Polyfluoroheterocyclic Compounds. Part XXII.[1] Preparation of and Nucleophilic Substitution in Perfluoro-3,5-dimethylpyridine and Perfluoro-3-methylpyridine

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Perfluoro-3-methylpyridine (II) and perfluoro-3,5-dimethylpyridine (III) are obtained as minor products in the reaction between pentachloropyridine and potassium fluoride at 500°. Compounds (II) and (III) are produced more efficiently by the known reaction of polytetrafluoroethylene with pentafluoropyridine (I) at elevated temperatures. Nucleophilic substitutions in (II) and (III) by ammonia, methoxide, and polyfluoroalkyl anions are described. Substitution occurs at the 2- and 6- as well as the 4-positions in (II) and (III). ^{19}F N.m.r. spectra of the perfluoroalkyl derivatives indicate fixed conformations of perfluoroisopropyl groups.

In a different series of papers [2] we are describing syntheses involving reactions of perfluoroaromatic compounds with carbanions which are generated by reaction of fluoride ion with fluoro-olefins. Perfluoromethyl compounds would result from an analogous route if trifluoromethyl anions could be produced from difluorocarbene. We have now made a number of

$$F^- + [CF_2] \rightleftharpoons {}^-CF_3 \xrightarrow{Ar_F\text{-}F} Ar_F\text{-}CF_3 + F^-$$

attempts to effect this type of process by reaction of perfluoroaromatic compounds with various sources of difluorocarbene, *e.g.* sodium chlorodifluoroacetate [3] or hexafluoropropene epoxide [4] in the presence of an excess of potassium or caesium fluoride, but, so far, these have been unsuccessful. Reactions involving sodium chlorodifluoroacetate and pentafluoropyridine (I) gave high yields of 4-chlorotetrafluoropyridine.

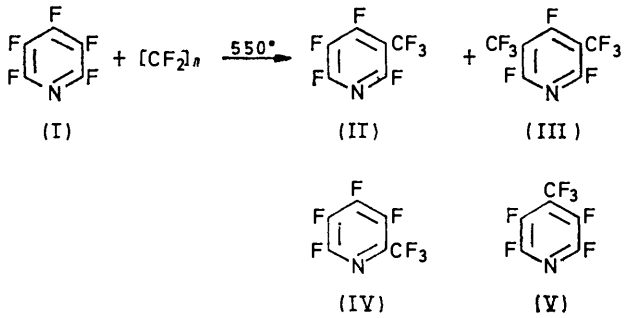
Russian workers [5] have shown that perfluoromethylbenzenes are obtained by heating hexafluorobenzene with potassium fluoride at 550° and were encouraged to suggest the intermediacy of difluorocarbene because reaction of hexafluorobenzene with polytetrafluoroethylene (PTFE) at 550°, without addition of metal fluoride, gave improved yields of perfluoromethylbenzenes.[6,7] Also, it has been reported [8] that a mixture of pentafluoropyridine and polytetrafluoroethylene at 550° gives mainly perfluoro-3-methylpyridine, with smaller amounts of the 2- and 4-isomers. Perfluoromethylpyridines have also been obtained by electrochemical fluorination of picolines followed by defluorination of the products over iron.[9]

We have now isolated small amounts of perfluoro-3-methylpyridine and perfluoro-3,5-dimethylpyridine from accumulated distillation fractions obtained in the preparation of pentafluoropyridine [10] from pentachloropyridine and potassium fluoride at *ca.* 500°, but we have been able to obtain these compounds much more effectively by reaction of pentafluoropyridine with polytetrafluoroethylene at 550°, without added metal fluoride; these observations are analogous to those of the earlier workers.[6-8] Some typical results which we have obtained are shown in the Table; depending

Synthesis of perfluoromethylpyridines

	Experiment		
Conditions	A	B	C
Pentafluoropyridine (I) (g)	25	25	50
PTFE (g)	50	50	25
Temperature (°C)	550	500	550
Time (h)	15½	15½	14
Yields and recovery (%)			
Pentafluoropyridine (I)	Trace	7	17
Perfluoro-3-methylpyridine (II)	6	35	42
Perfluoro-3,5-dimethylpyridine (III)	60	14	11

on the proportion of PTFE used, perfluoro-3-methylpyridine (II) or perfluoro-3,5-dimethylpyridine (III)



was the major product. No significant amounts of the 2- and 4-isomers, (IV) and (V), were isolated, although small amounts of unidentified products were present. These results differ from those of the Russian workers,[8] who did not report perfluoro-3,5-dimethylpyridine (III) but isolated small amounts of (IV) and (V).

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[2] S. L. Bell, R. D. Chambers, M. Y. Gribble, and J. R. Maslakiewicz, *J.C.S. Perkin, I*, 1973, 1716.
[3] J. M. Birchall, G. W. Cross, and R. N. Haszeldine, *Proc. Chem. Soc.*, 1960, 81.
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[6] J. M. Antonucci and L. A. Wall, *J. Res. Nat. Bur. Standards*, 1966, **70***A*, 473.
[7] N. N. Vorozhtsov, N. V. Ermolenko, S. A. Mazalov, O. M. Osina, V. E. Platonov, V. S. Tyurin, and G. G. Yakobson, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1969, 196.
[8] V. E. Platanov, N. V. Ermolenko, and G. G. Yakobson, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1970, 2843.
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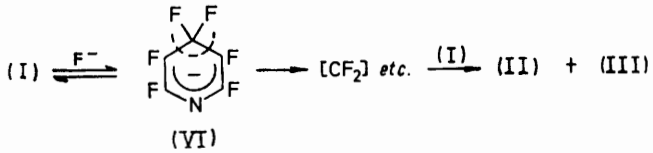
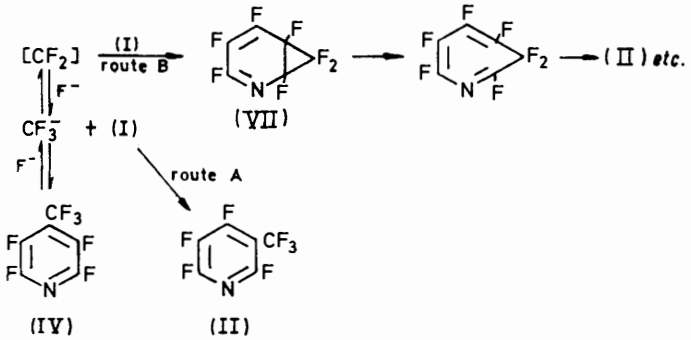
By analogy with suggestions made to account for the formation of trifluoromethyl derivatives from hexafluorobenzene [5] and tetrafluoropyrimidine,[11] formation of (II) and (III) in the reaction between potassium fluoride and pentachloropyridine probably arises from difluorocarbene produced by reaction of fluoride ion with pentafluoropyridine (I), which is the main product of



the reaction.[10] It is by no means clear, however, what happens to the rest of the molecule after loss of difluorocarbene from (VI). Nevertheless, our results with PTFE, like those of the Russian workers,[7,8] strongly support the involvement of difluorocarbene because pyrolysis of PTFE forms tetrafluoroethylene, which probably forms difluorocarbene at these temperatures since the carbene is produced on photolysis of the olefin.[12]

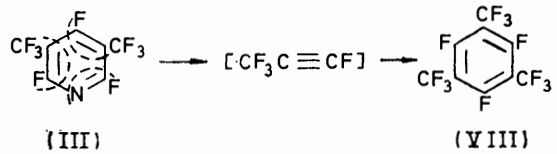
We can consider two possible mechanistic paths for the reaction of difluorocarbene with pentafluoropyridine. In the presence of added potassium fluoride, reaction of the carbene with fluoride ion could occur, followed by nucleophilic attack of the resultant trifluoromethyl-anion on pentafluoropyridine (route A). In the absence of added fluoride, direct addition of the carbene to pentafluoropyridine, either by insertion into a C–F bond or, more likely, *via* (VII) (route B) is probable.



Analogous to route B is the isolation of a tropylidene from reaction of hexafluorobenzene with bistrifluoromethylcarbene.[13] In route A we would expect nucleophilic attack to occur at the 4-position in pentafluoropyridine (I).[14] This, however, could be reversible at the temperatures involved, so that (II) is obtained, because displacement of trifluoromethyl by fluoride ion would be more difficult than from (IV). The reaction with PTFE occurs in the presence of potassium fluoride, but without much apparent effect on efficiency, and so there is little evidence to support route A. Surprisingly, variable amounts of perfluoromesitylene (VIII) were also obtained from these reactions.

The formation of (VIII) suggests that dissociation of perfluoro-3,5-dimethylpyridine (III) occurs, giving tetrafluoropropyne, followed by recombination. Tetrafluoropropyne has been characterised [15] but its behaviour under conditions of high temperature and pressure has not been reported, although hexafluorobut-2-yne is known to trimerise to hexakistrifluoromethylbenzene on heating under pressure.[16]

Hexafluoropropene epoxide is a useful source of difluorocarbene at 180°,[4] but when the epoxide was heated at this temperature with pentafluoropyridine (I), the latter was largely unchanged and only traces of



(II) were isolated, indicating that a high temperature is required for the perfluoroalkylation reaction. This is in keeping with the relatively low reactivity of difluorocarbene, which has been commented on previously.[17]

The perfluoroalkylpyridines (II) and (III) were obtained in reasonable purity for further reactions by fractional distillation, although analytical samples were obtained by g.l.c. They are very susceptible to nucleophilic substitution, the qualitative order of reactivity being (I) < (II) < (III), and reactions with methoxide, ammonia, and perfluoro-1-methylethanide are illustrated in Schemes 1 and 2. Monosubstitution in pentafluoropyridine, by a range of nucleophiles, occurs exclusively at the 4-position [14] *via* a transition state which resembles (IX); attack at the 2- and 6-positions *via* (X) is probably slightly inhibited by the fluorine atoms at the 3- and 5-positions which will raise the energy of adjacent planar [18] negatively charged centres, by electron-pair repulsions. In contrast, the presence of CF_3 at the 3- or 5-positions will encourage attack at the 2- and 6-positions *via* (XI); also steric crowding may well be more important at the 4-position and the overall effect makes substitution at the 2- and 6-positions in (II) and (III) more easy, relative to 4-attack, than in pentafluoropyridine. The results shown in Schemes 1 and 2 illustrate these points. Monosubstitution products of ammonia with both (II) and (III) and of methoxide with (III) show 2- or 6-substitution as well as attack at the 4-position and in some cases, *e.g.* with (III) and ammonia, the major product arises from 2-attack. Also, polysubstitution occurs

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[12] N. Cohen and J. Heicklen, *J. Chem. Phys.*, 1965, **43**, 871.
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[14] R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.*, 1964, 3736; R. E. Banks, J. E. Burgess, W. M. Cheng, and R. N. Haszeldine, *ibid.*, 1965, 575.
[15] R. E. Banks, M. G. Barlow, W. D. Davies, R. N. Haszeldine, and D. R. Taylor, *J. Chem. Soc.* (*C*), 1969, 1104.
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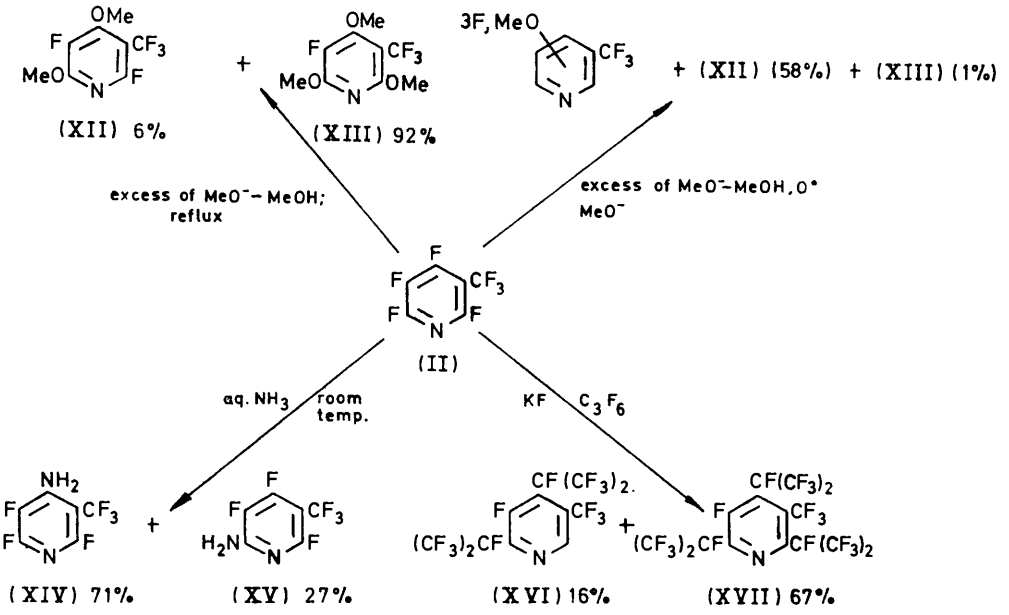
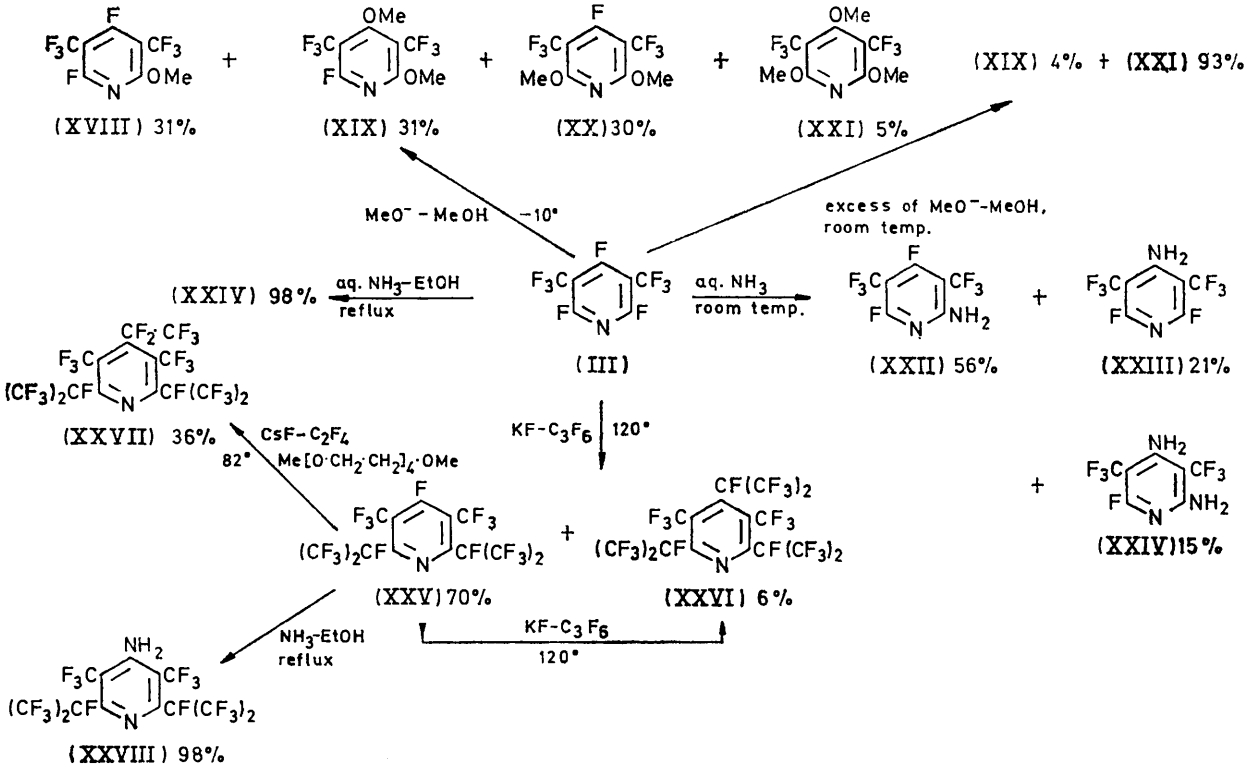
[17] J. F. Harrison, *J. Amer. Chem. Soc.*, 1971, **93**, 4112, and references therein.
[18] A. Streitwieser and F. Mares, *J. Amer. Chem. Soc.*, 1968, **90**, 2444.

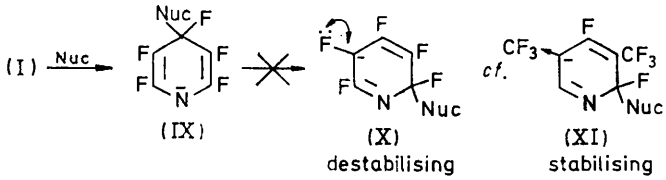


SCHEME 1 Reactions of perfluoro-3-methylpyridine (II)



SCHEME 2 Reactions of perfluoro-3,5-dimethylpyridine (III)

more readily than with pentafluoropyridine, *e.g.* trisubstitution occurs between methoxide and (III) at



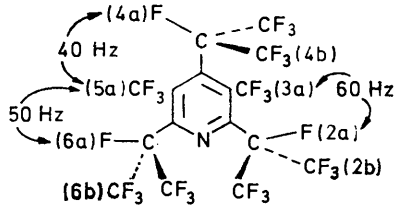
room temperature whereas pentafluoropyridine gives corresponding di- and tri-substitution products only after heating for prolonged periods with a concentrated solution of sodium methoxide.[14]

Polyfluoroalkylation[2] of both (II) and (III) is particularly interesting because of the difficulty involved in obtaining pyridines containing more than three perfluoroalkyl groups. Tetrakispentafluoroethylpyridine is obtained from fluoride-ion-initiated reactions of tetrafluoroethylene with pentafluoropyridine in very low yield and only with difficulty,[19] and a trace of perfluorotetra-isopropylpyridine has been obtained in a comparable reaction with hexafluoropropene.[20] Reaction occurred readily, however, with hexafluoropropene and either (II) or (III) in the presence of caesium fluoride. Introduction of two or three perfluoroisopropyl groups occurred and the results are shown in Schemes 1 and 2. Further substitution at the crowded 4-position in (XXV) occurred much more readily with pentafluoroethyl anions than with the larger perfluoroisopropyl anions. It is clearly much easier to obtain perfluoro-penta- and -tetra-alkyl derivatives starting from both (II) and (III) than from pentafluoropyridine; some photolysis studies of these perfluoropolyalkylated pyridines will be published later.

N.m.r. Spectra.—The data are available as Supplementary Publication No. SUP 20849 (4 pp.).* Assignments for perfluoro-3-methylpyridine (II) and -3,5-dimethylpyridine (III) are consistent with data reported by Lee and Orrell[21] for (I) and (II), and the data for the 6-fluorine atoms in (II) and the 2,6- and the 4-fluorine atoms in (III) allow the assignment of structures of methoxy- and amino-derivatives to be derived. Structures of the perfluoroalkyl derivatives were deduced on the basis of arguments analogous to those used previously.[22]

Earlier work with perfluoroisopropylpyridines[22,23] has shown that rotation of a perfluoroisopropyl group at the 4-position is restricted when there are two adjacent ring fluorine atoms. Consistent with these findings, the spectrum of (XXVI) suggests that the system is locked in the conformation shown (XXVIA). The difference in the values for $J_{2a,3a}$ (60 Hz) and $J_{5a,6a}$ (50 Hz) adds further support to the idea of through-space coupling,[23] the magnitude of the value depending on the separation. It is easy to see that the 3-CF_3(3aF) system will interact with the CF_3 groups of the 4-CF(CF_3)$_2$(4bF) system in conformation (XXVIA) and this resultant buttressing effect appears to account for the larger coupling with 3aF because these fluorine atoms are brought closer in space than are 5aF and 6aF.

The spectrum of (XVI) indicated that the compound exists as two conformational isomers; these are not interconverted up to 150°. However, this spectrum



(XXVIA)

is complicated and we have not yet been able to assign the structures of these conformers unambiguously.

EXPERIMENTAL

Synthesis of the Perfluoromethylpyridines (II) *and* (III).—*General technique.* Pentafluoropyridine (I) and PTFE turnings were sealed in an autoclave (550 ml capacity) which was heated at 500—550° for 14—15½ h. The products were distilled from the hot autoclave under vacuum and collected in a trap immersed in liquid air. After it had warmed to room temperature, the mixture was analysed by g.l.c. The results of some of the preparations are shown in the Table.

The products from five reactions, carried out as for experiment A, were combined and fractionated on a spinning band column to give a fraction (66 g), b.p. 118—120° at 751 mmHg, which contained perfluoro-3,5-dimethylpyridine (III) (97%) together with 3% of perfluoro-3-methylpyridine (II) and perfluoromesitylene[5] as impurities. A sample further purified by preparative scale g.l.c. (on di-n-decyl phthalate at 70°) gave *perfluoro-3,5-dimethylpyridine* (III) as an oil, b.p. 119° at 776 mmHg (Siwoloboff) (Found: C, 31·1; F, 63·1; N, 5·0%; *M*, 269. C_7F_9N requires C, 31·25; F, 63·55; N, 5·2%; *M*, 269); $\lambda_{max.}$ (cyclohexane) 218, 247, and 250 nm (log ε 2·68, 3·21, and 3·21).

The products of experiment B and two experiments under the conditions of C were combined and fractionated on a spinning band column to give a fraction (32 g), b.p. 102—103° at 747 mmHg, which contained perfluoro-3-methylpyridine (II) (95%) together with 5% of pentafluoropyridine (I) and an unidentified product as impurities. A small sample further purified by preparative scale g.l.c. (on di-n-decyl phthalate at 70°) gave perfluoro-3-methylpyridine (II) as an oil, b.p. 102° at 747 mmHg (Siwoloboff) (Found: C, 32·7; F, 61·0; N, 6·2%; *M*, 219. Calc. for C_6F_7N: C, 32·9; F, 60·7; N, 6·5%; *M*,

* For details of Supplementary Publications, see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20.

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[20] R. D. Chambers, R. P. Corbally, and W. K. R. Musgrave, *J.C.S. Perkin I*, 1972, 1281.

[21] J. Lee and K. G. Orrell, *J. Chem. Soc.*, 1965, 582.

[22] R. D. Chambers, J. A. Jackson, and W. K. R. Musgrave, *Tetrahedron*, 1970, **26**, 71.

[23] R. D. Chambers, L. H. Sutcliffe, and G. J. T. Tiddy, *Trans. Faraday Soc.*, 1970, **66**, 1025.

219). The ^{19}F n.m.r. spectrum was identical with that reported;[21] b.p. and $\lambda_{max.}$ (cyclohexane) (255 nm) also agree with reported data.[9]

Reactions of Perfluoro-3-methylpyridine (II).—(A) *With ammonia.* A mixture of perfluoro-3-methylpyridine (II) (2 g, 9·1 mmol) and aqueous ammonia (*d* 0·88; 10 ml) was shaken at room temperature without cooling. The mixture was then poured into water and the aqueous solution extracted with ether. The ethereal solution was dried (Na_2SO_4) and evaporated to leave a solid which was shown by g.l.c. to contain mainly 4-amino-2,5,6-trifluoro-3-trifluoromethylpyridine (XIV) (1·4 g, 71%) and 6-amino-2,4,5-trifluoro-3-trifluoromethylpyridine (XV) (0·53 g, 27%). The compounds were separated by preparative scale g.l.c. (20% polyethylene glycol *o*-phthalate on Celite; 180°) and recrystallised from petroleum (b.p. 60—80°), giving (XIV) as *platelets*, m.p. 79° (Found: C, 33·5; H, 0·9; F, 52·4; N, 13·1%; *M*, 216. $C_6H_2F_6N_2$ requires C, 33·35; H, 0·95; F, 52·75; N, 12·95%; *M*, 216); $\lambda_{max.}$ (cyclohexane) 210, 228, and 265 nm (log ε 3·59, 3·95, and 3·47); and (XV) as *crystals*, m.p. 77° (Found: C, 33·2; H, 1·1; F, 52·5; N, 13·0%; *M*, 216); $\lambda_{max.}$ (cyclohexane) 231 and 275 nm (log ε 4·02 and 3·84).

(B) *With sodium methoxide.* (i) Sodium methoxide (20% in methanol; 14 mmol) was added slowly with shaking to perfluoro-3-methylpyridine (II) (1 g, 4·6 mmol). The mixture was heated under reflux for 15 min, then poured into water, and the aqueous solution was extracted with ether. The ethereal solution was dried (Na_2SO_4) and evaporated to leave an oil, which was shown by g.l.c. to contain 5-fluoro-2,4,6-trimethoxy-3-trifluoromethylpyridine (XIII) (1·07 g, 92%) and 2,5-difluoro-4,6-dimethoxy-3-trifluoromethylpyridine (XII) (0·07 g, 6%), separated by preparative scale g.l.c. (silicone gum, 200°) to give (XIII) as an *oil*, b.p. 238° at 754 mmHg (Siwoloboff) (Found: C, 42·6; H, 3·5; F, 30·1; N, 5·7%; *M*, 255. $C_9H_9F_4NO_3$ requires C, 42·35; H, 3·55; F, 29·8; N, 5·5%; *M*, 255); $\lambda_{max.}$ (cyclohexane) 212, 228, and 278 nm (log ε 3·78, 3·79, and 3·88).

(ii) Sodium methoxide (20% in methanol; 29·2 mmol) was added slowly with shaking to perfluoro-3-methylpyridine (II) (4 g, 18·3 mmol) while the mixture was kept at 0° by cooling. The product was worked up as in (i) and the oil produced was shown by g.l.c. to contain an isomeric mixture of 3-trifluoromethylmethoxytrifluoropyridines (1·69 g, 40%), 2,5-difluoro-4,6-dimethoxy-3-trifluoromethylpyridine (XII) (2·57 g, 58%), and 5-fluoro-2,4,6-trimethoxy-3-trifluoromethylpyridine (XIII) (0·05 g, 1%). The isomeric monomethoxy-derivatives could not be isolated individually [preparative g.l.c. (silicone gum, 200°) gave an oil, b.p. 152° at 752 mmHg (Siwoloboff), containing mainly the 4- and 6-isomers (Found: C, 36·6; H, 1·5; F, 48·8; N, 6·2%; *M*, 231. Calc. for $C_7H_3F_6NO$: C, 36·4; H, 1·3; F, 49·35; N, 6·05%; *M*, 231)] but *2,5-difluoro-4,6-dimethoxy-3-trifluoromethylpyridine* (XII) was isolated as crystals, m.p. 32° (Found: C, 39·3; H, 2·8; F, 39·6; N, 5·9%; *M*, 243. $C_8H_6F_5NO_2$ requires C, 39·5; H, 2·5; F, 39·05; N, 5·75%; *M*, 243); $\lambda_{max.}$ (cyclohexane) 220 and 266 nm (log ε 3·71 and 3·71).

(C) *With perfluoroisopropyl anion.* The reaction was carried out as described later for reaction with (III), but with perfluoro-3-methylpyridine (7·7 g, 35·2 mmol). The product, analysed by g.l.c., contained perfluoro-2,4,6-triisopropyl-3-methylpyridine (XVII) (15·8 g, 67%) and perfluoro-4,6-di-isopropyl-3-methylpyridine (XVI) (3·0 g, 16%), together with dimers and trimers of hexafluoropropene. After fractionation to remove volatile material, the major products were isolated by preparative scale g.l.c. (di-n-decyl phthalate, 110°), giving (XVII) as an *oil*, b.p. 184° at 759 mmHg (Siwoloboff) (Found: C, 26·9; F, 70·7; N, 2·1%; *M*, 669. $C_{15}F_{25}N$ requires C, 26·95; F, 71·0; N, 2·1%; *M*, 669); $\lambda_{max.}$ (cyclohexane) 220 and 285 nm (log ε 3·47 and 3·49), and (XVI) as an *oil*, b.p. 167° at 759 mmHg (Siwoloboff) (Found: C, 28·0; F, 69·0; N, 2·5%; *M*, 519. $C_{12}F_{19}N$ requires C, 27·75; F, 69·55; N, 2·7%; *M*, 519); $\lambda_{max.}$ (cyclohexane) 217 and 286 nm (log ε 2·88 and 3·79).

Substitution Reactions of Perfluoro-3,5-dimethylpyridine (III).—(A) *With ammonia.* (i) Perfluoro-3,5-dimethylpyridine (III) (4 g, 14·9 mmol) and aqueous ammonia (*d* 0·88; 20 ml) were shaken together at room temperature; the mixture was then poured into water and the aqueous solution extracted with ether. The ethereal layer was dried (Na_2SO_4) and evaporated to leave a solid, analysed by g.l.c., containing 2-amino-4,6-difluoro-3,5-bistrifluoromethylpyridine (XXII) (2·22 g, 56%), 4-amino-2,6-difluoro-3,5-bistrifluoromethylpyridine (XXIII) (0·83 g, 21%), and 2,4-diamino-6-fluoro-3,5-bistrifluoromethylpyridine (XXIV) (0·59 g, 15%). The mixture was separated by preparative scale g.l.c. (silicone gum, 150°) and, after recrystallisation from petroleum (b.p. 60—80°), (XXII) was obtained as *crystals*, m.p. 86° (Found: C, 31·4; H, 0·7; F, 56·8; N, 10·4%; *M*, 266. $C_7H_2F_8N_2$ requires C, 31·6; H, 0·75; F, 57·1; N, 10·55%; *M*, 266); $\lambda_{max.}$ cyclohexane 237 and 274 nm (log ε 4·21 and 3·58). Similarly, (XXIII) was obtained as *crystals*, m.p. 66° (Found: C, 31·3; H, 0·8; F, 56·7; N, 10·2%; *M*, 266); $\lambda_{max.}$ (cyclohexane) 210, 234, and 263 nm (log ε 3·80, 4·03, and 3·02).

(ii) A mixture of perfluoro-3,5-dimethylpyridine (III) (4 g, 14·9 mmol), aqueous ammonia (*d* 0·88; 20 ml), and ethanol (20 ml) was heated under reflux for 4 h. The product was worked up as in (i) and was shown by g.l.c. to be mainly *2,4-diamino-6-fluoro-3,5-bistrifluoromethylpyridine* (XXIV) (3·83 g, 98%), which was recrystallised from petroleum (b.p. 60—80°)–ethanol to give needles, m.p. 122° (Found: C, 32·3; H, 1·7; F, 50·1; N, 16·2%; *M*, 263. $C_7H_4F_7N_3$ requires C, 31·95; H, 1·55; F, 50·55; N, 15·95%; *M*, 263); $\lambda_{max.}$ (cyclohexane) 222, 243, and 276 nm (log ε 4·60, 4·03, and 4·00).

(B) *With sodium methoxide.* (i) Sodium methoxide (20% in methanol; 40 mmol) was added slowly with shaking to perfluoro-3,5-dimethylpyridine (III) (2 g, 7·4 mmol) without cooling. The product mixture was analysed by g.l.c., after the addition of acetone to make up a single phase, and consisted of 2,4,6-trimethoxy-3,5-bistrifluoromethylpyridine (XXI) (2·11 g, 93%) and 6-fluoro-2,4-dimethoxy-3,5-bistrifluoromethylpyridine (XIX) (0·09 g, 4%). The major product was precipitated from the solutions by addition of water and filtered off. After recrystallisation from petroleum (b.p. 60—80°)–acetone, (XXI) was obtained as *crystals*, m.p. 81° (Found: C, 39·6; H, 3·0; F, 37·0; N, 4·5%; *M*, 305. $C_{10}H_9F_6NO_3$ requires C, 39·35; H, 2·95; F, 37·35; N, 4·6%; *M*, 305); $\lambda_{max.}$ (cyclohexane) 212, 235, and 272 nm (log ε 3·83, 3·94, and 3·76).

(ii) Sodium methoxide (20% in methanol; 31·6 mmol) was added slowly with shaking to perfluoro-3,5-dimethylpyridine (III) (5 g, 18·6 mmol) while the mixture was kept at *ca.* −10°. The product was poured into water,

after being allowed to attain room temperature, and the aqueous solution was extracted with ether. The ethereal layer was dried (Na_2SO_4) and evaporated to leave an oil which was shown by g.l.c. to contain 4,6-difluoro-2-methoxy-3,5-bistrifluoromethylpyridine (XVIII) (1·67 g, 31%), 6-fluoro-2,4-dimethoxy-3,5-bistrifluoromethylpyridine (XIX) (1·69 g, 31%), 4-fluoro-2,6-dimethoxy-3,5-bistrifluoromethylpyridine (XX) (1·63 g, 30%), and 2,4,6-trimethoxy-3,5-bistrifluoromethylpyridine (XXI) (0·28 g, 5%). The mixture was separated by preparative scale g.l.c. (silicone gum, 200°), giving (XVIII), which had to be rechromatographed (di-n-decyl phthalate, 125°), as an *oil*, b.p. 159° at 748 mmHg (Siwoloboff) (Found: C, 33·9; H, 1·3; F, 54·5; N, 5·3%; *M*, 281. $C_8H_3F_8NO$ requires C, 34·2; H, 1·1; F, 54·0; N, 5·0%; *M*, 281); $\lambda_{max.}$ (cyclohexane) 225 and 259 nm (log ε 3·91 and 3·55); (XIX) as an *oil*, b.p. 194° at 755 mmHg (Siwoloboff) (Found: C, 37·1; H, 2·2; F, 45·7; N, 5·0%; *M*, 293. $C_9H_6F_7NO_2$ requires C, 36·9; H, 2·05; F, 45·35; N, 4·8%; *M*, 293); $\lambda_{max.}$ (cyclohexane) 226 and 265 nm (log ε 3·84 and 3·52); and (XX) as *crystals*, m.p. 70° (Found: C, 36·6; H, 2·2; F, 45·8; N, 4·5%; *M*, 293); $\lambda_{max.}$ (cyclohexane) 233 and 265 nm (log ε 3·97 and 3·77).

(C) *With perfluoroisopropyl anion.* Polyperfluoroisopropylation reactions were carried out in the apparatus and by the technique described previously.[20] Potassium fluoride (20 g) and dry tetrahydrothiophen dioxide (150 ml) were placed in the flask and the apparatus was evacuated (to 10^{-2} mmHg) and then filled with hexafluoropropene until the bladder was inflated. Perfluoro-3,5-dimethylpyridine (III) (9·7 g, 36·1 mmol) was injected through the serum cap, the mixture was stirred rapidly, and the flask was heated at 120° for 2 h while the hexafluoropropene was circulated through the mixture. Volatile products were then transferred under high vacuum to a trap immersed in liquid air. The product, analysed by g.l.c., contained perfluoro-2,6-di-isopropyl-3,5-dimethylpyridine (XXV) (14·4 g, 70%), perfluoro-2,4,6-tri-isopropyl-3,5-dimethylpyridine (XXVI) (1·6 g, 6%), and perfluoro-3,5-dimethylpyridine (III) (1·0 g, 10%), together with dimers and trimers of hexafluoropropene. After further fractional distillation and fractional crystallisation by freezing, (XXV) was obtained as *crystals*, m.p. 37°, b.p. 181° at 770 mmHg (Siwoloboff) (Found: C, 27·2; F, 69·7; N, 2·3%; *M*, 569. $C_{13}F_{21}N$ requires C, 27·45; F, 70·1; N, 2·45%; *M*, 569); $\lambda_{max.}$ (cyclohexane) 221 nm (log ε 2·30). *Perfluoro-2,4,6-tri-isopropyl-3,5-dimethylpyridine* (XXVI) was isolated as an oil, b.p. 204° at 761 mmHg (Siwoloboff), from the residual liquors by preparative scale g.l.c. (di-n-decyl phthalate, 100°) followed by boiling with aqueous ammonia (*d* 0·88) and a final preparative g.l.c. separation (Found: C, 27·0; F, 70·9; N, 2·1%; *M*, 719. $C_{16}F_{27}N$ requires C, 26·7; F, 71·35; N, 1·95%; *M*, 719); $\lambda_{max.}$ (cyclohexane) 224 and 286 nm (log ε 3·35 and 3·15).

Reactions of Perfluoro-2,6-di-isopropyl-3,5-dimethylpyridine (XXV).—(A) *With ammonia.* A mixture of perfluoro-2,6-di-isopropyl-3,5-dimethylpyridine (XXV) (1·5 g, 2·6 mmol), ethanol (20 ml), and aqueous ammonia (*d* 0·88; 5 ml) was heated under reflux for 1 h, after which the mixture was poured into water. The aqueous solution was extracted with ether; the extract was washed with water, dried (Na_2SO_4), and evaporated to leave a solid. This was analysed by g.l.c. and contained 4-amino-2,6-bisheptafluoroisopropyl-3,5-bistrifluoromethylpyridine (XXVIII) (1·46 g, 98%). Recrystallisation from petroleum (b.p. 60—80°) gave *platelets*, m.p. 82·5° (Found: C, 27·3; H, 0·3; F, 66·5; N, 5·1%; *M*, 566. $C_{13}H_2F_{20}N_2$ requires C, 27·6; H, 0·35; F, 67·1; N, 4·95%; *M*, 566); $\lambda_{max.}$ (cyclohexane) 220, 246, and 308 nm (log ε 3·70, 3·99, and 3·38).

(B) *With pentafluoroethyl anion.* The apparatus consisted of a conical flask (100 ml) fitted with a three-way adaptor, the centre junction of which was surmounted by a reflux condenser topped by a rubber football bladder. The side-arms of the adaptor were used, one for evacuation of the apparatus and the second for injection of starting materials through a serum cap. The flask was heated in a thermostatically controlled oil-bath.

A stirred mixture of caesium fluoride (14·3 g) and dry 2,5,8,11,14-pentaoxapentadecane (70 ml) was heated at 82° under an atmosphere of tetrafluoroethylene (10 g, 757 mm). Perfluoro-2,6-di-isopropyl-3,5-dimethylpyridine (XXV) (20·2 g, 35·5 mmol) was injected through the serum cap and the mixture was stirred vigorously and heated at 82° for 4 h, after which it was poured into water. The precipitated solid was filtered off and sublimed and the sublimate was recrystallised from petroleum (b.p. 60—80°)–acetone to give *perfluoro-4-ethyl-2,6-di-isopropyl-3,5-dimethylpyridine* (XXVII) (8·55 g, 36%) as crystals, m.p. 104° (Found: C, 26·7; F, 70·6; N, 2·4%; *M*, 669. $C_{15}F_{25}N$ requires C, 26·95; F, 71·0; N, 2·1%; *M*, 669); $\lambda_{max.}$ (cyclohexane) 221 and 276 nm (log ε 3·32 and 3·22).

Reaction of Pentafluoropyridine with Sodium Chlorodifluoroacetate in the Presence of Caesium Fluoride (by S. Partington).—A mixture of sodium chlorodifluoroacetate (8 g, 52·8 mmol), caesium fluoride (4 g, 26·4 mmol), and pentafluoropyridine (5 g, 29·6 mmol) under dry nitrogen and contained in a sealed nickel tube was heated for 16 h at 170°. Volatile material (6 g) was transferred from the tube under vacuum and separation of the two-component mixture by g.l.c. gave 4-chlorotetrafluoropyridine (4·1 g), identical with an authentic sample[24] prepared from 4-aminotetrafluoropyridine,[25] and unchanged pentafluoropyridine.

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