are approximately the same. A substantially slower rate of displacement in tetraglyme, compared to sulpholan, may result from increased stabilisation of XII, decreased stabilisation of the transition state and intermediate (226) or a combination of both of these effects. A qualitative schematic representation of the energy profiles for the displacement reaction in both solvents is shown in Fig. 8 (p. 109).

4.4.2. Tetrafluoropyridazine.

(a) Conditions and products.

Atmospheric pressure fluoride ion-initiated reactions of chlorotrifluoroethylene and tetrafluoropyridazine at ca. 90°, using a combination of caesium fluoride and either sulpholan or tetraglyme in a static system, gave unreacted CF_2=CFCl and a colourless liquid. Chromatographic analysis of the latter indicated unreacted tetrafluoro-

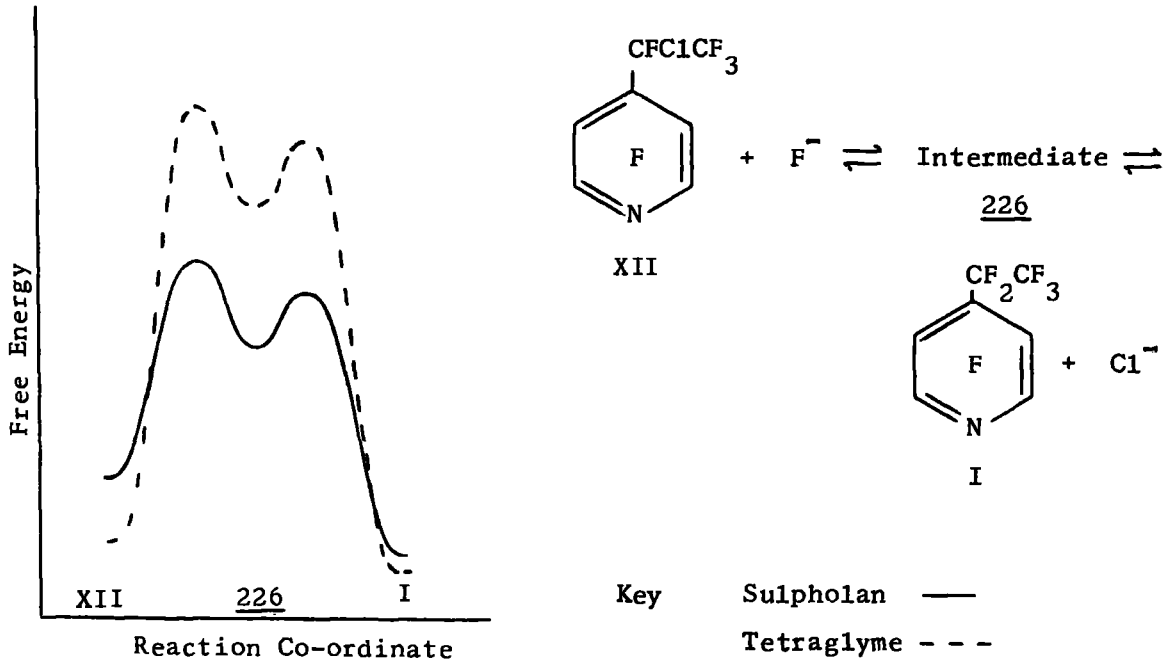
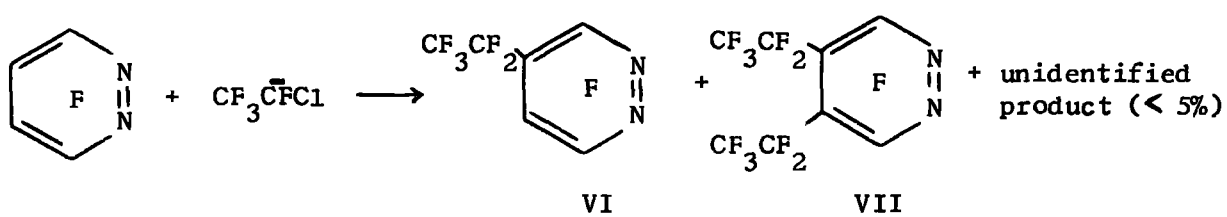


Fig. 8

pyridazine, two major products and one minor product.

The former products were identified as perfluoro(4-ethylpyridazine) (VI) and perfluoro-(4,5-di-ethylpyridazine) (VII) as shown in Scheme 4. Characterisation of the minor product was not possible owing to the low



Scheme 4

yield obtained, however, its v.p.c. retention time was identical with 4-chloro-3,5,6-trifluoropyridazine, which may be formed during the reaction due to attack of chloride ion on tetrafluoropyridazine, in an analogous

manner to that reported recently in reactions between lithium chloride and tetrafluoropyridazine.[155]

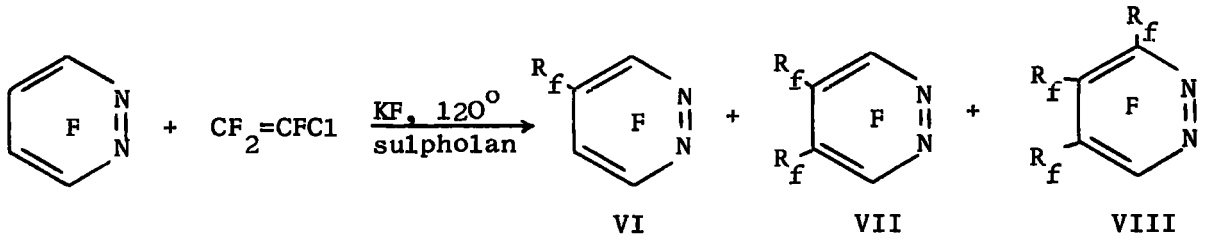
No chlorine containing polyfluoroalkylpyridazines were isolated from these reactions and, although the ratios of products were similar in both solvents, noticeably lower yields were obtained using tetraglyme (See Table 10), as mentioned previously for pentafluoroethylations of tetrafluoropyridazine (See Section 3.4.2.(a)).

Table 10

Solvent	Percentage Yields (%)*		Conversion
	VI	VII	%
Sulpholan	57	19	58
Tetraglyme	41	9	53

* Based on the weight of $C_4F_4N_2$ consumed.

A similar atmospheric pressure reaction at ca. 120°, using a combination of sulpholan and excess potassium fluoride in a static system, afforded three products, identified as VI, VII and perfluoro-(3,4,5-tri-ethyl-pyridazine) (VIII) in 23%, 32% and 9% yields respectively. A moderate amount of intractable tarry residue was also recovered but contained no identifiable products.



VI VII VIII

$R_f = CF_3CF_2$

(b) Structure.

The structures of VI, VII and VIII have been discussed previously in connection with perfluoroethylation reactions of tetrafluoropyridazine (See Section 3.4.2.(b)) and, apart from the fact that nucleophilic attack by $CF_3\bar{C}FCl$ occurs followed by chlorine displacement rather than by $CF_3CF_2^-$, the arguments are equally valid.

(c) Mechanism.

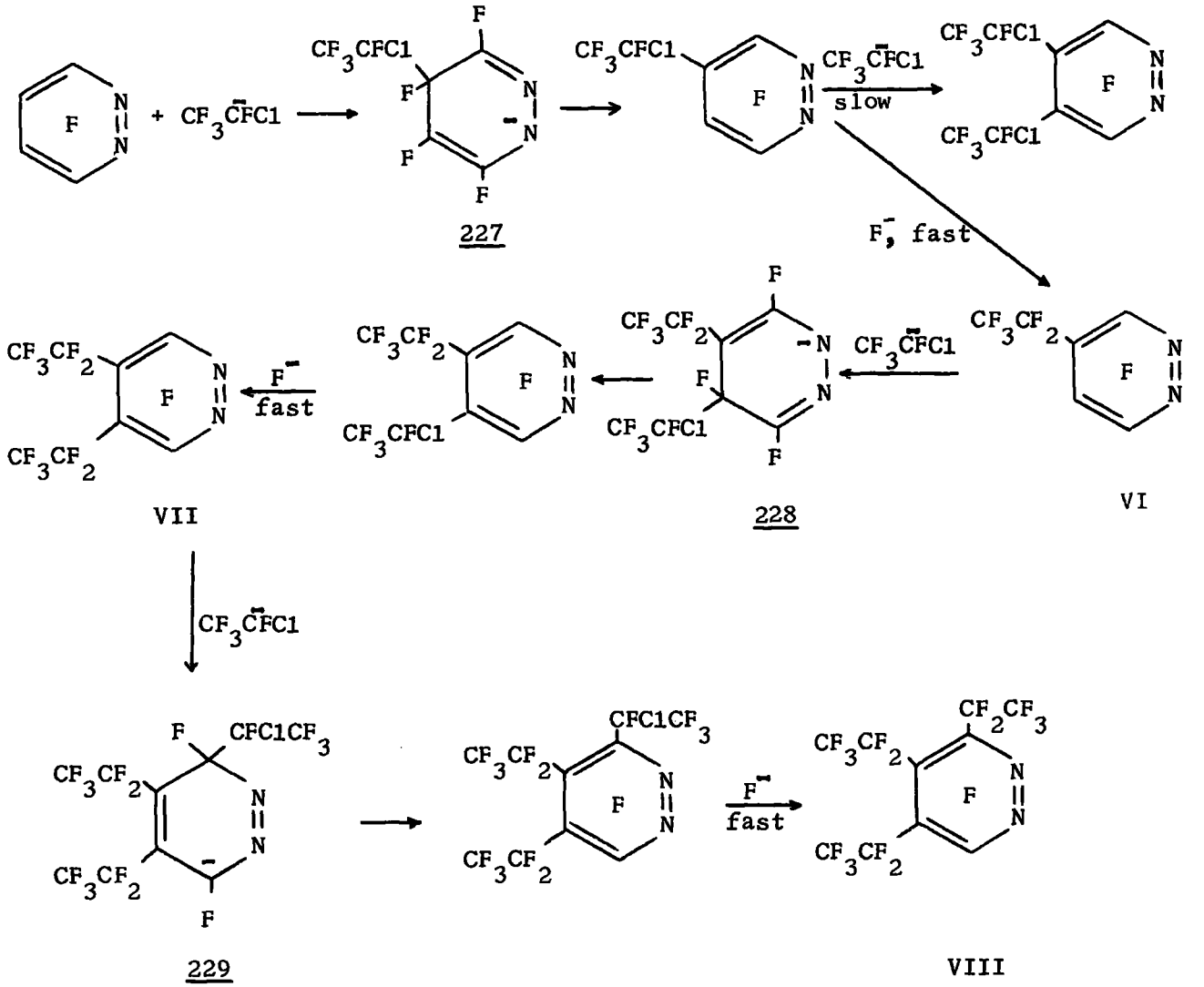
In contrast to fluoride ion-initiated reactions between chlorotrifluoroethylene and pentafluoropyridine, no chloropolyfluoroalkyl derivatives are observed in the analogous reactions with tetrafluoropyridazine. Therefore, the proposed mechanism for the latter reactions relies, to some extent, on the conclusions deduced from results for the former reactions.

(i) Chlorine displacement.

Since displacement of chlorine in the pyridine system was shown previously to occur after polyfluoroalkylation, it is reasonable to assume that a similar situation exists in analogous reactions of tetrafluoropyridazine. However, the rate of displacement of chlorine in the latter system must be substantially faster than in the former, a fact which must be accounted for in the displacement mechanism discussed later.

(ii) Nucleophilic aromatic substitution.

Mono- and di-substitution by $CF_3\bar{C}FCl$ in tetrafluoropyridazine are expected at the 4- and 4,5-positions, via 227 and 228 respectively. By analogy with the pyridine system, loss of chlorine is expected to occur prior to further substitution, as shown, to give VI and VII, although no direct evidence for this has been obtained. Since VII is not catalytically rearranged to the 3,5-isomer under these conditions, further substitution by $CF_3\bar{C}FCl$ in VII is expected at the 3-position via 229,



analogous to pentafluoroethylation reactions, followed by rapid chlorine displacement to give VIII.

4.5. Reactions with bromotrifluoroethylene.

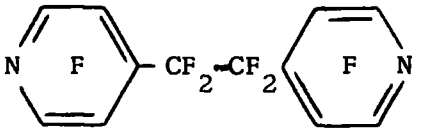
Atmospheric pressure fluoride ion-initiated reactions of bromotrifluoroethylene are conveniently discussed under the heading of the perfluoro-N-heteroaromatic compound used.

4.5.1. Pentafluoropyridine.

(a) Conditions and products.

Previously reported reactions of caesium fluoride, bromotrifluoroethylene and pentafluoropyridine in autoclaves at elevated temperatures (ca. 170°)

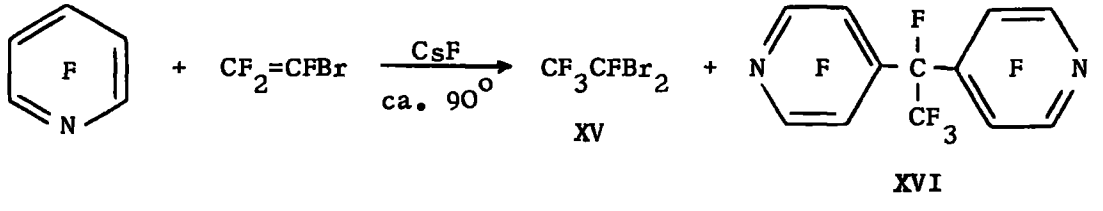
gave 1,1-dibromotetrafluoroethane (XV) and, allegedly, 1,2-bis-(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane (230).[101]



230

Atmospheric pressure reactions with a combination of caesium fluoride and sulpholan at ca. 90°, using a static system, gave unreacted CF_2=CFBr and a colourless liquid on vacuum distillation of the reaction mixture. Chromatographic analysis of the latter indicated two components which were identified as pentafluoropyridine and 1,1-dibromotetrafluoroethane (XV).

The involatile reaction mixture gave a water insoluble polymeric residue which contained carbon, fluorine and bromine but was not identified or investigated further. Ether extraction of the aqueous solution gave an orange oil containing several products, however, of the major components only 1,1-bis-(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane (XVI) was identifiable in low yield, as shown in Scheme 5.



XV

XVI

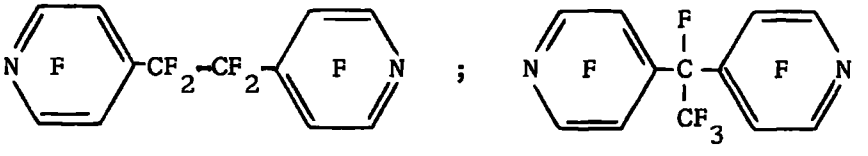
Scheme 5

No evidence was obtained from chromatographic analysis, i.r., mass or ^{19}F n.m.r. spectroscopy for the formation of either perfluoroethylpyridines or bromopolyfluoroalkylpyridines in these reactions.

(b) Structure.

The structure of 1,1-dibromotetrafluoroethane (XV) was determined previously by mass and ^{19}F n.m.r. spectroscopy.[101] However, although the

i.r. spectrum of the pyridine derivative isolated from the involatile reaction mixture was identical with that recorded previously, the observed ^{19}F n.m.r. spectrum contained an extra resonance, which was only observed owing to superior instrumentation, and consequently is not consistent with the previously proposed structure (230). The spectrum consists of four absorptions at 78·4, 90·4, 139·6 and 164·1 in the ratio 3:4:4:1 respectively. The absorptions at 78·4 and 164·1 are characteristic of a trifluoromethyl group and a tertiary fluorine respectively while those at 90·4 and 139·6 correlate with the calculated chemical shifts, derived from s.c.s. data for perfluoro-(4-ethylpyridine) of 89 and 140 for the 2,6- and 3,5-ring fluorines in a 4-perfluoroalkyl substituted pyridine nucleus. These results are therefore consistent with the postulated structure (XVI), rather than 230, for which only three absorptions of equal area are expected, as reported previously.[101]



230 XVI

(c) Mechanism.

Formation of 1,1-dibromotetrafluoroethane (XV) was previously rationalised as removal of Br^+ from CF_2=CFBr by fluoride ion to give trifluorovinylanion (231) and BrF; subsequent addition of the latter to the olefin would give XV. To investigate the proposed abstraction of Br^+ by F^-, caesium fluoride and carbon tetrabromide were heated at ca. 90° in acetonitrile. In order to trap any CBr_3^- formed, tetrafluoropyridazine was also added to the reaction mixture, however, only quantitative recovery of the starting material was obtained. Consequently there is no evidence to date to substantiate this type of mechanism.

$$CF_2{=}CFBr + F^- \not\longrightarrow CF_2{=}CF^- + BrF$$

$$\downarrow CF_2{=}CFBr$$

$$CF_3CFBr_2$$

XV

A more likely mechanism is nucleophilic attack of $CF_3\bar{C}FBr$ (232) on bromine in $CF_2{=}CFBr$ to displace the carbon-bromine bonding electrons, by analogy with results reported by Miller and co-workers in reactions of fluoroperhalocarbanions and perhaloalkanes,[115] to give XV and 231. Formation of XV in similar reactions of $CF_2{=}CFBr$ by itself indicates that pentafluoropyridine is not involved in the process.[101]

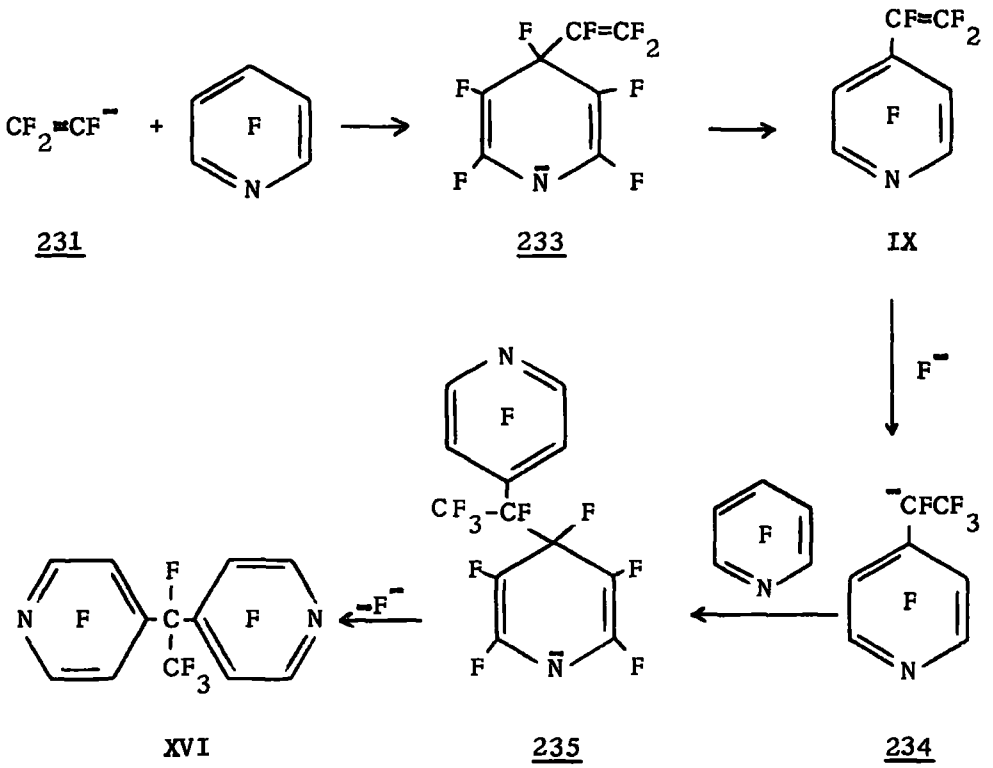
$$CF_2{=}CFBr \rightleftharpoons[F^-] CF_3\bar{C}FBr + Br\text{-}\underset{F}{C}{=}CF_2 \longrightarrow CF_3CFBr_2 + CF_2{=}CF^-$$

232 XV 231

In contrast to analogous reactions of $CF_2{=}CFCl$, fluoride ion-initiated reactions between $CF_2{=}CFBr$ and pentafluoropyridine give no polyfluoroalkylpyridines, however, significant quantities of CF_3CFBr_2 are formed. These contrasting results emphasize the competition between polyfluoroalkylation of Ar-F and halogen exchange with $CF_2{=}CFX$ by $CF_3\bar{C}FX$. The preferential nucleophilic attack on halogen, rather than carbon, in this system by $CF_3\bar{C}FBr$ can probably be attributed to a combination of the increased steric requirements and increased stability of $CF_3\bar{C}FBr$, compared to $CF_3\bar{C}FCl$, making halogen exchange energetically more favourable.

However, formation of 1,1-bis-(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane (XVI) clearly requires nucleophilic aromatic substitution of some description. Since the mechanism for the formation of XV affords highly reactive trifluorovinylanions (231), aromatic substitution is

expected at the 4-position of pentafluoropyridine, via 233, to give perfluoro-(4-vinylpyridine) (IX). Subsequent rapid addition of fluoride ion to IX to give 234 is expected, which can substitute at the 4-position in pentafluoropyridine to give the observed product (XVI) via 235.



Confirmatory evidence for this mechanism was obtained on isolation of XVI in 60% yield from a fluoride ion-initiated reaction of IX, prepared by defluorination of perfluoro-(4-ethylpyridine), with pentafluoropyridine. A similar reaction with 2-(2',3',5',6'-tetrafluoropyridyl)-pentafluoropropene (X) and pentafluoropyridine afforded 2,2-bis-(2',3',5',6'-tetrafluoropyridyl)hexafluoropropane (XVII) as the only product in 60% yield, which further substantiated the proposed mechanism for the formation of XVI in fluoride ion-catalysed reactions of $CF_2{=}CFBr$ and pentafluoropyridine.

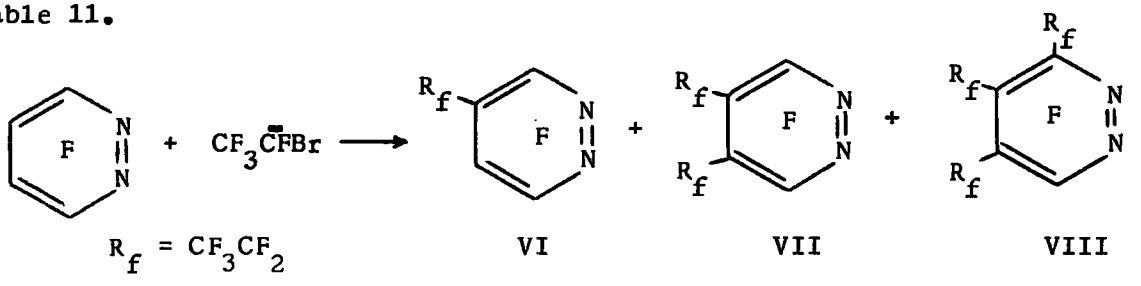
Formation of complex intractable residues in these reactions is quite consistent with the existence of such highly reactive intermediate carbanions as 231 and 234 in the reaction mixture. Similar results have

been observed previously in fluoride ion-initiated reactions of tetrafluoroethylene.[83]

4.5.2. Tetrafluoropyridazine.

(a) Conditions and products.

Atmospheric pressure fluoride ion-initiated reactions of bromotrifluoroethylene and tetrafluoropyridazine at ca. 90° and 120°, using a combination of caesium fluoride and either sulpholan or tetraglyme in a static system, gave unreacted $CF_2{=}CFBr$ and a colourless liquid. Chromatographic analysis of the latter indicated unreacted tetrafluoropyridazine, two products at ca. 90° and the same two products plus a third at ca. 120°. The components were identified as perfluoro-(4-ethylpyridazine) (VI) and perfluoro-(4,5-di-ethylpyridazine) (VII) at both temperatures and perfluoro-(3,4,5-tri-ethylpyridazine) (VIII) at ca. 120° only, as shown in Scheme 6. The results obtained are summarised in Table 11.



No bromine containing polyfluoroalkylpyridazines were isolated from these reactions and, although the ratios of products were similar in both solvents, substantially lower yields were obtained for reactions in tetraglyme, as seen from Table 11, analogous to previous polyfluoroalkylations with this solvent and substrate (See Sections 3.4.2.(a) and 4.4.2.(a)).

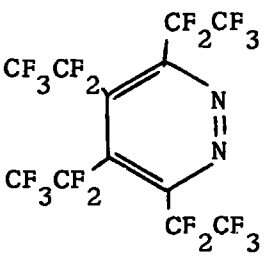
Using a combination of caesium fluoride and sulpholan in a static system at ca. 90° with a much longer reaction time afforded not only VI, VII and VIII, but also a fourth product which was identified as

Table 11

Solvent	Temp. °C	Percentage Yields (%)* VI	VII	VIII	Conversion %
Tetraglyme	90	30	9	-	62
Sulpholan	90	51	18	-	64
Tetraglyme	120	52	25	5	66
Sulpholan	120	41	28	5	80

* Based on the quantity of $C_4F_4N_2$ consumed.

tetrakis(pentafluoroethyl)pyridazine (XXXIII) in low yield. This product



XXXIII

had not been observed previously in similar reactions with either $CF_2{=}CF_2$ or $CF_2{=}CFCl$ to give perfluoroethylpyridazines.

A combination of potassium fluoride and sulpholan at ca. 120° in a static system was also found to be suitable for the formation of perfluoroethylpyridazines, giving VI, VII and VIII in 27%, 33% and 6% yields respectively.

(b) Structure.

The structures of VI, VII and VIII have been discussed previously in connection with perfluoroethylation of tetrafluoropyridazine (See Section 3.4.2.(b)) and, despite the fact that the attacking nucleophile is $CF_3\bar{C}FBr$ with subsequent rapid bromine displacement and not

$CF_3\dot{C}F_2$, the arguments are equally valid.

Only one structure is possible for tetrakis(pentafluoroethyl)pyridine (XXXIII) and broad absorptions in the ^{19}F n.m.r. spectrum and low extinction coefficients in the u.v. spectrum (λ_{max} = 260 mμ, ε_{max} = 743; λ_{max} = 356 mμ, ε_{max} = 200; cf. perfluoro-(4,5-di-ethylpyridazine) (VII), ε_{max} = 4990) indicates extreme steric crowding and possibly distortion of the aromatic ring.

(c) Mechanism.

In contrast to analogous reactions of CF_2=CFBr and pentafluoropyridine, no 1,1-dibromotetrafluoroethane (XV) or perfluoro-1,1-bis-arylethane were observed, which indicates that $CF_3\dot{C}FBr$ preferentially polyfluoroalkylates tetrafluoropyridazine instead of abstracting Br^+ from CF_2=CFBr. Since no bromopolyfluoroalkyl derivatives of perfluoro-pyridine or -pyridazine have been isolated, the proposed mechanism for the formation of VI - VIII and XXXIII in these reactions is based largely on the conclusions deduced from similar reactions of CF_2=CFCl, especially with C_5F_5N.

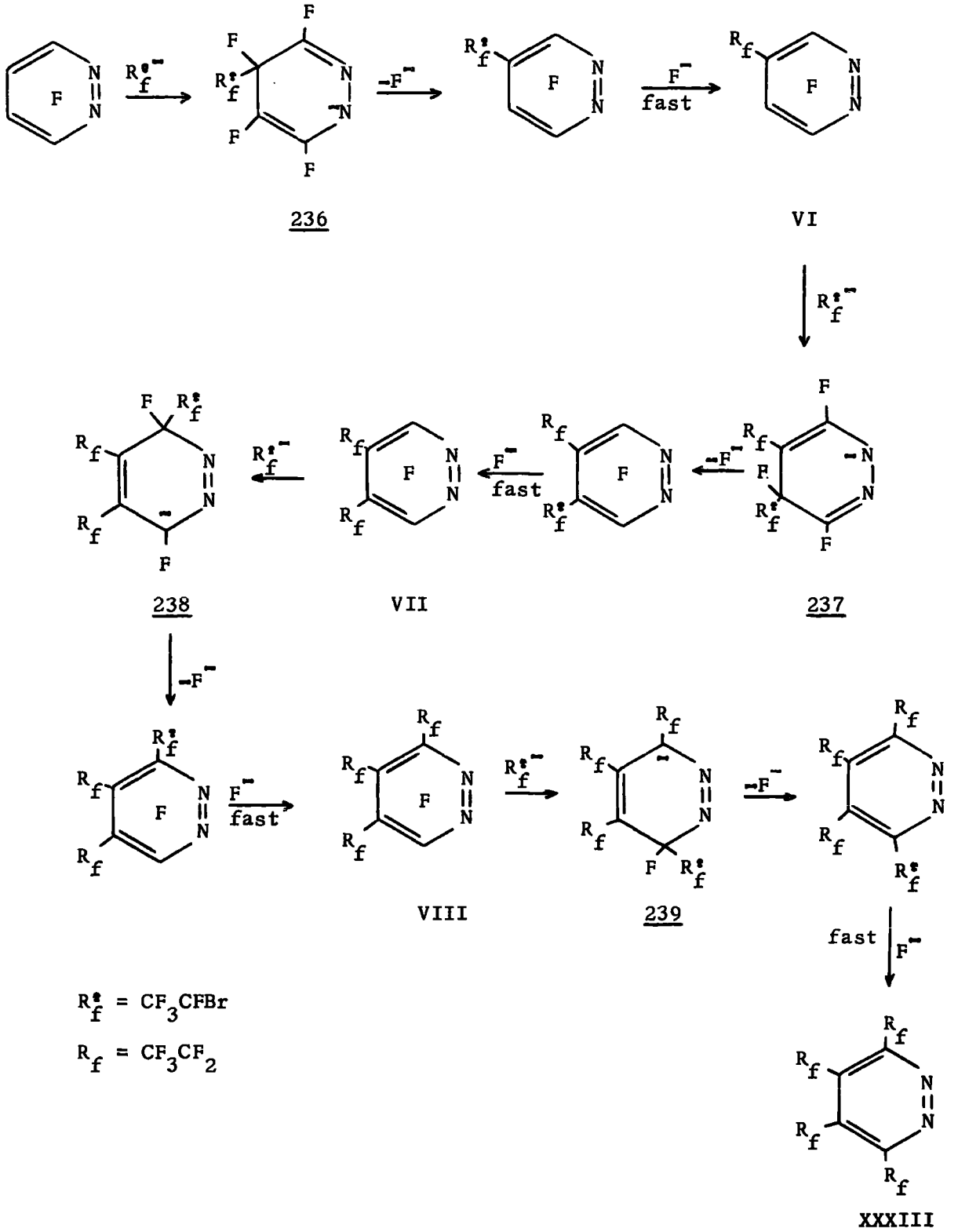
(i) Bromine displacement.

Displacement of bromine from CF_2=CFBr by vinylic substitution or an α-elimination process are not expected; the analogous processes do not occur with CF_2=CFCl. Alternatively, displacement of bromine after polyfluoroalkylation by $CF_3\dot{C}FBr$ is expected by analogy with previous results.

(ii) Nucleophilic aromatic substitution.

Mono- and di-substitution by $CF_3\dot{C}FBr$ in tetrafluoropyridazine are expected at the 4- and 4,5-positions, via 236 and 237 respectively. By analogy with the CF_2=CFCl/C_5F_5N system, rapid displacement of bromine is

expected to occur prior to further substitution as shown to give VI and VII, although no direct evidence for this has been obtained. Since VII is not catalytically rearranged to the 3,5-isomer, further substitution by $CF_3\bar{C}FBr$ is expected at the 3- and 6-positions, via 238 and 239 respectively, followed by rapid bromine displacement to give VIII and XXXIII.

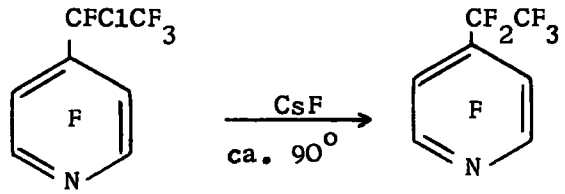


$R_f^{\bullet} = CF_3CFBr$

$R_f = CF_3CF_2$

4.6. Mechanism of halogen displacement from polyfluoroalkyl derivatives.

From the results obtained in fluoride ion-initiated reactions of CF_2=CFCl with itself, pentafluoropyridine and cyclohexene, and the action of fluoride ion on XII to give I, it was concluded in a preliminary discussion that halogen displacement occurs after substitution by the

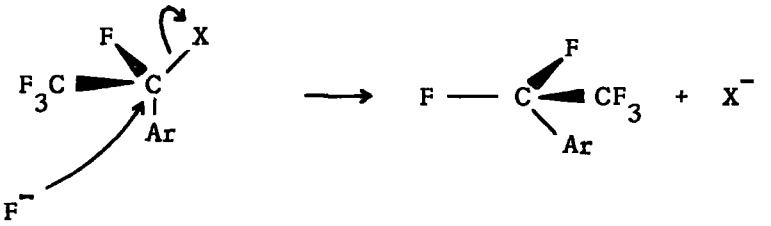


XII I

polyfluoroalkylanion, $CF_3\bar{C}FX$, in the perfluoro-N-heteroaromatic compound. However, differentiation of the previously postulated possible processes for displacement of halogen from a polyfluoroalkyl derivative is potentially much more difficult. The mechanism must account for not only the formation of the observed products, but also the observed differences between the perfluoro-pyridine and -pyridazine systems. In particular, a substantial increase in the rate of halogen displacement is evident in reactions with the latter compared to those with the former since, in contrast to the isolation of XII, no analogous chloro- or bromo-polyfluoroalkylpyridazines have been isolated.

4.6.1. Direct benzylic-type displacement.

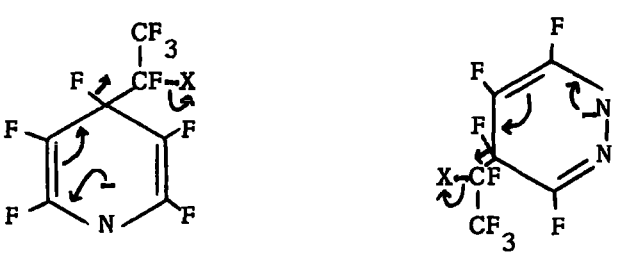
Classically, a direct benzylic-type displacement of the halide ion (X^-) by fluoride ion is the obvious mechanism for this type of reaction and accounts for the formation of the perfluoroethyl derivatives. The marked increase in the rate of displacement of X^- on changing the aryl substituent (Ar) from tetrafluoropyridyl to trifluoropyridazyl is less obvious. However, it was found previously[156] in displacement reactions of benzyl halides that if bond formation predominated in the transition state (i.e. $\Longrightarrow S_N2$-type



mechanism) then electron withdrawing substituents in the aromatic ring stabilised the transition state, compared to the unsubstituted compound, increasing the rate of halide substitution. In contrast, if bond breaking predominated in the transition state (i.e. $\Longrightarrow$ S_N1-type mechanism) the converse applied. It is possible, therefore, that the different observed rates of displacement of halide from polyfluoroalkyl-pyridines and -pyridazines may be attributed to a "substituent effect" of the nitrogen(s) in the aromatic ring, although no evidence for this was reported previously.

4.6.2. Concerted benzylic-type displacement.

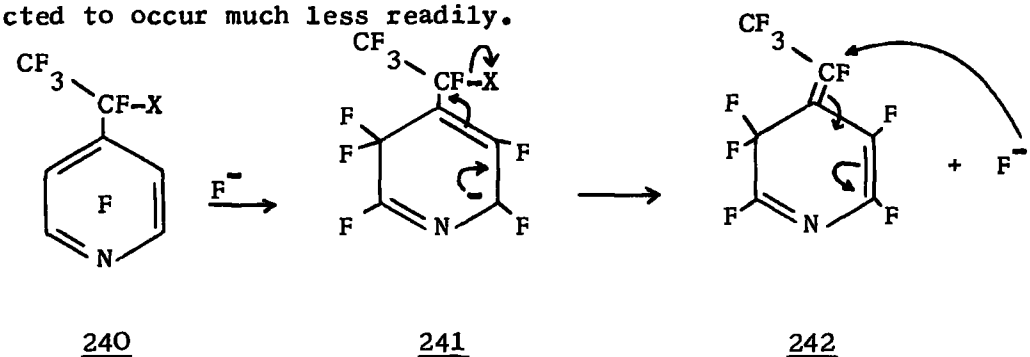
Extension of the direct benzylic-type mechanism to a concerted process involving the aromatic nucleus, as shown, also accounts for the formation of perfluoroethyl derivatives. Experimentally it is impossible to distinguish between these processes and, therefore, similar considerations are expected to apply to the concerted mechanism as apply to the direct mechanism.



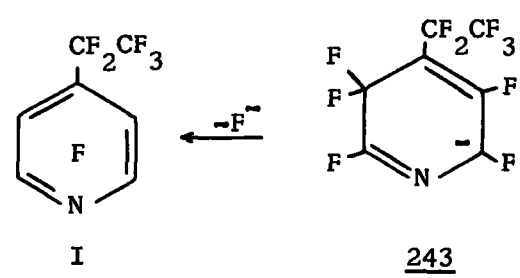
4.6.3. Pseudo-S_N2^2-type displacement.

The stages involved in displacement of X via the recently proposed

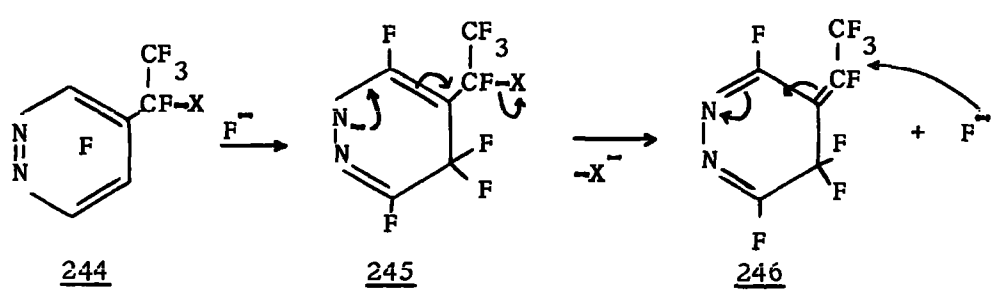
pseudo-S_N2' process[144,145] are shown for both systems, however, confirmatory experimental evidence for such a mechanism has not been obtained to date. The relative rates of displacement of X from the mono-substituted derivatives is attributed to the relative susceptibilities of the hetero-aromatic nuclei to attack by fluoride ion ortho, or para, to the poly-fluoroalkyl substituent. Since ortho attack at the 5-position in 244 is preferred, rapid displacement of X is predicted via this process, however, ortho attack at the 3-position of 240 is not favoured hence displacement is expected to occur much less readily.



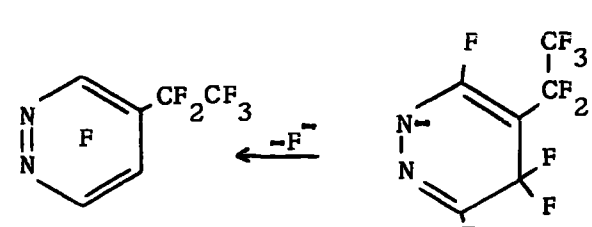
240 241 242



I 243

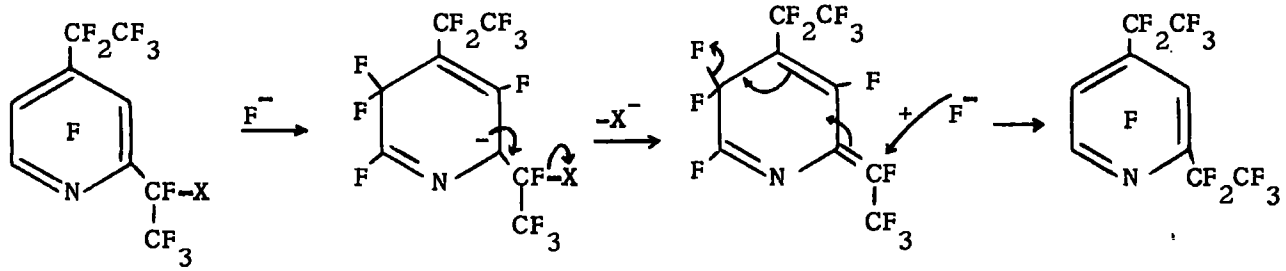


244 245 246



VI 247

Since no evidence for halogen (X) containing polysubstituted derivatives of either system was obtained, subsequent displacement of X must be rapid. Extension of the previous argument similarly accounts for these observations since ortho or para attack to CF_3CFX by fluoride ion is favourable, as shown for example, in the di-substituted pyridine (248).



248 249 250 II

4.6.4. Conclusion.

From experimental evidence it is difficult to decide which of the mechanisms discussed is operating. The direct benzylic-type process is a well established mechanism in organic chemistry and, consequently, it is the immediately obvious choice. However, the pseudo-S_N2^{ar} process does appear to account for the observed results quite nicely and several subtle experiments are required to provide some factual evidence for or against such a novel mechanism.

4.7. Reactions with trifluoroethylene.

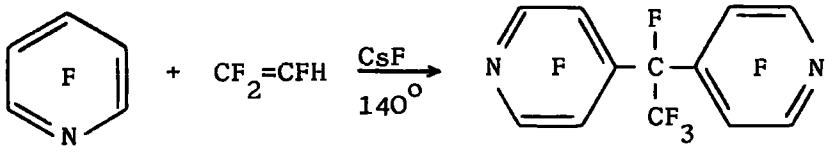
Atmospheric pressure fluoride ion-initiated reactions of trifluoroethylene are conveniently discussed under the heading of the perfluoro-N-heteroaromatic compound used.

4.7.1. Pentafluoropyridine.

(a) Conditions and products.

Previously reported fluoride ion-initiated reactions of trifluoroethylene and pentafluoropyridine in an autoclave at ca. 200° gave only

recovered starting material. An atmospheric pressure reaction with a combination of caesium fluoride and sulpholan at ca. 140°, using a static system, gave unreacted starting materials and a low yield of 1,1-bis-(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane (XVI). Ether extraction of an aqueous solution of the involatile reaction mixture gave a substantial amount of intractable tarry residue which was not investigated further.



XVI

(b) Structure.

The structure of XVI was determined principally from the observed ^{19}F n.m.r. spectrum and is discussed in Section 4.3.1.(b).

(c) Mechanism.

Nucleophilic substitution in pentafluoropyridine by trifluorovinyl-anions (231), generated by abstraction of a proton from CF_2=CFH by either F^- or $CF_3\bar{C}FH$, gives perfluoro-(4-vinylpyridine) (IX), which subsequently affords XVI as shown. The low yield of XVI (~10%) and formation of substantial quantities of intractable tarry residues are attributed to side reactions of the very reactive intermediate carbanions and solvent decomposition, which are more pronounced at elevated temperatures.

4.7.2. Tetrafluoropyridazine.

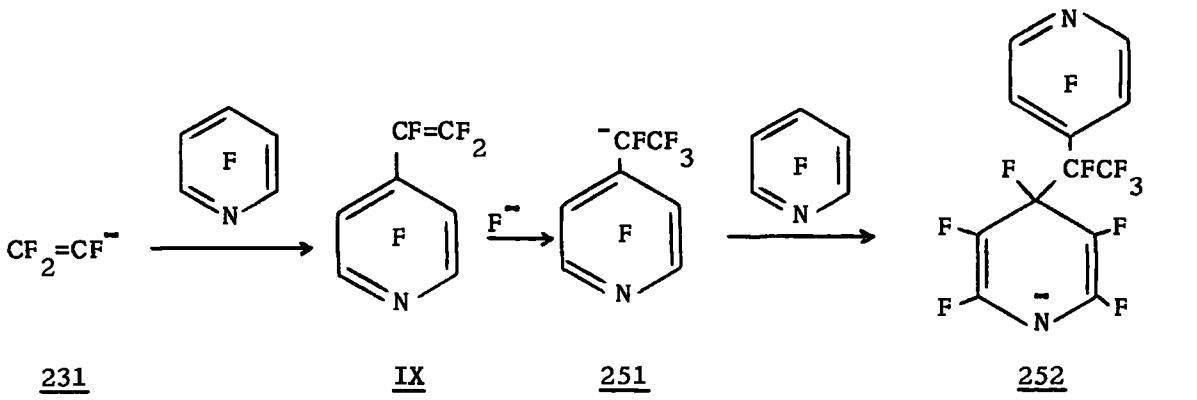
A fluoride ion-initiated reaction between trifluoroethylene and tetrafluoropyridazine at ca. 90° in a static system gave only recovered olefin and an intractable tarry residue which contained no identifiable

$$CF_2{=}CFH + F^- \longrightarrow CF_2{=}CF^- + HF$$

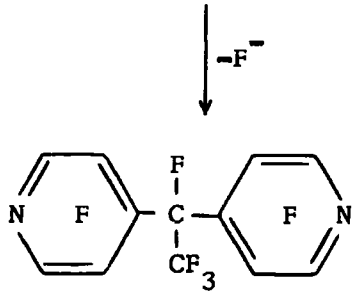
231

or $CF_2{=}CFH + F^- \rightleftharpoons CF_3\bar{C}FH \xrightarrow{CF_2=CFH} CF_3CFH_2 + CF_2{=}CF^-$

231



231 IX 251 252



XVI

products. This result may be due to either non-formation of the intermediate carbanion, $CF_3\bar{C}FH$, under these conditions or, if formed, it is not reactive enough to substitute in tetrafluoropyridazine. However, no tetrafluoropyridazine was recovered after the reaction and, therefore, it is more likely that side reactions involving the solvent occurred in preference to polyfluoroalkylation, to give the observed high molecular weight involatile material.

CHAPTER 5

Fluoride Ion-Induced Rearrangement Reactions of Perfluoroalkylheteroaromatic Compounds.

Introduction.

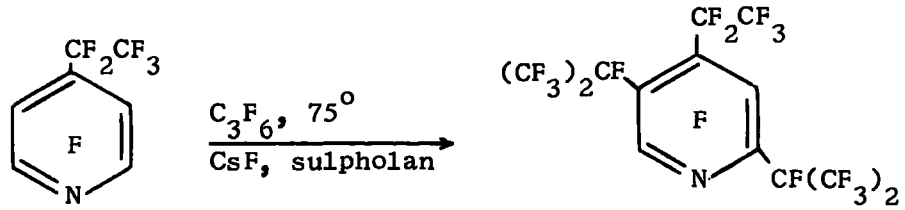
Previous polyfluoroalkylations of pentafluoropyridine using $CF_3CF_2^-$, $(CF_3)_2CF^-$ and $(CF_3)_3C^-$, as discussed in Chapter 3, indicated that kinetically controlled or thermodynamically controlled tri-substituted products can be obtained, depending upon the perfluoroalkylanion and the conditions employed.[146] In an attempt to distinguish the possible effects influencing these reactions, a series of mixed perfluoroalkylpyridines were prepared in atmospheric pressure reactions at moderate temperatures (ca. 70^o - 80^o) and, where possible, the effect of fluoride on the tri-substituted derivatives at elevated temperatures (ca. 150^o - 190^o) was investigated. The discussion is conveniently presented, therefore, in sections concerned with the polyfluoroalkylation reactions and the attempted aromatic rearrangement reactions, followed by the conclusions drawn from these results about the relative importance of steric effects, the ability of different perfluoroalkyl substituents to stabilise an intermediate carbanion and the migratory aptitude or stability of the perfluoroalkylanion in rearrangement reactions.

5.1. Polyfluoroalkylation reactions.

5.1.1. Heptafluoroisopropylation of perfluoro-(4-ethylpyridine) (I).

(a) Conditions and products.

Fluoride ion-catalysed reaction of hexafluoropropene and I in a static system at ca. 75^o for 40 minutes afforded dimers and trimers of the olefin and a single product, identified as perfluoro-(2,5-di-isopropyl-4-ethyl-pyridine) (XVIII) in quantitative yield. No di-substituted derivative was observed in this reaction.



I XVIII

(b) Structure.

The observed chemical shifts for I in conjunction with the previously reported[33,141] s.c.s. for 2-substitution by $(CF_3)_2CF^-$ afford calculated chemical shifts for the ring fluorines of perfluoro-(2-isopropyl-4-ethyl-pyridine) (254). Using these calculated values and the known s.c.s. for introduction of $(CF_3)_2CF$ at C-5 and C-6,[33,141] calculated shifts for the 2,4,5- and 2,4,6-isomers are obtained which are, as shown below, in close agreement with the observed results for XVIII and XXV respectively; see later for rearrangement of the former to the latter.

Chemical shifts for ring fluorines

	3	5	6
Obs. (XVIII)	113·9	-	52·2
Calc.	113	-	50
Obs. (XXV)	111·4	111·4	-
Calc.	108	108	

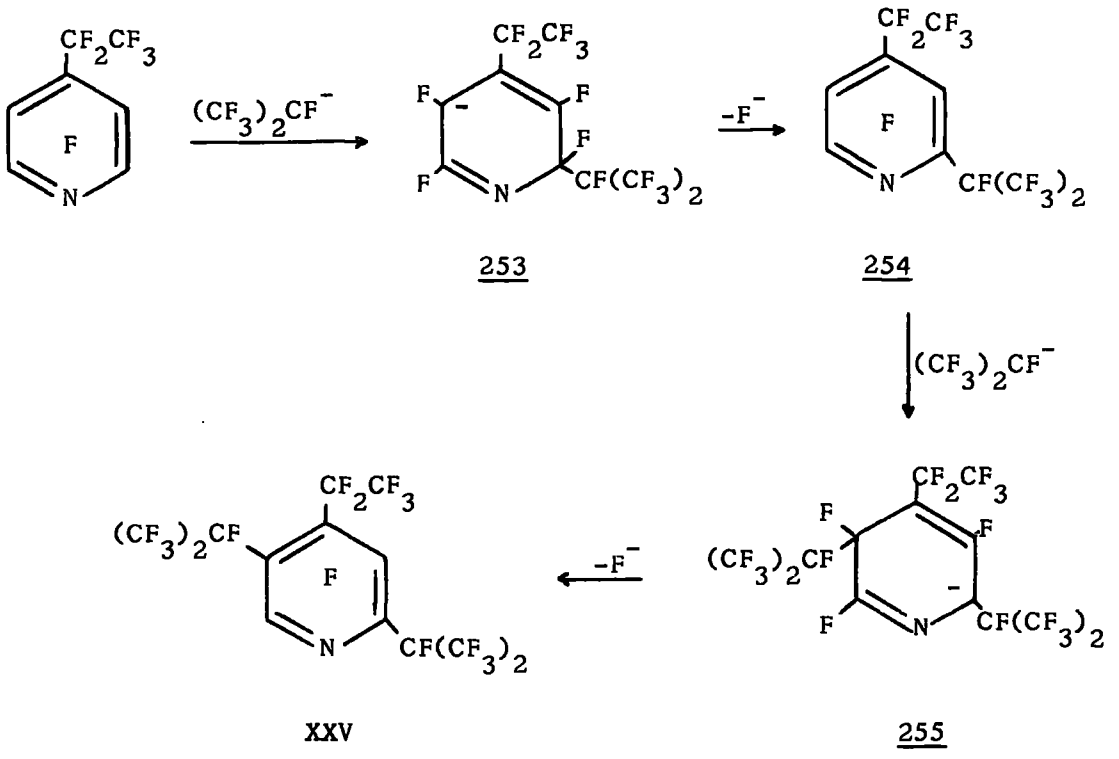
(c) Mechanism.

Mono- and di-substitution in I by $(CF_3)_2CF^-$ are expected at the 2- and 2,5-positions, via 253 and 255 respectively, by analogy with perfluoro-ethylation and isopropylation of pentafluoropyridine. (See page 129).

5.1.2. Heptafluoroisopropylation of perfluoro-(2,4-di-ethylpyridine) (II).

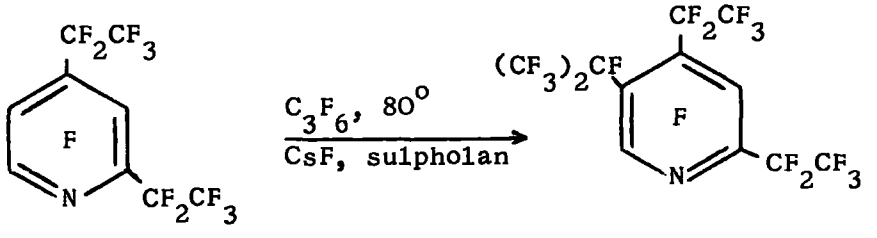
(a) Conditions and products.

Reaction of hexafluoropropene and II in a static system at ca. 80°



253 254 XXV 255

for 60 minutes gave dimers and trimers of the olefin, unreacted starting material and a single product, identified as perfluoro-(5-isopropyl-2,4-di-ethylpyridine) (XIX) in 65% yield.



II XIX

(b) Structure.

The substituent chemical shifts which arise from introduction of $(CF_3)_2CF$ at C-5 and C-6 have been previously determined;[33,141] with perfluoro-(2,4-di-ethylpyridine) as reference, the calculated and observed shifts for XIX and XXVI are in close agreement, as shown. Rearrangement of XIX to XXVI is discussed later.

Chemical shifts for ring fluorines

	3	5	6
Obs. (XIX)	115•2	-	53•6
Calc.	114	-	50
Obs. (XXVI)	111•5	108•6	-
Calc.	108	107	-

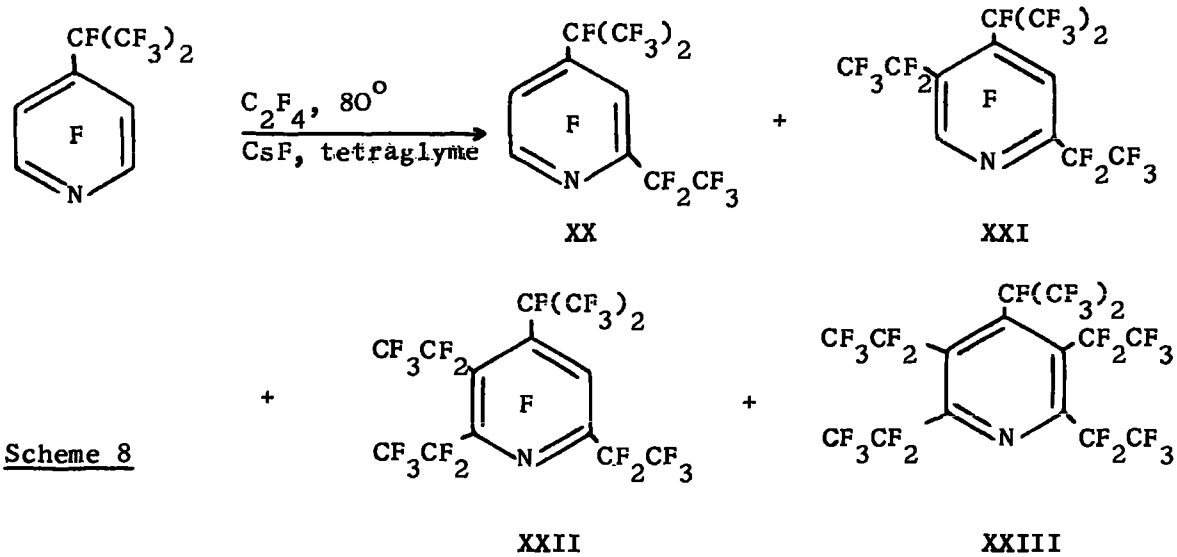
(c) Mechanism.

Substitution in II by $(CF_3)_2CF^-$ is expected at the 5-position, via a similar mechanism to that indicated previously, and by analogy with similar perfluoro-ethylation and -isopropylation reactions.

5.1.3. Pentafluoroethylation of perfluoro-(4-isopropylpyridine).

(a) Conditions and products.

Analogous reactions of tetrafluoroethylene and perfluoro-(4-isopropyl-pyridine) at ca. 80° for 5 hours gave unreacted starting materials and a mixture of four products, which were separated with difficulty. They were identified as perfluoro-(2-ethyl-4-isopropylpyridine) (XX), perfluoro-(2,5-di-ethyl-4-isopropylpyridine) (XXI), perfluoro-(2,5,6-tri-ethyl-4-isopropylpyridine) (XXII) and perfluoro-(tetraethyl-4-isopropylpyridine) (XXIII), as shown in Scheme 8, and were obtained in low to moderate yields.



Scheme 8

(b) Structure.

The chemical shifts which arise from introduction of CF_3CF_2 at C-2 and C-5 have been previously determined.[157] With perfluoro-(4-isopropylpyridine) as reference, the calculated and observed shifts for XX are in close agreement, as shown. Similarly, with XX as reference, the calculated and observed shifts for XXI are also in close agreement.

Chemical shifts for ring fluorines in XX

	3	5	6
Obs.	115·7	123·3	83·8
Calc.	115	123	83

Chemical shifts for ring fluorines in XXI

	3	5	6
Obs.	114·8	-	52·9
Calc.	113	-	55
Calc.*	102	102	-

* assuming a 2,4,6-isomer formed.

Since no absorption is observed below 73·9 in the complex ^{19}F n.m.r. spectrum of XXII, the calculated shifts for the remaining ring fluorine, with XXI as reference and utilising the previously determined s.c.s. for introduction of CF_3CF_2,[157] indicate quite conclusively that 6-substitution in XXI occurs to give XXII.

Calculated chemical shifts for ring fluorines

	3	6
2,3,4,5-isomer	-	40-50
2,4,5,6-isomer	100-110	-

Assuming that the 4-heptafluoroisopropyl group is not displaced during these reactions, there is only one possible aromatic structure for XXIII, as indicated.

(c) Mechanism.

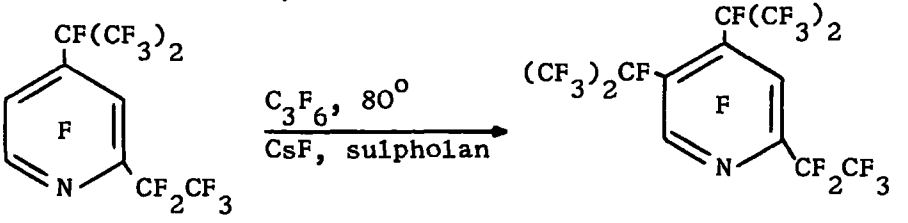
Substitution in perfluoro-(4-isopropylpyridine) by $CF_3CF_2^-$ to give XX - XXIII is as expected from previously discussed perfluoroethylations of

pentafluoropyridine and occurs via an analogous mechanism.

5.1.4. Heptafluoroisopropylation of perfluoro-(2-ethyl-4-isopropylpyridine) (XX).

(a) Conditions and products.

A similar reaction of hexafluoropropene and XX at ca. 80° for 150 minutes gave dimers and trimers of the olefin, unreacted starting materials and a single product, identified as perfluoro-(2-ethyl-4,5-di-isopropyl-pyridine) (XXIV) in ca. 80% yield.



XX XXIV

(b) Structure.

The chemical shifts which arise from introduction of $(CF_3)_2CF$ at C-5 and C-6 have been previously determined;[33,141] with XX as reference, the calculated and observed shifts for XXIV are in close agreement, as shown.

Chemical shifts for ring fluorines in XXIV

	3	5	6
Obs.	113·6	-	52·4
Calc.	111	-	50
Calc.*	106	104	-

* assuming a 2,4,6-isomer formed.

(c) Mechanism.

5-Substitution in XX is expected via an analogous mechanism to previously discussed perfluoroisopropylations.

5.2. Rearrangement reactions.

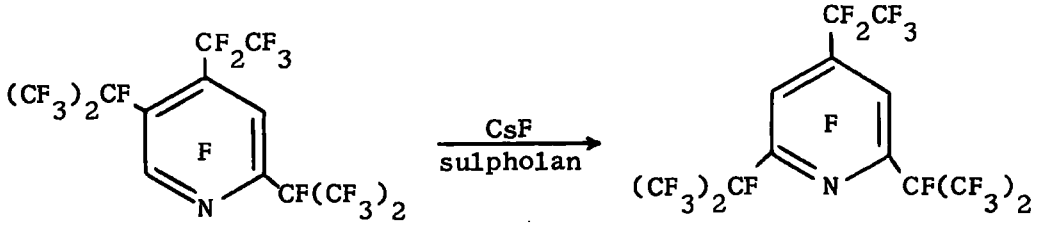
The effect of fluoride ion on a series of 2,4,5-tri-substituted

perfluoroalkylpyridines at elevated temperatures gives a variety of results depending upon the particular system, and these are discussed in the following sections.

5.2.1. Perfluoro-(2,5-di-isopropyl-4-ethylpyridine) (XVIII).

(a) Conditions and products.

Attempted fluoride ion-catalysed rearrangement of XVIII at ca. 160° gave a 3:2 mixture of XVIII and a single product, perfluoro-(2,6-di-isopropyl-4-ethylpyridine) (XXV) in ca. 55% yield. A similar reaction at ca. 180° gave XXV only in ca. 30% yield.



XVIII XXV

(b) Structure.

The proposed structure of XXV was shown previously, in Section 5.1.1.(b), to be consistent with the observed spectroscopic data.

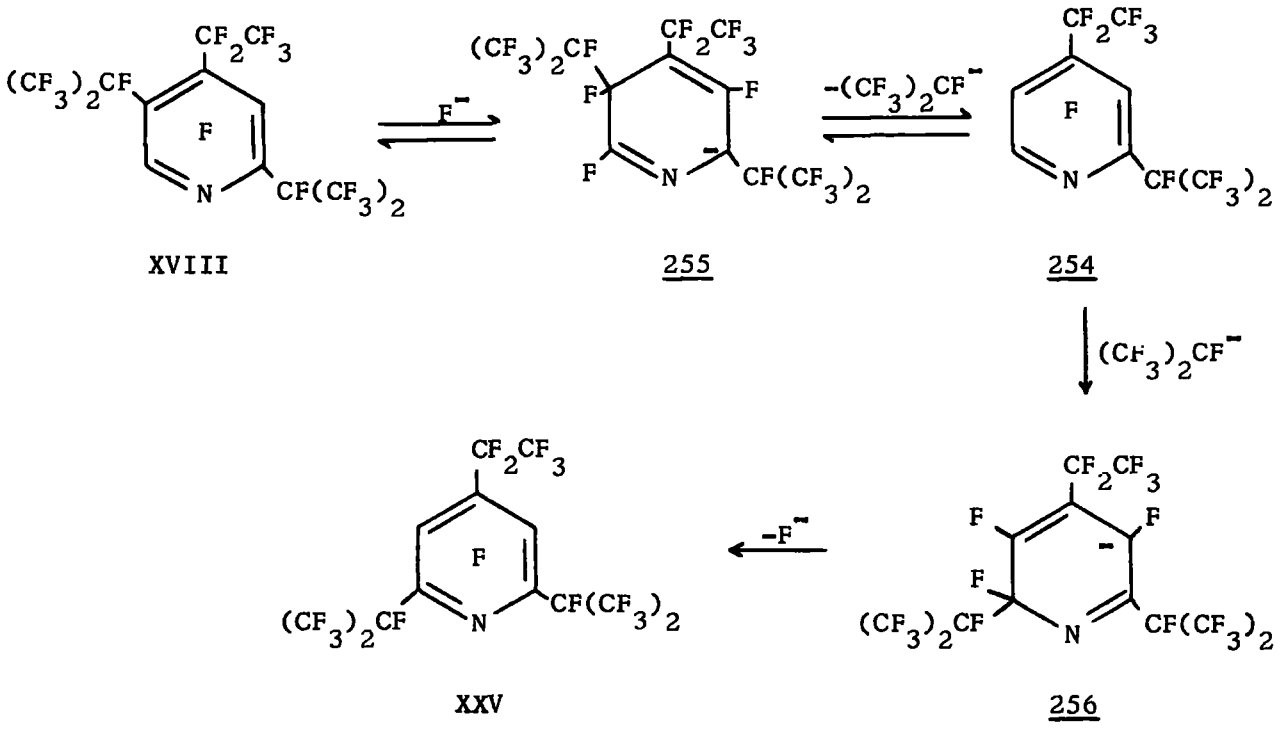
(c) Mechanism.

Loss of the 5-substituent in this type of aromatic rearrangement reaction was recently proposed[39,102] to be the reverse of its introduction. Regeneration of the 2,4-di-substituted derivative and subsequent attack at the 6-position by the liberated perfluoroalkylanions gives the thermodynamically stable 2,4,6-isomer. Hence the proposed mechanism for the rearrangement of XVIII to XXV is as shown, via 255 and 256.

5.2.2. Perfluoro-(5-isopropyl-2,4-di-ethylpyridine) (XIX).

(a) Conditions and products.

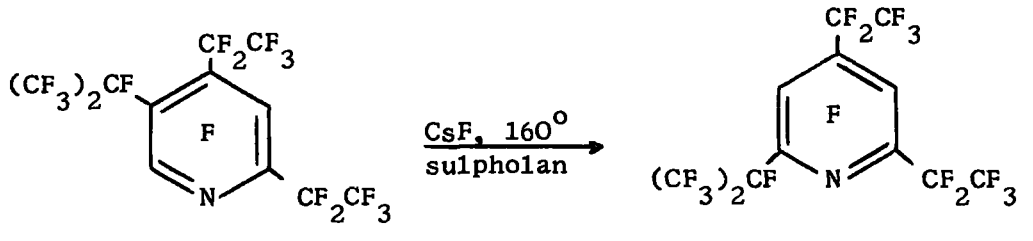
A similar reaction of XIX at ca. 160° gave a 2:3 mixture of XIX and



XVIII 255 254

XXV 256

a single product, perfluoro-(6-isopropyl-2,4-di-ethylpyridine) (XXVI) in ca. 50% yield.



XIX XXVI

(b) Structure.

The proposed structure of XXVI was shown previously, in Section 5.1.2.(b), to be consistent with the observed spectroscopic data.

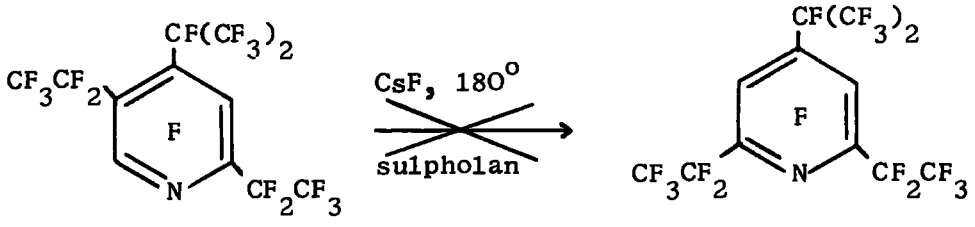
(c) Mechanism.

The mechanism for rearrangement of XIX to XXVI is analogous to that discussed for rearrangement of XVIII to XXV in Section 5.2.1.(c).

5.2.3. Perfluoro-(2,5-di-ethyl-4-isopropylpyridine) (XXI).

In contrast to previously discussed related reactions, attempted fluoride ion-initiated rearrangement of XXI at ca. 180° gave neither

recovered starting material nor identifiable products. It is feasible that, by analogy with equivalent rearrangements of perfluoro-(2,4,5-tri-isopropylpyridine),[39] the 4-heptafluoroisopropyl substituent is displaced rather than the 5-pentafluoroethyl group, and that the resultant 2,5-di-substituted derivative is unstable under these conditions. Further investigation of this system at lower temperatures is therefore required, however, due to the difficulties encountered in the preparation of XXI in sufficient quantities for such reactions, this has not been possible to date.



XXI 257

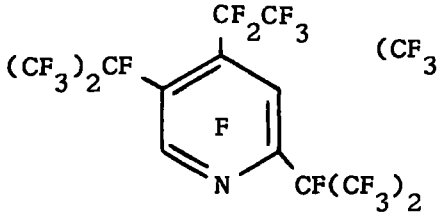
5.3. Rationalisation of the possible effects controlling catalytic rearrangement of some tri-substituted perfluoroalkylpyridines.

The possible effects which determine whether a 2,4,5-perfluoroalkyl-pyridine is catalytically rearranged to the 2,4,6-isomer, under suitable conditions, are considered to be: steric interactions between the 4- and 5-substituents; the relative stabilising effect of the 2-substituent on the intermediate carbanion for loss of the 5-substituent; and the migratory aptitude of the perfluoroalkylanion, primarily determined by its relative stability. From the observed results for polyfluoroalkylation reactions and fluoride ion-induced rearrangements it is possible to comment on the relative importance of each of these effects.

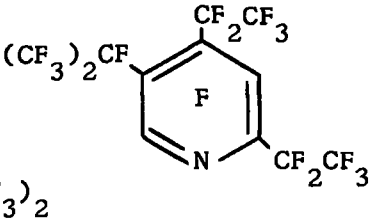
5.3.1. Steric effects.

In contrast to perfluoro-(2,4,5-tri-isopropylpyridine), which readily rearranged to the 2,4,6-isomer at ca. 160°,[146] perfluoro-(2,4,5-tri-ethylpyridine) was unaffected by fluoride ion, even at ca. 190°. If the

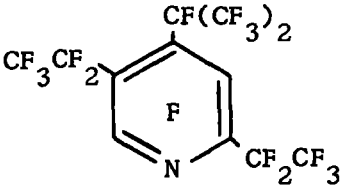
relief of adverse steric crowding is the driving force in the former, then XVIII, XIX and XXI, which should have identical steric interactions between the 4- and 5-substituents, would be expected to either all rearrange,



XVIII



XIX



XXI

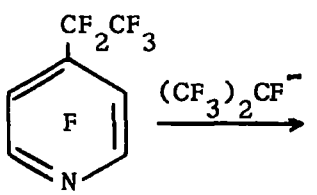
or all not rearrange under similar conditions. In practice, XVIII and XIX partially rearrange at ca. 160°, however, in contrast to complete rearrangement of XVIII at ca. 180°, XXI does not afford any identifiable products.

Since only partial isomerisation of XVIII and XIX occurs at ca. 160°, unlike perfluoro-(2,4,5-tri-isopropylpyridine), variation in the steric interactions does affect the ease of rearrangement to some extent, however, non-isolation of a 2,4,6-isomer of XXI, under identical conditions with those for successful rearrangement of XVIII, clearly indicates that steric interactions are not the major effect in this type of reaction.

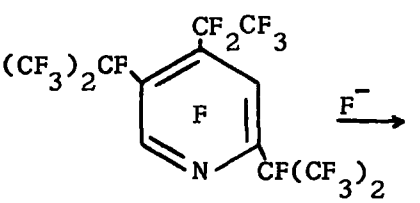
5.3.2. Stabilising effect of the 2-substituent.

The relative ease of loss of a 5-substituent in attempted rearrangements of 2,4,5-perfluoroalkylpyridines may be related to the effect of the para perfluoroalkyl substituent on the stability of the transition state and intermediate carbanion. Variation of the free energy of the transition state and intermediate carbanion alter the activation energies for the addition and displacement of the 5-perfluoroalkyl substituent, thus changing the possibility of polyfluoroalkylation of the 2,4-di-substituted derivative and rearrangement of the 2,4,5-tri-substituted compound.

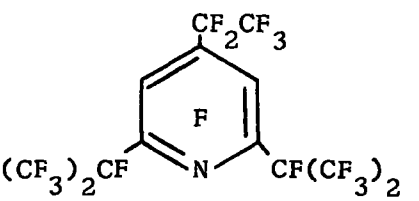
Since heptafluoroisopropylation of I and II gives quantitative and partial conversion to XVIII and XIX respectively, and rearrangement of XIX to XXVI gives a slightly higher conversion than rearrangement of XVIII to XXV under identical conditions, it appears that a 2-CF_3CF_2 group increases the activation energy for addition of $(CF_3)_2CF^-$ at the 5-position and decreases the activation energy for loss of $(CF_3)_2CF^-$ from the 5-position. However, this argument does not appear to be true when



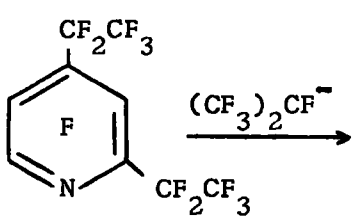
I



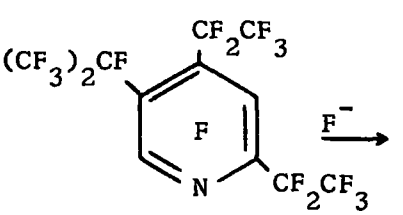
XVIII



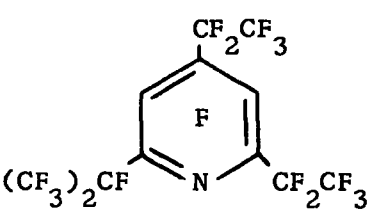
XXV



II

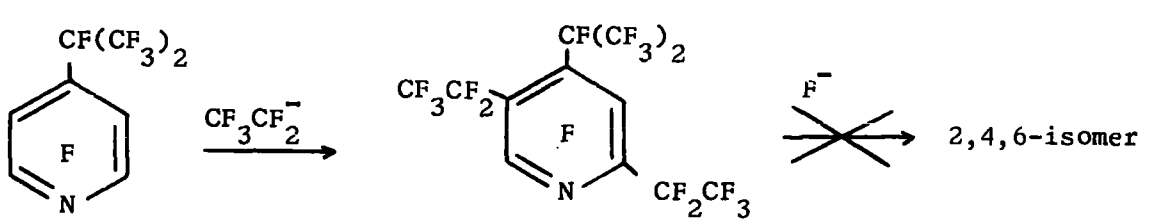


XIX



XXVI

the 5-substituent is CF_3CF_2, since XXI does not readily afford a 2,4,6-isomer, which therefore suggests that the nature of the 5-substituent, and not the 2-substituent, is the controlling factor.



XXI

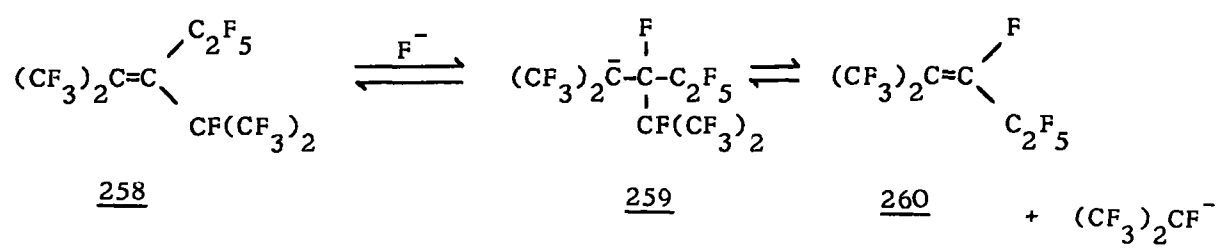
5.3.3. Migratory aptitude of the 5-perfluoroalkyl substituent.

The available evidence to date indicates that the possibility of fluoride ion-induced rearrangement of a 2,4,5-perfluoroalkylpyridine to the 2,4,6-isomer is governed primarily by the nature of the 5-substituent, and the relative stability of the perfluoroalkylanion formed on displacement. Since rearrangement of XIX is observed, in contrast to perfluoro-(2,4,5-triethylpyridine), the stability of the leaving perfluoroalkylanion is clearly the important factor, assuming that steric interactions are of secondary importance as shown earlier.

Clearly, loss of $(CF_3)_3C^-$ is extremely easy, due to its high stability, since no 2,4,5-isomer was observed; $(CF_3)_2CF^-$ is of intermediate stability and is displaced reasonably readily at elevated temperatures; $CF_3CF_2^-$, the least stable anion considered, was not displaced even under forcing conditions. Hence the following order of migratory aptitude for this system is postulated:-

$$(CF_3)_3C^- > (CF_3)_2CF^- > CF_3CF_2^-$$

which is substantiated to some extent by the action of fluoride ion on 258 to give 259, which losses $(CF_3)_2CF^-$, in preference to $CF_3CF_2^-$, to give 260.[93]



258 259 260

EXPERIMENTAL

Reagents.

Hexafluoropropene, trifluoroethylene and bromotrifluoroethylene, purchased from Peninsular Chem. Research Inc., were utilised without further purification. Vacuum and atmospheric pyrolyses at ca. 600-700°C of powdered Teflon,[158,159] kindly donated by I.C.I., provided, after rigorous vacuum fractionation, pure samples of tetrafluoroethylene and perfluoroisobutene respectively. Chlorotrifluoroethylene was prepared in high yield on dechlorination of Isceon 113, $CF_2Cl\text{-}CFCl_2$, with zinc dust suspended in ethanol.[160]

Pentafluoropyridine and tetrafluoropyridazine were prepared as described in the literature.[37,161] The latter was stored over magnesium carbonate and phosphorus pentoxide to exclude any traces of moisture.

The caesium fluoride was reagent grade, dried by heating under high vacuum for several days, powdered in a glove bag, stored under vacuum and, when required, equilibriated to atmospheric pressure with dry nitrogen. Attempted purification of the caesium fluoride by extracting a neutralised aqueous solution of it with methylene chloride, to remove any organic impurities, gave only identical material, as shown by i.r. spectroscopy. Caesium fluoride roasted in air in a platinum crucible was shown to be contaminated, possibly due to the formation of caesium carbonate. The potassium fluoride was reagent grade, dried by heating strongly over a bunsen flame for several days, and stored in an oven at 150°.

Sulpholan and tetraglyme were purified by fractional vacuum distillation; the middle fraction, collected over suitably dried molecular sieves (Type IVA), was retained and stored under dry nitrogen at room temperature.

Instrumentation.

Infra-red spectra were recorded on a Grubb-Parsons "Spectromaster" spectrometer and a Perkin-Elmer Model 157 spectrophotometer. Volatile

liquid or gaseous samples were vaporized into an evacuated cylindrical cell with potassium bromide end windows; liquid and low melting point solid samples were in the form of thin contact films between potassium bromide plates; solid samples were pressed into homogeneous thin discs with potassium bromide.

Ultra-violet spectra, in cyclohexane (Spectrosol grade) as solvent, were recorded using a Unicam S.P. 800 spectrophotometer.

Proton (^{1}H) and fluorine (^{19}F) nuclear magnetic resonance spectra were recorded on a Varian A56/60D spectrometer, operating at 60 and 56·4 Mc/s. respectively. Chemical shifts are quoted in p.p.m. relative to T.M.S. and $CFCl_3$ respectively. Variable temperature facilities permitted spectra to be recorded at temperatures different from 40°C, the standard condition.

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

Carbon, nitrogen and hydrogen analyses were obtained using a Perkin-Elmer 240 Elemental Analyser. Analysis for halogens was as described in the literature.[162]

Quantitative vapour phase chromatographic analysis (v.p.c.) was carried out on a Griffin and George, D6, Gas Density Balance (G.D.B.), using columns packed with silicone elastomer on Celite (column "O") and di-n-decyl-phthalate on Celite (column "A"). For this instrument, when correctly standardised, the number of moles of any compound in a mixture is directly proportional to its peak area. Calibration of the instrument with standard mixtures indicated that, within experimental error, this relationship was valid. Further non-quantitative chromatographic analysis was performed using Perkin-Elmer "Fractometer" models 451 and 452 with the same column packings ("O" and "A"). Preparative scale vapour phase chromatography was

performed on either a Varian "Aerograph" instrument or a Perkin-Elmer "F-21" instrument, using columns "O" and "A" in both instruments.

Boiling points were determined by Siwoloboff's Method and are not corrected for changes in atmospheric pressure.

Experimental Procedure.

Introduction.

A static atmospheric pressure system was developed, as discussed previously (See Section 3.2.2.), for fluoride ion-initiated reactions of some fluoro-olefins with perfluoro-N-heteroaromatic substrates. The experimental procedure was identical in all cases, perfluoroisobutene reactions excepted, and a detailed description is most relevant at this stage.

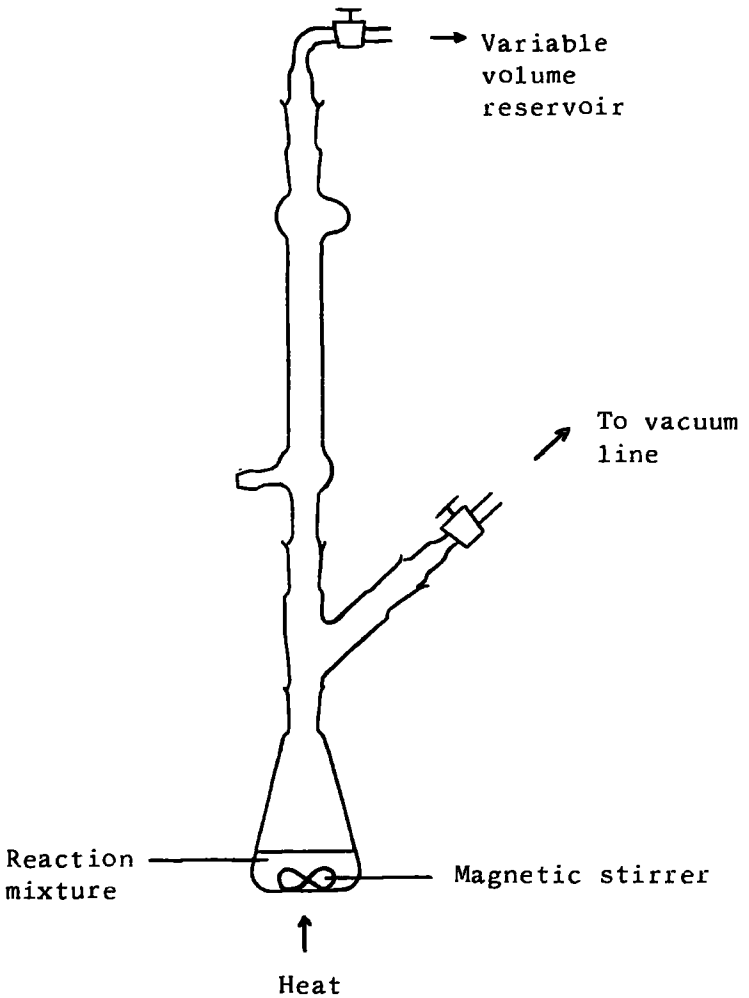
Procedure.

The required quantities of dry caesium fluoride and dry dipolar aprotic solvent were rapidly introduced into the baked, purged reaction apparatus (Fig. 9) against a flow of dry nitrogen. Evacuation of the apparatus was accompanied by degassing of the solvent, after which the flask was heated to the required reaction temperature. Sufficient gaseous polyfluoro-olefin was admitted to the system to equilibrate it to atmospheric pressure and approximately half-fill the reservoir. The perfluoro-N-heteroaromatic substrate was rapidly added to the reaction mixture which was vigorously stirred.

Partial collapse of the reservoir and colouration of the reaction mixture were usually observed during the reaction.

On completion, the volatile material was vacuum transferred from the reaction mixture into a cold trap (liquid air) at temperatures up to ca. 90°C. An atmospheric pressure fractionation of the recovered

Fig. 9



volatile reaction mixture was utilised for the removal of gaseous components, which were identified initially by infra-red spectroscopy and frequently shown to be unreacted polyfluoro-olefin. Exploitation of the Gas Density Balance (column "O", 78°C) permitted analysis of, and product yield estimation in the residual colourless or pale yellow liquid, the components of which were frequently separated by preparative scale gas chromatography.

The residual involatile reaction material was poured into water (400 mls.), extracted with ether (4 x 25 mls.) and the combined extracts washed with water (2 x 10 mls.). After drying ($MgSO_4$) and filtering the extracts, removal of the solvent invariably left a dark brown tarry residue, vacuum distillation of which gave small amounts of yellow oil and intractable tar.

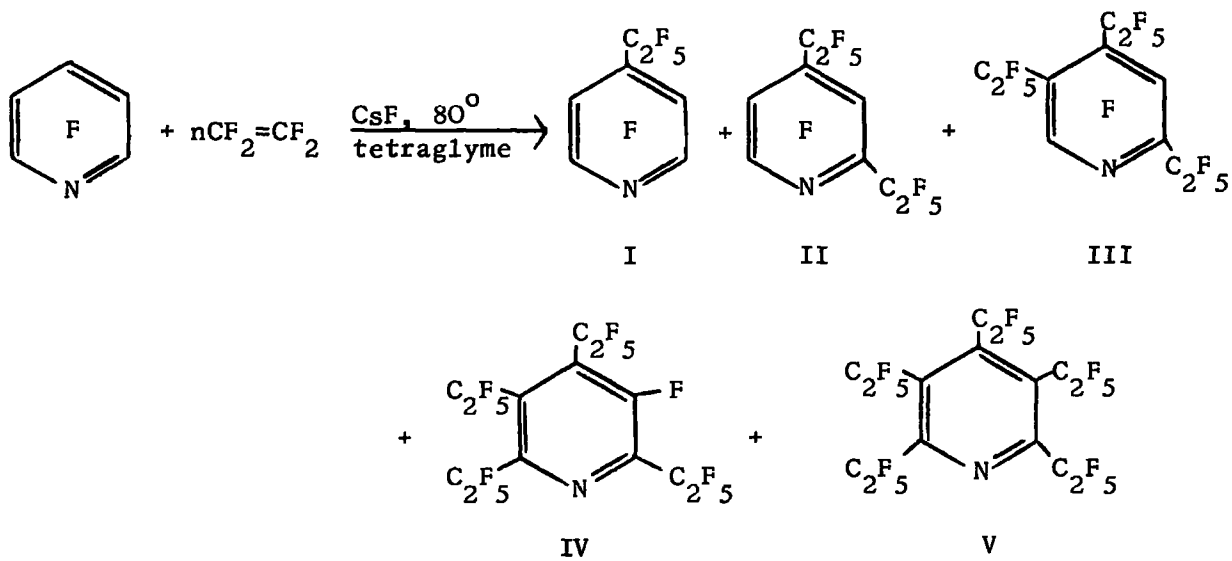
Chromatographic analysis (G.D.B., column "O", 150°C) of the oil frequently indicated the presence of extracted dipolar aprotic solvent and higher boiling material, possibly olefin oligomers, formed in side reactions.

CHAPTER 6

Experimental for Chapter 3

6.1. Reactions of tetrafluoroethylene with pentafluoropyridine.

Atmospheric pressure, fluoride ion-initiated reactions of tetrafluoroethylene and pentafluoropyridine resulted in the formation of perfluoroethylpyridines as shown in Scheme 1.



Scheme 1

6.1.1. Short reaction times.

A series of reactions was undertaken to investigate the effect of reaction time upon product distribution at 80°. The standard experimental procedure was adopted (See p. 141), using caesium fluoride (3·0 g., 20 m.moles), tetraglyme (40 mls.), pentafluoropyridine (3·0 g., 17·8 m.moles) and excess tetrafluoroethylene (10·0 g., 100 m.moles).

The gaseous material recovered was shown, by infra-red spectroscopy, to be entirely unreacted tetrafluoroethylene. Chromatographic analysis (G.D.B., column "O", 78°) of the volatile material indicated unreacted pentafluoropyridine and perfluoroethylpyridines, I (shortest ret. time)

to V (longest ret. time), in various proportions depending upon the reaction time. Similar analysis of the extracted material showed, for the longer reaction times, small amounts of III, IV and V only. Total yields of products, calculated from the chromatogram and based on the weight of pentafluoropyridine consumed, are summarised in Table 12.

Separation of the mixtures obtained from the above reactions was effected, with difficulty, by preparative scale gas chromatography (Aerograph, column "O", 80°). Only products I, II and III were characterised fully since IV was difficult to obtain pure in reasonable quantities, and V has been characterised previously.[101]

I was shown to be perfluoro-(4-ethylpyridine) b.pt. 114-115°. (Found: C, 31·5; F, 64·1%; M, 269. C_7F_9N requires C, 31·2; F, 63·6%; M, 269). I.R. spectrum No. 1. λ_{max} (cyclohexane) = 280·5 mμ; (ε, 3865).

Broad absorptions in the ^{19}F n.m.r. at 89·0 and 140·3, due to two fluorines each, were assigned to the 2,6 and 3,5 ring positions respectively, consistent with calculated chemical shifts. Further absorptions at 86·6, (CF_3-) and 113·2, (CF_2-) were also observed.

II was shown to be perfluoro-(2,4-diethylpyridine), b.pt. 140-141°. (Found: C, 29·5; F, 66·5%; M, 369. $C_9F_{13}N$ requires C, 29·3; F, 66·9%; M, 369). I.R. spectrum No. 2. λ_{max} (cyclohexane) = 275·5 mμ; (ε, 4747).

Broad absorptions in the ^{19}F n.m.r. at 83·8, 118·5 and 126·4, due to single fluorines, were assigned to the 6, 3 and 5 ring positions respectively and were consistent with calculated chemical shifts for 2 substitution by C_2F_5- in I. Further absorptions at 84·9, (2-CF_3); 86·6, (4-CF_3); 113·5, (4-CF_2) and 116·9, (2-CF_2) were assigned from the chemical shift and observed fine structure.

Table 12

Reaction Time (hours)	Weight of recovered C_2F_4	Weight of recovered volatile material	Products: Percentage Yields* (%)					Conversion %
			C_7F_9N I	$C_9F_{13}N$ II	$C_{11}F_{17}N$ III	$C_{13}F_{21}N$ IV	$C_{15}F_{25}N$ V	
1	8•5 g.	3•1 g.	76	-	-	-	-	16
2	7•5 g.	3•25 g.	49	13	4	-	-	53
3	7•0 g.	3•6 g.	46	17	10	-	-	62
4	7•0 g.	3•6 g.	41	18	10	-	-	63
5	7•5 g.	3•8 g.	38	19	12	1•5	-	68
6	6•5 g.	3•8 g.	37	15	13	3	-	72
7	6•5 g.	3•9 g.	36	16	30	3	5	76
8	6•0 g.	3•8 g.	27	20	32	6•5	5•5	79

* Based on the weight of C_5F_5N consumed.

III was characterised as perfluoro-(2,4,5-triethylpyridine), b.pt. 165-166°. (Found: C, 28·2; F, 68·5%; M, 469. $C_{11}F_{17}N$ requires C, 28·2; F, 68·8%; M, 469). I.R. spectrum No. 3. λ_{max} (cyclohexane) = 285 mμ; (ε, 6470).

Broad absorptions in the ^{19}F n.m.r. at 55·5 and 115·7, due to single fluorines, were assigned to the 6 and 3 ring positions respectively, and were consistent with the calculated chemical shifts for 5 substitution by C_2F_5- in II. Further resonances at 81·4, (4 and 5-CF_3); 83·2, (2-CF_3); 103·3, (4 and 5-CF_2) and 116·0, (2-CF_2) were observed; assignments were based upon the similarity of the electronic environment of the 4 and 5 pentafluoroethyl groups.

6.1.2. Long reaction times.

Two identical atmospheric pressure reactions at (a) ca. 80° and (b) ca. 120° for 7 days were carried out using caesium fluoride, tetraglyme, pentafluoropyridine and tetrafluoroethylene (for quantities, See Table 13). The recovered gaseous material was identified as unreacted tetrafluoroethylene, by comparison of the i.r. spectrum with that of an authentic sample. Recovered products, for both reactions, consisted of a colourless liquid and a white crystalline solid, identified as V by comparison of the i.r. spectrum with that of an authentic sample obtained previously.[101]

In both cases, chromatographic analysis (G.D.B., column "O", 78°) of the colourless liquid indicated the presence of III, IV, V and an unknown product of almost identical retention time to IV. Attempted preparative scale v.p.c. separation (Aerograph, columns "O" and "A", 80°) was futile, and gave only sufficient of the unknown compound for a mass spectrum, which had a similar breakdown pattern to known perfluoroalkylpyridines and $^m/e$ = 769. It is tentatively suggested that such a product results

Table 13

	C_5F_5N	C_2F_4	CsF	Tetra-glyme	Weight of recovered C_2F_4	Weight of volatile product	Weight of white solid	Weight of residual yellow oil	Estimated Yields* III	V
(a)	3·0 g., 17·8 m.moles	10·0 g., 100 m.moles	3·0 g., 20·0 m.moles	40 mls.	2·0 g., 20 m.moles	3·0 g.	1·6 g.	4·4 g.	8%	20%
(b)	3·0 g., 17·8 m.moles	10·0 g., 100 m.moles	3·0 g., 20·0 m.moles	40 mls.	1·0 g., 10 m.moles	3·2 g.	0·95 g.	3·0 g.	7%	12%

* Based on 100% conversion.

from the dimerisation of tetrafluoroethylene and subsequent reaction of the perfluoro-sec.-butyl anion with pentafluoropyridine, II or IV.

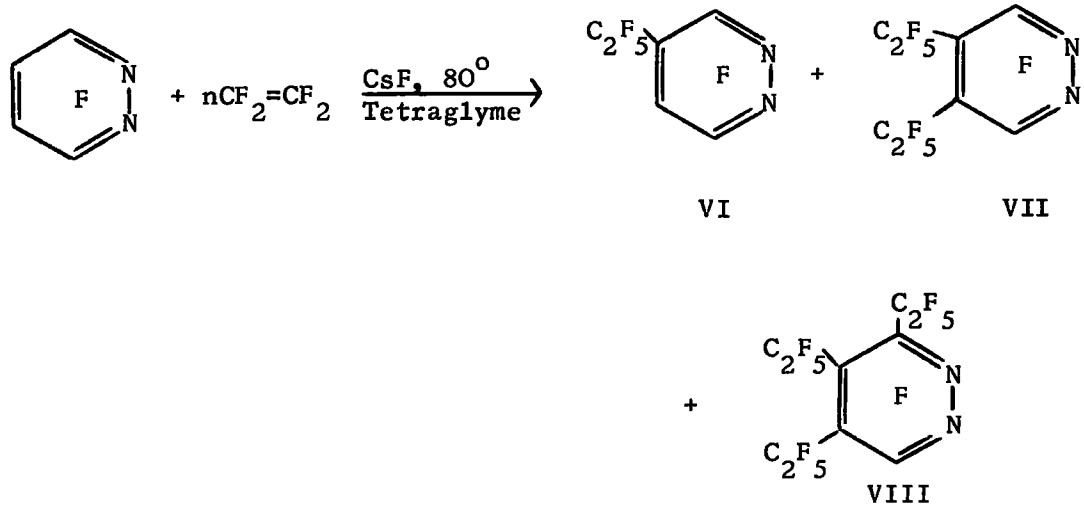
The involatile reaction mixtures were worked up as usual and resulted in yellow oils which, on analysis (G.D.B., column "O", 78°), did not contain any perfluoroethylpyridines.

6.2. Reactions of tetrafluoroethylene with tetrafluoropyridazine.

Atmospheric pressure, fluoride ion-initiated reactions of tetrafluoroethylene and tetrafluoropyridazine, of less than 5 hours and analogous to 6.1.1., resulted in the formation of perfluoroethylpyridazines as shown in Scheme 2.

6.2.1. Short reaction times.

The standard experimental procedure was adopted (See p. 141). Reaction times exceeding five hours were not investigated owing to the



Scheme 2

low recovery of volatile products and the increased formation of intractable tarry residues. Caesium fluoride (3·0 g., 20·0 m.moles), tetraglyme (35 mls.), tetrafluoropyridazine (3·0 g., 19·7 m.moles) and excess tetrafluoroethylene (10·0 g., 100 m.moles) were stirred vigorously at ca. 80°.

The recovered gaseous material was identified, by comparison of the i.r. spectrum with that of an authentic sample, as unreacted tetrafluoroethylene. Chromatographic analysis (G.D.B., column "O", 78°) of the recovered volatile material indicated unreacted tetrafluoropyridazine and perfluoroethylpyridazines, VI (shortest ret. time) to VIII (longest ret. time), in various proportions depending upon the reaction time. A similar analysis of the extracted involatile reaction mixture showed the absence of VI, VII and VIII. The quantities of recovered materials and yields of products, calculated from the chromatogram and based on the weight of tetrafluoropyridazine consumed, are summarised in Table 14.

The mixtures obtained were separated, with difficulty by preparative scale v.p.c. ("F21" and Aerograph, column "O", 80°). The products, VI to VIII were subsequently characterised.

VI was shown to be perfluoro-(4-ethylpyridazine), b.pt. 144°. (Found: C, 28·3; F, 60·6%; M, 252. $C_6F_8N_2$ requires C, 28·5; F, 60·4%; M, 252). I.R. spectrum No. 4. λ_{max} (cyclohexane) = 262·5 mμ; (ε, 2582).

Broad absorptions in the ^{19}F n.m.r. at 77·4, 97·5 and 120·6, due to single fluorines, were assigned to the 3, 6 and 5 ring positions respectively, and were consistent with calculated chemical shifts for 4-substitution in tetrafluoropyridazine. Further resonances at 87·0, (CF_3) and 115·0, (CF_2) were also observed.

VII was identified as perfluoro-(4,5-di-ethylpyridazine), m.pt. 37-37·5°. (Found: C, 27·5; F, 64·2%; M, 352. $C_8F_{12}N_2$ requires C, 27·3; F, 64·8%; M, 352). I.R. spectrum No. 5. λ_{max} (cyclohexane), 277 and 285·5 infl. mμ; (ε, 4990 and 4475 respectively).

A broad absorption in the ^{19}F n.m.r. at 77·7, due to two fluorines, was assigned to the 3,6 ring positions and was consistent with the calculated chemical shift for 5 substitution by C_2F_5- in VI. Two resonances at 82·6, (4 and 5-CF_3) and 107·2, (4 and 5-CF_2) confirmed the

Table 14

Reaction Time hrs.	Weight of recovered C_2F_4	Weight of recovered volatile material	Weight of recovered involatile material	Products: Percentage Yields* (%) $C_6F_8N_2$ VI	$C_8F_{12}N_2$ VII	$C_{10}F_{16}N_2$ VIII	Conversion %
1	9•0 g.	2•7 g.	0•9 g.	37	7	-	45
2	8•5 g.	2•1 g.	1•9 g.	21	11	2	94
3	7•5 g.	1•7 g.	2•85 g.	13	8	3	100
4	7•0 g.	1•35 g.	4•2 g.	9	6	5	100
5	7•0 g.	0•75 g.	4•9 g.	4	3	4	100

* Based on the weight of $C_4F_4N_2$ consumed.

symmetrical substitution pattern.

VIII was shown to be perfluoro-(3,4,5-tri-ethylpyridazine), b.pt. 174-175°. (Found: C, 26·3; F, 66·7%; M, 452. $C_{10}F_{16}N_2$ requires C, 26·5; F, 67·3%; M, 452). I.R. spectrum No. 6. λ_{max} (cyclohexane) = 268 mμ; (ε, 3130).

A broad absorption in the ^{19}F n.m.r. at 70·2, due to a single fluorine, was assigned to the 6 ring position and was consistent with the calculated chemical shift for 3 substitution by C_2F_5- in VII. Complex resonances at 81·0, (4 and 5-CF_3) and 74·5, (3-CF_3), and broad absorptions at 93·0, 104·7 and 108·0, due to the difluoromethylene moieties, were also observed.

6.3. Reaction of perfluoroisobutene with pentafluoropyridine.

6.3.1. Excess perfluoroisobutene.

The hazardous nature of perfluoroisobutene necessitated the use of a slightly modified experimental technique for atmospheric pressure reactions. Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan (35 mls.) and pentafluoropyridine (3·0 g., 17·8 m.moles) were introduced into the baked, purged apparatus (Fig. 10), which was subsequently sealed. After cooling the reaction flask in liquid air, the apparatus was evacuated. Perfluoroisobutene, from a pre-weighed cylinder, was admitted to the isolated apparatus, as it was heated to ca. 80°, until a small positive pressure was exerted. Rapid vacuum formation was observed when the reaction mixture was stirred vigorously, and further quantities of olefin were admitted to the apparatus. After ca. 30 mins. the rate of reaction decreased, even with a small positive pressure, and stirring was continued for a further 6½ hr.; a vacuum was formed slowly owing to dimerisation[84] of the olefin. The weight of perfluoroisobutene consumed (15·0 g.,

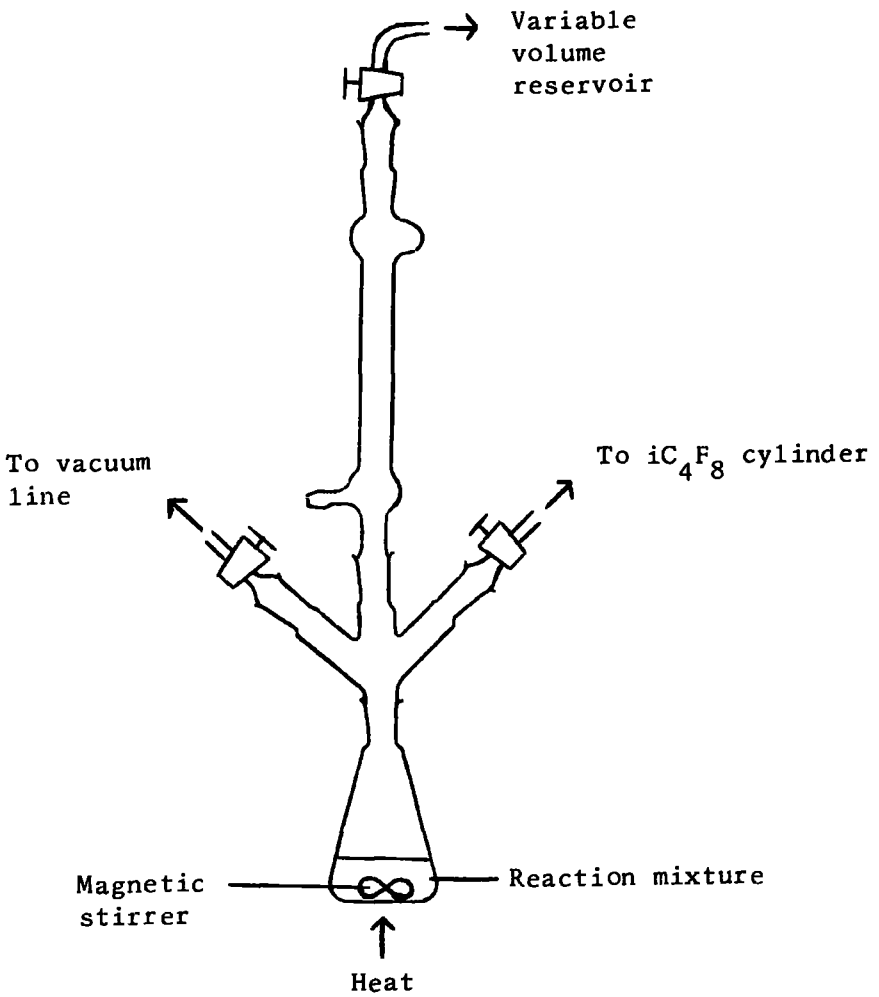


Fig. 10

75 m.moles) was obtained, after the reaction, on weighing the cylinder.

Removal of the volatile reaction product, under vacuum at temperatures up to ca. 90°, gave a colourless liquid (4·0 g.) and a white solid, which was contaminated with sulpholan. Chromatographic analysis (G.D.B., column "O", 78°) of the former indicated dimers of perfluoroisobutene and dissolved white solid. The contaminated solid was washed with boiling water to remove the sulpholan, filtered and recrystallised from ethyl acetate to give a white crystalline solid (10·0 g.), perfluoro-(2,4,6-tri-t-butylpyridine) (85% yield) m.pt. 161-162°. (Found: C, 26·4; F, 71·9%; M, 769. $C_{17}F_{29}N$ requires C, 26·5; F, 71·7%; M, 769). I.R. spectrum No. 7.

^{19}F n.m.r. (ca. 180°) showed three absorptions, two of which overlapped, at (a) 60·7, (4-$(CF_3)_3C$); (b) 61·8, (2,6-$(CF_3)_3C$); (c) 87·3, (3,5-F); integration of (a + b):c was 27:2.

The residual involatile reaction mixture was worked up in the usual manner and gave only a small amount (0·2 g.) of intractable tar.

6.4. Reaction of perfluoroisobutene with tetrafluoropyridazine.

6.4.1. Excess perfluoroisobutene.

The procedure adopted was identical with that described in 6.3.1. Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan (35 mls.), tetrafluoropyridazine (3·0 g., 19·7 m.moles) and perfluoroisobutene (12·0 g., 60·0 m.moles) were stirred vigorously at ca. 80° for 10 hours; a vacuum was formed. Removal of the volatile reaction products under vacuum at temperatures up to ca. 90° gave a colourless liquid (1·4 g.). Chromatographic analysis (G.D.B., column "O", 78°) showed oligomers of the olefin and two products. The major product had an identical retention time to the crystalline solid isolated from the involatile reaction mixture.

A sulpholan and water insoluble product, which had partially sublimed, was filtered off during the standard work-up procedure and recrystallised from acetone to give a white solid (7·5 g.), perfluoro-(3,6-di-t-butylpyridazine), m.pt. 135-136° (75% yield). (Found: C, 26·3; F, 69·3%; M, 552. $C_{12}F_{20}N_2$ requires C, 26·1; F, 68·8%; M, 552). I.R. spectrum No. 8.

Absorptions in the ^{19}F n.m.r. (acetone) at 62·4 and 129·2 in the ratio 9:1 were assigned to the 3,6-$(CF_3)_3C$ and 4,5 ring fluorines respectively; the latter was consistent with approximate calculated chemical shifts for 3,6 rather than 4,5 di-substitution.

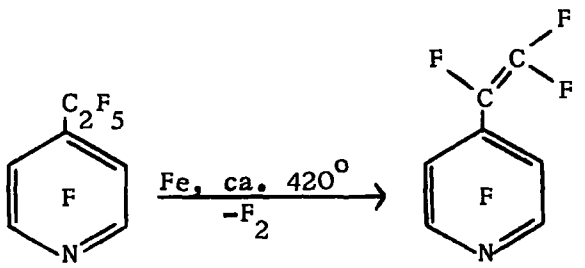
Extraction of the aqueous involatile reaction mixture gave only a small amount (0·35 g.) of intractable tar.

6.5. Reactions of perfluoroalkylpyridines.

6.5.1. Defluorination Reactions.

The standard procedure employed in these reactions was to pass the compound to be defluorinated through a silica tube (ca. 75 cms. in length), containing a suitable defluorinating agent (coarse iron filings or zinc dust/shavings as specified), by means of a steady flow of nitrogen, and application of heat to the sample. The defluorination tube was heated by a cylindrical heater and the products were collected in a cold trap. The average nitrogen flow rate was approximately 1 litre/hour.

(a) Defluorination of perfluoro-(4-ethylpyridine), C_7F_9N.



I IX

C_7F_9N (I) was passed in the vapour phase through the silica tube containing coarse iron filings. The reaction was investigated over a range of temperatures (See Table 15). Chromatographic analysis (G.D.B., column "A", 78°) of the products indicated unreacted starting material and a single product (IX).

The product obtained, after separation (Aerograph, column "O", 90°) was a colourless liquid, identified as perfluoro-(4-vinylpyridine), b.pt. 130°. (Found: C, 36·1; F, 58·0%; M, 231. C_7F_7N requires C, 36·4; F, 57·6%; M, 231). I.R. spectrum No. 9. λ_{max} (cyclohexane) = 249 and 282 mμ; (ε, 7430 and 6550).

Table 15

Temp. °C	C_7F_9N	Weight recovered	Products Yield* C_7F_7N	Conversion
410	1·0 g., 3·7 m.moles	0·8 g.	50%	35%
420	1·0 g., 3·7 m.moles	0·6 g.	40%	60%
450	1·0 g., 3·7 m.moles	0·25 g.	25%	95%

* Based on the weight of C_7F_9N consumed.

Broad absorptions in the ^{19}F n.m.r. at 89·2 and 138·8, due to two fluorines each, were assigned to the 2,6 and 3,5 ring positions respectively. Further absorptions at 93·8, 124·1 and 175·6 were assigned, by comparison with the spectrum of octafluorostyrene,[151] to the vinylic fluorines.

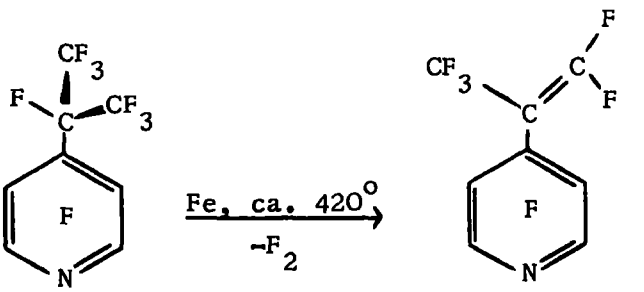
(b) Attempted defluorination of C_7F_9N over zinc.

C_7F_9N (I) was passed in the vapour phase through a silica tube packed with a mixture of zinc dust and shavings at various temperatures (See Table 7). Chromatographic analysis (G.D.B., columns "O" and "A", 78°) of the recovered product showed unreacted starting material and, for higher temperatures, low yields of C_7F_7N (IX); the yield of product at ca. 380° was ~12%.

Table 7

Temp. °C	C_7F_9N	Products
280	1·0 g., 3·7 m.moles	0·8 g. unchanged C_7F_9N
320	0·6 g., 2·2 m.moles	0·55 g. unchanged C_7F_9N
380	0·7 g., 2·6 m.moles	0·2 g. mixture of C_7F_9N and C_7F_7N

(c) Defluorination of perfluoro-(4-isopropylpyridine), $C_8F_{11}N$.



X

$C_8F_{11}N$ was passed in the vapour phase through the silica tube containing coarse iron filings. The reaction was investigated over a range of temperatures (See Table 8).

Table 8

Temp. °C	$C_8F_{11}N$	Weight	Products Yield* C_8F_9N	Conversion
350	1·0 g., 3·14 m.moles	0·5 g.	45%	85%
420	1·0 g., 3·14 m.moles	0·4 g.	45%	100%
450	1·0 g., 3·14 m.moles	Only gaseous material recovered		

*Yield of C_8F_9N based on the weight of $C_8F_{11}N$ consumed.

The product obtained, X, was a colourless liquid identified as 2-(2′,3′,5′,6′-tetrafluoropyridyl)-pentafluoropropene, b.pt. 135°. (Found: C, 34·1; F, 60·5%; M, 281. C_8F_9N requires C, 34·2; F, 60·1%; M, 281). I.R. spectrum No. 10. λ_{max} (cyclohexane) = 276·5 mμ; (ε, 3760).

Broad absorptions in the ^{19}F n.m.r. at 89·2 and 139·8, both due to two fluorines, were assigned to the 2,6 and 3,5 ring positions respectively. Further resonances at 59·5 and 68·5 were assigned to the trifluoromethyl and vinyl fluorines respectively; the latter was complex.

6.5.2. Nucleophilic substitution with methoxide ion.

The standard procedure employed for nucleophilic substitution reactions with methoxide ion (CH_3O^-) was the addition of a predetermined volume of standard methanolic sodium methoxide solution, diluted with a similar volume of dry methanol, to a dry methanolic solution (30 mls.) of the compound at room temperature in baked, purged apparatus. The dropwise addition, with stirring, was carried out over a period of approximately one hr. The reaction mixture was stirred for a further 3 hr., with heat if necessary, poured into water (300 mls.), acidified, and the aqueous mixture extracted with methylene chloride (4 x 25 mls.). The combined extracts were washed with water (2 x 10 mls.), dried ($MgSO_4$), and the product obtained on removal of the solvent.

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

The standard experimental procedure was adopted, with addition of 28·3 mls. 0·08M methanolic sodium methoxide (2·3 m.moles) and dry methanol (25 mls.) to a stirred solution of perfluoro-(4-ethylpyridine) (0·6 g., 2·2 m.moles) in dry methanol (30 mls.). The recovered product, after the work-up procedure, was a single component (column "A", 125°), pale yellow liquid which was shown to be 4-pentafluoroethyl-2-methoxy-3,5,6-trifluoropyridine, (0·5 g., 80% yield), b.pt. 164-165°. (Found: C, 34·3; H, 1·3; F, 53·5%; M, 281. $C_8H_3F_8NO$ requires C, 34·2; H, 1·1; F, 54·1%; M, 281). I.R. spectrum No. 11. λ_{max} (cyclohexane) = 299 mμ; (ε, 5180).

Broad absorptions in the ^{19}F n.m.r. at 91·6, 139·0 and 151·5, due to single fluorines, were assigned to the 6, 3 and 5 ring positions and were consistent with the calculated chemical shifts. Further resonances at 86·0, (4-CF_3); 112·9, (4-CF_2) and, in the ^1H n.m.r., 4·0, (OCH_3) were also observed.

(b) Preparation of 2,4-perfluorodi-ethyl-5-methoxy-3,6-difluoropyridine.

Two reactions were carried out, at ca. 20° and 70°, between perfluoro-(2,4-di-ethylpyridine) (0·5 g., 1·36 m.moles) in dry methanol (30 mls.) and 17·2 mls. 0·08M methanolic sodium methoxide (1·38 m.moles) in dry methanol (15 mls.) using the standard procedure. Solvent extraction with methylene chloride gave, in both cases, identical, single component (column "A", 125°), pale yellow liquids which were shown to be 2,4-perfluorodi-ethyl-5-methoxy-3,6-difluoropyridine, (0·45 g., 85% yield), b.pt. 195-196°. (Found: C, 31·2; H, 1·0; F, 59·8%; M, 381. $C_{10}H_3F_{12}NO$ requires C, 31·5; H, 0·8; F, 59·8%; M, 381). I.R. spectrum No. 12. λ_{max} (cyclohexane) = 286 mμ; (ε, 5025).

Broad absorptions in the ^{19}F n.m.r. at 77·8 and 123·2, due to single fluorines, were assigned to the 6 and 3 ring positions respectively and were consistent with the calculated chemical shifts, which were sufficiently different for 5 and 6 substitution to differentiate the two possibilities. Further absorptions at 85·5, (2-CF_3); 86·4, (4-CF_3); 116·4, (4-CF_2); 117·2, (2-CF_2) and, in the ^1H n.m.r., at 3·9, (OCH_3) were also observed.

(c) Preparation of 2,4-perfluorodi-isopropyl-5-methoxy-3,6-difluoro-pyridine.

Reaction of perfluoro-(2,4-di-isopropylpyridine) (0·5 g., 1·07 m.moles) in dry methanol (30 mls.) with 13·6 mls. 0·08M methanolic sodium methoxide (1·09 m.moles) in dry methanol (10 mls.), using the standard procedure at ca. 20° and 85°, gave a single component (column "A", 125°), pale yellow liquid which was shown to be 2,4-perfluorodi-isopropyl-5-methoxy-3,6-difluoropyridine, (0·45 g., 88% yield), b.pt. 199-200°. (Found: C, 29·7; H, 0·6; F, 63·1%; M, 481. $C_{12}H_3F_{16}NO$ requires C, 29·9; H, 0·6; F, 63·2%; M, 481). I.R. spectrum No. 13. λ_{max} (cyclohexane) = 286 mμ; (ε, 5620).

Broad absorptions in the ^{19}F n.m.r. at 78•7 and 120•2, comparable to (b) previously and due to single fluorines, were similarly assigned to the 6 and 3 ring positions respectively. Absorptions were also observed for the trifluoromethyl groups, (76•2), and tertiary fluorines, (179•6 and 185•5), of the isopropyl substituents and, in the ^{1}H n.m.r., for the methoxyl group, (3•8).

6.6. Reactions of perfluoroalkylpyridazines.

6.6.1. Nucleophilic substitution with methoxide ion.

(a) Preparation of 4-pentafluoroethyl-5-methoxy-3,6-difluoropyridazine.

Reaction of perfluoro-(4-ethylpyridazine) (0•5 g., 1•98 m.moles) in dry methanol (30 mls.) with 22•0 mls. 0•096M methanolic sodium methoxide in dry methanol (20 mls.), using the standard procedure (6.5.2.) at ca. 70°, gave a single component (column "A", 125°), yellow liquid which was shown to be 4-pentafluoroethyl-5-methoxy-3,6-difluoropyridazine, (0•4 g., 75% yield), decomposed above 100°. (Found: C, 32•0; H, 1•3; F, 50•1%; M, 264. $C_7H_3F_7N_2O$ requires C, 31•8; H, 1•1; F, 50•4%; M, 264). I.R. spectrum No. 14.

Broad absorptions in the ^{19}F n.m.r. at 81•4 and 90•2, due to single fluorines, were assigned to the 3 and 6 ring positions respectively and were consistent with the calculated chemical shifts, which were sufficiently different for 3,5 and 6 substitution to differentiate the possibilities. Further resonances were observed at 85•5, ($4-CF_3$); 113•6, ($4-CF_2$) and, in the ^{1}H n.m.r., 4•2, (OCH_3).

6.6.2. Attempted hydrolysis reactions of perfluoro-(3,6-di-t-butyl-pyridazine).

(a) Sulphuric acid.

i) $C_{12}F_{20}N_2$ (0•5 g., 0•9 m.moles) in concentrated sulphuric

acid (12 mls.) was treated dropwise with water (35 mls.) during 90 mins. with vigorous stirring. The mixture was stirred for a further 60 mins. at ca. 80°, cooled and then extracted with 4 x 25 ml. aliquots of ether. The combined extracts were washed with saturated sodium sulphate solution, dried ($MgSO_4$) and removal of the solvent left a white solid (0·5 g.). This was recrystallised from acetone and was shown, by infra-red and ^{19}F n.m.r. spectroscopy, to be entirely unreacted starting material.

ii) $C_{10}F_{20}N_2$ (1·0 g., 1·8 m.moles) in conc. sulphuric acid (10 mls.) and water (5 drops) was heated to ca. 160° for 45 hr. A white sublimate collected in the condenser and was recrystallised from acetone to give unreacted starting material (0·3 g.) m.pt. 139-140°, identified by comparison of the infra-red spectrum with that of an authentic sample. The remaining sulphuric acid solution was poured into water and the resulting precipitate (0·5 g.) washed with water, sublimed (220°/0·001 mm.) with difficulty to give a light brown powdery solid similar to that obtained in (b), and thought to be polymeric in nature.

(b) Potassium hydroxide in t-butanol.

i) $C_{12}F_{20}N_2$ (0·9 g., 1·6 m.moles), potassium hydroxide (0·4 g., 7·15 m.moles) and t-butanol (9 mls.) were stirred under reflux at ca. 70° for 5 hr. Water (15 mls.) was then added and the alcohol distilled off, giving a white precipitate. The cooled reaction mixture was acidified (dil. HCl) and methylene chloride added; the insoluble precipitate was filtered off. The solid was dried under vacuum at ca. 190°, since an attempted sublimation was unsuccessful, to give a light brown involatile solid (0·7 g.), stable at 350°, (Found: C, 24·1; N, 4·8; F, 56·8%). I.R. spectrum No. 15. Too involatile to obtain a mass spectrum. ^{19}F n.m.r. indicated the possibility of perfluoro-t-

butyl groups but no ring fluorines were observed.

The combined methylene chloride extracts were dried ($MgSO_4$) and removal of the solvent left a small quantity (< 0·1 g.) of intractable residue which was not investigated further.

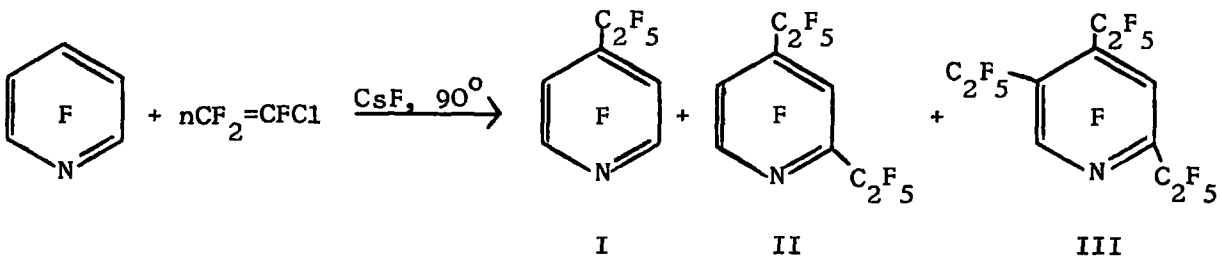
ii) $C_{12}F_{20}O^{N}_{2}$ (0·65 g., 1·2 m.moles), potassium hydroxide (0·2 g., 3·55 m.moles) and t-butanol (9 mls.) were stirred at ca. 25° for 17 hr. Water (15 mls.) was then added and the alcohol distilled off, giving a white precipitate. The cooled reaction mixture was acidified, the precipitate filtered off and dried under vacuum at ca. 190° to give a light brown solid (0·5 g.), the infra-red spectrum of which was identical with that obtained in (i) previously. Extraction of the aqueous solution with methylene chloride gave a yellow oil (< 0·1 g.) which was not identified.

CHAPTER 7

Experimental for Chapter 4

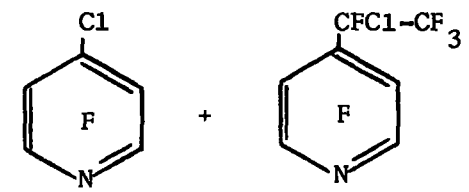
7.1. Chlorotrifluoroethylene, CF_2=CFCl.

7.1.1. Reactions of chlorotrifluoroethylene with pentafluoropyridine.



I II III

Scheme 3



XI XII

Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan or tetraglyme (35 mls.), C_5F_5N (3·0 g., 17·8 m.moles) and CF_2=CFCl (for quantities and reaction conditions, See Table 16) were stirred, in a standard atmospheric pressure reaction (See p. 141), at ca. 90°. Removal of the volatile products under vacuum gave unreacted CF_2=CFCl, identified by i.r. spectroscopy, and a colourless liquid. Chromatographic analysis (G.D.B., column "O", 78°) of the latter showed, in order of increasing retention times, unreacted C_5F_5N, I, II, III, XI and XII, 1-chloro-1-(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane, (Scheme 3). The products were separated by preparative scale v.p.c. (Aerograph, column "O", 80°) and identified by comparison of the i.r. spectra with those of authentic samples. Vacuum distillation of the extracts of the involatile reaction mixtures gave small quantities of yellow oily liquids which did not contain any identifiable products.

Table 16

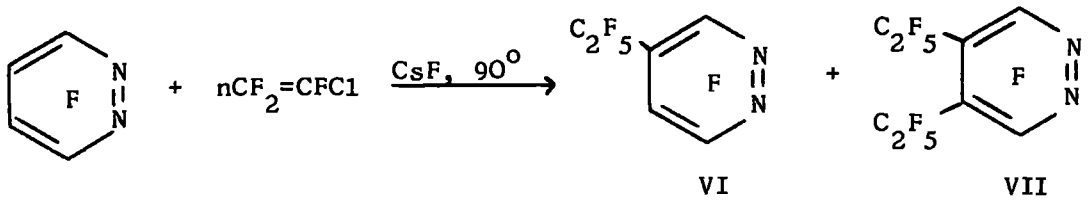
Solvent	Reaction Time	CF_2=CFCl Initially	CF_2=CFCl Recovered	Weight of Volatile Products	Weight of Residue	Percentage Yields* I	II	III	XI	XII	Conversion
S	4 hr.	9·0 g., 77·2 m.moles	2·0 g.	2·3 g.	0·8 g.	15	4	3	4	15	78%
S	24 hr.	12·0 g., 103 m.moles	3·0 g.	3·1 g.	1·0 g.	19	8	8	5	17	82%
T	4 hr.	8·0 g., 68·6 m.moles	1·8 g.	3·2 g.	1·2 g.	-	6	4	8	46	67%
T	24 hr.	9·0 g., 77·2 m.moles	1·9 g.	3·1 g.	1·0 g.	-	5	8	9	40	76%

* Based on the weight of C_5F_5N consumed.

S = Sulpholan.

T = Tetraglyme.

7.1.2. Reactions of chlorotrifluoroethylene and tetrafluoropyridazine.



VI VII

Scheme 4 + unidentified product (< 5%)

(a) Two identical atmospheric pressure reactions (See p. 141) with (i) sulpholan and (ii) tetraglyme were carried out in which caesium fluoride (3·0 g., 20·0 m.moles), solvent (35 mls.), $C_4F_4N_2$ (4·0 g., 26·3 m.moles) and CF_2=CFCl (for quantities and yields, See Table 17) were stirred at ca. 90° for 24 hr. Removal of the volatile products under vacuum gave unreacted CF_2=CFCl, identified by i.r. spectroscopy, and a pale yellow lachrymatory liquid. Chromatographic analysis (G.D.B., column "O", 78°) of the latter showed unreacted $C_4F_4N_2$, two products (VI) and (VII) (Scheme 4) and a small quantity of unidentified material (< 5%) with similar retention time to 4-chloro-3,5,6-trifluoropyridazine. VI and VII were separated by preparative scale v.p.c. (Aerograph, column "O", 95°) and identifed by comparison of the i.r. and ^{19}F n.m.r. spectra with those of authentic samples.

Table 17

	CF_2=CFCl		Weight of volatile product	Percentage Yield*		Conversion
	Initially	Recovered		VI	VII	
(i)	8·0 g., 68·6 m.moles	5·0 g.	5·3 g.	57	19	58%
(ii)	10·0 g., 85·8 m.moles	2·0 g.	4·2 g.	41	9	53%

* Based on the weight of $C_4F_4N_2$ consumed.

Extraction of the involatile reaction mixture gave small quantities (approx. 0·1 g.) of yellow oily residue which did not contain any identifiable products.

(b) Potassium fluoride (7·0 g., 120·7 m.moles), sulpholan (45 mls.), $C_4F_4N_2$ (5·0 g., 32·8 m.moles) and CF_2=CFCl (11·0 g., 94·4 m.moles) were stirred in a standard atmospheric pressure reaction (See p. 141), at ca. 120° for 9 hr. Removal of the volatile products under vacuum gave unreacted CF_2=CFCl (2·0 g.), identified by i.r. spectroscopy, and a pale yellow liquid (7·0 g.). Chromatographic analysis (G.D.B., column "O", 78°) of the latter showed a three component mixture of VI, VII and perfluoro-(3,4,5-tri-ethylpyridazine) in 23%, 32% and 9% yields respectively. The products were separated by preparative scale v.p.c. (Aerograph, column "O", 95°) and identified by comparison of the i.r. and ^{19}F n.m.r. spectra with those of authentic samples. Extraction of the involatile reaction mixture gave an intractable tarry residue (3·6 g.).

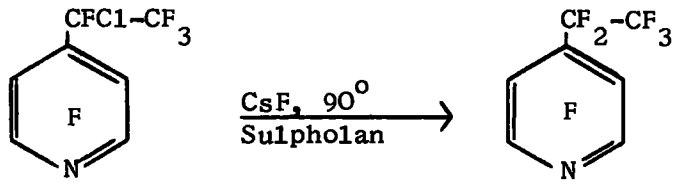
7.1.3. Reaction of chlorotrifluoroethylene and cyclohexene.

Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan (35 mls.), cyclohexene (12·0 g., 146·3 m.moles) and CF_2=CFCl (8·0 g., 68·6 m.moles) were stirred, in a standard atmospheric pressure reaction (See p. 141), at ca. 90° for 17 hr. Removal of the volatile products under vacuum gave unreacted CF_2=CFCl (0·5 g.), identified by i.r. spectroscopy, and a colourless liquid (11·6 g.). Chromatographic analysis (G.D.B., column "O", 78°) of the latter showed a single component which was identified as cyclohexene by comparison of the i.r. spectrum with that of an authentic sample. Vacuum distillation of the extracts of the involatile reaction mixture gave a small quantity of yellow oil (0·3 g.), identified by i.r. spectroscopy as sulpholan, and an intractable tarry residue (5·7 g.).

7.1.4. Reactions of C_7F_8NCl, (XII).

(a) With caesium fluoride.

i) Atmosphere of nitrogen.

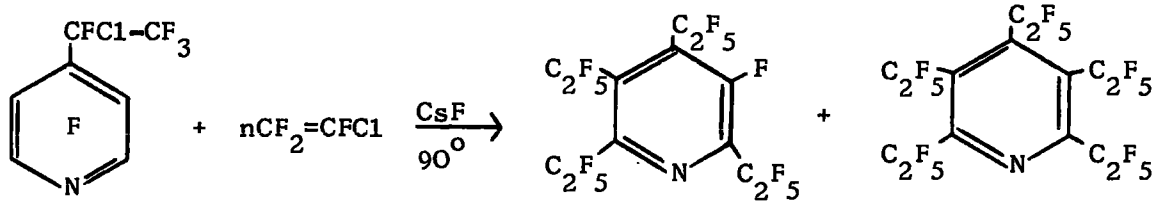


XII I

Caesium fluoride (2·0 g., 13·3 m.moles), sulpholan (20 mls.) and C_7F_8NCl (XII) (0·95 g., 3·3 m.moles) were stirred under an atmosphere of dry nitrogen at ca. 90° for 24 hr. Removal of the volatile products under vacuum gave a colourless liquid (0·6 g.) which was shown to be a single component (G.D.B., column "O", 78°) and identified by i.r. and ^{19}F n.m.r. spectroscopy as perfluoro-(4-ethylpyridine) (60% yield; 100% conversion). Extraction of the involatile reaction mixture gave an intractable tarry residue (0·1 g.).

ii) Atmosphere of CF_2=CFCl.

Two atmospheric pressure reactions (See p. 141) for (a) 1 hr. and (b) 48 hr. at ca. 90° were carried out using caesium fluoride, sulpholan,



XII IV V

C_7F_8NCl (XII) and CF_2=CFCl (for quantities, See Table 18). Removal of the volatile products under vacuum gave, in both cases, unreacted CF_2=CFCl, identified by i.r. spectroscopy, and a pale yellow liquid. Chromatographic

Table 18

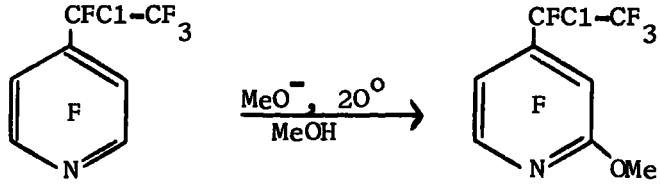
	CsF	Sulpholan	C_7F_8NCl XII	$CF_2=CFCl$ Initially	$CF_2=CFCl$ Recovered	Weight of Volatile product	Weight of Residue
(a)	2·5 g., 16·7 m.moles	10 mls.	1·0 g., 3·5 m.moles	7·0 g., 60·1 m.moles	5·0 g.	0·15 g.	3·1 g.
(b)	3·0 g., 20·0 m.moles	35 mls.	3·0 g., 10·5 m.moles	8·0 g., 68·7 m.moles	1·0 g.	0·55 g.	3·0 g.

analysis (G.D.B., column "O", 78°) of the latter showed the major products to be perfluoro-(tetraethylpyridine) (IV) and pentakis(pentafluoroethyl)pyridine (V), which were separated by preparative scale v.p.c. (F21, column "O", 80°) and identified by comparison of the i.r. spectra with those of authentic samples. Extraction of the involatile reaction mixtures gave intractable tarry residues.

Reaction (iia) was repeated using caesium fluoride (2·5 g., 16·7 m.moles), tetraglyme (10 mls.), C_7F_8NCl (0·9 g., 3·2 m.moles) and CF_2=CFCl (7·0 g., 60·1 m.moles). Chromatographic analysis (G.D.B., column "O", 78°) of the recovered volatile product (0·25 g.) showed it to be similar to (iia). Sublimation of the extracted involatile reaction product (2·0 g.) gave a white crystalline solid (0·05 g.) which was identified as pentakis-(pentafluoroethyl)pyridine (V) by comparison of the i.r. spectrum with that of an authentic sample.

(b) With methoxide ion.

i) One molecular proportion of methoxide ion.



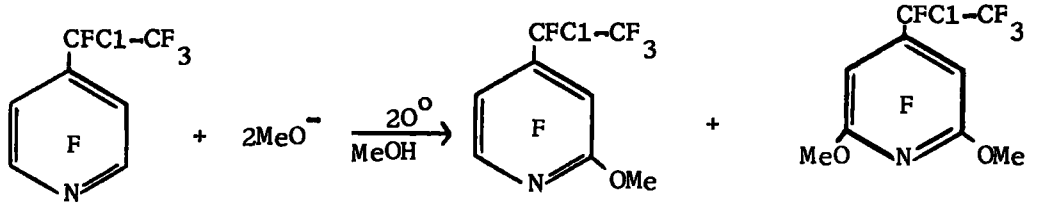
XII XIII

The standard experimental procedure (See 6.5.2) was adopted, with addition of 22·2 mls. 0·08M methanolic sodium methoxide (1·8 m.moles) and dry methanol (20 mls.) to a stirred solution of C_7F_8NCl (XII) (0·5 g., 1·75 m.moles) in dry methanol (30 mls.). The recovered product, after the work-up procedure, was a single component (column "A", 125°), pale yellow liquid which was shown to be 1-chloro-1-(2'-methoxy-3',5',6'-trifluoropyridyl)-

tetrafluoroethane, (0·45 g., 85% yield), b.pt. 192°. (Found: C, 32·0; H, 1·1; Cl, 11·9; F, 44·2%; M,, 297 and 299. $C_8H_3F_7NCl$ requires C, 32·3; H, 1·0; Cl, 11·9; F, 44·7%; M, 297 and 299). I.R. spectrum No. 16. λ_{max} (cyclohexane) = 301 br. mμ; (ϵ, 4265).

Broad absorptions in the ^{19}F n.m.r. at 93·4, 137·2 and 150·0, due to single fluorines were assigned to the 6, 3 and 5 ring positions respectively and were consistent with the calculated chemical shifts. Further resonances were observed at 83·2, (4-CF_3); 125·3, (4-CFCl) and, in the ^1H n.m.r., at 4·1, (OCH_3).

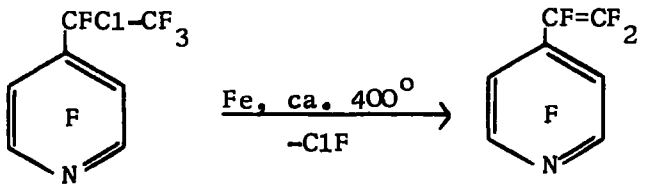
ii) Two molecular proportions of methoxide ion.



XII XIII XIV

Reaction (i) was repeated with addition of 44·4 mls. 0·08M methanolic sodium methoxide (3·6 m.moles) to a stirred solution of C_7F_8NCl (XII) (0·5 g., 1·75 m.moles) in dry methanol (30 mls.). The recovered product (0·5 g.), after the work-up procedure was shown, by ^{19}F n.m.r. and mass spectrometry, to be a 50:50 mixture of XIII and XIV, the mono- and di-methoxy derivatives of C_7F_8NCl (XII) respectively. The three absorptions in the ^{19}F n.m.r. due to XIV at 83·0, (4-CF_3); 124·5, (4-CFCl) and 148·3, (3,5-F) showed that the 2,4,6-substituted isomer, and not the 2,4,5-isomer, was formed. Calculated chemical shifts for the two possible products were sufficiently different to be consistent with the former but not the latter.

(c) Defluorochlorination of C_7F_8NCl.



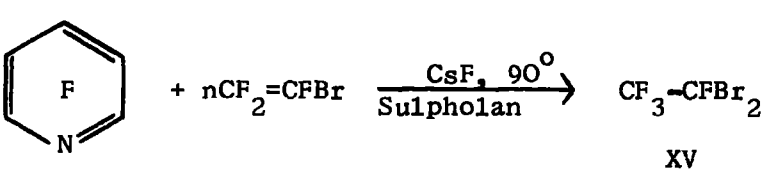
XII IX

A mixture (0·5 g.) containing predominantly C_7F_8NCl (XII) and small amounts of perfluoroethylpyridines was passed in the vapour phase through the silica tube packed with coarse iron filings heated to ca. 400°. Chromatographic analysis (column "A", 75°) of the recovered product (0·2 g.) showed a major component, identified by i.r. spectroscopy as perfluoro-(4-vinylpyridine) (IX), traces of C_7F_8NCl (XII) and perfluoroethylpyridines.

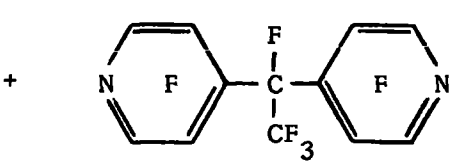
This was not a quantitative result since the preparation of XII in a pure state and high yield had not then been perfected, however it suggested that this was a superior route to IX.

7.2. Bromotrifluoroethylene, CF_2=CFBr.

7.2.1. Reaction of bromotrifluoroethylene with pentafluoropyridine.



XV



Scheme 5

XVI

Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan (35 mls.), C_5F_5N (3·0 g., 17·8 m.moles) and CF_2=CFBr (16·0 g., 100 m.moles) were stirred, in a standard atmospheric pressure reaction (See p. 141), at ca. 90° for 2 hr. Removal of the volatile products under vacuum gave unreacted CF_2=CFBr (5·0 g.), identified by i.r. spectroscopy, and a colourless liquid (4·1 g.). Chromatographic analysis (G.D.B., column "A", 78°) of the latter showed 1,1-dibromotetrafluoroethane (XV) (25% yield, based on the quantity of CF_2=CFBr consumed) and C_5F_5N (17% recovery), both identified by i.r. spectroscopy.

The involatile reaction mixture was washed with water (400 mls.), the insoluble material (4·3 g.) was separated and the aqueous solution extracted. Removal of the solvent, after drying ($MgSO_4$), gave a dark brown oily liquid (2·45 g.) which was vacuum distilled. The collected orange oil (1·2 g.) was shown, by comparison of i.r. and ^{19}F n.m.r. spectra with authentic samples, to contain approximately 35% by weight of 1,1-bis-(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane (XVI), (approx. 15% yield, based on the quantity of C_5F_5N consumed).

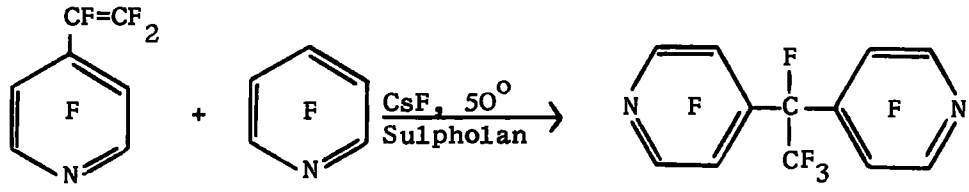
The insoluble material was dissolved in acetone, water (50 mls.) was added to remove the insoluble caesium fluoride, the acetone was then removed under vacuum and the residual aqueous slurry was extracted with ether. The residual orange gum (2·7 g.) did not contain any readily identifiable products.

7.2.2. Attempted reaction of caesium fluoride and carbon tetrabromide.

Caesium fluoride (3·0 g., 20·0 m.moles), acetonitrile (30 mls.), carbon tetrabromide (10·0 g., 30·0 m.moles) and tetrafluoropyridazine (4·0 g., 26·3 m.moles) under dry nitrogen were stirred at ca. 90° for 7 hr.

Chromatographic analysis (G.D.B., column "O", 78 and 150°) of an ether solution of the reaction mixture showed only quantitative recovery of the starting materials.

7.2.3. Preparation of 1,1-bis(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane, $C_{12}F_{12}N_2$.



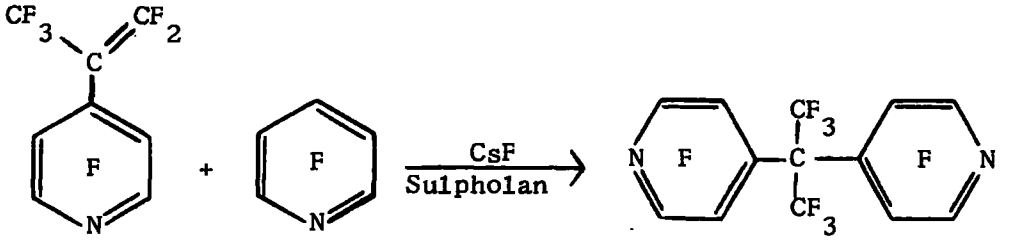
IX XVI

C_7F_7N (IX) (0·9 g., 4·1 m.moles) was added dropwise over 15 min. to stirred caesium fluoride (0·5 g., 3·3 m.moles), sulpholan (3 mls.) and pentafluoropyridine (0·9 g., 5·3 m.moles) under dry nitrogen at ca. 50°. Removal of the volatile products under vacuum, after a further 45 min., gave a colourless liquid (0·5 g.) and a white crystalline solid (0·9 g.). Chromatographic analysis (G.D.B., column "O", 78°) of the former showed a two component mixture of unreacted C_5F_5N (50% recovery) and C_7F_7N (7% recovery). The solid was recrystallised from methanol and shown to be 1,1-bis-(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane (XVI), (60% yield, based on the weight of C_7F_7N consumed) m.pt. = 91-92°. (Found: C, 35·8; F, 56·5%; M, 400. $C_{12}F_{12}N_2$ requires C, 36·0; F, 57·0%; M, 400). I.R. spectrum No. 17. λ_{max} (cyclohexane) = 280·5 mμ; (ε, 8251).

Broad absorptions in the ^{19}F n.m.r. at 90·4 and 139·6, due to four fluorines, were assigned to the 2,6 and 3,5 ring positions respectively. Two further absorptions were observed at 78·4, ($-CF_3$) and 164·1, (-CF) and confirmed the postulated unsymmetrical rather than the isomeric symmetrical structure.

Extraction of the involatile reaction mixture gave a pale yellow residue (0·75 g.) which was sublimed. The recovered white crystalline solid (0·05 g.) was shown to be XVI by comparison of the i.r. spectrum with that of an authentic sample.

7.2.4. Preparation of 2,2-bis-(2',3',5',6'-tetrafluoropyridyl)hexafluoropropane, $C_{13}F_{14}N_2$.



X XVII

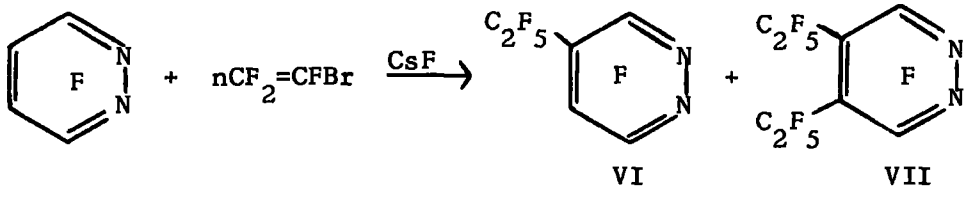
(a) C_8F_9N (X) (2·0 g., 7·1 m.moles) was added dropwise over 1 hr. to stirred caesium fluoride (2·0 g., 13·3 m.moles), sulpholan (10 mls.) and pentafluoropyridine (1·5 g., 8·9 m.moles) under dry nitrogen at ca. 75°. Removal of the volatile products under vacuum, after a further 2 hr., gave a colourless liquid (3·0 g.) which was shown by chromatographic analysis (G.D.B., column "A", 78°) to be unreacted starting materials.

(b) Caesium fluoride (1·0 g., 6·7 m.moles), sulpholan (6 mls.), C_5F_5N (1·4 g., 8·3 m.moles) and C_8F_9N (X) (1·6 g., 5·7 m.moles) were sealed in a glass ampoule and heated to ca. 150° for 18 hr. The tube was then cooled, opened, and the volatile products, a colourless liquid (1·0 g.) and a white crystalline solid (0·8 g.), were transferred under vacuum to a cold trap. Chromatographic analysis (G.D.B., column "A", 78°) of the former showed mainly unreacted C_5F_5N (55% recovery) and the latter was recrystallised from ethanol. Extraction of the involatile reaction mixture gave a brown oily residue (1·1 g.) from which a white crystalline solid

(0·7 g.), identical with the material obtained previously, was sublimed (80°/0·01 mm.). The recrystallised solid (XVII) was shown to be 2,2-bis-(2',3',5',6'-tetrafluoropyridyl)hexafluoropropane, (60% yield, based on the weight of C_8F_9N (X) consumed), m.pt. = 99·5°. (Found: C, 34·4; F, 58·9%; M, 450. $C_{13}F_{14}N_2$ requires C, 34·7; F, 59·1%; M, 450). I.R. spectrum No. 18. λ_{max} (cyclohexane) = 279·5 mμ; (ϵ, 8041).

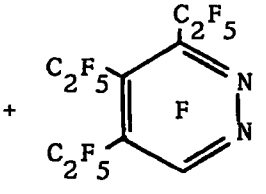
Broad absorptions in the ^{19}F n.m.r. at 89·6 and 136·1, due to four fluorines, were assigned to the 2,6 and 3,5 ring positions respectively. A further resonance at 64·9 ($-CF_3$), due to six fluorines, was also observed.

7.2.5. Reactions of bromotrifluoroethylene with tetrafluoropyridazine.



VI VII

Scheme 6



VIII

(a) Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan or tetraglyme (35 mls.), $C_4F_4N_2$ (3·0 g., 19·7 m.moles) and CF_2=CFBr (16·0 g., 100 m.moles) were stirred for 2 hr. in a standard atmospheric pressure reaction (for further quantities and reaction conditions, See Table 19). Removal of the volatile products under vacuum gave unreacted bromotrifluoroethylene, identified by i.r. spectroscopy, and a pale yellow liquid. Chromatographic analysis (G.D.B., column "O", 78°) of the latter showed, in order of

Table 19

	Solvent	Temp.	Weight of CF_2=CFBr recovered	Weight of volatile product	Weight of residue	Percentage Yields*			Conversion
						VI	VII	VIII	
(i)	T	90°	6·0 g.	2·8 g.	1·0 g.	30	9	-	62%
(ii)	S	90°	6·0 g.	4·0 g.	0·2 g.	51	18	-	64%
(iii)	T	120°	4·0 g.	6·0 g.	1·25 g.	52	25	5	66%
(iv)	S	120°	9·5 g.	4·8 g.	0·4 g.	41	28	5	80%

* Based on the weight of $C_4F_4N_2$ consumed.

T = Tetraglyme.

S = Sulpholan.

increasing retention times, unreacted $C_4F_4N_2$, VI, VII and VIII (See Scheme 6); the products were separated by preparative scale v.p.c. (Aerograph, column "O", 95°) and were identified by comparison of the i.r. spectra with those of authentic samples. Extraction of the involatile reaction mixture gave small quantities of intractable tarry residues.

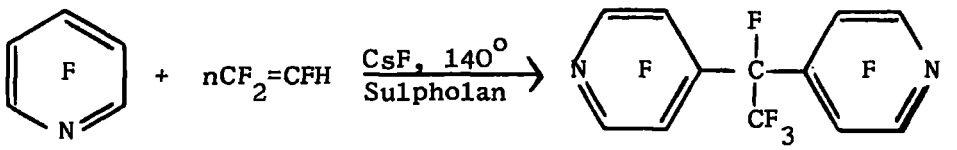
When reaction (ii) (Table 19) was repeated for a prolonged reaction time (18 hr.) a further component of longer retention time was observed, separated (Aerograph, column "O", 95°) and shown to be tetrakis(pentafluoroethyl)pyridazine, m.pt. 37-38°. (Found: C, 25·8; F, 68·2%; M, 552. $C_{12}F_{20}N_2$ requires C, 26·1; F, 68·8%; M, 552). I.R. spectrum No. 19. λ_{max} (cyclohexane) = 260 br. and 356 br. mμ; (ε, 743 and 200 respectively).

Three broad absorptions in the ^{19}F n.m.r. at 73·2, (3 and 6-CF_3); 91·2, (3 and 6-CF_2) and 108·8, (4 and 5-CF_2) and a singlet at 80·8, (4 and 5-CF_3), due to 6, 4, 4 and 6 fluorines respectively, were assigned by extrapolation of the observed spectra of VII and VIII.

(b) Potassium fluoride (7·0 g., 120·5 m.moles), sulpholan (45 mls.), $C_4F_4N_2$ (5·0 g., 32·8 m.moles) and CF_2=CFBr (16·0 g., 100 m.moles) were stirred, in a standard atmospheric pressure reaction (See p. 141), at ca. 120° for 4 hr. Removal of the volatile products under vacuum gave unreacted CF_2=CFBr (1·0 g.), identified by i.r. spectroscopy, and a pale yellow liquid (8·0 g.). Chromatographic analysis (G.D.B., column "O", 78°) of the latter showed unreacted $C_4F_4N_2$ (95% conversion), VI, VII and VIII in 27%, 33% and 6% yields respectively. The products were separated by preparative scale v.p.c. (Aerograph, column "O", 95°) and identified by comparison of the i.r. spectra with those of authentic samples. Extraction of the involatile reaction mixture gave an intractable tarry residue (4·0 g.).

7.3. Trifluoroethylene, CF_2=CFH.

7.3.1. Reaction of trifluoroethylene with pentafluoropyridine.



XVI

Scheme 7

Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan (40 mls.), C_5F_5N (3·0 g., 17·8 m.moles) and trifluoroethylene (10·0 g., 121·9 m.moles) were stirred, in a standard atmospheric pressure reaction (See p. 141), at ca. 140° for 46 hr. Removal of the volatile products under vacuum gave unreacted trifluoroethylene (3·0 g.), identified by i.r. spectroscopy, a colourless liquid (0·8 g.) which was shown by chromatographic analysis (G.D.B., column "O", 78°) to be a single component identified as C_5F_5N (70% conversion) by i.r. spectroscopy, and a white crystalline solid (XVI) (Scheme 7) (0·3 g.) XVI was shown to be 1,1-bis-(2',3',5',6'-tetrafluoro-pyridyl)tetrafluoroethane, (11% yield, based on weight of C_5F_5N consumed) by comparison of the i.r. spectrum with that of an authentic sample. Extraction of the involatile reaction mixture gave an intractable tarry residue (4·5 g.).

7.3.2. Reaction of trifluoroethylene with tetrafluoropyridazine.

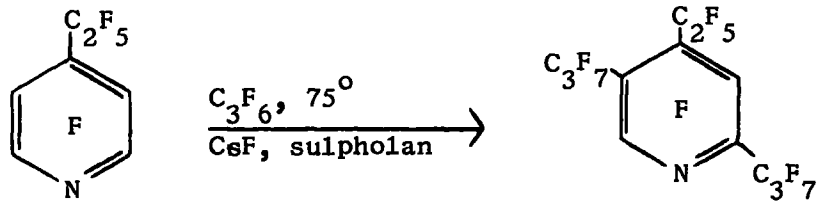
Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan (40 mls.), $C_4F_4N_2$ (4·0 g., 26·3 m.moles) and trifluoroethylene (6·0 g., 73·2 m.moles) were stirred, in a standard atmospheric pressure reaction (See p. 141), at ca. 90° for 96 hr. Removal of the volatile products under vacuum gave only unreacted CF_2=CFH (4·0 g.), identified by comparison of the i.r. spectrum with that of an authentic sample. Extraction of the involatile reaction mixture gave an intractable tarry residue (4·0 g.).

CHAPTER 8

Experimental for Chapter 5

8.1. Polyfluoroalkylation reactions.

8.1.1. Preparation of perfluoro-(2,5-di-isopropyl-4-ethylpyridine).

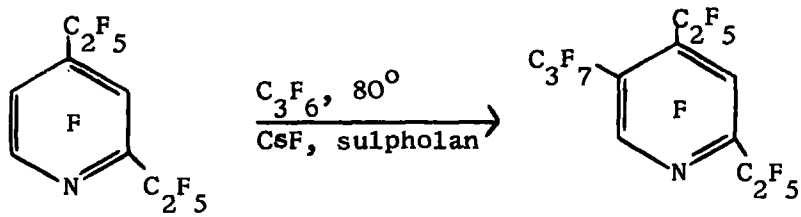


I XVIII

Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan (35 mls.), C_7F_9N (I) (5·0 g., 18·6 m.moles) and hexafluoropropene (16·0 g., 106·7 m.moles) were stirred, in a standard atmospheric pressure reaction (See p.141), for 40 min. at ca. 75°. Removal of the volatile products under vacuum, at temperatures up to ca. 90°, gave unreacted C_3F_6 (0·5 g.), identified by i.r. spectroscopy, and a colourless liquid (19·5 g.). Chromatographic analysis (G.D.B., column "O", 78°) of the latter showed dimers and trimers of C_3F_6, identified by i.r. spectroscopy, and a single product (XVIII) which was separated by distillation and shown to be perfluoro-(2,5-di-isopropyl-4-ethylpyridine) in quantitative yield, b.pt. 176°. (Found: C, 27·1; F, 70·7%; M, 569. $C_{13}F_{21}N$ requires C, 27·4; F, 70·3%; M, 569). I.R. spectrum No. 20. λ_{max} (cyclohexane) = 286 br. mμ; (ϵ ; 6780).

Broad absorptions in the ^{19}F n.m.r. at 52·2 and 113·9, due to single fluorines, were assigned to the 6 and 3 ring positions respectively and were consistent with calculated chemical shifts. Further resonances were observed at 72·3, (5-CF_3); 74·1, (2-CF_3); 80·3, (4-CF_3); 99·7, (4-CF_2); 170·5, (5-CF) and 183·8, (2-CF).

8.1.2. Preparation of perfluoro-(5-isopropyl-2,4-di-ethylpyridine).



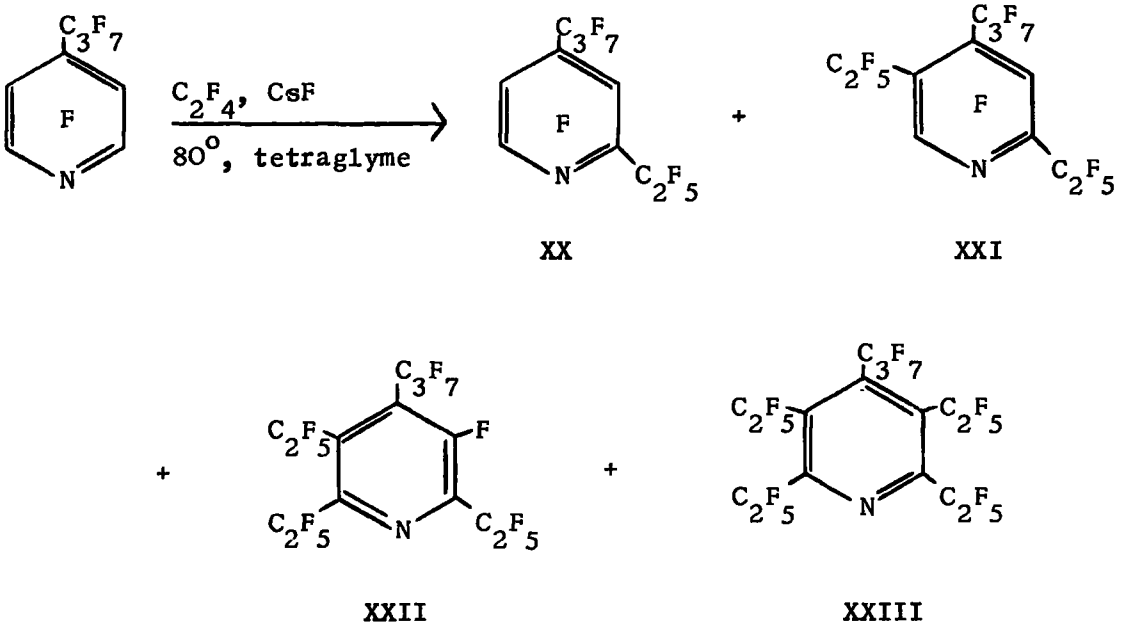
II XIX

Caesium fluoride (3·0 g., 20·0 m.moles), sulpholan (35 mls.), $C_9F_{13}N$ (II) (4·0 g., 10·8 m.moles) and hexafluoropropene (11·0 g., 73·4 m.moles) were stirred, in a standard atmospheric pressure reaction (See p.141), at ca. 80° for 1 hr. Removal of the volatile products under vacuum, at temperatures up to ca. 90°, gave unreacted C_3F_6 (0·5 g.), identified by i.r. spectroscopy, and a colourless liquid (13·4 g.). Chromatographic analysis (G.D.B., column "O", 78°) of the latter indicated a four component mixture of dimers and trimers of C_3F_6, II, and a single product (XIX), which was separated by distillation and preparative scale v.p.c. (Aerograph, column "O", 80°). XIX was shown to be perfluoro-(5-isopropyl-2,4-di-ethylpyridine), (65% yield), b.pt. 175°. (Found: C, 27·6; F, 69·0%; M, 519. $C_{12}F_{19}N$ requires C, 27·8; F, 69·6%; M, 519). I.R. spectrum No. 21. λ_{max} (cyclohexane) = 286 br. mμ; (ϵ, 6240).

Broad absorptions in the ^{19}F n.m.r. at 53·6 and 115·2, due to single fluorines, were assigned to the 6 and 3 ring positions respectively and were consistent with calculated chemical shifts. Further resonances were observed at 72·3, (5-CF_3); 81·0, (4-CF_3); 83·1, (2-CF_3); 100·1, (4-CF_2); 116·1, (2-CF_2) and 170·2, (5-CF).

A similar reaction at ca. 60° for 2 hr. resulted in an 80% yield of XIX.

8.1.3. Perfluoroethylation of perfluoro-(4-isopropylpyridine), $C_8F_{11}N$.



Caesium fluoride (6·0 g., 40·0 m.moles), tetraglyme (100 mls.), $C_8F_{11}N$ (10·0 g., 31·4 m.moles) and tetrafluoroethylene (14·0 g., 140 m.moles) were stirred, in a standard atmospheric pressure reaction (See p. 141), at ca. 80° for 5 hr. Removal of the volatile products under vacuum, at temperatures up to ca. 90°, gave unreacted C_2F_4 (10·0 g.), identified by i.r. spectroscopy, and a colourless liquid (11·0 g.). Chromatographic analysis (G.D.B., column "O", 78°) of the latter showed a five component mixture comprised of unreacted $C_8F_{11}N$ (67% conversion), XX, XXI, XXII and XXIII which were separated by preparative scale v.p.c. (Aerograph, column "O", 80°). Vacuum distillation of the extracts of the involatile reaction mixture gave an oily liquid (1·5 g.) and an intractable tar (1·3 g.); XXII and XXIII were detected on analysis of the former (G.D.B., column "O", 78°).

XX was shown to be perfluoro-(2-ethyl-4-isopropylpyridine), (37% yield), b.pt. 158°. (Found: C, 28·4; F, 67·5%; M, 419. $C_{10}F_{15}N$ requires

C, 28·7; F, 68·0%; M, 419). I.R. spectrum No. 22. λ_{max} (cyclohexane) = 274·5 mμ; (ϵ, 4796).

Broad absorptions in the ^{19}F n.m.r. at 83·8, 115·7 and 123·3, due to single fluorines, were assigned to the 6, 3 and 5 ring positions respectively and were consistent with calculated chemical shifts. Further resonances were observed at 75·1, (4-CF_3); 83·5, (2-CF_3); 115·0, (2-CF_2) and 180·0, (4-CF).

XXI was identified as <u>perfluoro-(2,5-di-ethyl-4-isopropylpyridine)</u>, (27% yield), b.pt. 170°. (Found: C, 27·6; F, 69·3%; M, 519. $C_{12}F_{19}N$ requires C, 27·8; F, 69·6%; M, 519). I.R. spectrum No. 23. λ_{max} (cyclohexane) = 285 br. mμ; (ϵ, 6150).

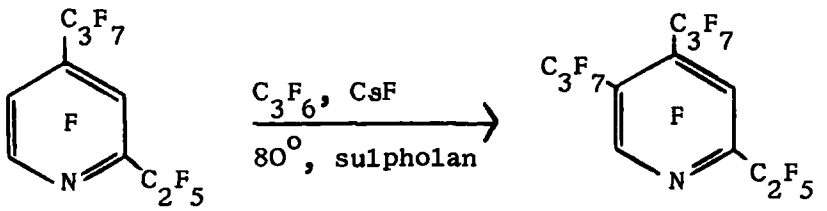
Broad absorptions in the ^{19}F n.m.r. at 52·9 and 114·8, due to single fluorines, were assigned to the 6 and 3 ring positions respectively and were consistent with calculated chemical shifts. Further resonances were observed at 72·1, (4-CF_3); 80·1, (5-CF_3); 83·0, (2-CF_3); 100·0, (5-CF_2); 116·3, (2-CF_2) and 170·1, (4-CF).

XXII was shown to be <u>perfluoro-(2,5,6-tri-ethyl-4-isopropylpyridine)</u>, (18% yield), b.pt. 185° (Found: C, 27·4 ; F, 70·0%; M, 619. $C_{14}F_{23}N$ requires C, 27·1; F, 70·6%; M, 619). I.R. spectrum No. 24.

The ^{19}F n.m.r. consisted of complex bands centred at 73·9, 81·4, 84·8, 108·7, 117·3 and 171·9 which could not be fully analysed. The absence of an absorption at ca. 45, calculated from substituent chemical shifts, indicated that the 6, and not the 3, fluorine of XXI had been replaced.

XXIII was shown to be <u>perfluoro-(tetraethyl-4-isopropylpyridine)</u>, (4% yield), m.pt. 35°. (Found: M, 719. $C_{16}F_{27}N$ requires M, 719). I.R. spectrum No. 25.

8.1.4. Preparation of perfluoro-(2-ethyl-4,5-di-isopropylpyridine).



XX XXIV

Caesium fluoride (2·0 g., 13·6 m.moles), sulpholan (20 mls.), $C_{10}F_{15}N$ (XX) (1·8 g., 4·3 m.moles) and hexafluoropropene (10·0 g., 66·7 m.moles) were stirred, in a standard atmospheric pressure reaction (See p.141), at ca. 80° for 2·5 hr. Removal of the volatile products under vacuum, at temperatures up to ca. 90°, gave unreacted C_3F_6 (5·6 g.), identified by i.r. spectroscopy, and a colourless liquid (5·5 g.). Chromatographic analysis (G.D.B., column "O", 78°) of the latter indicated a four component mixture of dimers and trimers of C_3F_6, XX (50% conversion) and a single product (XXIV), which was separated by preparative scale v.p.c. (Aerograph, column "O", 80°). XXIV was shown to be perfluoro-(2-ethyl-4,5-di-isopropylpyridine), (80% yield), b.pt. 183°. (Found: C, 27·2; F, 70·5%; M, 569. $C_{13}F_{21}N$ requires C, 27·4; F, 70·2%; M, 569). I.R. spectrum No. 26. λ_{max} (cyclohexane) = 288 br. mμ; (ϵ, 3890).

Broad absorptions in the ^{19}F n.m.r. at 52·4 and 113·6, due to single fluorines, were assigned to the 6 and 3 ring positions respectively and were consistent with calculated chemical shifts. Further resonances were observed at 74·0, (4 and 5-CF_3); 85·4, (2-CF_3); 117·9, (2-CF_2) and 167·8, (4 and 5-CF).

8.2. Fluoride ion-initiated aromatic rearrangement reactions.

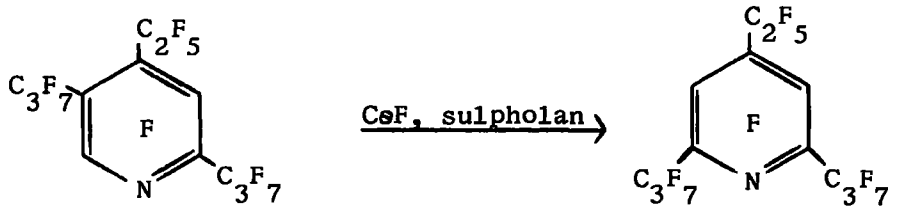
8.2.1. Attempted rearrangement of perfluoro-(2,4,5-tri-ethylpyridine), $C_{11}F_{17}N$.

(a) $C_{11}F_{17}N$ (3·0 g., 6·4 m.moles), caesium fluoride (3·0 g., 20·0 m.moles) and sulpholan (30 mls.) were sealed in a nickel tube and heated to ca. 160° for 16 hr. with continuous rotation. The tube was then cooled, opened, and the volatile products transferred under vacuum to a cold trap. The recovered colourless liquid (2·6 g.) was analysed with ^{19}F n.m.r. and shown to be identical with the starting material. The involatile material was poured into water (400 mls.), ether extracted (4 x 20 mls.) and the combined extracts dried ($MgSO_4$). Removal of the solvent left an intractable tarry residue (0·5 g.).

(b) Reaction (a) was repeated in the presence of heptafluoroquinoline (3·0 g., 11·8 m.moles) using $C_{11}F_{17}N$ (1·2 g., 2·6 m.moles), caesium fluoride (3·0 g., 20·0 m.moles) and sulpholan (30 mls.) heated to ca. 160° for 72 hr. The recovered volatile products, a pale yellow liquid (0·9 g.) and a white crystalline solid (2·7 g.), were identified as perfluoro-(2,4,5-tri-ethylpyridine) and heptafluoroquinoline respectively by i.r. and ^{19}F n.m.r. spectroscopy. Extraction of the involatile material gave no tractable products.

(c) Reaction (a) was repeated using identical quantities of material and heated to ca. 190° for 18 hr. The recovered colourless liquid (1·2 g.) was analysed with ^{19}F n.m.r. and shown to be perfluoro-(2,4,5-tri-ethyl-pyridine). Extraction of the involatile reaction mixture gave an intractable tarry residue (3·5 g.) owing to reactant and solvent decomposition.

8.2.2. Rearrangement of perfluoro-(2,5-di-isopropyl-4-ethylpyridine), $C_{13}F_{21}N$.



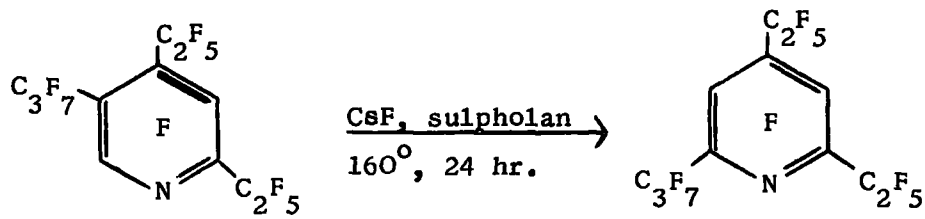
XVIII XXV

(a) $C_{13}F_{21}N$ (XVIII) (2·0 g., 3·5 m.moles), caesium fluoride (1·0 g., 6·7 m.moles) and sulpholan (10 mls.) were sealed in a glass ampoule and heated to ca. 160° for 24 hr. with continuous rotation. The tube was then cooled, opened, and the volatile products transferred under vacuum to a cold trap. Chromatographic analysis (G.D.B., column "O", 78°) of the recovered colourless liquid (1·5 g., 75% recovery) showed a two component mixture of the 2,4,5 (XVIII) and 2,4,6 (XXV) isomers of $C_{13}F_{21}N$ in the ratio 60:40 respectively, estimated from ^{19}F n.m.r. data. Extraction of the involatile reaction mixture gave an intractable tarry residue (0·2 g.).

(b) $C_{13}F_{21}N$ (2·5 g., 4·4 m.moles), caesium fluoride (4·0 g., 26·6 m. moles) and sulpholan (30 mls.) were sealed in a nickel tube and heated to ca. 180° for 24 hr. with continuous rotation. The tube was then cooled, opened, and the volatile products transferred under vacuum to a cold trap. Chromatographic analysis (G.D.B., column "O", 78°) of the recovered colourless liquid (0·8 g.) showed a single component (XXV) which was identified as perfluoro-(2,6-di-isopropyl-4-ethylpyridine), (32% yield), b.pt. 180°. (Found: C, 26·9; F, 70·0%; M, 569. $C_{13}F_{21}N$ requires C, 27·4; F, 70·3%; M, 569). I.R. spectrum No. 27. λ_{max} (cyclohexane) = 274 mμ; (ε, 4540).

A broad absorption in the relatively straightforward ^{19}F n.m.r. at 111·4, due to two fluorines, was assigned to the 3,5 ring positions and was consistent with the calculated chemical shift. Further absorptions were observed at 74·5, (2 and 6-CF_3); 85·5, (4-CF_3); 112·3, (4-CF_2) and 185·2, (2 and 6-CF).

8.2.3. Rearrangement of perfluoro-(5-isopropyl-2,4-di-ethylpyridine), $C_{12}F_{19}N$.



XIX XXVI

$C_{12}F_{19}N$ (XIX) (2·0 g., 3·9 m.moles), caesium fluoride (1·0 g., 6·7 m.moles) and sulpholan (10 mls.) were sealed in a glass ampoule and heated to ca. 160° for 24 hr. with continuous rotation. The tube was then cooled, opened, and the volatile products transferred under vacuum to a cold trap. Chromatographic analysis (G.D.B., column "O", 78°) of the recovered colourless liquid (1·3 g.) showed a two component mixture of the 2,4,5 (XIX) and 2,4,6 (XXVI) isomers of $C_{12}F_{19}N$ in the ratio 40:60 respectively, estimated from the chromatogram. The product (XXVI) was separated by preparative scale v.p.c. (Aerograph, column "O", 80°) and shown to be perfluoro-(6-isopropyl-2,4-di-ethylpyridine), (52% yield), b.pt. 168-169°. (Found: C, 27·5; F, 69·2%; M, 519. $C_{12}F_{19}N$ requires C, 27·8; F, 69·6%; M, 519). I.R. spectrum No. 28. λ_{max} (cyclohexane) = 274 br. mμ; (ε, 4230).

Broad absorptions in the ^{19}F n.m.r. at 108·6 and 111·5, due to single fluorines, were assigned to the 5 and 3 ring positions respectively

and were consistent with calculated chemical shifts. Further absorptions were observed at 76·4, (6-CF_3); 85·2, (2-CF_3); 87·4, (4-CF_3); 113·5, (4-CF_2); 116·8, (2-CF_2) and 186·9, (6-CF).

Extraction of the involatile reaction mixture gave an intractable tarry residue (0·3 g.).

8.2.4. Attempted rearrangement of perfluoro-(2,5-di-ethyl-4-isopropyl-pyridine), $C_{12}F_{19}N$.

$C_{12}F_{19}N$ (2·0 g., 3·9 m.moles), caesium fluoride (3·0 g., 20·0 m.moles) and sulpholan (30 mls.) were sealed in a nickel tube and heated to ca. 180° for 24 hr. with continuous rotation. The tube was then cooled, opened, and the volatile products transferred under vacuum to a cold trap. ^{19}F n.m.r. analysis of the small quantity of recovered colourless liquid (0·05 g.) did not indicate a perfluoroalkylpyridine. Extraction of the involatile reaction mixture gave a dark brown liquid (0·8 g.) which did not contain any identifiable products.

8.2.5. Attempted rearrangement of perfluoro-(4,5-di-ethylpyridazine), $C_8F_{12}N_2$.

$C_8F_{12}N_2$ (0·6 g., 1·7 m.moles), caesium fluoride (0·5 g., 3·3 m.moles) and sulpholan (3 mls.) were sealed in a glass ampoule and heated to ca. 150° for 18 hr. with continuous rotation. The tube was then cooled, opened, its contents poured into water, and extracted with ether, the organic layer was washed with water and dried ($MgSO_4$). Removal of the solvent left a dark brown residue (0·5 g.), which was shown by v.p.c. (column "O", 75° and 150°) to be a single volatile component. A white crystalline solid (0·2 g.), identified as starting material by i.r. and ^{19}F n.m.r. spectroscopy, was sublimed (50°/0·01 mm.) from the residue to leave an intractable tar (0·3 g.).

CHAPTER 9

Nuclear Magnetic Resonance Data

Introduction.

In recent years, ^{19}F n.m.r. spectroscopy has emerged as an important method for determining the structures of fluorinated compounds. Of particular interest has been its effective use, in conjunction with substituent chemical shifts (s.c.s.),[142,163] for differentiating the orientation of nucleophilic substitution in polyfluoro-aromatic and -heterocyclic compounds.[17,141,164]

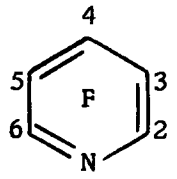
Substituent chemical shifts, or the effect of a substituent on the ring fluorines ortho, meta and para to it, are obtained from a comparison of the observed shifts for the same ring fluorine in the substituted and unsubstituted compounds. Using these s.c.s. for a particular substituent, it is possible to determine substitution patterns in other compounds containing the same substituent. Similarly, for fluorinated benzenes in which substituent effects have been shown to be approximately additive,[163] it is possible to predict the spectra for multisubstitution. For fluorinated-N-heteroaromatic compounds the concept of s.c.s. is a useful one in determining the orientation of substitution and, despite variations in s.c.s. values, the assignments are often quite unambiguous due to the large differences in chemical shifts of non-equivalent ring fluorines in the parent compound.

Since the results presented are mainly concerned with perfluoroalkyl-pyridines and -pyridazines, and their respective derivatives, it is advantageous to first discuss the general features of the ^{19}F n.m.r. spectra of these systems under the heading of the perfluoro-N-heteroaromatic compound.

9.1. Polyfluoropyridine derivatives.

9.1.1. Chemical shifts.

The spectrum of pentafluoropyridine, which has been fully analysed previously,[165] contains three resonances at 88·1 (2,6F),



134·5 (4F) and 162·6 (3,5F), relative to $CFCl_3$, in the ratio 2:1:2. Introduction of a perfluoroalkyl substituent affords characteristic resonances due to aliphatic fluorines and also alters the chemical shifts of the remaining ring fluorines, as described later. Other substituents, e.g. CH_3O^- have significant, though less pronounced, effects on the chemical shifts of the ring fluorines.

9.1.2. Coupling constants.

Analysis of the ^{19}F n.m.r. spectra of polyfluoropyridines indicated that, in general, meta-coupling constants are smaller than either ortho- or para-constants.[142] However, it was also observed that such spectra are frequently complicated by the broadening effect of the quadrupolar nitrogen nucleus on the 2,6-ring fluorine resonance. For perfluoroalkyl-pyridines, the coupling constants between aliphatic fluorines and neighbouring ring fluorines are often quite large, possibly indicative of a "through space" mechanism.[141,166,167] Coupling constants are quoted where possible and some assignments have been made on the basis of them.

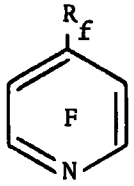
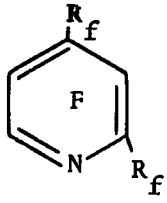
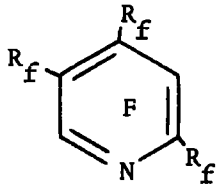
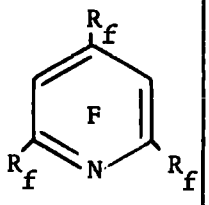
9.1.3. Substituent shifts.

The same s.c.s. cannot be used for a particular substituent in all pyridines since variations in ortho, meta and para shifts have been observed for several substituents in a series of fluorinated pyridines.[142] Similar results were found for perfluoroisopropylpyridines,[33,141] as shown.

These s.c.s. for $(CF_3)_2CF$ substitution in fluorinated pyridines have been used to predict the ^{19}F n.m.r. spectra of, and determine the orientation of substitution in related compounds, including those discussed later.

Substituent chemical shifts due to $(CF_3)_2CF$ in perfluoroisopropylpyridines.

(Position of fluorine atom in parentheses)

Compound	Internal shifts arising from:-	Effect on ^{19}F shifts (p.p.m.) ortho	meta	para	Ref. compound
 A	$4(CF_3)_2CF$	-24•4(3,5)	-2•1(2,6)	-	C_5F_5N
 B	$2(CF_3)_2CF$	-22•4(3)	-5•2(6)	-13•2(3)	A
	$5(CF_3)_2CF$	-33•6(6)	-5•0(3)	-	B
	$6(CF_3)_2CF$	-19•3(5)	-	-10•1(3)	B

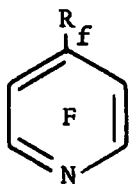
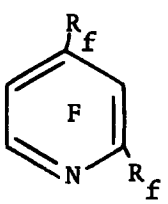
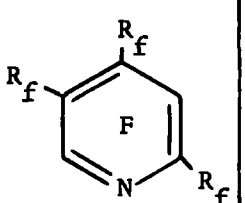
R_f = $(CF_3)_2CF$

Emsley and Phillips have tentatively proposed that alkyl groups in fluorinated pyridines have similar s.c.s.[142] The possibility of a similar situation with perfluoroalkyl substituents is justified to some extent

from a comparison of the above results for $(CF_3)_2CF$ with the analogous observed s.c.s. for CF_3CF_2. The latter results have also been used for structure determinations of related compounds.

Substituent chemical shifts due to CF_3CF_2 in perfluoroethylpyridines.

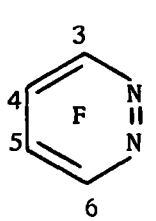
(Position of fluorine in parentheses)

Compound	Internal shifts arising from:-	Effect on ^{19}F shifts (p.p.m.) ortho	meta	para	Ref. compound
 I	4 CF_3CF_2	-22•3(3,5)	+0•9(2,6)	-	C_5F_5N
 II	2 CF_3CF_2	-21•8(3)	-5•2(6)	-13•9(5)	I
 III	5 CF_3CF_2	-28•3(6)	-2•8(3)	-	II
	$R_f = CF_2CF_3$				

9.2. Polyfluoropyridazine derivatives.

9.2.1. Chemical shifts.

The spectrum of tetrafluoropyridazine contained two resonances at 93•95 (3,6F) and 147•6 (4,5F) of equal intensity. Substituents



give similar effects to those discussed previously for the pyridine system.

9.2.2. Coupling constants.

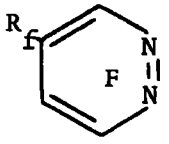
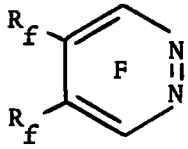
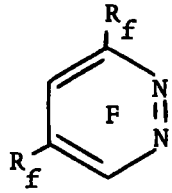
Detailed analyses of the ^{19}F n.m.r. spectrum of tetrafluoropyridazine or the effects of substituents on the various coupling constants have not yet been published. Due to the broadening effect of the quadrupolar nitrogen nucleic on the 3,6-ring fluorines, the observed spectra of perfluoroalkylpyridazines are frequently complicated, however, where possible the extracted coupling constants are given.

9.2.3. Substituent shifts.

A detailed investigation of the specific effect of substituents on the chemical shifts of the ring fluorines is not available to date, however, preliminary results using CH_3O^- and $(CF_3)_2CF^-$ indicate that similar principles to the pyridine system are applicable. The observed s.c.s. for $(CF_3)_2CF$ in fluorinated pyridazines are shown, and have been used for structure determinations in related compounds, as indicated later.

Substituent chemical shifts due to $(CF_3)_2CF$ in perfluoroisopropylpyridazines.

(Position of fluorine atom in parentheses)

Compound	Internal shifts arising from:-	Effect on ^{19}F shifts (p.p.m.) ortho a	ortho b	meta	para	Reference compound
 C	4 $(CF_3)_2CF$	-23·0(3)	-29·3(5)	+3·2(6)	-	Tetrafluoro-pyridazine
	5 $(CF_3)_2CF$	-26·2(6)	-	+1·0(3)	-	C
	3 $(CF_3)_2CF$	-	-14·6(4)	-	-2·3(6)	C

R_f = $(CF_3)_2CF$

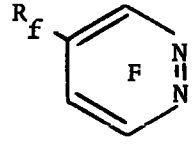
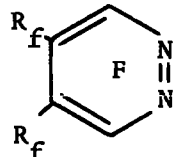
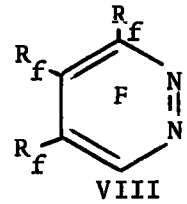
a = fluorine adjacent to nitrogen, i.e. 3 or 6.

b = fluorine adjacent to carbon, i.e. 4 or 5.

The following shifts were observed for CF_3CF_2 substitution in fluorinated pyridazines.

Substituent chemical shifts due to CF_3CF_2 in perfluoroethylpyridazines.

(Position of fluorine atom in parentheses)

Compound	Internal shift arising from:-	Effect on ^{19}F shifts (p.p.m.) ortho a	ortho b	meta	para	Reference compound
 VI	4 CF_3CF_2	-16·6(3)	-27·0(5)	+3·6(6)	-	Tetrafluoro-pyridazine
 VII	5 CF_3CF_2	-19·8(6)	-	+0·3(3)	-	VI
 VIII	3 CF_3CF_2	-	-	-	-7·5(6)	VII

R_f = CF_3CF_2

a = fluorine adjacent to nitrogen, i.e. 3 or 6.

b = fluorine adjacent to carbon, i.e. 4 or 5.

9.3. Data for polyfluoropyridine derivatives.

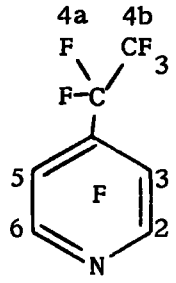
The following abbreviations have been used in presenting data concerning the fine structure of absorptions:-

S = singlet; D = doublet; T = triplet; Q = quartet; P = quintet; H = heptet.

9.3.1. Mono-substituted compounds.

(a) Perfluoro-(4-ethylpyridine).

Shift (p.p.m.) Obs.	Shift (p.p.m.) Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
86·6	-	T($J_{4b-3,5}$ = 7) of T(J_{4b4a} = 2)	3	4b
89·0	86	Broad	2	2,6
113·2	-	T($J_{4a-3,5}$ = 29·5)	2	4a
140·3	138	T($J_{3,5-4a}$ = 29·5) of Q($J_{3,5-4b}$ = 7)	2	3,5



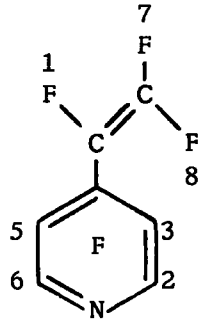
I

* Reference compound = pentafluoropyridine; s.c.s. for 4-$(CF_3)_2CF$. Recorded in ether solution with an internal $CFCl_3$ reference.

Using a variable temperature probe, spectra of I were recorded over the temperature range -100° to +40°, however, apart from a slight broadening of the absorptions, there was no significant change in the spectrum.

(b) Perfluoro-(4-vinylpyridine).

Shift (p.p.m.) Obs.	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
89·2	Broad	2	2,6
93·8	$D(J_{78} = 52)$ of $D(J_{71} = 36)$ of $T(J_{7\text{-}3,5} = 2{\cdot}5)$	1	7
124·1	$D(J_{81} = 116)$ of $D(J_{87} = 52)$ of $T(J_{8\text{-}3,5} = 16)$	1	8
138·8	Complex multiplet	2	3,5
175·6	$D(J_{18} = 116)$ of $D(J_{17} = 36)$ of $T(J_{1\text{-}3,5} = 9{\cdot}5)$	1	1



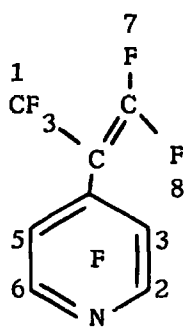
IX

Recorded in ether solution with an internal $CFCl_3$ reference.

This spectrum was analysed by comparison with the previously reported data for octafluorostyrene.[151,168]

(c) 2-(2′,3′,5′,6′-Tetrafluoropyridyl)-pentafluoropropene .

Shift (p.p.m.) Obs.	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
59•5	$D(J_{17} = 17)$ of $D(J_{18} = 11)$ of $T(J_{1-3,5} = 5•3)$	3	1
68•0	$Q(J_{71} = 17)$ of $D(J_{78} = 7)$	1	7
68•9	$Q(J_{81} = 11)$ of $D(J_{87} = 7)$ of $T(J_{8-3,5} = 6)$	1	8
89•2	Broad	2	2,6
139•8	Complex multiplet*	2	3,5



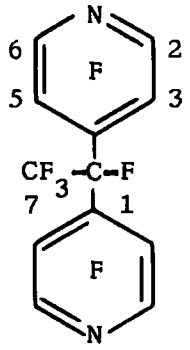
X

* Badly resolved due to weak sample.

Recorded in ether solution with an internal $CFCl_3$ reference.

(d) 1,1-Bis-(2′,3′,5′,6′-tetrafluoropyridyl)tetrafluoroethane.

Shift (p.p.m.) Obs.	Shift (p.p.m.) Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
78·4	-	$P(J_{7-3,5} = 13{\cdot}5)$ of $D(J_{71} = 9)$	3	7
90·4	86	Broad	4	2,6
139·6	138	Complex multiplet	4	3,5
164·1	-	$P(J_{1-3,5} = 26)$ of $Q(J_{17} = 9)$	1	1



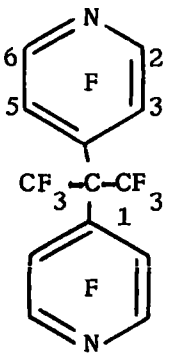
XVI

* Reference compound = pentafluoropyridine; s.c.s. for $(CF_3)_2CF$.

Recorded in acetone solution with an external $CFCl_3$ reference.

(e) 2,2-Bis-(2′,3′,5′,6′-tetrafluoropyridyl)hexafluoropropane.

Shift (p.p.m.) Obs.	Shift (p.p.m.) Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
64·9	-	$P(J_{1-3,5} = 17)$	6	1
89·6	86	Broad	4	2,6
136·1	138	Broad	4	3,5



XVII

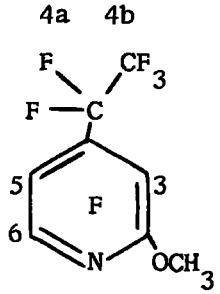
* Reference compound = pentafluoropyridine; s.c.s. for $(CF_3)_2CF$.

Recorded in acetone solution with an external $CFCl_3$ reference.

9.3.2. Di-substituted compounds.

(a) 4-Pentafluoroethyl-2-methoxy-3,5,6-trifluoropyridine.

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
86·0	-	$T(J_{4b-3,5} = 7)$ of $T(J_{4b4a} = 2)$	3	4b
91·6	93	$D(J_{63} = 32)$ of $D(J_{65} = 20)$	1	6
112·9	-	$T(J_{4a-3,5} = 29)$ of $Q(J_{4a4b} = 2)$	2	4a
139·0	140	Complex multiplet†	1	3
151·5	151		1	5



XXVII

* Reference compound = perfluoro-(4-ethylpyridine); s.c.s. for CH_3O obtained from 4-heptafluoroisopropyl-2-methoxy-3,5,6-trifluoropyridine.[33]

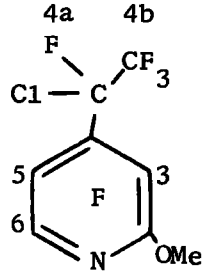
† Badly resolved due to weak sample.

Recorded in carbon tetrachloride solution with an internal $CFCl_3$ reference.

The ^1H n.m.r. consisted of a singlet at -4·0 (downfield from $(CH_3)_4Si$).

(b) 1-Chloro-(2'-methoxy-3',5',6'-trifluoropyridyl)tetrafluoroethane.

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
83·2	-	D(J_{4b4a} = 7·5) of T($J_{4b-3,5}$ = 10)	3	4b
93·4	93	D(J_{63} = 31) of D(J_{65} = 21)	1	6
125·3	-	T($J_{4a-3,5}$ = 43·5) of Q(J_{4a4b} = 7·5)	1	4a
137·2	137	D(J_{34a} = 43·5) of D(J_{36} = 31) of D(J_{35} = 13) of Q(J_{34b} = 10)	1	3
150·0	148	D(J_{54a} = 43·5) of D(J_{56} = 21) of D(J_{53} = 13) of Q(J_{54b} = 10)	1	5



XIII

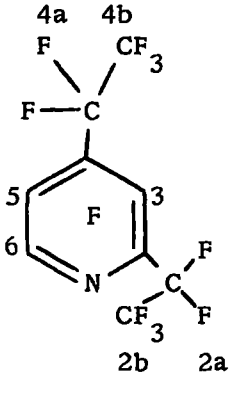
* Reference compound = 1-chloro-(tetrafluoropyridyl)tetrafluoroethane; s.c.s. for CH_3O were obtained from 4-heptafluoroisopropyl-2-methoxy-3,5,6-trifluoropyridine.[33]

Recorded as a neat liquid with an external $CFCl_3$ reference.

The ^1H n.m.r. consisted of a singlet -4·1 (downfield from $(CH_3)_4Si$).

(c) Perfluoro-(2,4-di-ethylpyridine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
83·8	83	D(J_{63} = 32) of D(J_{65} = 24)	1	6
84·9	-	D(J_{2b3} = 7) of T(J_{2b2a} = 1·5)	3	2b
86·6	-	D(J = 8·1) of D(J = 6·5) of T(J_{4b4a} = 2·1)	3	4b
113·5	-	T($J_{4a-3,5}$ = 31)	2	4a
116·9	-	D(J_{2a3} = 24) of Q(J_{2a2b} = 1·5)	2	2a
118·5	119	Broad	1	3
126·4	126	Complex multiplet	1	5



II

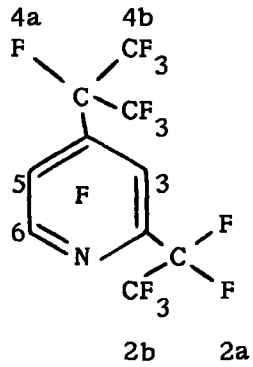
* Reference compound = perfluoro-(4-ethyl-pyridine); s.c.s. for 2-$(CF_3)_2CF$.

Recorded as a neat liquid with an internal $CFCl_3$ reference.

Using a variable temperature probe, spectra of II were recorded over the range -100° to +40°, however, apart from a slight broadening of the absorptions, there was no significant change in the spectrum.

(d) Perfluoro-(2-ethyl-4-isopropylpyridine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
75·1	-	Complex multiplet	6	4b
83·5	83	Complex, overlapping resonances	4	2b, 6
115·3	115	Complex, overlapping resonances	3	2a, 3
123·3	123	Broad	1	5
180·0	-	Broad	1	4a



XX

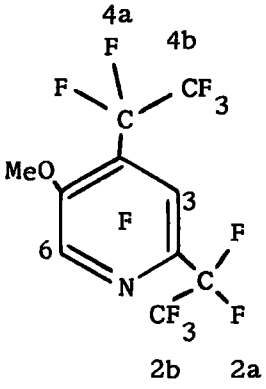
* Reference compound = perfluoro-(4-isopropylpyridine); s.c.s. for 2-CF_3CF_2.

Recorded as a neat liquid with an internal $CFCl_3$ reference.

9.3.3. Tri-substituted compounds.

(a) 2,4-Perfluorodi-ethyl-5-methoxy-3,6-difluoropyridine.

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
77·8	82	D(J_{63} = 32) of Q($J_{6\text{-}OMe}$ = 4)	1	6
85·5	-	D(J_{2b3} = 7) of T(J_{2b2a} = 1·5)	3	2b
86·8	-	D(J_{4b3} = 7·3) of T(J_{4b4a} = 2)	3	4b
116·4	-	Broad D(J_{4a3} = 39)	2	4a
117·2	-	Broad D(J_{2a3} = 24·5)	2	2a
123·2	123	Broad	1	3



XXVIII

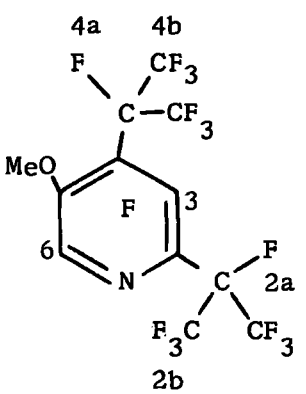
* Reference compound = perfluoro-(2,4-di-ethylpyridine); s.c.s. for 4-OCH_3.[142]

Recorded as a neat liquid with an external $CFCl_3$ reference.

The ^1H n.m.r. consisted of a doublet ($J_{6\text{-}OCH_3}$ = 4) at -3·9 (downfield from $(CH_3)_4Si$).

(b) 2,4-Perfluorodi-isopropyl-5-methoxy-3,6-difluoropyridine.

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
76·2	-	Complex, overlapping absorptions	12	4b, 2b
78·7	81	Broad D(J_{63} = 32)	1	6
120·2	119	Broad	1	3
179·6	-	Broad D(J_{4a3} = 112)	1	4a
185·5	-	Broad D(J_{2a3} = 56)	1	2a



XXIX

* Reference compound = perfluoro-(2,4-di-isopropylpyridine); s.c.s. for 4-OCH_3.[142]

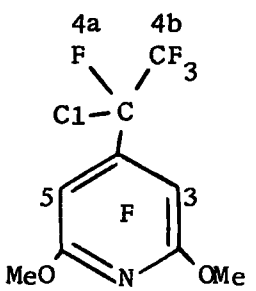
Recorded as a neat liquid with an external $CFCl_3$ reference.

The ^1H n.m.r. consisted of a doublet (J = 4) at -3·8 (downfield from $(CH_3)_4Si$).

High temperature studies of XXIX, especially at ca. 80°, gave, in general, sharper absorptions, however, complications due to rotational isomerism are also possible under such conditions.

(c) 1-Chloro-(2',6'-di-methoxy-3',5'-difluoropyridyl)tetrafluoroethane.

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
83·0	-	$T(J_{4b-3,5} = 10)$ of $D(J_{4b4a} = 8)$	3	4b
124·5	-	$T(J_{4a-3,5} = 44)$ of $Q(J_{4a4b} = 8)$	1	4a
148·3	147	$D(J_{3,5-4a} = 44)$ of $Q(J_{3,5-4b} = 10)$	2	3,5



XIV

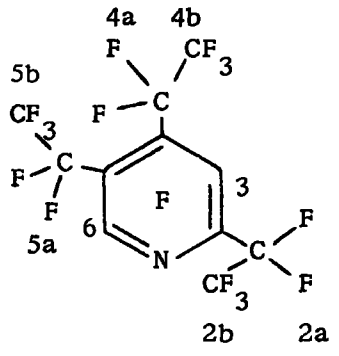
* Reference compound = 1-chloro-(2-methoxy-3,5,6-trifluoropyridyl)tetrafluoroethane; s.c.s. for 6-OCH_3.[142]

Recorded as a neat mixture (ca. 50:50) of the mono- and di-methoxy derivatives of 1-chloro-(tetrafluoropyridyl)tetrafluoroethane with an external $CFCl_3$ reference.

The ^1H n.m.r. consisted of a singlet at -3·8 (downfield from $(CH_3)_4Si$).

(d) Perfluoro-(2,4,5-tri-ethylpyridine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
55•5	50	Broad	1	6
81•4	-	Complex, overlapping absorptions	6	4b,5b
83•2	-	D(J = 6) of D(J = 1•5)	3	2b
103•3	-	Broad multiplet	4	4a,5a
115•8	114	Complex, overlapping absorptions	3	2a, 3

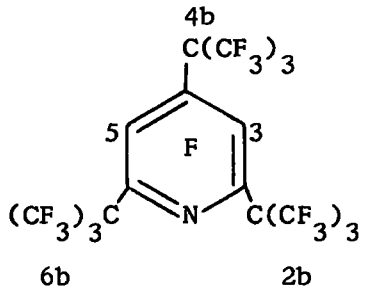


* Reference compound = perfluoro-(2,4-di-ethylpyridine); s.c.s. for 5-$(CF_3)_2CF$.

Recorded as a neat liquid with an internal $CFCl_3$ reference.

(e) Perfluoro-(2,4,6-tri-t-butylpyridine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure	Relative intensity	Assignment
60·7	-	Broad overlapping resonances	27	4b
61·8	-			2b, 6b
87·3	85	Broad	2	3,5



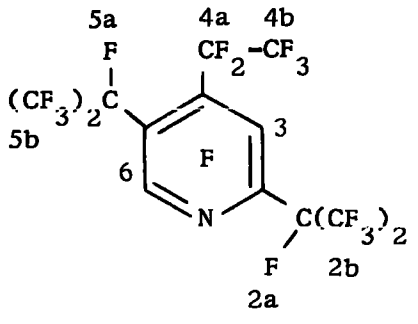
XXXI

* Reference compound = perfluoro-(4-t-butylpyridine)[143]; s.c.s. for 4-$(CF_3)_3C$ and 2,6-$(CF_3)_2CF$.

Recorded as a neat liquid at ca. 180° with an external $CFCl_3$ reference.

(f) Perfluoro-(2,5-di-isopropyl-4-ethylpyridine).

Shift (p.p.m.) Obs.	Shift (p.p.m.) Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
52•2	50	$D(J_{63} = 32)$ of $H(J_{65b} = 30)$	1	6
72•3	-	$D(J_{5b6} = 30)$ of $T(J_{5b4a} = 7)$ of $D(J_{5b5a} = 2•5)$	6	5b
74•1	-	$D(J_{2b3} = 7•5)$ of $D(J_{2b2a} = 6)$	6	2b
80•3	-	$D(J_{4b5a} = 31)$ of $D(J_{4b3} = 15)$	3	4b
99•7	-	$D(J_{4a5a} = 86)$ of $D(J_{4a3} = 52)$ of $H(J_{4a5b} = 7)$	2	4a
113•9	113	Broad complex multiplet	1	3
170•5	-	$T(J_{5a4a} = 86)$ of $Q(J_{5a4b} = 31)$	1	5a
183•8	-	$D(J_{2a3} = 60)$ or $H(J_{2a2b} = 6)$	1	2a



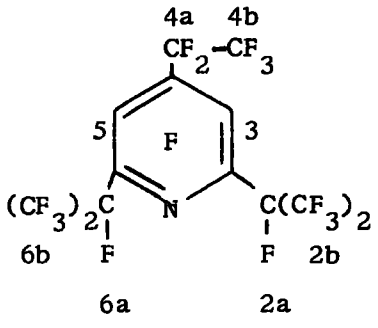
XVIII

* Reference compound = perfluoro-(4-ethyl-pyridine); s.c.s. for 2- and 5-$(CF_3)_2CF$.

Recorded as a neat liquid with an external $CFCl_3$ reference.

(g) Perfluoro-(2,6-di-isopropyl-4-ethylpyridine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
74•5	-	D(J_{6b6a} = 5) of D(J_{6b5} = 4•5)	12	2b, 6b
85•5	-	Broad T($J_{4b-3,5}$ = 7)	3	4b
111•4	108	Broad	2	3, 5
112•3	-	T($J_{4a-3,5}$ = 32)	2	4a
185•2	-	Broad D(J_{6a5} = 59)	2	2a, 6a



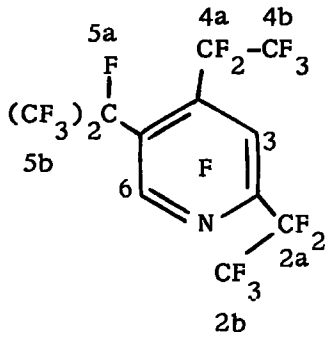
XXV

* Reference compound = perfluoro-(4-ethylpyridine); s.c.s. for 2,6-$(CF_3)_2CF$.

Recorded as a neat liquid with an external $CFCl_3$ reference.

(h) Perfluoro-(5-isopropyl-2,4-di-ethylpyridine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
53·6	50	Broad H(J_{65b} = 29)	1	6
72·3	-	D(J_{5b6} = 29) of T(J_{5b4a} = 6·5)	6	5b
81·0	-	D(J_{4b5a} = 32) of D(J_{4b3} = 14)	3	4b
83·1	-	D(J_{2b3} = 7)	3	2b
100·1	-	Broad D(J_{4a5a} = 87) of D(J_{4a3} = 45)	2	4a
115·2	114	Broad	1	3
116·1	-	D(J_{2a3} = 23)	2	2a
170·2	-	T(J_{5a4a} = 87) of Q(J_{5a4b} = 32)	1	5a



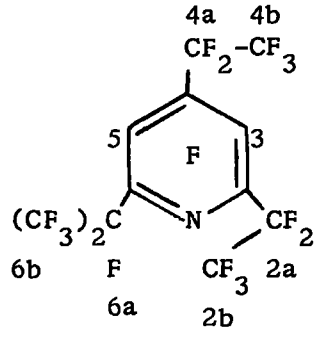
XIX

* Reference compound = perfluoro-(2,4-di-ethylpyridine); s.c.s. for 5-$(CF_3)_2CF$.

Recorded as a neat liquid with an external $CFCl_3$ reference.

(i) Perfluoro-(6-isopropyl-2,4-di-ethylpyridine).

Shifts (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
76·4	-	D(J_{6b6a} = 6) of D(J_{6b5} = 6)	6	6b
85·2	-	D(J_{2b3} = 5)	3	2b
87·4	-	Broad T($J_{4b-3,5}$ = 14)	3	4b
108·6	107	Broad	1	5
111·5	108	Broad	1	3
113·5	-	T($J_{4a-3,5}$ = 32)	2	4a
116·8	-	D(J_{2a3} = 23)	2	2a
186·9	-	D(J_{6a5} = 56) of H(J_{6a6b} = 6)	1	6a



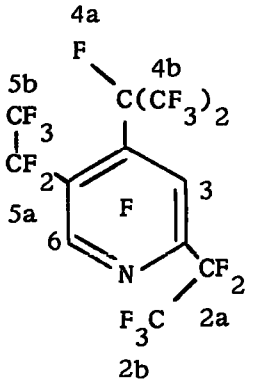
XXVI

* Reference compound = perfluoro-(2,4-di-ethylpyridine); s.c.s. for 6-$(CF_3)_2CF$.

Recorded as a neat liquid with an external $CFCl_3$ reference.

(j) Perfluoro-(2,5-di-ethyl-4-isopropylpyridine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
52·9	55	T(J_{65a} = 47) of D(J_{63} = 31) of Q(J_{65b} = 14)	1	6
72·1	-	Broad D(J_{4b3} = 32)	6	4b
80·1	-	D(J_{5b4a} = 33) of D(J_{5b6} = 14)	3	5b
83·0	-	D(J_{2b3} = 8	3	2b
100·0		D(J_{5a4a} = 86) of D(J_{5a6} = 47) of H(J_{5a4b} = 6)	2	5a
114·8	113	Broad multiplet	1	3
116·3	-	D(J_{2a3} = 26)	2	2a
170·1	-	T(J_{4a5a} = 86) of Q(J_{4a5b} = 33)	1	4a



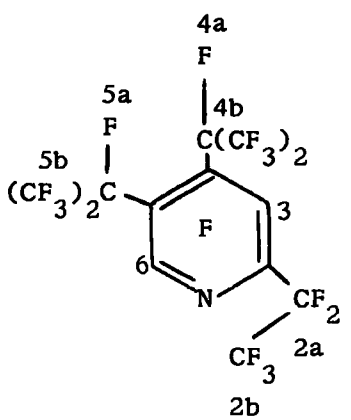
XXI

* Reference compound = perfluoro-(2-ethyl-4-isopropylpyridine); s.c.s. for $5CF_3CF_2$.

Recorded as a neat liquid with an external $CFCl_3$ reference.

(k) Perfluoro-(2-ethyl-4,5-di-isopropylpyridine).

Shifts (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
52·4	50	D(J_{63} = 31) of H(J_{65b} = 32)	1	6
74·0	-	D(J_{4b3} = 32; J_{5b6} = 32) of T(J_{4b4a} = 7·5; J_{5b5a} = 7·5)	12	4b,5b
85·4	-	D(J_{2b} = 7·5)	3	2b
113·6	111	Broad multiplet	1	3
117·9	-	D(J_{2a3} = 25)	2	2a
167·8	-	Broad	2	4a,5a



XXIV

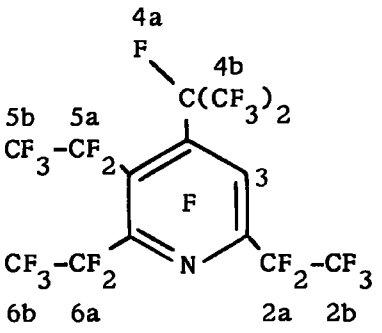
* Reference compound = perfluoro-(2-ethyl-4-isopropylpyridine); s.c.s. for 5-$(CF_3)_2CF$.

Recorded as a neat liquid with an external $CFCl_3$ reference.

9.3.4. Tetra-substituted compounds.

(a) Perfluoro-(2,5,6-tri-ethyl-4-isopropylpyridine).

Shifts (p.p.m.) Obs.	Calc.*	Relative intensity	Assignment
73•9	-	9	4b,6b
81•4	-	3	5b
84•8	-	3	2b
-	100		3
108•7	-	4	2a,6a
117•3	-	2	5a
171•9	-	1	4a



XXII

* Reference compound = perfluoro-(2,5-di-ethyl-4-isopropylpyridine); s.c.s. for 2-CF_3CF_2.

Recorded as a neat liquid with an external $CFCl_3$ reference.

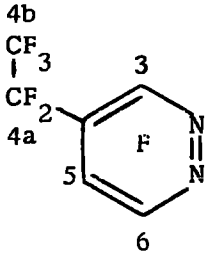
The observed spectrum of XXII consisted of broad resonances with little or no fine structure; assignments were made by comparison with the spectrum of the reference compound. An absorption due to the remaining ring fluorine (3) was not observed, however, large couplings with the substituent groups are expected to result in an extremely broad absorption of similar amplitude to the background.

9.4. Data for polyfluoropyridazine derivatives.

9.4.1. Mono-substituted compounds.

(a) Perfluoro-(4-ethylpyridazine).

Shift (p.p.m.) Obs.	Shift (p.p.m.) Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
77•4	71	D(J_{36} = 34) of T(J_{34a} = 26•5) of D(J_{35} = 15) of Q(J_{34b} = 8)	1	3
87•0	-	D(J_{4b3} = 8) of D(J_{4b5} = 6) of T(J_{4b4a} = 2)	3	4b
97•5	97	D(J_{63} = 34) of D(J_{65} = 25)	1	6
115•0	-	T($J_{4a-3,5}$ = 26•5)	2	4a
120•6	118	T(J_{54a} = 26•5) of D(J_{56} = 25) of D(J_{53} = 15) of Q(J_{54b} = 6)	1	5



VI

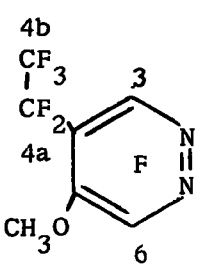
* Reference compound = tetrafluoropyridazine; s.c.s. for 4-$(CF_3)_2CF$.

Recorded as a neat liquid with an internal $CFCl_3$ reference.

9.4.2. Di-substituted compounds.

(a) 4-Pentafluoroethyl-5-methoxy-3,6-difluoropyridazine.

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
81·4	80	D(J_{36} = 34) of T(J_{34a} = 33) of Q(J_{34b} = 7)	1	3
85·5	-	Broad D(J_{4b3} = 7)	3	4b
90·2	92	D(J_{63} = 34) of Q(J_{6OMe} = 5·5)	1	6
113·6	-	D(J_{4a3} = 33)	2	4a



XXX

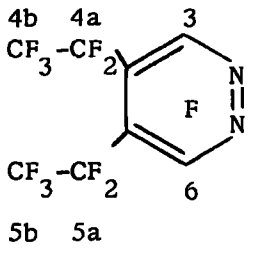
* Reference compound = perfluoro-(4-ethyl-pyridazine); s.c.s. for 5-OCH_3 obtained from 3,6-difluoro-4,5-dimethoxypyridazine.[37]

Recorded as a neat liquid with an external $CFCl_3$ reference.

The ^1H n.m.r. consisted of a doublet (J = 5·5) at -4·2 (downfield from $(CH_3)_4Si$).

(b) Perfluoro-(4,5-di-ethylpyridazine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure	Relative intensity	Assignment
77·7	81	Broad complex multiplet	2	3,6
82·6	-	Complex multiplet	6	4b,5b
107·2	-	Complex multiplet	4	4a,5a



VII

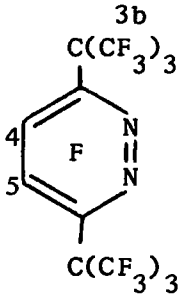
* Reference compound = perfluoro-(4-ethyl-pyridazine); s.c.s. for 5-$(CF_3)_2CF$.

Recorded in acetone solution with an external $CFCl_3$ reference.

Variable temperature studies of VII at ca. 0°, 70°, 140° and 180° gave only broadened resonances and did not simplify analysis of the spectrum.

(c) Perfluoro-(3,6-di-t-butylpyridazine).

Shifts (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
62·4	-	D(J = 19·5	18	3b,6b
129·2	133	Broad multiplet	2	4,5



XXXII

* Reference compound = tetrafluoropyridazine; s.c.s. for 3-$(CF_3)_2CF$, obtained from perfluoro-(3,5-di-isopropylpyridazine).

Recorded in acetone solution with an external $CFCl_3$ reference.

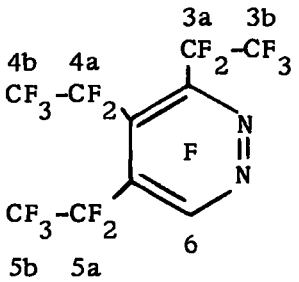
The calculated chemical shifts for the other possible di-substitution patterns are as shown.

	3	5	6
4,5-isomer	70	-	71
4,6-isomer	67	103	-

9.4.3. Tri-substituted compounds.

(a) Perfluoro-(3,4,5-tri-ethylpyridazine).

Shift (p.p.m.) Obs.	Calc.*	Fine structure (Coupling constants in Hz)	Relative intensity	Assignment
70•2	75	T(J_{65a} = 26) of Q(J_{65b} = 17)	1	6
74•5	-	T(J = 15•5) of T(J = 15)	3	3b
80•9	-	D(J_{5b6} = 17) of T(J = 17)	3	5b
81•7	-	Broad singlet	3	4b
93•0	-	Broad	2	3a
104•7	-	Broad	2	4a
108•0	-	Broad	2	5a



VIII

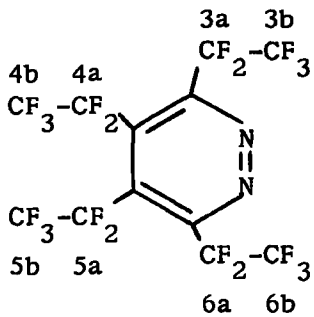
* Reference compound = perfluoro-(4,5-di-ethylpyridazine); s.c.s. for 3-$(CF_3)_2CF$.

Recorded as a neat liquid with an external $CFCl_3$ reference.

9.4.4. Tetra-substituted compounds.

(a) Tetrakis(pentafluoroethyl)pyridazine.

Shift (p.p.m.) Obs.	Fine structure	Relative intensity	Assignment
73·2	Broad	6	3b,6b
80·8	Singlet	6	4b,5b
91·2	Broad	4	3a,6a
108·8	Broad	4	4a,5a



XXXIII

Recorded as an acetone solution with an external $CFCl_3$ reference.

APPENDIX 1

Mass Spectral Data

Mass Spectral Data of Polyfluoro-pyridine and -pyridazine Derivatives [^{m}/e values; relative abundance (% of base peak) in parentheses].

All peaks > 5% of the base peak (arbitrarily 100%) are recorded; * indicates parent peak.

Perfluoro-(4-ethylpyridine)(I).

269 (23)*, 250 (8), 201 (6), 200 (100), 150 (7), 131 (5), 117 (8), 105 (6), 100 (16), 93 (9), 86 (5), 69 (46), 31 (19).

Perfluoro-(2,4-di-ethylpyridine) (II).

369 (18)*, 350 (20), 301 (11), 300 (100), 269 (22), 250 (25), 231 (18), 201 (5), 200 (62), 181 (9), 131 (5), 117 (6), 100 (7), 93 (5), 69 (25), 31 (5).

Perfluoro-(2,4,5-tri-ethylpyridine) (III).

469 (12)*, 450 (28), 400 (79), 350 (44), 331 (12), 319 (5), 312 (7), 300 (27), 281 (42), 262 (35), 250 (8), 231 (10), 219 (14), 212 (13), 200 (16), 193 (7), 181 (6), 169 (5), 167 (5), 162 (13), 131 (14), 124 (7), 119 (5), 117 (14), 100 (10), 93 (11), 69 (100), 31 (10).

Perfluoro-(4-ethylpyridazine) (VI).

253(6), 252 (79)*, 233 (13), 184 (7), 183 (100), 155 (15), 152 (22), 124 (6), 119 (5), 105 (11), 93 (25), 74 (10), 69 (57), 55 (6), 31 (25).

Perfluoro-(4,5-di-ethylpyridazine) (VII).

353 (10), 352 (95)*, 333 (48), 305 (6), 284 (10), 283 (92), 267 (5), 255 (8), 234 (9), 233 (100), 205 (14), 186 (7), 183 (11), 177 (8), 155 (18), 150 (11), 119 (23), 117 (16), 100 (10), 93 (15), 86 (22), 69 (70).

Perfluoro-(3,4,5-tri-ethylpyridazine) (VIII).

452 (29)*, 433 (22), 383 (10), 352 (12), 333 (7), 305 (16), 286 (8), 283 (17), 267 (10), 255 (13), 236 (9), 233 (21), 217 (10), 205 (6), 183 (7), 155 (6), 119 (18), 117 (13), 100 (7), 93 (13), 69 (100), 31 (13).

Perfluoro-(2,4,6-tri-t-butylpyridine) (XXXI).

770 (7), 769 (29)*, 751 (10), 750 (41), 700 (19), 681 (14), 662 (5), 612 (7), 600 (11), 69 (100).

Perfluoro-(3,6-di-t-butylpyridazine) (XXXII).

553 (7), 552 (38)*, 534 (6), 533 (35), 454 (5), 367 (13), 317 (7), 255 (7), 120 (11), 109 (5), 97 (5), 95 (7), 69 (100), 57 (7), 55 (27).

Perfluoro-(4-vinylpyridine) (IX).

232 (9), 231 (100)*, 212 (20), 200(9), 186 (9), 182 (5), 181 (69), 162 (61), 136 (21), 131 (43), 124 (13), 117 (69), 112 (7), 105 (9), 100 (11), 98 (10), 93 (24), 86 (14), 81 (5), 74 (11), 69 (43), 31 (38).

2-(2',3',5',6'-Tetrafluoropyridyl)pentafluoropropene (X).

282 (7), 281 (72)*, 262 (36), 231 (10), 219 (12), 212 (20), 200 (30), 193 (8), 181 (7), 169 (11), 162 (17), 155 (13), 124 (9), 117 (22), 100 (10), 93 (13), 69 (100), 31 (17).

4-Pentafluoroethyl-2-methoxy-3,5,6-trifluoropyridine (XXVII).

282 (11), 281 (100)*, 280 (13), 262 (32), 253 (9), 252 (71), 251 (28), 250 (7), 238 (7), 213 (7), 212 (56), 201 (9), 200 (26), 197 (14), 188 (35), 185 (7), 184 (83), 182 (34), 181 (11), 171 (9), 169 (49), 164 (8), 162 (14), 155 (12), 150 (7), 143 (19), 134 (9), 132 (10), 131 (16), 124 (17), 119 (11), 117 (8), 105 (10), 100 (34), 93 (39), 92 (9), 86 (10), 84 (14), 80 (10), 74 (24), 69 (79), 48 (22), 31 (32).

2,4-Perfluorodi-ethyl-5-methoxy-3,6-difluoropyridine (XXVIII).

382 (7), 381 (34)*, 362 (17), 312 (100), 278 (16), 250 (6), 228 (15), 200 (23), 155 (8), 138 (17), 117 (7), 69 (37), 33 (9), 31 (7).

2,4-Perfluoro-di-isopropyl-5-methoxy-3,6-difluoropyridine (XXIX).

482 (8), 481 (47)*, 463 (6), 462 (37), 428 (8), 413 (15), 412 (90), 363 (8), 362 (60), 328 (15), 263 (5), 262 (5), 250 (8), 200 (9),

167 (5), 117 (7), 93 (6), 69 (100).

4-Pentafluoroethyl-5-methoxy-3,6-difluoropyridazine (XXX).

265 (9), 264 (100)*, 245 (11), 216 (7), 195 (7), 193 (7), 165 (5), 164 (24), 155 (12), 147 (74), 143 (19), 137 (31), 135 (7), 124 (10), 119 (14), 117 (8), 105 (11), 100 (5), 93 (37), 90 (14), 87 (11), 86 (7), 76 (8), 74 (12), 71 (22), 69 (8), 60 (7), 51 (11), 33 (22), 31 (26).

1-Chloro-1-(2'-methoxy-3',5',6'-trifluoropyridyl)tetrafluoroethane (XIII).

299 (36)*, 298 (16), 297 (100)*, 296 (15), 278 (10), 270 (21), 269 (13), 268 (63), 267 (20), 262 (25), 234 (29), 230 (15), 228 (41), 216 (17), 212 (38), 200 (43), 199 (15), 198 (21), 197 (10), 185 (16), 184 (12), 182 (12), 181 (19), 178 (11), 169 (25), 162 (18), 159 (10), 155 (10), 150 (10), 143 (10), 131 (12), 124 (13), 117 (12), 109 (9), 105 (13), 100 (23), 93 (27), 92 (9), 85 (13), 74 (18), 69 (73), 31 (36).

1,1-Bis-(2',3',5',6'-tetrafluoropyridyl)tetrafluoroethane (XVI).

401 (14), 400 (97)*, 381 (15), 332 (15), 331 (100), 293 (12), 286 (18), 282 (6), 281 (48), 262 (19), 236 (6), 231 (10), 217 (5), 200 (23), 186 (6), 117 (8), 100 (8), 93 (8), 69 (58), 31 (12).

2,2-Bis-(2',3',5',6'-tetrafluoropyridyl)hexafluoropropane (X).

451 (11), 450 (66)*, 431 (10), 382 (5), 381 (26), 331 (14), 312 (11), 293 (25), 287 (8), 286 (63), 281 (15), 262 (16), 248 (7), 200 (7), 117 (6), 100 (8), 93 (6), 69 (100), 31 (9).

Tetrakis(pentafluoroethyl)pyridazine (XXXIII).

553 (18), 552 (98)*, 531 (51), 505 (7), 455 (16), 417 (8), 240 (42), 386 (6), 367 (29), 355 (21), 336 (9), 317 (47), 305 (10), 297 (6), 286 (8), 267 (40), 255 (6), 248 (7), 243 (8), 229 (5), 217 (19), 198 (7), 193 (32), 181 (8), 179 (10), 174 (5), 169 (5), 167 (13), 155 (11), 148 (20), 143 (24), 131 (10), 129 (6), 124 (21), 120 (6), 119 (100), 117 (8), 100 (25), 93 (10), 69 (99), 31 (14).

Perfluoro-(2,5-di-isopropyl 4-ethylpyridine) (XVIII).

570 (5), 569 (31)*, 551 (7), 550 (48), 501 (8), 500 (58), 462 (7), 451 (8), 450 (63), 412 (13), 400 (21), 362 (11), 312 (10), 274 (5), 69 (100).

Perfluoro-(5-isopropyl-2,4-di-ethylpyridine) (XIX).

519 (13)*, 500 (20), 450 (55), 400 (28), 381 (6), 362 (9), 350 (17), 312 (13), 93 (5), 69 (100).

Perfluoro-(2-ethyl-4-isopropylpyridine) (XX).

419 (16)*, 400 (19), 350 (100), 300 (12), 281 (16), 250 (19), 231 (10), 219 (9), 131 (6), 69 (44).

Perfluoro-(2,5-di-ethyl-4-isopropylpyridine) (XXI).

520 (5), 519 (30)*, 501 (10), 500 (74), 451 (17), 450 (99), 412 (7), 400 (17), 381 (10), 362 (16), 350 (24), 312 (24), 293 (5), 274 (5), 262 (11), 224 (7), 119 (5), 117 (5), 93 (7), 69 (100).

Perfluoro-(2,5,6-tri-ethyl-4-isopropylpyridine) (XXII).

619 (8)*, 601 (9), 600 (47), 551 (14), 550 (78), 500 (15), 462 (8), 450 (8), 412 (14), 400 (5), 362 (7), 350 (6), 267 (5), 119 (14), 93 (5), 69 (100).

Perfluoro-(2-ethyl-4,5-di-isopropylpyridine) (XXIV).

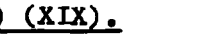
569 (17)*, 551 (5), 550 (30), 501 (9), 500 (52), 462 (5), 450 (20), 431 (5), 412 (10), 362 (11), 350 (5), 312 (6), 274 (5), 119 (8), 69 (100).

Perfluoro-(2,6-di-isopropyl-4-ethylpyridine) (XXV).

569 (33)*, 550 (73), 501 (9), 500 (96), 451 (12), 450 (100), 400 (6), 381 (8), 362 (6), 331 (5), 219 (32), 131 (22), 119 (6), 100 (8), 69 (99), 31 (47).

Perfluoro-(6-isopropyl-2,4-di-ethylpyridine) (XXVI).

519 (15)*, 501 (6), 500 (32), 451 (14), 450 (100), 400 (27), 381 (8), 331 (9), 117 (5), 69 (32).



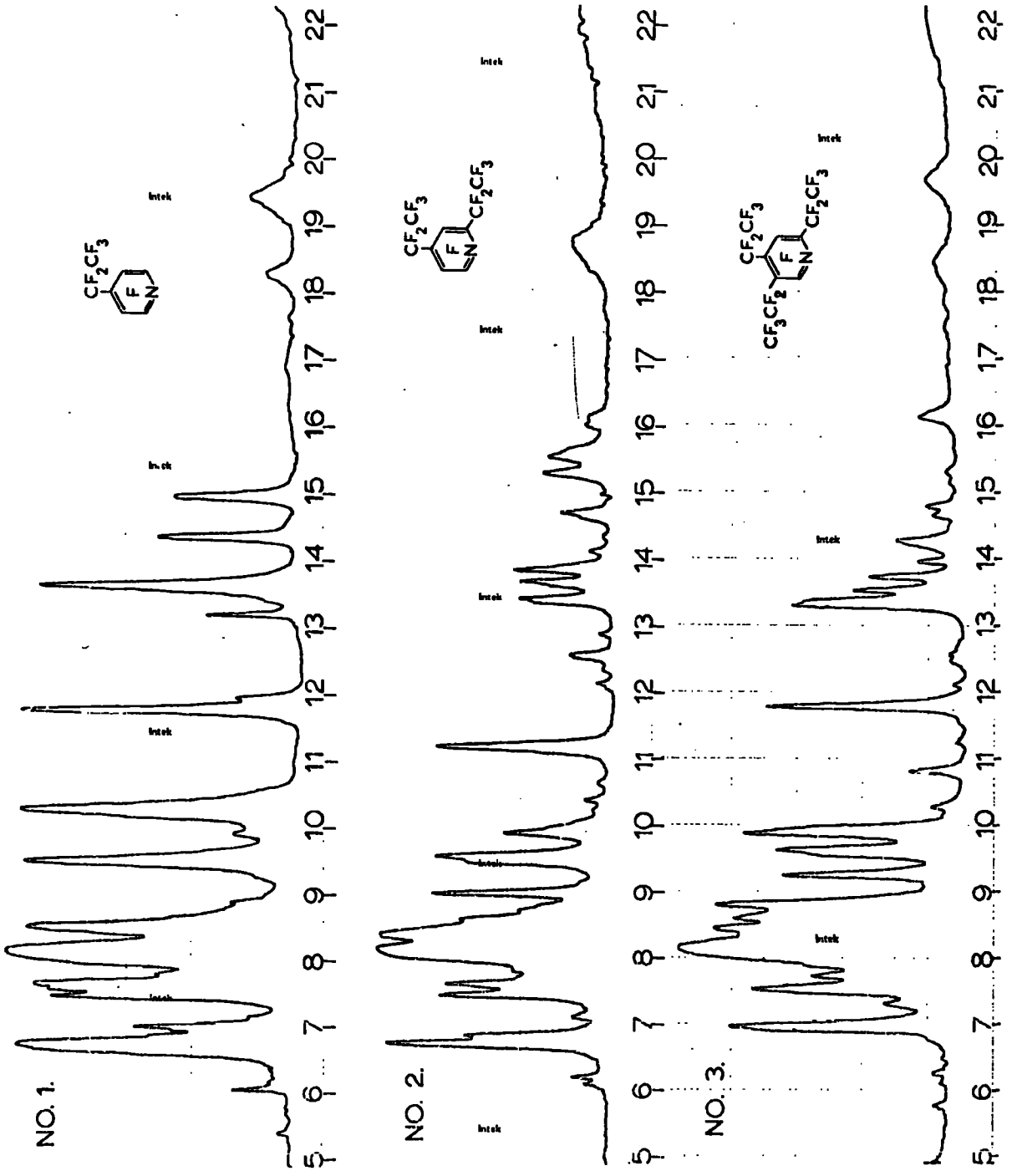
APPENDIX 2

Infra-red Spectra

Solid samples were recorded as KBr discs and liquid or low melting solid samples as contact films between KBr plates.

Spectrum No.	Compound	
1	Perfluoro-(4-ethylpyridine)	(l)
2	Perfluoro-(2,4-di-ethylpyridine)	(l)
3	Perfluoro-(2,4,5-tri-ethylpyridine)	(l)
4	Perfluoro-(4-ethylpyridazine)	(l)
5	Perfluoro-(4,5-di-ethylpyridazine)	(l)
6	Perfluoro-(3,4,5-tri-ethylpyridazine)	(l)
7	Perfluoro-(2,4,6-tri-t-butylpyridine)	(s)
8	Perfluoro-(3,6-di-t-butylpyridazine)	(s)
9	Perfluoro-(4-vinylpyridine)	(l)
10	2-(2',3',5',6'-Tetrafluoropyridyl)-pentafluoropropene	(l)
11	4-Pentafluoroethyl-2-methoxy-3,5,6-trifluoropyridine	(l)
12	2,4-Perfluorodi-ethyl-5-methoxy-3,6-difluoropyridine	(l)
13	2,4-Perfluorodi-isopropyl-5-methoxy-3,6-difluoropyridine	(l)
14	4-Pentafluoroethyl-5-methoxy-3,6-difluoropyridazine	(l)
15	Polymer from hydrolysis of perfluoro-(3,6-di-t-butylpyridazine)	(s)
16	1-Chloro-(2'-methoxy-3',5',6'-trifluoropyridyl)tetrafluoroethane	(l)
17	1,1-Bis-(2',3',5',6'-tetrafluoropyridyl)-tetrafluoroethane	(s)
18	2,2-Bis(2',3',5',6'-tetrafluoropyridyl)-hexafluoropropane	(s)
19	Tetrakis(pentafluoroethyl)pyridazine	(l)
20	Perfluoro-(2,5-di-isopropyl-4-ethyl-pyridine)	(l)

Spectrum No.	Compound	
21	Perfluoro-(5-isopropyl-2,4-di-ethylpyridine)	(1)
22	Perfluoro-(2-ethyl-4-isopropylpyridine)	(1)
23	Perfluoro-(2,5-di-ethyl-4-isopropylpyridine)	(1)
24	Perfluoro-(2,5,6-tri-ethyl-4-isopropylpyridine)	(1)
25	Perfluoro-(tetraethyl-4-isopropylpyridine)	(1)
26	Perfluoro-(2-ethyl-4,5-di-isopropylpyridine)	(1)
27	Perfluoro-(2,6-di-isopropyl-4-ethylpyridine)	(1)
28	Perfluoro-(6-isopropyl-2,4-di-ethylpyridine)	(1)
29	Perfluoro-(4,5-di-ethylpyridazine) (a) ca. 60°	(1)
	(b) ca. 15°	(1)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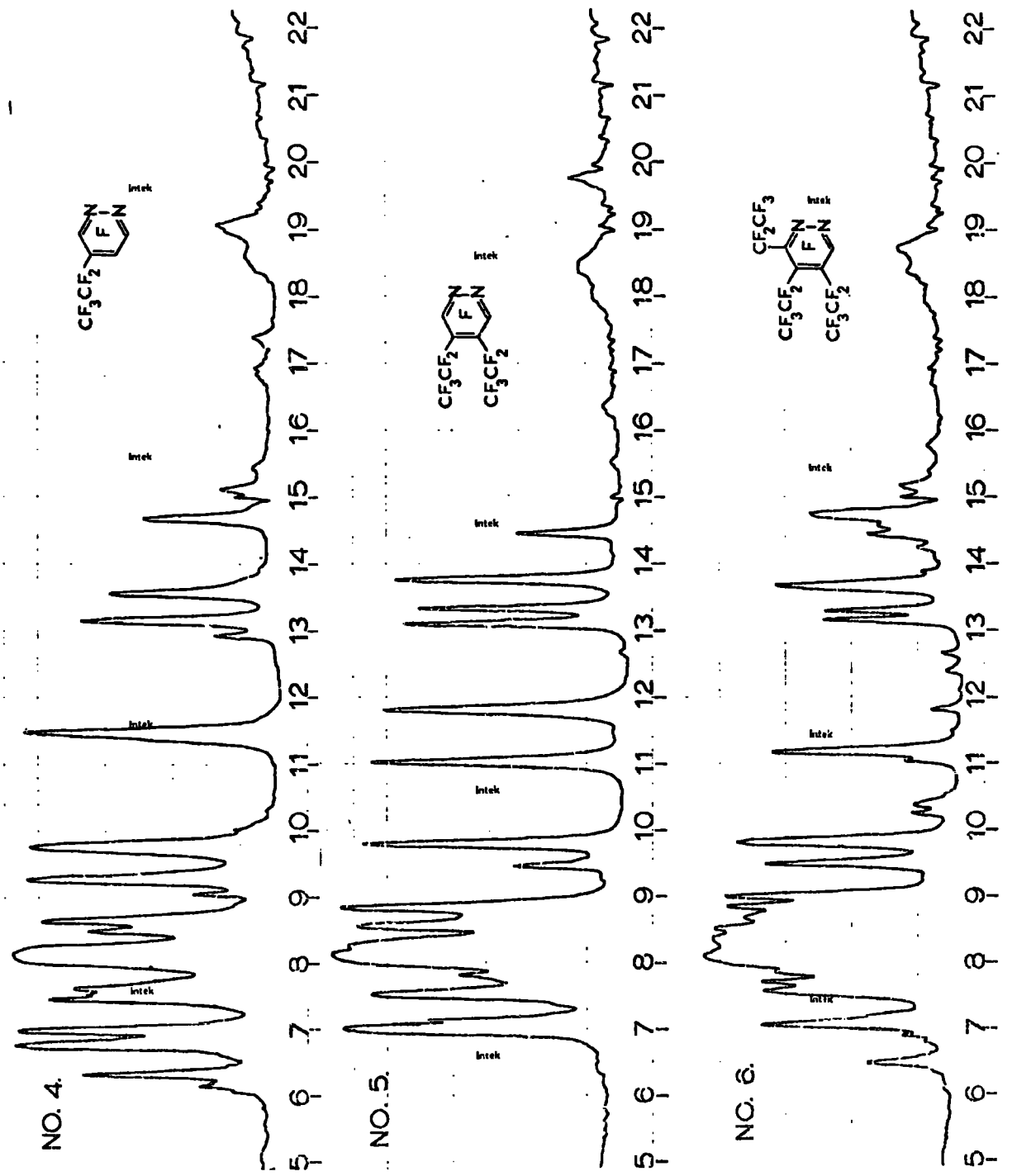
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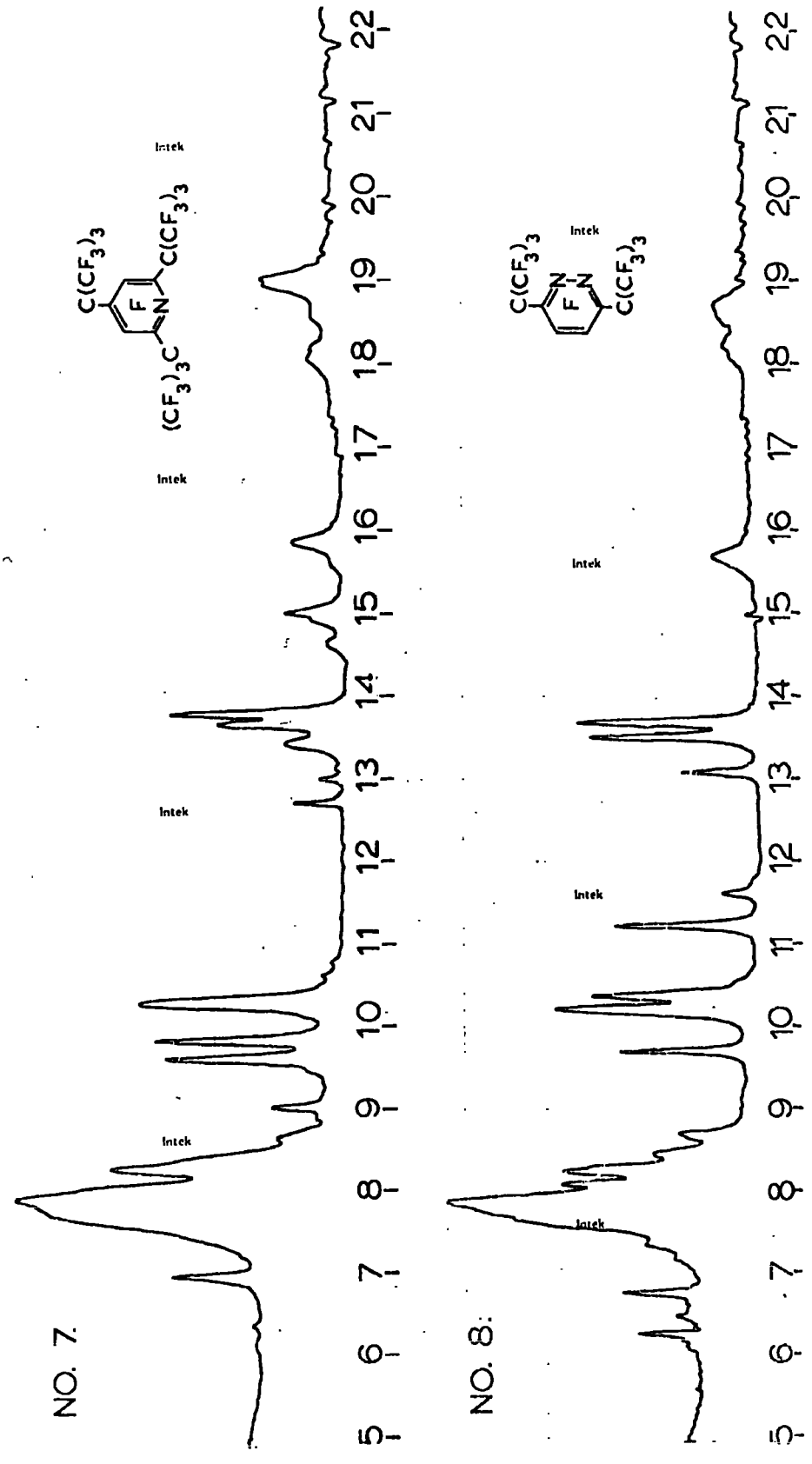
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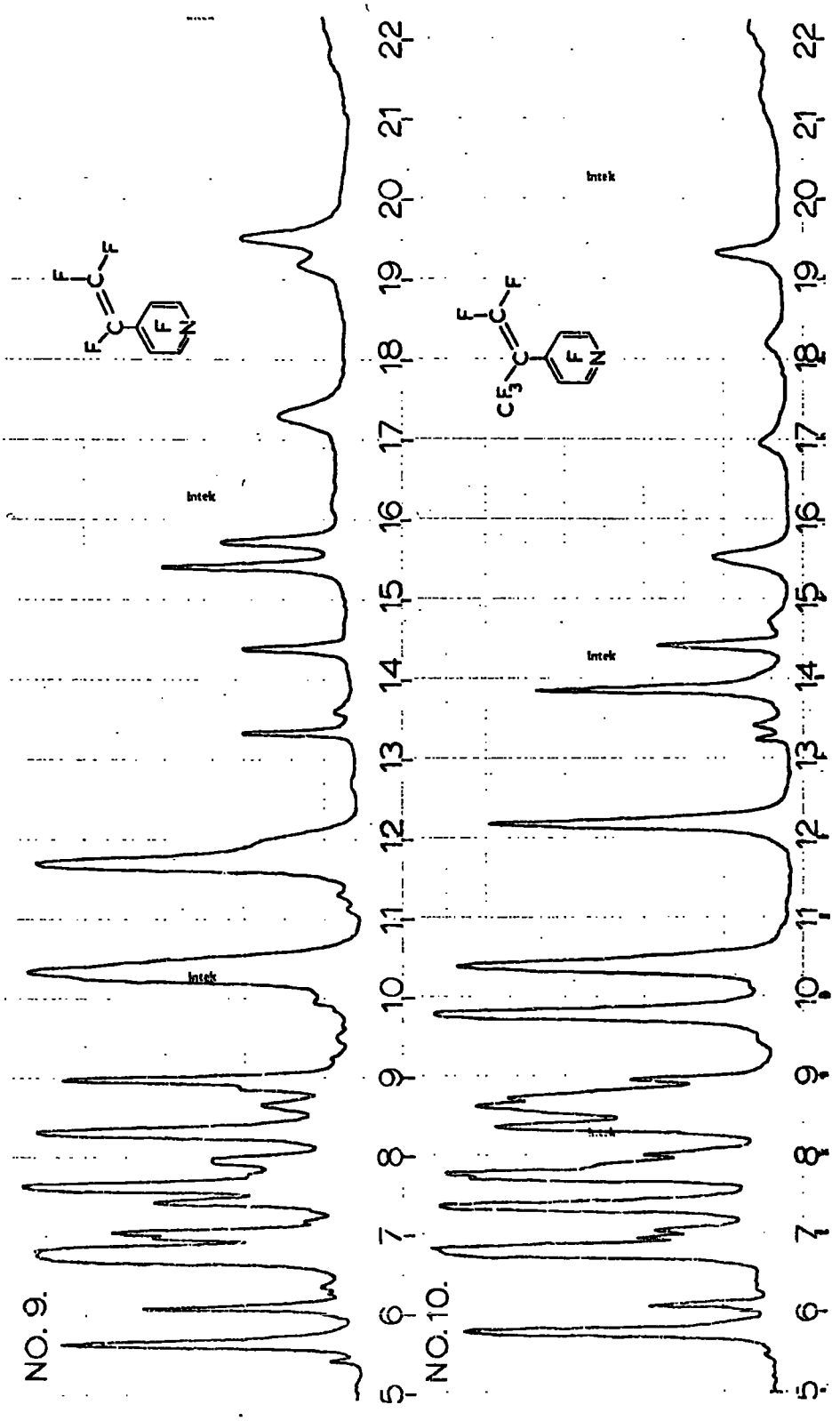
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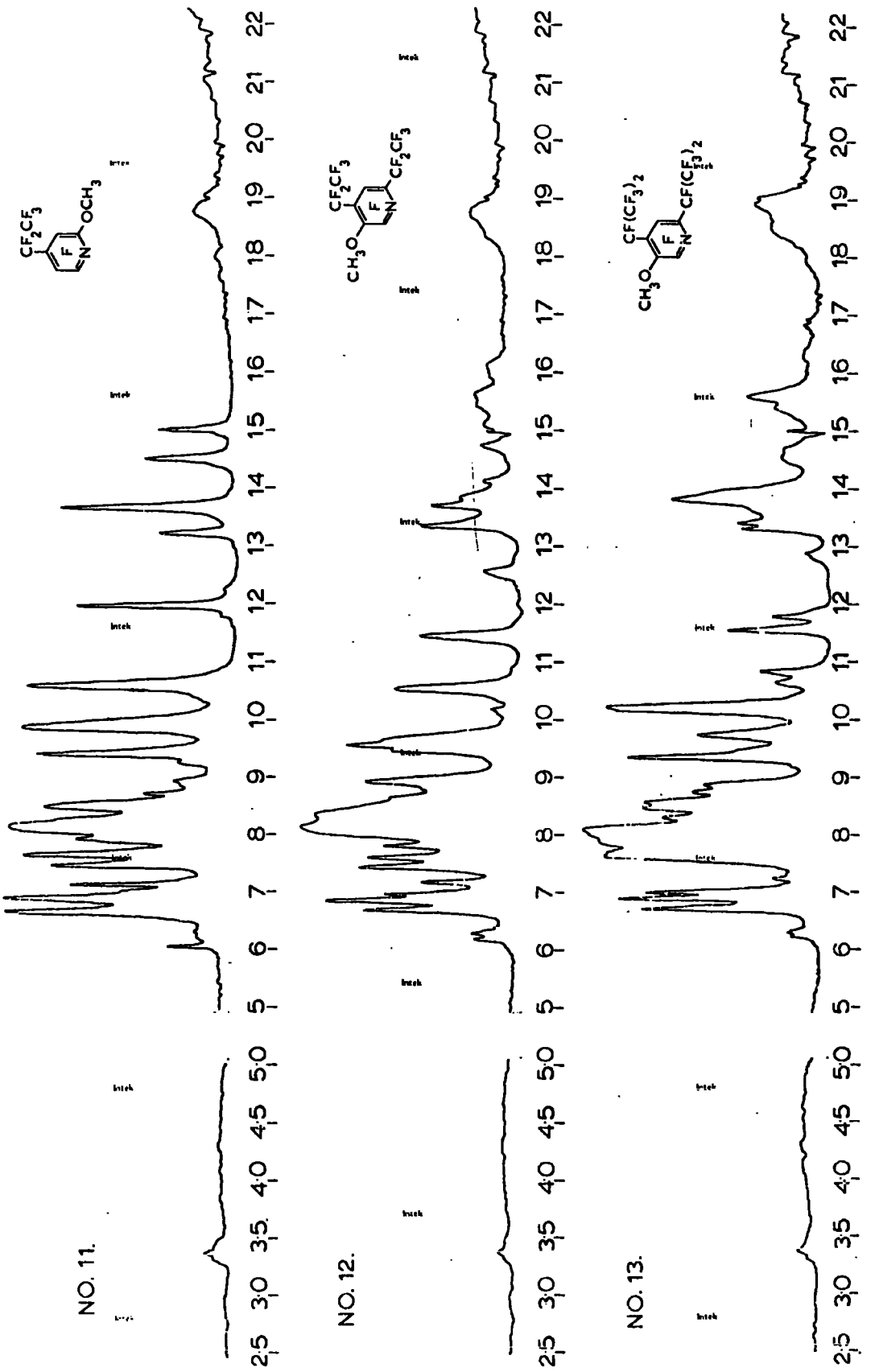
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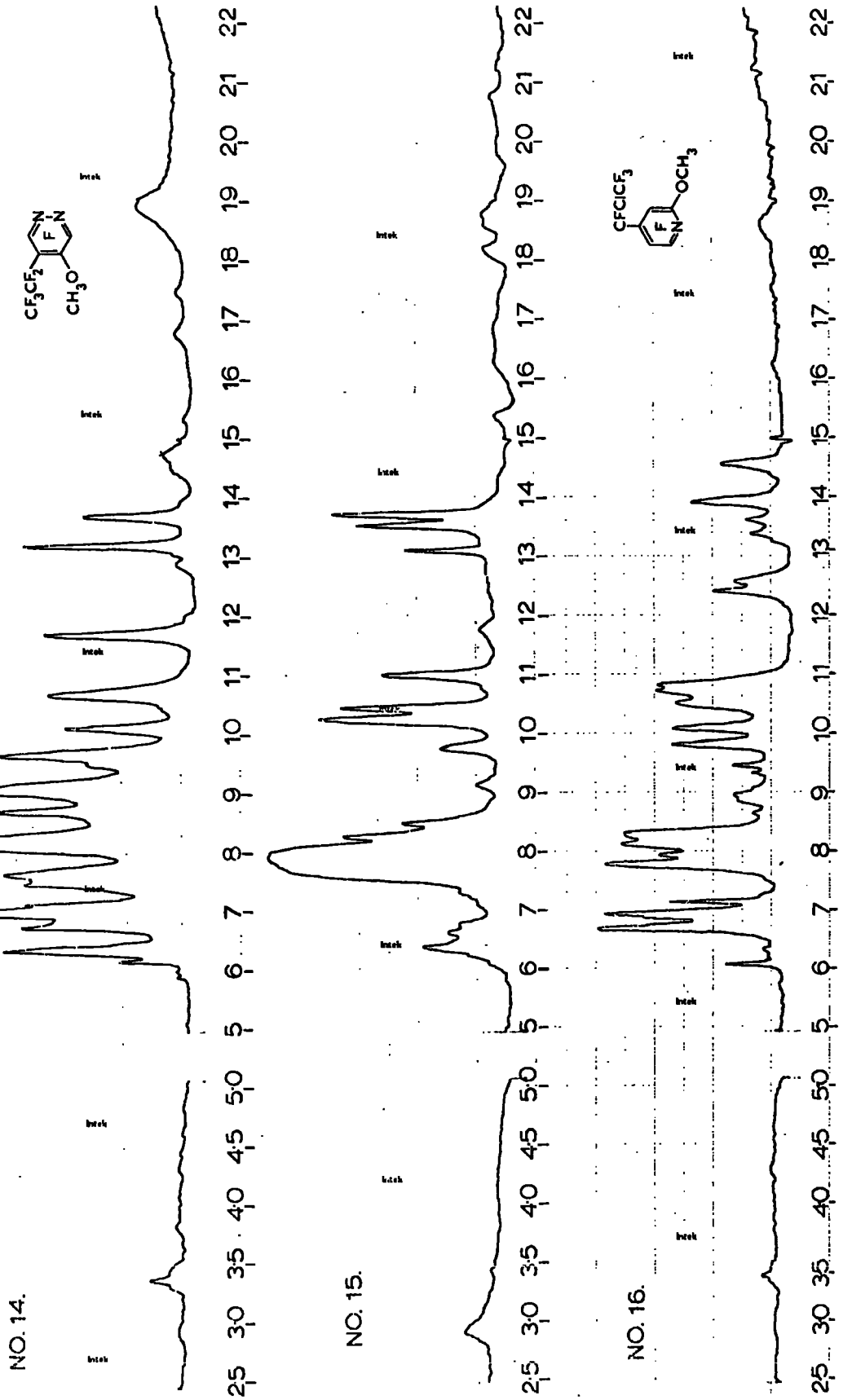
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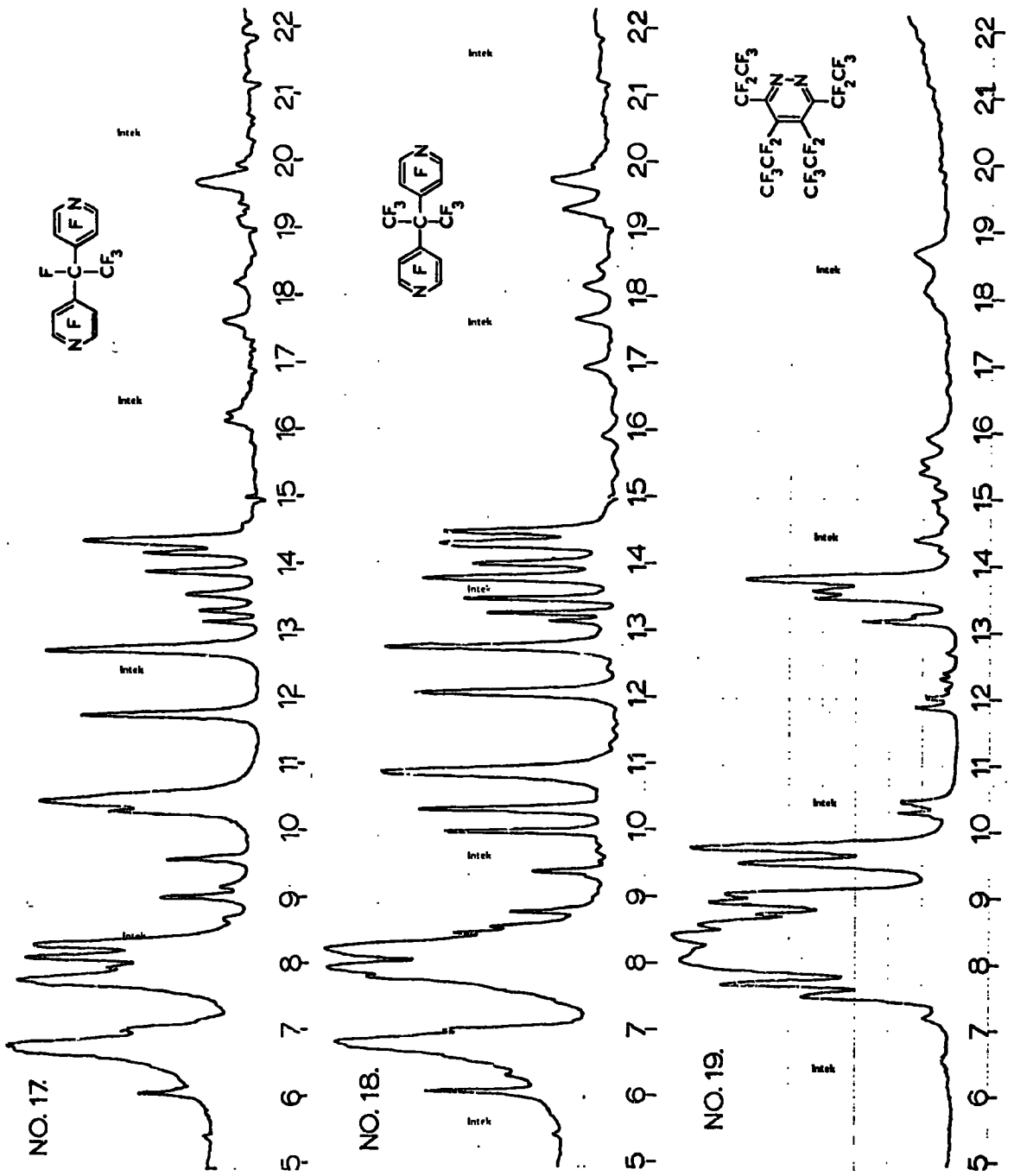
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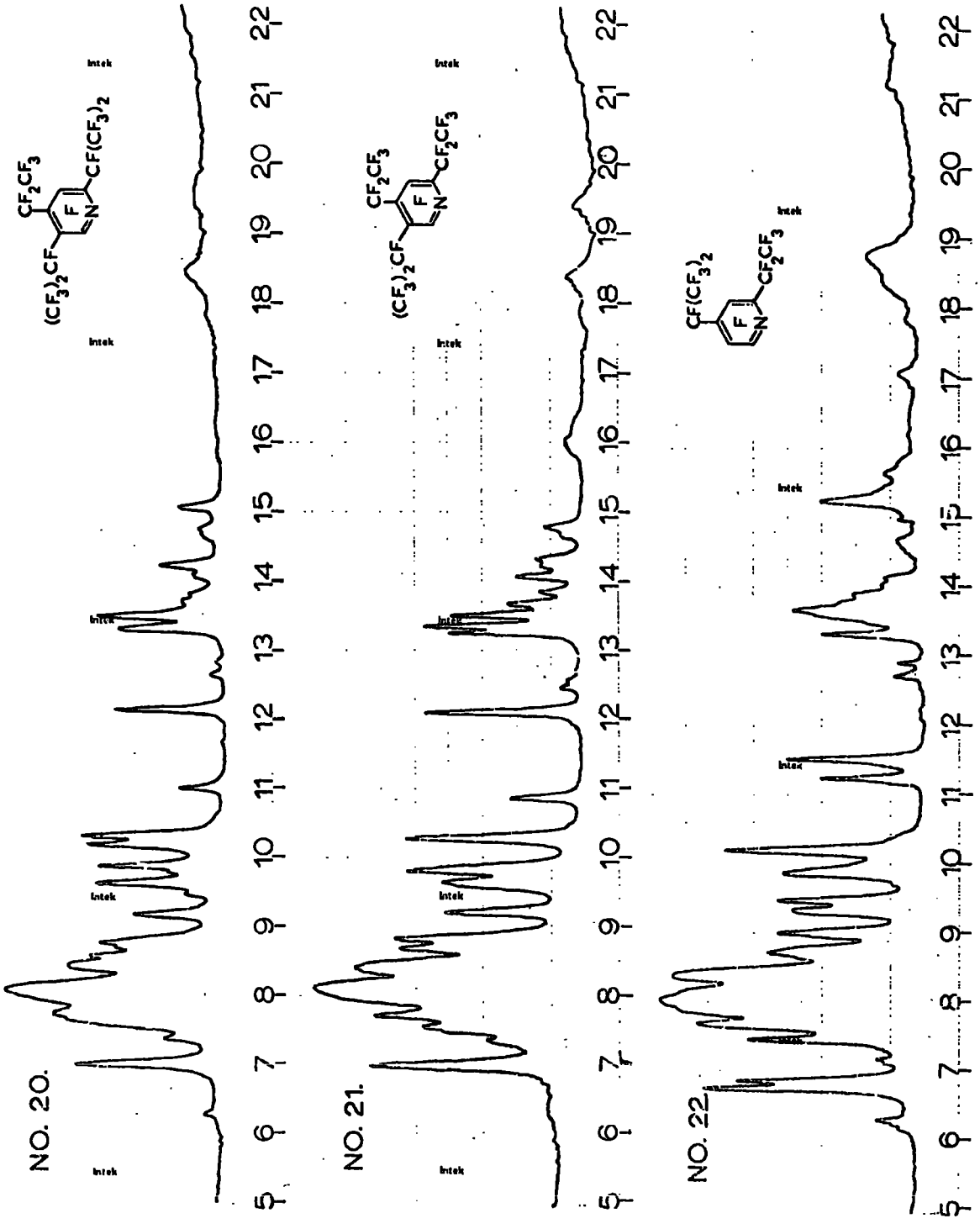
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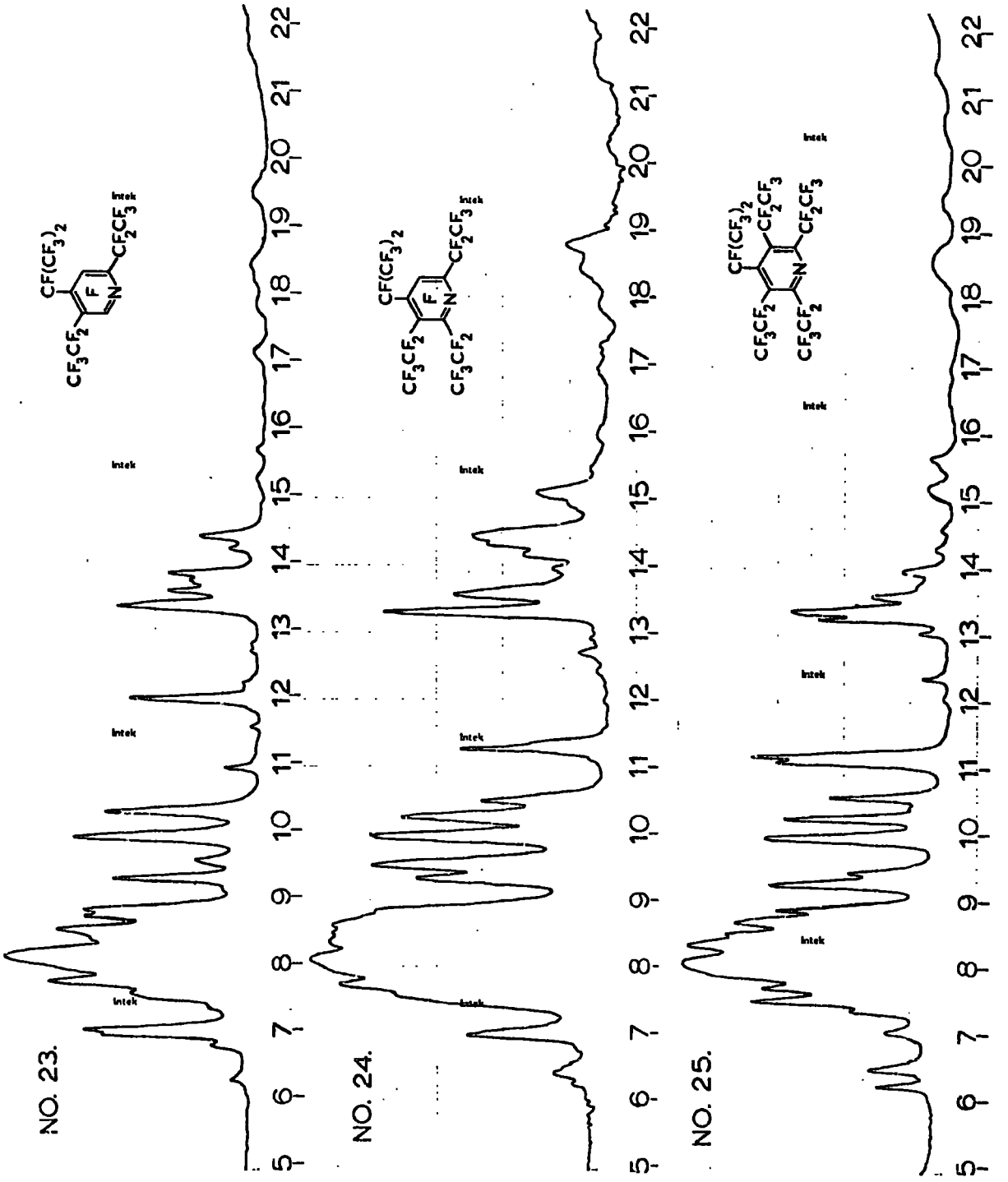
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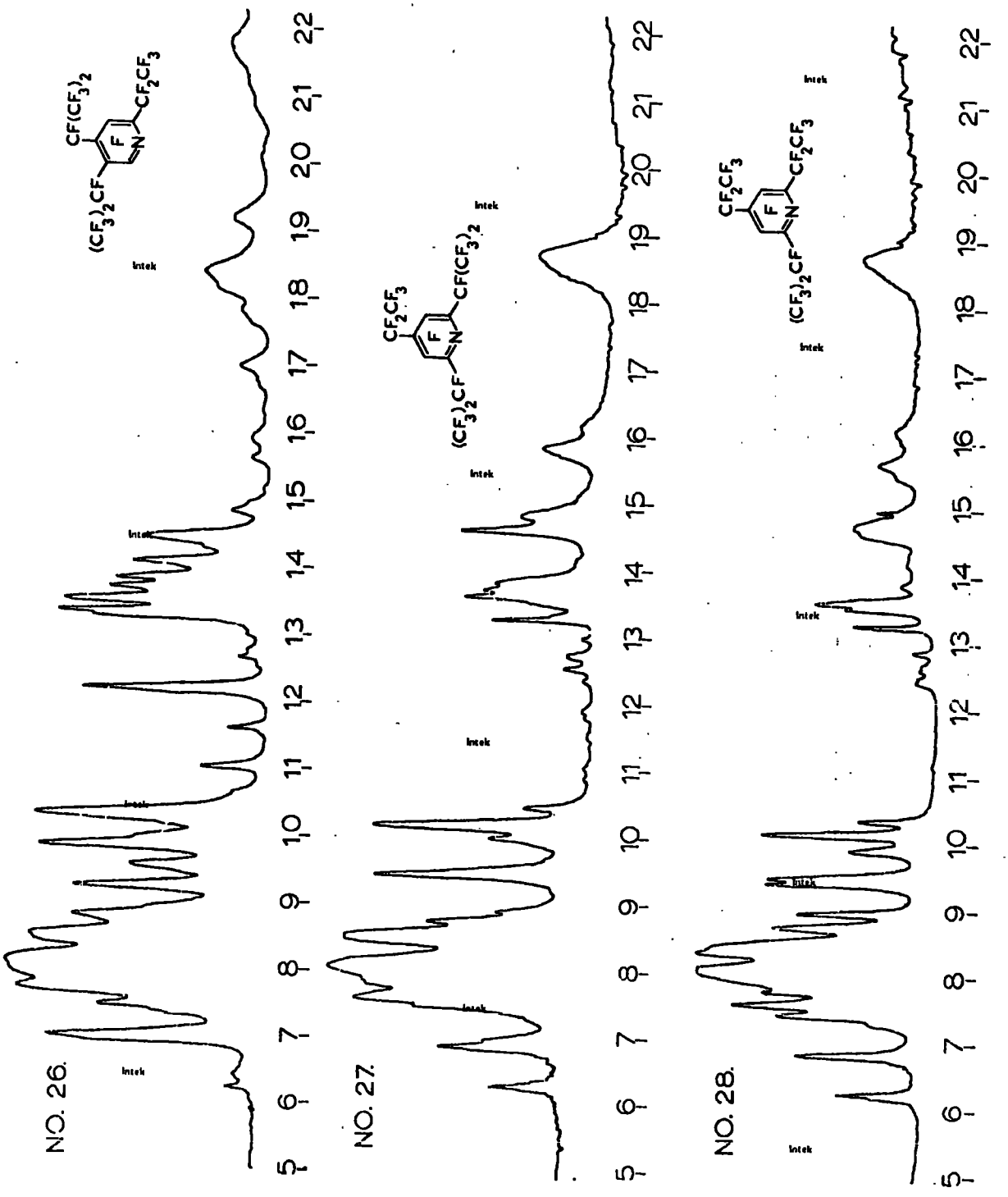
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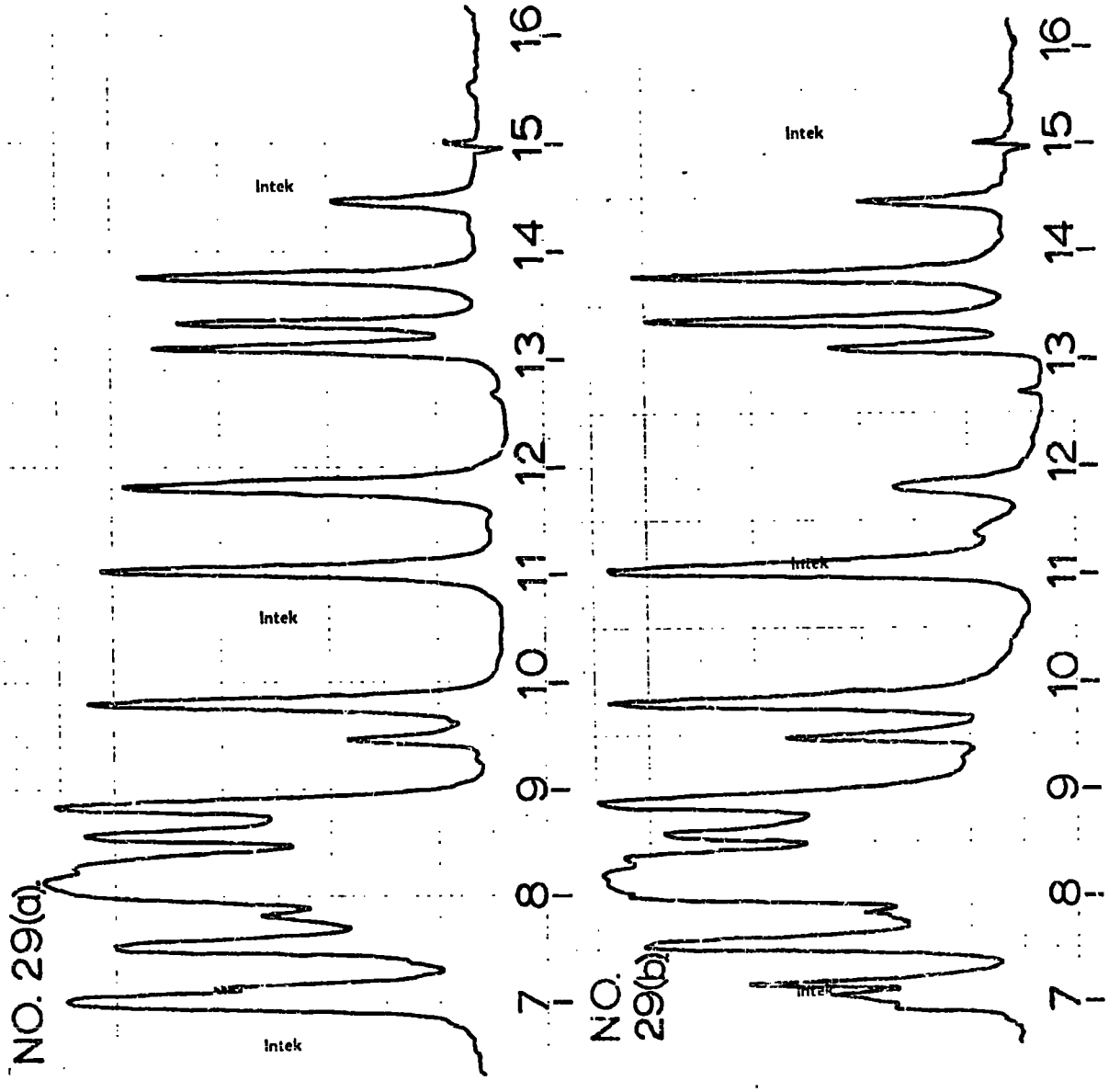
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