187. *Aromatic Polyfluoro-compounds. Part XX.[1] Nucleophilic Reactions of Pentafluoronitrobenzene.*

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Sodium methoxide, methylamine, and dimethylamine react with pentafluoronitrobenzene to replace the fluorine atoms *ortho* and *para* to the nitro-group. For the mono-replacement products, *para* : *ortho* ratios of 92 : 8, 35 : 65, and 81 : 19, respectively, have been found for these nucleophiles.

It is suggested that the fluorine *para* to the nitro-group is the one normally replaced most easily, but that the amines, by hydrogen-bonding to the nitro-group, give larger proportions of *ortho*-replacement; a steric effect in opposition to this hydrogen-bonding is also invoked. Further reaction of the mono-replacement products gives compounds disubstituted *ortho–ortho* and *ortho–para* with reference to the nitro-group.

IN a previous Paper[2] we reported that, when pentafluoronitrobenzene reacted with ammonia, 69% of the mono-replacement derivative had lost the *ortho*- and 31% the *para*-fluorine, the products being 2,3,4,5-tetrafluoro-6-nitroaniline (VI) and 2,3,5,6-tetrafluoro-4-nitroaniline (IX). In giving this high proportion of the *ortho*-product, pentafluoronitrobenzene was unique among compounds of the type C_6F_5X. In most other cases[3] the fluorine *para* to X is the one which is most easily replaced by nucleophiles; in a few cases[3] the position *meta* to X is the most reactive. We have now shown that, in fact, preferential *ortho*-fluorine replacement from pentafluoronitrobenzene does not occur with all nucleophiles and that preferential *para*-replacement is to be expected in many cases.

RESULTS

Gas–liquid chromatography (g.l.c.) of the crude product from the reaction of one equivalent of sodium methoxide with pentafluoronitrobenzene showed two major peaks whose areas were in the ratio 7·5 : 92. [1]H Nuclear magnetic resonance (n.m.r.) * on the same material showed, in the methoxyl region of the spectrum, a doublet and a triplet, in intensity ratio 8 : 92. We attribute the doublet to the *ortho*- (II) and the triplet to the *para*-isomer (I), since other work[4]

TABLE 1.

Nuclear magnetic resonance data (for acetone solutions).

Compound	[1]H Spectrum [a]		[19]F Spectrum
	Chemical shift [b]	*J* (c./sec.) [b]	Chemical shift [c]
(I)	4·21t	2·0	75·5, 82·7 [d]
(II)	4·07d	2·05	—
(IV) [c]	3·99d, 4·11t [d]	1·7d, 1·7t	—
(VII)	3·05d [f]	5·6	71·2, 74·2, 80·8, 97·8 [d]
(VIII)	2·97d	1·8	—
(X)	3·18t [f]	3·1	73·3, 86·6 [d]
(XI)	3·11t	2·7	71·0, 74·0 [d]
(XVI)	3·05d,[f] 3·18t [df]	7·0d, 3·2t	69·8, 79·8, 92·2 [d]
(XVII)	2·74d, 2·97t [d]	1·65d, 2·45t	57·0, 75·0 [g]

[a] Side-chain methyl groups only (OMe, 3·7—4·3; NHMe, 3·0—3·2; NMe₂, 2·7—3·2). [b] d, doublet; t, triplet. [c] Centres of complex multiplets given. [d] Equal intensity. [e] In CCl₄. [f] All the peaks in these multiplets were further split into doublets (*J* = 5·2—5·4 c./sec.). [g] Intensities 1 and 2, respectively.

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* Chemical shifts are given in p.p.m. downfield from tetramethylsilane as internal standard for ^{1}H spectra and upfield from trifluoroacetic acid for ^{19}F spectra.

[1] Part XIX, Burdon, Castaner, and Tatlow, *J.*, 1964, 5017.
[2] Brooke, Burdon, and Tatlow, *J.*, 1961, 802.
[3] Tatlow, *Endeavour*, 1963, **22**, 89.
[4] Burdon, *Tetrahedron*, in the press.

has shown that methyl protons in side-chains of the type $-Y-CH_3$ (Y = O, N, S, SO$_2$, or C:O) attached to polyfluorophenyl compounds couple with the fluorine atoms *ortho* to the side-chain. Thus, when there are no *ortho*-fluorines, the side-chain methyl protons show only a singlet, when there is one, a doublet, and two, a triplet (cf. Table 1). In the present case, the doublet could possibly have arisen from the disubstituted product 2,3,5-trifluoro-4,6-dimethoxynitro-benzene (IV), with the triplet also shown by this compound being hidden by the stronger triplet from the *para*-isomer (I). Separation of the two components showed that this was not so; the minor one, even though it was present in too small an amount to purify completely, showed only a doublet in the methoxyl region. Further, when compound (IV) was made (see later) it was found to give a doublet distinguishable from the present one (Table 1).

The methoxide reactions are outlined in the accompanying scheme.
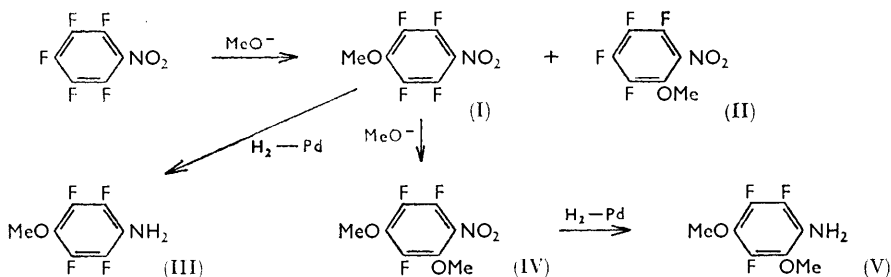
The structure of the *para*-isomer (I) was indicated by ^{19}F n.m.r. (the ^{1}H spectrum cannot distinguish between the *meta*- and *para*-isomers; both would be expected to give triplets); only two types of fluorine atom were present in the molecule (Table 1). Also, reduction of compound (I) gave 2,3,5,6-tetrafluoro-*p*-anisidine (III); the same compound was formed [5] by methylation of the known [6] 4-aminotetrafluorophenol. Oxidation of this amino-phenol to tetrafluoro-*p*-benzoquinone had proved [6] it to be the *para*-isomer. Wall's group also reported [7] this anisidine (III) from the reaction of pentafluoroanisole with sodamide; the structure was not proved chemically however.

Further treatment of the *p*-nitroanisole (I) with methoxide gave the expected dimethoxy-compound (IV). Since this showed a doublet and a triplet of equal intensity in the methoxyl region of its ^{1}H n.m.r. spectrum, we allocated to it the formula shown. This compound was reduced to the dimethoxyaniline (V), also obtained [5] from decafluoroazobenzene, where we have further n.m.r. evidence for this type of structure.

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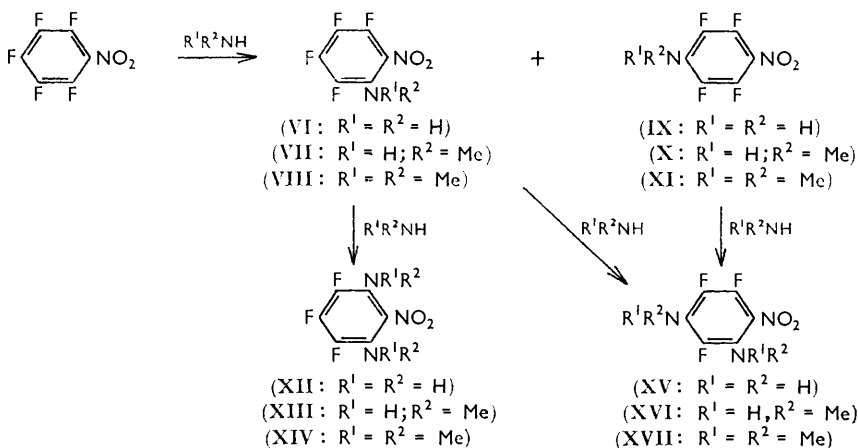
[5] Burdon, Morton, and Thomas, *J.*, in the press.
[6] Brooke, Forbes, Richardson, Stacey, and Tatlow, *J.*, in the press.
[7] Wall, Pummer, Fearn, and Antonucci, *J. Res. Nat. Bur. Stand.*, 1963, **67**A, 481.

The reactions of pentafluoronitrobenzene with ammonia,[2] methylamine, and dimethylamine are summarised in the above scheme, the isomer ratios for the mono-replacement products being given in Table 2.   These reactions were carried out in ethanol–ether at room
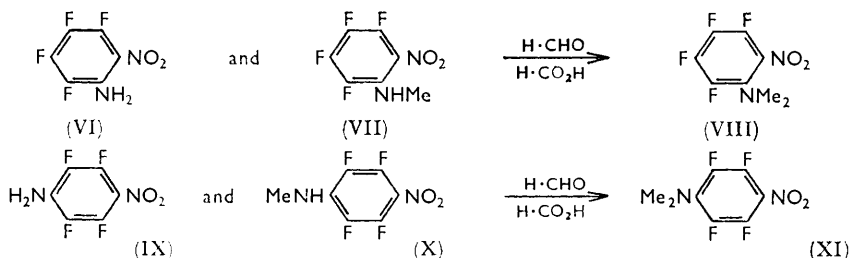
TABLE 2.

Isomer distribution in the reactions of pentafluoronitrobenzene with nucleophiles.

Nucleophile	NH_3 *	NH_2Me	$NHMe_2$	$NaOMe$
ortho-Replacement (%)	69	65	19	8
para-Replacement (%)	31	35	81	92

* Ref. 2.

temperature and the coloured products were separated by chromatography on alumina.   In every case, by using calculated quantities of the amines, the reactions could be controlled to give mono-replacement products, with very little of the di-replacement products.   Further reactions of the monoamines with another equivalent of the nucleophiles did give the direplacement products.   Very small amounts of another product were formed in each case; these could well have been the tri-replacement compounds (cf. the ammonia reaction[2]) as they ran so slowly on the alumina, but they were not investigated.

The mono-replacement products (VII), (VIII), (X), and (XI) from the methylamine and dimethylamine reactions were related to the known[2] tetrafluoro-*o*- (VI) and -*p*-nitro-aniline (IX) by methylation[8] with formaldehyde and formic acid (Eschweiler–Clarke methylation).   The yields were low, however, particularly with the *ortho*-isomers.   Further, the [19]F

and [1]H n.m.r. spectra of the four monoamines were consistent only with the structures established by methylation (Table 1).

The di-replacement product obtained from treatment of both tetrafluoro-*N*-methylnitro-anilines (VII) and (X) could only be the 2,4-isomer (XVI); its [1]H n.m.r. spectrum was consistent with this, showing that one methylamino-group was flanked by one *ortho*-fluorine (a doublet) and the other by two (a triplet).   The other (minor) di-replacement product from the *ortho*-isomer (VII) was most probably compound (XIII) by analogy with the ammonia reaction.[2]

The di-replacement product from the tetrafluoro-*NN*-dimethyl-*p*-nitroaniline (XI)–dimethyl-amine reaction, by analogy with the methylamine and ammonia[2] reactions, would be expected to have the analogous structure (XVII); the ^{19}F and [1]H n.m.r. spectra fitted only such a formula (Table 1).   No attempt was made to prepare the di-*ortho*-isomer (XIV) as the amount of *ortho*-replacement in the dimethylamine reactions is so low.

DISCUSSION

We suggest that, besides the general factors which control replacement of fluorine in compounds of type C_6F_5X, at least two extra effects are needed to rationalise the nucleophilic replacement reactions of pentafluoronitrobenzene so far studied.   First, hydrogen-bonding between certain nucleophiles and the nitro-group, and secondly, a steric effect.

We regard methoxide ion as a " normal " nucleophile, since in reaction with it penta-fluoronitrobenzene resembles almost all other C_6F_5X compounds[3] in giving mainly the

[8] Clarke, Gillespie, and Weisshaus, *J. Amer. Chem. Soc.*, 1933, **55**, 4571.

isomer in which the fluorine *para* to X has been replaced. However, the factors which control these *para*-replacements are incompletely understood.
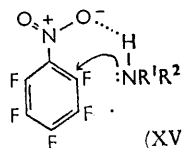
(XVIII)

With the amine nucleophiles, we attribute the high percentage of *ortho*-replacement to hydrogen-bonding between the attacking amine and the nitro-group, as in (XVIII).

A similar hydrogen-bonding effect has previously [9,10] been invoked to explain why nitro-groups activate *ortho*- more than *para*-halogen substituents towards amine nucleophiles. Although this explanation has been disputed,[11] it seems the most satisfactory advanced so far.[10] A few reports of apparently anomalous preferential *ortho*-halogen replacement reactions have been collected [11] however, involving nucleophiles which should not hydrogen-bond. These cases cannot at present be rationalised; amongst other factors, preference for *ortho*- or *para*-replacement depends on the solvent in some systems.[12] Further work is clearly necessary.

A hydrogen-bonding effect alone would suggest that the percentage of *ortho*-fluorine replacement in pentafluoronitrobenzene with the amine nucleophiles should decrease in the order: ammonia > methylamine > dimethylamine, since this is the expected order of decreasing strength of the hydrogen-bonds formed by these bases when they act as proton donors. Although this sequence is, in fact, the observed one, there is a very marked fall in the *ortho*-replacement with dimethylamine (Table 2). We therefore suggest that steric hindrance between the attacking amine and the nitro-group can operate to hinder the formation of a suitably hydrogen-bonded intermediate, providing the amine is large enough.

Our results so far, we suggest, indicate that pentafluoronitrobenzene will be attacked almost entirely at the position *para* to the nitro-group by nucleophiles which cannot hydrogen-bond to, or otherwise complex with, this group, and at the *ortho*-position by nucleophiles which can, the precise amount of *ortho*-replacement being governed both by the strength of the hydrogen-bond or complex and by the size of the nucleophile; the smaller it is, the greater the amount of *ortho*-replacement. Other examples to test these postulates are being studied.

EXPERIMENTAL

Reaction of Pentafluoronitrobenzene with Sodium Methoxide.—Sodium methoxide in methanol (13·3 ml.; 1·06N) was added dropwise over 90 min. at room temperature to a stirred solution of pentafluoronitrobenzene (3·00 g.) in methanol (50 ml.). After being stirred for 1 hr., the mixture was distilled through a 6 in. column, packed with glass helices, to remove most of the methanol (50 ml.). The residue was poured into water (300 ml.) and the crude product isolated by ether-extraction. G.l.c. on silicone gum showed it to contain five components; the first two (which were minor) had retention times corresponding to ether or methanol, and pentafluoronitrobenzene. The relative areas under the three longer-retained peaks were 7·5 : 92 : <1. The ^{1}H n.m.r. spectrum of the crude mixture showed, in the methoxyl region (3·7—4·3), a doublet ($J = 2·05$ c./sec.) and a triplet ($J = 2·0$ c./sec.), in intensity ratio 8 : 92, attributable to the *o*-nitroanisole (II) and its *p*-isomer (I), respectively.

Only the third and fourth components were present in sufficient quantity to be isolated by preparative-scale g.l.c. [column 35 mm. × 4·8 m., packed with silicone gum on Celite, 175°, N_2 flow-rate 20 l./hr.]. Even so, the third component could only be isolated in a crude state as a yellow oil (0·17 g.) contaminated with volatile silicon compounds. The ^{1}H n.m.r. spectrum of this crude material, in acetone, showed a doublet ($J = 2·05$ c./sec.) at 4·07, and no other peaks in the 3·7—4·3 region, suggesting that it contained 2,3,4,5-tetrafluoro-6-nitroanisole (II).

The fourth component was a pale yellow solid (2·04 g.) which crystallised from light petroleum (b. p. 80—100°) to give colourless needles of 2,3,5,6-*tetrafluoro-4-nitroanisole* (I) (1·48 g.), m. p. 39—39·5° (Found: C, 37·2; H, 1·4. $C_7H_3F_4NO_3$ requires C, 37·3; H, 1·3%).

  [9] Bishop, Cavell, and Chapman, *J.*, 1952, 437.
  [10] Ross, *Progr. Phys. Org. Chem.*, 1963, 1, 31.
  [11] Bunnett and Morath, *J. Amer. Chem. Soc.*, 1955, 77, 5051, 5055.
  [12] Hertog and Jouwersma, *Rec. Trav. chim.*, 1953, 72, 44.

2,3,5-Trifluoro-4,6-dimethoxynitrobenzene (IV).—The *p*-nitroanisole (I) (2·00 g.) in methanol (50 ml.) was treated with sodium methoxide in methanol (10 ml.; 1·06N) as described above, but for 3 hr. at room temperature after the methoxide had been added, followed by 10 min. reflux. Separation of the crude product (2·20 g.) as in the previous experiment gave (i) a white solid (0·21 g.) which crystallised from light petroleum (b. p. 60—80°) to yield starting material (0·14 g.), m. p. and mixed m. p. 39—39·5°; and (ii) a liquid which was distilled at 120° (bath)/0·5 mm. to give *2,3,5-trifluoro-4,6-dimethoxynitrobenzene* (IV) (1·60 g.) (Found: C, 40·5; H, 2·4. $C_8H_6F_3NO_4$ requires C, 40·5; H, 2·6%).

2,3,5,6-Tetrafluoro-p-anisidine.—The nitroanisole (I) (0·70 g.) in ethanol (50 ml.) was hydrogenated over 10% palladium–charcoal at atmospheric pressure and room temperature. After 2 hr., 330 ml. of hydrogen had been absorbed. Filtration, evaporation, and then crystallisation of the residue from light petroleum (b. p. 80—100°) gave 2,3,5,6-tetrafluoro-*p*-anisidine (III) (0·60 g.), m. p. and mixed [5] m. p. 77·5—78° (lit.,[7] 75—76·5°) (Found: C, 42·9; H, 2·7. Calc. for $C_7H_5F_4NO$: C, 43·1; H, 2·6%).

2,3,5-Trifluoro-4,6-dimethoxyaniline (V).—Reduction of 2,3,5-trifluoro-4,6-dimethoxynitrobenzene (IV) (1·02 g.) as in the previous experiment gave 2,3,5-trifluoro-4,6-dimethoxyaniline (V) (0·33 g.), m. p. and mixed [5] m. p. 45—46°.

Reaction of Ammonia with Pentafluoronitrobenzene.—This reaction was carried out as described previously [2] on pentafluoronitrobenzene (5·10 g.), except that the products (4·91 g.) were separated completely on alumina by elution with light petroleum (b. p. 40—60°)–benzene (1 : 1, v/v) They were, after further chromatography of the individual bands on alumina in ether (to remove traces of high-boiling petroleum fractions): 2,3,4,5-tetrafluoro-6-nitroaniline (VI) (2·59 g.); 4,5,6-trifluoro-2-nitro-1,3-phenylenediamine (XII) (0·26 g.), m. p. 158—160° (lit.,[2] 162—163·5°); 2,3,5,6-tetrafluoro-4-nitroaniline (IX) (1·13 g.), and 2,4,5-trifluoro-6-nitro-1,3-phenylenediamine (XV) (0·71 g.); all were identified by infrared spectroscopy. When benzene alone was the eluent, the first three compounds ran together to some extent.[2]

Reaction of Methylamine with Pentafluoronitrobenzene.—A solution of ethanolic methylamine (33%, w/w; 2·50 g.) in ether (30 ml.) was added dropwise at room temperature to a stirred solution of pentafluoronitrobenzene (2·80 g.) in ether (30 ml.). After 1 hr., the mixture was washed with water, the washings extracted with ether, and the combined, dried ($MgSO_4$) extracts evaporated to leave a red oil (2·80 g.). This oil, in 0·2 g. portions, was chromatographed on alumina (commercial chromatography-grade alumina, deactivated with one-tenth its weight of water) with light petroleum (b. p. 40—60°)–benzene (4 : 1, v/v) as eluent. Four bands separated; the first two were washed from the column with the above eluent and the last two with a 1 : 1 (v/v) mixture of the same solvents. The solvents were removed from each fraction *in vacuo* to avoid losses by co-distillation.

The crude product (1·75 g.) from the first band was crystallised from light petroleum (b. p. 60—80°) to give orange plates of *2,3,4,5-tetrafluoro-N-methyl-6-nitroaniline* (VII) (0·89 g.), m. p. 46·5—48° (Found: C, 37·7; H, 2·0. $C_7H_4F_4N_2O_2$ requires C, 37·5; H, 1·8; F, 33·9%). Crystallisation of the crude material (0·05 g.) from the second, purple band as above gave 4,5,6-trifluoro-*NN'*-dimethyl-2-nitro-1,3-phenylenediamine (XIII) (0·01 g.) m. p. and mixed m. p. with the specimen prepared later, 163—164°. The third band (0·94 g.) yielded yellow needles of *2,3,5,6-tetrafluoro-N-methyl-4-nitroaniline* (X) (0·38 g.), m. p. 99·5—101·5° [from light petroleum (b. p. 80—100°)–benzene] (Found: C, 37·7; H, 2·2; F, 34·4%). Crystallisation of the crude product (0·14 g.) from the fourth, orange band from light petroleum (b. p. 60—80°)–benzene gave 2,4,5-trifluoro-*NN'*-dimethyl-6-nitro-1,3-phenylenediamine (XVI) (0·03 g.), m. p. and mixed m. p. with the compound obtained later, 123—124°.

Reaction of Dimethylamine with Pentafluoronitrobenzene.—Pentafluoronitrobenzene (2·50 g.) in ether (30 ml.) was treated with ethanolic dimethylamine (33%, w/w; 3·20 g.) as in the methylamine experiment. The crude product (2·64 g.) was a green solid. An acetone solution of it showed, in the 2·7—3·2 range (NMe₂ region) of the ^{1}H n.m.r. spectrum, a doublet ($J = 1·8$ c./sec.) and a triplet ($J = 2·7$ c./sec.) in intensity ratio 19 : 81.

The crude product was washed with light petroleum (b. p. 40—60°) (10 ml.) and the washings were chromatographed on alumina as above but with light petroleum (b. p. 40—60°) as the eluent. Four bands developed; the first three were washed from the column with the eluent and the last with light petroleum (b. p. 40—60°)–benzene (1 : 1, v/v). The undissolved green solid was washed three more times with light petroleum (b. p. 40—60°) (10 ml.) and the washings were again chromatographed. Neither the first band nor second bands were present in the

last washings. The remaining green solid was dissolved in benzene and chromatographed on alumina with light petroleum (b. p. 40—60°)–benzene (1 : 1, v/v) as the eluent. Only the last two bands appeared. The appropriate solutions containing the various fractions were combined and evaporated *in vacuo*.

The first band yielded a yellow viscous liquid (0·45 g.) which decomposed on attempted simple distillation *in vacuo*. Slow distillation at 15°/0·1 mm. into a liquid air-cooled trap gave, as a yellow oil, 2,3,4,5-*tetrafluoro*-NN-*dimethyl*-6-*nitroaniline* (VIII) (Found: C, 40·3; H, 2·3. $C_8H_6F_4N_2O_2$ requires C, 40·3; H, 2·5%). The compound did not form a hydrochloride in dry ether. The second band gave an orange liquid (0·08 g.) which crystallised from light petroleum (b. p. 40—60°) at 0° to give 2,4,5-trifluoro-*NNN'N'*-tetramethyl-6-nitro-1,3-phenylenediamine (XVII) (0·03 g.), m. p. and mixed m. p. with the specimen prepared later, 24—25°. The crude product (2·10 g.) from the third band gave yellow needles of 2,3,5,6-*tetrafluoro*-NN-*dimethyl*-4-*nitroaniline* (XI) (1·40 g.), m. p. 99—99·5° [from light petroleum (b. p. 80—100°)] (Found: C, 40·4; H, 2·4; F, 31·8. $C_8H_6F_4N_2O_2$ requires C, 40·3; H, 2·5; F, 31·9%). The fourth band yielded a brown solid (0·03 g.) which was not investigated.

Treatment of the Tetrafluoro-N-methylnitroanilines with Methylamine.—(a) 2,3,4,5-*Tetrafluoro-N-methyl*-6-*nitroaniline* (VII). This compound (1·50 g.) in ether (20 ml.) was treated with ethanolic methylamine (30%, w/w; 1·38 g.) in ether (30 ml.) as in the previous methylamine experiment. Four bands developed on alumina. The first yielded crude starting material (0·36 g.) which, on crystallisation from light petroleum (b. p. 60—80°), gave the pure compound (0·19 g.), m. p. and mixed m. p. 46—48°. The crude product (0·37 g.) from the second band gave deep purple crystals (with a green sheen) of 4,5,6-*trifluoro*-NN'-*dimethyl*-2-*nitro*-1,3-*phenylenediamine* (XIII) (0·16 g.), m. p. 163·5—164° [from light petroleum (b. p. 60—80°)] (Found: C, 41·1; H, 3·6. $C_8H_8F_3N_3O_2$ requires C, 40·9; H, 3·4; F, 24·2%).

The product (0·79 g.) from the third band, crystallised from benzene–light petroleum (b. p. 60—80°), gave orange 2,4,5-*trifluoro*-NN'-*dimethyl*-6-*nitro*-1,3-*phenylenediamine* (XVI) (0·24 g.), m. p. 123·5—125° (Found: C, 41·1; H, 3·4; F, 24·6%). The fourth band gave a brown oil (0·08 g.) which was not investigated.

(b) 2,3,5,6-*Tetrafluoro-N-methyl*-4-*nitroaniline* (X). Treatment of this compound (0·80 g.) with ethanolic methylamine (33%, w/w; 0·67 g.) as before gave three bands on alumina with benzene–light petroleum (b. p. 40—60°) (1 : 1, v/v) as eluent. The first yielded starting material (0·21 g.); crystallisation from light petroleum (b. p. 60—80°)–benzene gave the pure compound (0·08 g.), m. p. and mixed m. p. 99—101°. The crude product (0·50 g.) from the second band gave 2,4,5-trifluoro-*NN'*-dimethyl-6-nitro-1,3-phenylenediamine (XVI) (0·13 g.), m. p. and mixed m. p. with the sample obtained in (a), 123—125° [from light petroleum (b. p. 60—80°)–benzene]. The third band yielded a red-brown oil (0·12 g.) which was not investigated.

*Reaction of 2,3,5,6-Tetrafluoro-*NN-*dimethyl*-4-*nitroaniline* (XI) *with Dimethylamine.*—This compound (2·00 g.) was treated as before, in ether, with ethanolic dimethylamine (33%, w/w; 2·43 g.) and the product was chromatographed on alumina in light petroleum (b. p. 40—60°)– benzene (1 : 1, v/v). Three bands developed. The product from the first, a liquid (1·03 g.) which solidified in ice, gave the orange 2,4,5-*trifluoro*-NNN'N'-*tetramethyl*-6-*nitro*-1,3-*phenyl-enediamine* (XVII) (0·26 g.), m. p. 26·5° [from light petroleum (b. p. 40—60°) at 0°] (Found: C, 45·6; H, 4·7; F, 22·0. $C_{10}H_{12}F_3N_3O_2$ requires C, 45·6; H, 4·6; F, 21·7%). The second band yielded starting material (0·31 g.), which crystallised from light petroleum (b. p. 80—100°) to give the pure compound (0·21 g.), m. p. and mixed m. p. 98—99·5°. The third band yielded a brown solid (0·07 g.) which was not investigated.

Methylation of the Nitroamines.—Each nitroamine was refluxed with about (these quantities are not very critical) 30 times its weight of a mixture (3 : 1, v/v) of 90% aqueous formic acid and 40% (w/v) aqueous formaldehyde for 2 days when a further amount of formalin (*ca.* 1—5 times the weight of the compound) was added. The reflux was continued for 2 more days when more of the original mixture of formic acid and formalin (*ca.* 10 times the weight of the compound) was added. After a further 2 days reflux, the mixture was poured into water (100 ml.), and the product extracted with ether. The extracts were washed with aqueous sodium hydrogen carbonate, dried (MgSO₄), and evaporated. The residue was chromatographed on alumina in light petroleum (b. p. 40—60°). When these methylations were carried out for 1 day at reflux, they only proceeded to about 15% of completion.

(a) 2,3,4,5-*Tetrafluoro*-6-*nitroaniline* (VI).—This compound [2] (3·00 g.) gave a crude product (0·62 g.) which showed only one moving band on the alumina, and much tar. The band yielded

a yellow liquid (0·45 g.) which distilled very slowly *in vacuo* to give 2,3,4,5-tetrafluoro-*NN*-di-methyl-6-nitroaniline (VIII) (0·31 g.), identified by infrared spectroscopy.

(*b*) 2,3,5,6-*Tetrafluoro-4-nitroaniline* (IX).—The crude product (0·21 g.) from this compound [2] (0·40 g.) gave three bands on alumina, but only the first in any significant amount. It was 2,3,5,6-tetrafluoro-*NN*-dimethyl-4-nitroaniline (XI), 0·15 g. crude, 0·07 g. pure, m. p. and mixed m. p. 98—99° [from light petroleum (b. p. 80—100°)].

(*c*) 2,3,4,5-*Tetrafluoro*-N-*methyl*-6-*nitroaniline* (VII).—The product from reaction of this compound (0·60 g.) showed only one moving band on alumina. This yielded, after slow distillation *in vacuo*, 2,3,4,5-tetrafluoro-*NN*-dimethyl-6-nitroaniline (VIII) (0·02 g.), identified by infrared spectroscopy.

(*d*) 2,3,5,6-*Tetrafluoro*-N-*methyl*-4-*nitroaniline* (X).—This compound (0·25 g.), after methylation, showed only one band on alumina. This yielded a brown solid (0·08 g.), which gave yellow needles of 2,3,5,6-tetrafluoro-*NN*-dimethyl-4-nitroaniline (XI) (0·03 g.), m. p. and mixed m. p. 99—99·5°, [from light petroleum (b. p. 60—80°)].

Nuclear Magnetic Resonance Spectra.—The ^{1}H spectra were measured on a Varian A60 instrument at 60 Mc./sec., and the ^{19}F spectra on either a Mullard SL44 Mark 2 at 30·1 Mc./sec. or on a Varian HR100 instrument at 94·1 Mc./sec.

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