Polyfluoroarenes. Part XVII.[1] Some Reactions of Pentafluorobenzonitrile

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Pentafluorobenzonitrile reacts with ammonia, aniline, and *o*-phenylenediamine and with chloride, bromide, iodide, methoxide, hydroxide, acetate, benzoate, and azide ions mainly by displacement of the 4-fluorine atom. Reaction with an excess of chloride ion yields pentachlorobenzonitrile. Tetrafluoro-4-iodobenzonitrile undergoes attack at the iodine atom itself in the presence of iodide ion, and 4-benzoyloxytetrafluorobenzonitrile yields tetrafluoro-4-hydroxybenzonitrile when it is treated with dimethylformamide. Pentafluorobenzonitrile may be converted into pentafluorobenzaldehyde by reaction with Raney nickel and into pentafluorobenzophenone by reaction with phenylmagnesium bromide.

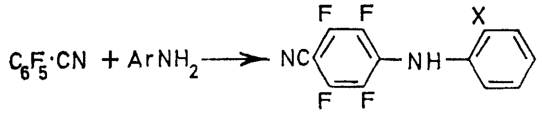
THE reactions of pentafluorobenzonitrile with ammonia,[2] hydrazine,[3] dimethylformamide,[4] methoxide ions,[4] pentafluorophenoxide ions,[5] heptafluoroisopropyl carbanions,[6] and certain metal carbonyl anions [7] lead to predominant nucleophilic displacement of the 4-fluorine atom. Substitution at the 2-position has sometimes been observed to follow or accompany this process, and it has been estimated that about 10% of the reaction with pentafluorophenoxide ion occurs at this position.[5] The high reactivity of pentafluorobenzonitrile towards methoxide ion has also been demonstrated,[8] and suggests that this compound should react under relatively mild conditions with reagents which are usually considered to be too weakly nucleophilic for use in the polyfluoroarene field. Reactions with a number of such reagents are discussed here, and some reactions with more conventional nucleophiles have also been examined.

Reactions with Ammonia and Amines.—The reported reaction of pentafluorobenzonitrile with a large excess of aqueous ammonia at 80° apparently gave 4-aminotetrafluorobenzonitrile as the only identified product.[2] Following the reaction under our conditions (equimolar quantities of the nitrile and aqueous ammonia, 60°), this compound was isolated in 70% yield, and a fraction containing 90% of the 2-isomer, identified by n.m.r. spectroscopy, was also obtained. Analysis of the crude product from this reaction revealed that these compounds are produced in a 19 : 1 ratio.

The hydrolysis of 4-aminotetrafluorobenzonitrile by boiling 80% sulphuric acid is accompanied by decarboxylation of the acid initially formed, and 2,3,5,6-tetrafluoroaniline (60% yield) is the only product isolated. Reactions of this type can provide a means of ready identification of the substituted nitrile; the hydrolysis of polyfluorobenzonitriles under milder conditions yields the expected amide or acid.

The reactivity of pentafluorobenzonitrile towards more weakly basic amino-compounds was investigated with aniline, *o*-phenylenediamine, and diphenylamine. Aniline does not react to a significant extent with hexafluorobenzene, even at 165°,[9] although reaction *via* the $Ph\bar{N}H$ ion occurs in the presence of sodium hydride, and pentafluorodiphenylamine is formed in 49% yield.[10] Sodium hydride also promotes reaction between pentafluoroaniline and hexafluorobenzene.[11]

However, pentafluorobenzonitrile undergoes ready reaction with aniline (2 moles) in refluxing ethanol to give 4-cyano-2,3,5,6-tetrafluorodiphenylamine (I) (63%) and with *o*-phenylenediamine under similar conditions to give 2′-amino-4-cyano-2,3,5,6-tetrafluorodiphenylamine (II) (92%). No products resulting from displacement at the 2-position in the nitrile were detected in these reactions, the increased selectivity being in accord with the reduced nucleophilicity of the attacking amino-group.



(I) X = H
(II) X = NH_2

Further substantial reduction in the nucleophilicity of the amine completely inhibits reaction under these mild conditions, pentafluorobenzonitrile and diphenylamine being effectively unchanged after prolonged contact (16 hours) in refluxing ethanol; similar results were obtained at higher temperatures in the absence of a solvent. The effect of strongly basic catalysts on the reaction with diphenylamine was not investigated.

Reactions with Halide Ions.—Although hexafluorobenzene does not react with iodide ion in pyridine, the

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[1] Part XVI, J. M. Birchall, R. N. Haszeldine, and M. E. Jones, preceding paper.

[2] Netherlands Appl. 6,613,001/1967 (*Chem. Abs.*, 1968, **68**, 68,762).

[3] C. Tamborski and E. J. Soloski, *J. Org. Chem.*, 1966, **31**, 746.

[4] E. Felstead, H. C. Fielding, and B. J. Wakefield, *J. Chem. Soc.* (*C*), 1966, 708.

[5] R. J. De Pasquale and C. Tamborski, *J. Org. Chem.*, 1968, **33**, 1658.

[6] R. D. Chambers, J. A. Jackson, W. K. R. Musgrave, and R. A. Storey, *J. Chem. Soc.* (*C*), 1968, 2221.

[7] B. L. Booth, R. N. Haszeldine, and M. B. Taylor, *J. Organometallic Chem.*, 1966, **6**, 570; M. I. Bruce and F. G. A. Stone, *J. Chem. Soc.* (*A*), 1966, 1837.

[8] K. C. Ho and J. Miller, *Austral. J. Chem.*, 1966, **19**, 423.

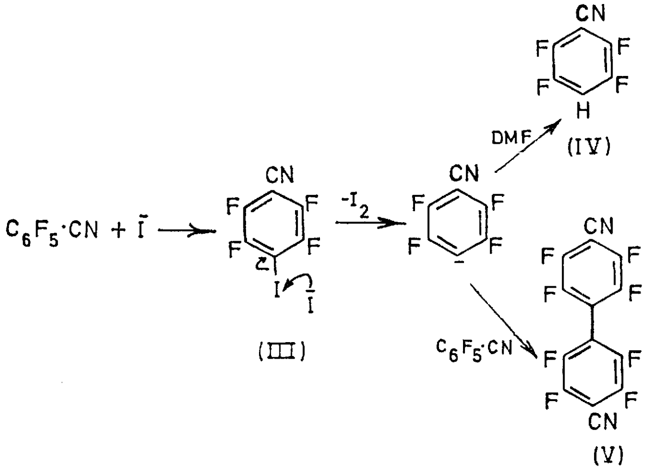
[9] G. M. Brooke, J. Burdon, M. Stacey, and J. C. Tatlow, *J. Chem. Soc.*, 1960, 1768.

[10] J. Burdon, J. Castaner, and J. C. Tatlow, *J. Chem. Soc.*, 1964, 5017.

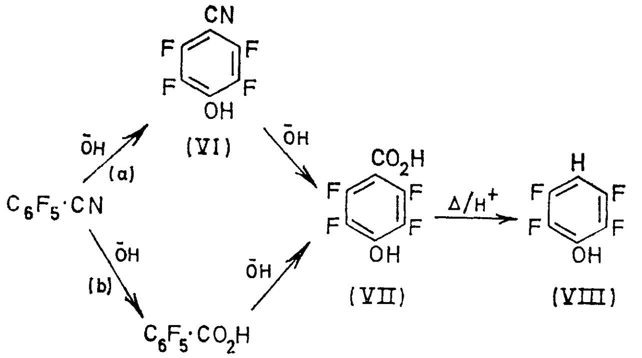
[11] G. Baum and C. Tamborski, *Chem. and Ind.*, 1964, 1949.

displacement of fluoride ion by other halogens has been achieved with tetrafluorophthalonitrile (chloride and bromide ion)[12] and with pentafluoropyridine (iodide ion),[13] both relatively reactive aromatic systems. Pentafluorobenzonitrile is also sufficiently reactive to undergo this type of halogen exchange under relatively mild conditions, and reacts with an equimolar proportion of either lithium chloride or lithium bromide in refluxing *N*-methylpyrrolidone to give mainly the corresponding 4-halogenotetrafluorobenzonitrile in moderate yield (52—55%). The use of an excess of lithium chloride in this reaction gives a quantitative conversion into pentachlorobenzonitrile, a reversal of the preferred method of preparation of the pentafluoro-compound.[1] A similar reaction with an excess of lithium bromide failed to yield a clear-cut product, although tetrafluorophthalonitrile does give some of the tetrabromo-compound under these conditions.[12]

The reaction of pentafluorobenzonitrile with sodium iodide was carried out in dimethylformamide before the discovery that this solvent can itself react with the polyfluoroarene nucleus.[4,12] The products, tetrafluoro-4-iodobenzonitrile (III), 2,3,5,6-tetrafluorobenzonitrile (IV), 4,4′-dicyano-octafluorobiphenyl (V), and elemental iodine, formed in yields dependent upon the proportion of sodium iodide used, parallel those isolated from the reaction of pentafluoropyridine under these conditions. The suggested mechanism for their formation, which has been discussed in detail for the pyridine reaction,[13] is supported by the formation of the tetrafluoro-nitrile (IV) (15%), when the iodo-compound (III) is treated with sodium iodide in dimethylformamide; none of the biphenyl (V) is formed in this last reaction. The trace (1%) of tetrafluorobenzonitrile (IV) which is formed when the iodo-compound (III) is heated alone in dimethylformamide may be attributed to an alternative, slow, homolytic fission of the carbon–iodine bond. The generation of aromatic carbanions by nucleophilic attack at an iodine atom has been observed in other systems[14] and may become a useful synthetic method in polyfluoroarene chemistry.



Reaction with Oxygen Nucleophiles.—Felstead, Fielding, and Wakefield have obtained tetrafluoro-4-methoxybenzonitrile in 69% yield by the reaction of pentafluorobenzonitrile with sodium cyanide in methanol; gas-liquid chromatography also indicated the formation of 5% of a second product, believed to be the 2-methoxy-compound.[4] We have obtained very similar results by treatment of pentafluorobenzonitrile with one equivalent of sodium methoxide in methanol, the two methoxy-compounds being formed in a 15 : 1 ratio. Use of an excess of the reagent gave difluoro-2,4,6-trimethoxybenzonitrile (75%), a compound previously obtained by the reaction of pentafluorobenzonitrile with an excess of sodium cyanide or potassium carbonate in methanol.[4] Tetrafluoro-4-methoxybenzonitrile reacts with boiling 70% sulphuric acid to give 2,3,5,6-tetrafluoroanisole (61%).



The product of prolonged treatment of pentafluorobenzonitrile with aqueous sodium hydroxide is tetrafluoro-4-hydroxybenzoic acid (VII) (40%), obtained as the monohydrate and converted into 2,3,5,6-tetrafluorophenol (VIII) in boiling 80% sulphuric acid. The fact that tetrafluoro-4-hydroxybenzonitrile (VI) may be obtained in 83% yield from the reaction of pentafluorobenzonitrile with potassium hydroxide in t-butyl alcohol suggests that the polyfluoroarene ring is more susceptible to attack by hydroxide ion than the cyano-group in this system and that the reaction with aqueous base follows route (a). However, pentafluorobenzonitrile reacts with aqueous sodium carbonate to give a low yield of pentafluorobenzamide,[15] suggesting that attack at the cyano-group is likely to precede substitution of fluorine in an aqueous medium [route (b); pentafluorobenzoic acid is known to undergo attack by methoxide ion at the 4-position[16]]. These results are in accord with the suggestion[15] that the degree of solv-

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[12] J. M. Birchall, R. N. Haszeldine, and J. O. Morley, *J. Chem. Soc.* (*C*), 1970, 456.

[13] R. E. Banks, R. N. Haszeldine, E. Phillips, and I. M. Young, *J. Chem. Soc.* (*C*), 1967, 2091.

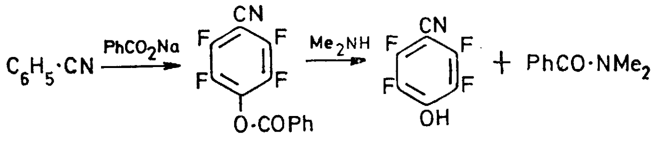
[14] J. M. Birchall, M. Green, R. N. Haszeldine, and J. E. Waller, unpublished results.

[15] E. V. Aroskar, P. J. N. Brown, R. G. Plevey, aud R. Stephens, *J. Chem. Soc.* (*C*), 1968, 1569.

[16] J. Burdon, W. B. Hollyhead, and J. C. Tatlow, *J. Chem. Soc.*, 1965, 6336.

ation of the nucleophile may influence its preference for the alternative sites in the pentafluorobenzonitrile molecule. It is, perhaps, significant that, although nearly all the reactions of pentafluorobenzonitrile which have been studied result in attack at the aromatic nucleus, the reagents have usually been employed in systems where solvation of the nucleophile might be expected to be severely limited.

The behaviour of pentafluorobenzonitrile towards a weaker nucleophile in the oxygen series was investigated initially with sodium acetate in refluxing dimethylformamide, a reaction which yields *NN*-dimethylacetamide and tetrafluoro-4-hydroxybenzonitrile (49%). An analogous reaction occurs with sodium benzoate in dimethylformamide. 4-Benzoyloxytetrafluorobenzonitrile (IX) may be obtained from pentafluorobenzonitrile and sodium benzoate in refluxing *N*-methylpyrrolidone (56% yield) or in the absence of a solvent at 185° (88%), or by conventional benzoylation of the 4-hydroxy-compound (78%). The benzoyloxy-compound yields *NN*-dimethylbenzamide and tetrafluoro-4-hydroxybenzonitrile when it is heated in dimethylformamide, and this step is clearly involved in the earlier reaction in this solvent. The electron-withdrawing power of the cyanotetrafluorophenyl-group must be partially responsible for the reactivity of the ester carbonyl group towards nucleophilic attack by dimethylamine, traces of which are probably present in the dimethylformamide at the beginning of the reaction.[17] The phenolic product is likely to be a sufficiently strong acid to catalyse continuous decomposition of more dimethylformamide into dimethylamine and carbon monoxide in the manner proposed earlier.[12]



(IX)

Reaction with Azide Ion.—Pentafluorophenyl azide may be prepared from pentafluorophenylhydrazine and nitrosyl chloride, but not by a direct displacement reaction between hexafluorobenzene and sodium azide in refluxing aqueous acetone.[18] However, displacement reactions of activated aryl halides with cyanide ion are not uncommon,[19] and pentafluorobenzonitrile reacts exothermically with sodium azide in acetone to give the 4-azido-compound in 54% yield. This is believed to be the first successful reaction with azide ion in the polyfluoroarene field. No substitution at other positions was detected.

Product Orientation.—Where necessary, the orientation of attack on pentafluorobenzonitrile has been established mainly by ^{19}F n.m.r. spectroscopy, the 4-substituted products giving clear-cut AA′XX′ patterns in all cases, with chemical shifts and coupling constants (where measurable) in good agreement with predicted values.

The tetrafluoro-4-iodobenzonitrile obtained from the reactions of pentafluorobenzonitrile with iodide ion was identified by comparison with a specimen obtained by treatment of tetrafluoro-4-hydrazinobenzonitrile with silver oxide in iodomethane. An analogous reaction has been used to convert pentafluorophenylhydrazine into pentafluoroiodobenzene.[18]

Reactions of the Cyano-Group.—The ready availability of pentafluorobenzonitrile[1] could make this compound an attractive precursor of other polyfluoroarenes, but few conversions of the cyano-group have been reported.

We have found that the nitrile does not undergo conventional Stephen reduction with tin(II) chloride, but it may be converted into pentafluorobenzaldehyde by treatment with Raney nickel in formic acid. Reaction of the nitrile with phenylmagnesium bromide yields 2,3,4,5,6-pentafluorobenzophenone *via* the intermediate imine hydrochloride, $C_6F_5\cdot CPh{:}\overset{+}{N}H_2\overset{-}{Cl}$, and it seems likely that most conventional reactions of the cyano-group could be achieved with little difficulty.

EXPERIMENTAL

Spectroscopic techniques have been described previously;[1] ^{19}F chemical shifts are to high field of an external trifluoroacetic acid reference. A Griffin and George D6 instrument (gas-density balance detector) was used for g.l.c. analyses; unless otherwise stated, the instrument was fitted with a 2-m. column packed with 30% by weight of Silicone MS550 on Celite.

Aminotetrafluorobenzonitriles.— Pentafluorobenzonitrile (10·0 g., 51·8 mmoles)[1] and aqueous ammonia (*d*, 0·880; 6·4 ml., *ca.* 52·0 mmoles) were heated in a sealed tube at 60° for 24 hr. Extraction with ether (3 × 30 ml.) then yielded a pale yellow solid (8·9 g.), which was sublimed at 90°/0·2 mm. and recrystallised from light petroleum (b.p. 100—120°) to give white needles of 4-aminotetrafluorobenzonitrile (6·9 g., 70%) (Found: C, 43·9; H, 1·3. Calc. for $C_7H_2F_4N_2$: C, 44·2; H, 1·1%), m.p. 94·5—95·5° (lit.,[2] m.p. 94—96°) [$\delta_2 = \delta_6 = 62{\cdot}3$, $\delta_3 = \delta_5 = 85{\cdot}2$ p.p.m. (in acetone)]. Evaporation of the mother liquors and repeated recrystallisation of the residue from light petroleum (b.p. 30—40°) gave a solid, m.p. 75—83°, shown by n.m.r. spectroscopy to consist mainly (*ca.* 90%) of 2-aminotetrafluorobenzonitrile [$\delta_3 = 84{\cdot}3$, $\delta_4 = 74{\cdot}0$, $\delta_5 = 98{\cdot}6$, and $\delta_6 = 60{\cdot}9$ p.p.m. (in acetone)]. Analysis of the crude product by g.l.c. (145°) showed that the two major products were present in a 19 : 1 ratio.

2,3,5,6-Tetrafluoroaniline.— 4-Aminotetrafluorobenzonitrile (0·95 g., 5 mmoles) was heated under reflux with aqueous 80% sulphuric acid (25 ml.) for 1 hr. Carbon dioxide was evolved. The cooled mixture was poured onto crushed ice, and extraction with ether (2 × 25 ml.) gave a low-melting solid, sublimation of which at 20°/0·2 mm.

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[17] A. B. Thomas and E. G. Rochow, *J. Amer. Chem. Soc.*, 1957, **79**, 1843.

[18] J. M. Birchall, R. N. Haszeldine, and A. R. Parkinson, *J. Chem. Soc.*, 1962, 4966.

[19] See, for example, E. Muller and K. Weisbrod, *J. prakt. Chem.*, 1926, **113**, 30.

yielded 2,3,5,6-tetrafluoroaniline (0·49 g., 60%), m.p. 28—30° (lit.,[20] m.p. 29—31·5°), identified by i.r. spectroscopy.

Cyanotetrafluorodiphenylamine.— Pentafluorobenzonitrile (4·82 g., 25 mmoles) and aniline (4·66 g., 50 mmoles) were heated under reflux in ethanol (50 ml.) for 90 min. The solid product, which separated when the mixture was poured onto crushed ice, was recrystallised from ethanol to give white needles of 4-*cyano*-2,3,5,6-*tetrafluorodiphenylamine* (4·20 g., 63%) (Found: C, 58·8; H, 2·3; N, 10·8. $C_{13}H_6F_4N_2$ requires C, 58·7; H, 2·3; N, 10·5%), m.p. 121—123°, showing $-C{\equiv}N$ absorption at 4·46 μm [$\delta_2 = \delta_6 = 59{\cdot}5$, $\delta_3 = \delta_5 = 73{\cdot}1$ p.p.m. (in acetone)].

2′-*Amino*-4-*cyanotetrafluorodiphenylamine.*— Pentafluorobenzonitrile (1·93 g., 10 mmoles) and *o*-phenylenediamine (2·16 g., 20 mmoles), heated in refluxing ethanol (10 ml.) for 4 hr., similarly gave pink crystals of 2′-*amino*-4-*cyano*-2,3,5,6-*tetrafluorodiphenylamine* (2·60 g., 92%) (Found: C, 55·5; H, 2·2; N, 15·0. $C_{13}H_7F_4N_3$ requires C, 55·5; H, 2·5; N, 15·0%), m.p. 212—214° (from ethanol).

4-*Chlorotetrafluorobenzonitrile.*— Pentafluorobenzonitrile (0·965 g., 5·0 mmoles), lithium chloride (0·22 g., 5·0 mmoles), and *N*-methyl-2-pyrrolidone (5 ml.) were heated under reflux for 30 min. The mixture was poured into water (50 ml.), the resulting semisolid was extracted with ether (3 × 15 ml.), and the combined extracts were dried ($MgSO_4$) and evaporated. Analysis of the crude, low-melting, product by g.l.c. (180°) showed it to contain two components in the ratio 1 : 17. Sublimation at 40° *in vacuo* and two recrystallisations from light petroleum (b.p. 30—40°) yielded fine white needles of 4-*chloro*-2,3,5,6-*tetrafluorobenzonitrile* (0·58 g., 56%) (Found: C, 40·0; N, 6·5. C_7ClF_4N requires C, 40·1; N, 6·7%), m.p. 66—67°, showing $-C{\equiv}N$ absorption at 4·46 μm [$\delta_2 = \delta_6 = 53{\cdot}8$, $\delta_3 = \delta_5 = 59{\cdot}2$ p.p.m. (in CCl_4)].

Pentachlorobenzonitrile.—Pentafluorobenzonitrile (0·965 g., 5·0 mmoles), lithium chloride (4·25 g., 100 mmoles), and *N*-methyl-2-pyrrolidone (5 ml.) were heated under reflux for 4 hr. The white solid, which separated when the mixture was poured into water, was washed repeatedly with water, dried, powdered, and extracted with ether. The ether-insoluble portion was then sublimed at 140° *in vacuo* to give pentachlorobenzonitrile (1·41 g., 100%), m.p. and mixed m.p. 216—217°, identified by i.r. spectroscopy.

4-*Bromotetrafluorobenzonitrile.*—An exothermic reaction occurred when pentafluorobenzonitrile (0·965 g., 5·0 mmoles), lithium bromide (0·45 g., 5·0 mmoles), and *N*-methyl-2-pyrrolidone (5 ml.) were mixed, and heating under reflux was continued for 30 min. The mixture was cooled, an excess of water was added, and the resulting off-white solid was washed with water and dried. G.l.c. (185°) showed that the crude product (0·70 g.) contained two components in a 1 : 18 ratio. Sublimation at 50° *in vacuo* and several recrystallisations from light petroleum (b.p. 30—40°) gave pure (g.l.c.) 4-bromo-2,3,5,6-tetrafluorobenzonitrile (0·43 g., 55%) (Found: C, 31·3; N, 5·3. Calc. for C_7BrF_4N: C, 31·5; N, 5·5%), m.p. 76—76·5° (lit.,[2] m.p. 77—79°) [$\delta_2 = \delta_6 = 53{\cdot}2$, $\delta_3 = \delta_5 = 50{\cdot}9$ p.p.m. (in CCl_4)].

Tetrafluoro-4-iodobenzonitrile.— 4-Hydrazinotetrafluorobenzonitrile (3·90 g., 19 mmoles) [3] was added during 1 hr. to a stirred suspension of silver oxide (6·80 g., 29 mmoles) in iodomethane (50 ml.). The vigorous reaction, which began after a short induction period, was controlled by cooling in ice, and the mixture was heated under reflux for 30 min. after the addition was complete. The liquid products were filtered, dried ($MgSO_4$), and distilled, to give 2,3,5,6-tetrafluorobenzonitrile (1·60 g., 48%), b.p. 78—80°/20 mm., m.p. 40° (lit.,[3] m.p. 40—41°), identified by i.r. spectroscopy, and impure tetrafluoro-4-iodobenzonitrile (0·4 g.), b.p. 80—100°. The solid residue was sublimed at 40°/0·2 mm. to give a white crystalline sublimate of pure 2,3,5,6-*tetrafluoro*-4-*iodobenzonitrile* (0·57 g., 10%) (Found: C, 28·1; I, 42·3; N, 4·8. C_7F_4IN requires C, 27·9; I, 42·2; N, 4·7%), m.p. 89° [$\delta_2 = \delta_6 = 53{\cdot}5$, $\delta_3 = \delta_5 = 38{\cdot}2$ p.p.m. (in CCl_4)].

Reaction of Pentafluorobenzonitrile with Sodium Iodide.—(a) 1 : 1 *Mole ratio.* The nitrile (4·82 g., 25 mmoles), anhydrous sodium iodide (3·75 g., 25 mmoles), and *NN*-dimethylformamide (25 ml.) were heated under reflux for 4 hr. and then poured into an excess of water. The mixture was extracted with ether (3 × 25 ml.), and the combined extracts were washed with aqueous sodium thiosulphate to remove iodine and dried ($MgSO_4$). Distillation gave a fraction (2·52 g.), b.p. 80—100°/20 mm., shown by g.l.c. to consist of pentafluorobenzonitrile (1·26 g., 26% recovery) and 2,3,5,6-tetrafluorobenzonitrile (1·26 g., 39% based on $C_6F_5{\cdot}CN$ transformed). The residue (2·31 g.) solidified on cooling and was sublimed at 40° *in vacuo* to give tetrafluoro-4-iodobenzonitrile (0·55 g., 10%), m.p. and mixed m.p. 89°, identified by i.r. spectroscopy. Recrystallisation from light petroleum (b.p. 100—120°) of the residue from the sublimation gave white needles of 4,4′-*dicyano*-2,2′,3,3′,5,5′,6,6′-*octafluorobiphenyl* (1·05 g., 33%) [Found: C, 48·1; N, 8·2%; *M* (mass spec.), 348. $C_{14}F_8N_2$ requires C, 48·3; N, 8·1%; *M*, 348], m.p. 129·5—131·5° [$\delta = 56{\cdot}1$ and 58·9 p.p.m. (in acetone)].

(b) 1 : 5 *Mole ratio.* A similar experiment, in which the nitrile (4·82 g., 25 mmoles), sodium iodide (18·75 g., 125 mmoles), and dimethylformamide (20 ml.) were heated under reflux for 4 hr., gave pentafluorobenzonitrile (0·88 g., 18% recovery), 2,3,5,6-tetrafluorobenzonitrile (0·88 g., 25%), tetrafluoro-4-iodobenzonitrile (0·70 g., 11%), and 4,4′-dicyano-octafluorobiphenyl (0·48 g., 13%), identified by i.r. spectroscopy.

Reactions of Tetrafluoro-4-iodobenzonitrile.—(a) *With dimethylformamide.* The iodo-compound (0·50 g., 1·7 mmoles) and dimethylformamide (5 ml.) were heated under reflux for 4 hr., poured into water (30 ml.), and extracted with ether (3 × 15 ml.). Distillation of the dried ($MgSO_4$) extracts left a solid (0·48 g.), shown by g.l.c. to consist of 2,3,5,6-tetrafluorobenzonitrile (1%) and tetrafluoro-4-iodobenzonitrile (99%).

(b) *With sodium iodide in dimethylformamide.* Tetrafluoro-4-iodobenzonitrile (0·50 g., 1·7 mmoles) and sodium iodide (0·25 g., 1·7 mmoles) were heated under reflux in dimethylformamide (5 ml.) for 4 hr. The mixture was poured into water (30 ml.) and extracted with ether (3 × 15 ml.), and the combined extracts were washed with aqueous sodium thiosulphate and dried ($MgSO_4$). Distillation of the ether left an oily solid (0·31 g.) shown to consist of 2,3,5,6-tetrafluorobenzonitrile (15%) and tetrafluoro-4-iodobenzonitrile (85%) by g.l.c. and i.r. spectroscopy.

Tetrafluoro-4-methoxybenzonitrile.—Sodium methoxide (50 mmoles) in methanol (55·6 ml.) was added dropwise to a stirred solution of pentafluorobenzonitrile (9·65 g., 50 mmoles) in methanol (25 ml.). The mixture became warm during the addition, and was heated under reflux for 2 hr. and then poured into water. Extraction with ether (4 × 50 ml.) gave a low-melting solid (9·52 g.), which was re-

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[20] G. M. Brooke, J. Burdon, and J. C. Tatlow, *J. Chem. Soc.*, 1962, 3253.

crystallised twice from light petroleum (b.p. 40—60°), to give white needles of 2,3,5,6-tetrafluoro-4-methoxybenzonitrile (7·60 g., 74%) (Found: C, 46·5; H, 1·5; N, 6·8. Calc. for $C_8H_3F_4NO$: C, 46·8; H, 1·5; N, 6·8%), m.p. 53—54° (lit.,[4] m.p. 53·5—54·5°), identified by n.m.r. spectroscopy. Analysis of the crude product by g.l.c. (2-m. column; polyethyleneglycol adipate; 120°) showed it to consist of pentafluorobenzonitrile (3%), a component believed to be tetrafluoro-2-methoxybenzonitrile (6%), and the 4-methoxy-compound (90%). The pure 4-methoxy-compound (3·23 g.) was heated under reflux in aqueous 70% sulphuric acid (60 ml.) for 1 hr.; dilution with water and extraction with ether then gave 2,3,5,6-tetrafluoroanisole (1·72 g., 61%), b.p. 145—146° (lit.,[21] b.p. 145°), identified by i.r. spectroscopy.

Difluoro-2,4,6-*trimethoxybenzonitrile*.—Sodium methoxide (36 mmoles) in methanol (40 ml.) was added dropwise to pentafluorobenzonitrile (1·93 g., 10 mmoles) in methanol (5 ml.), and the mixture was heated under reflux for 4 hr. and then poured into cold water. The resulting solid (1·83 g.), m.p. 79·5—80°, was recrystallised from light petroleum (b.p. 60—80°) to give 3,5-difluoro-2,4,6-trimethoxybenzonitrile (1·72 g., 75%) (Found: C, 52·2; H, 4·0; N, 6·4. Calc. for $C_{10}H_9F_2NO_3$: C, 52·4; H, 3·9; N, 6·1%), m.p. 79—80° (lit.,[4] m.p. 78°), identified by n.m.r. spectroscopy.

Tetrafluoro-4-*hydroxybenzoic Acid*.—Pentafluorobenzonitrile (2·90 g., 15 mmoles) was heated under reflux in aqueous 20% sodium hydroxide (50 ml.) until the evolution of ammonia ceased (14 hr.). The cooled mixture was neutralised with aqueous 5N-sulphuric acid, filtered, and extracted with ether (3 × 50 ml.), and the combined extracts were dried ($MgSO_4$) and evaporated. The resulting solid was recrystallised from benzene to give fine white needles of 2,3,5,6-tetrafluoro-4-hydroxybenzoic acid monohydrate (1·37 g., 40%) (Found: C, 37·0; H, 1·9. Calc. for $C_7H_4F_4O_4$: C, 36·9; H, 1·8%), m.p. 154—156° (lit.,[22] m.p. 157°). The monohydrate (2·80 g.) was heated under reflux for 1 hr. in aqueous 80% sulphuric acid (50 ml.); dilution with water, extraction with ether, and distillation of the extract gave 2,3,5,6-tetrafluorophenol (0·84 g., 41%), b.p. 141—143°, which solidified when kept (lit.,[23] b.p. 146°, m.p. 30°) and was identified by i.r. spectroscopy.

Tetrafluoro-4-*hydroxybenzonitrile*.— Pentafluorobenzonitrile (9·65 g., 50 mmoles), potassium hydroxide (5·60 g., 100 mmoles), and t-butyl alcohol (100 ml.) were stirred and heated under reflux for 2 hr. and then poured into water (200 ml.). Distillation removed the t-butyl alcohol, and the residual aqueous phase was acidified with aqueous 5N-hydrochloric acid (160 ml.) and extracted with ether (4 × 50 ml.). The combined extracts were dried ($MgSO_4$) and evaporated, and the residual solid (8·29 g.), m.p. 120—123°, was recrystallised from benzene to give white crystals of 2,3,5,6-tetrafluoro-4-hydroxybenzonitrile (7·90 g., 83%) (Found: C, 44·1; H, 0·6; N, 7·6. Calc. for C_7HF_4NO: C, 44·0; H, 0·5; N, 7·3%), m.p. 128—129° (lit.,[15] m.p. 124°), identified by n.m.r. spectroscopy. Reaction of the hydroxy-compound (0·96 g.) with benzoyl chloride (0·75 ml.) in pyridine (3 ml.) on a water-bath gave 4-*benzoyloxy*-2,3,5,6-*tetrafluorobenzonitrile* (1·15 g., 78%) (Found: C, 57·0; H, 1·5; N, 4·9. $C_{14}H_5F_4NO_2$ requires C, 57·0; H, 1·7; N, 4·8%), m.p. 113—114° (from ethanol).

Reaction of Pentafluorobenzonitrile with Sodium Acetate in Dimethylformamide.—The nitrile (0·97 g., 5·0 mmoles) and anhydrous sodium acetate (0·41 g., 0·5 mmoles) were heated under reflux in dimethylformamide (5 ml.) for 4 hr. Distillation under reduced pressure, followed by evacuation at room temperature, gave a colourless liquid, identified as a mixture of dimethylformamide and *NN*-dimethylacetamide by i.r. spectroscopy and g.l.c. Aqueous 5N-hydrochloric acid (25 ml.) was added to the solid residue, and extraction of the mixture with ether (2 × 25 ml.) gave a red solid. This was sublimed at 80° *in vacuo* to give white tetrafluoro-4-hydroxybenzonitrile (0·47 g., 49%), m.p. 128—129°, identified by i.r. spectroscopy.

Reaction of Pentafluorobenzonitrile with Sodium Benzoate.—(a) *In dimethylformamide*. The nitrile (4·83 g., 25 mmoles), anhydrous sodium benzoate (3·60 g., 25 mmoles), and dimethylformamide (50 ml.) were heated under reflux for 4 hr., cooled, and extracted with ether (2 × 50 ml.). Distillation of the ethereal solution gave dimethylformamide (40 ml.), b.p. 153°, and *NN*-dimethylbenzamide (3·10 g., 83%), b.p. 270°, identified by i.r. spectroscopy. The ether-insoluble solid was treated with aqueous 5N-hydrochloric acid, and extraction of the mixture with ether (3 × 25 ml.), followed by sublimation at 80° *in vacuo*, gave tetrafluoro-4-hydroxybenzonitrile (1·34 g., 28%).

(b) *In* N-*Methyl-2-pyrrolidone*. Pentafluorobenzonitrile (0·97 g., 5·0 mmoles), anhydrous sodium benzoate (0·72 g., 5·0 mmoles), and *N*-methylpyrrolidone (10 ml.) were heated under reflux for 2 hr. Dilution with water (50 ml). and extraction with ether (3 × 25 ml.) gave a dark brown liquid (1·20 g.), distillation of which yielded 4-benzoyloxy-2,3,5,6-tetrafluorobenzonitrile (0·83 g., 56%), b.p. 260°, m.p. 113—114°, identified by i.r. spectroscopy.

(c) *Without a solvent*. Pentafluorobenzonitrile (1·93 g., 10 mmoles) and anhydrous sodium benzoate (1·44 g., 10 mmoles) were heated in an evacuated sealed tube at 185° for 16 hr. The mixture was allowed to cool, and pentafluorobenzonitrile (0·96 g., 50%) was distilled out *in vacuo*. The residual solid was washed with water, dried, and recrystallised from benzene to give 4-benzoyloxytetrafluorobenzonitrile (1·30 g., 88% based on C_6F_5·CN transformed), m.p. 113—114°.

Reaction of 4-*Benzoyloxytetrafluorobenzonitrile with Dimethylformamide*.—The benzoyloxy-compound (2·95 g., 10 mmoles) and dimethylformamide (25 ml.) were heated under reflux for 4 hr., and the cooled mixture was then poured into water (50 ml.). Aqueous 5N-sodium hydroxide (40 ml.) was added, and extraction with ether (3 × 30 ml.) followed by distillation of the dried ($MgSO_4$), combined, extracts gave dimethylformamide (18 ml.) and *NN*-dimethylbenzamide (1·20 g., 81%). The aqueous solution was acidified with aqueous 5N-hydrochloric acid (60 ml.), and extraction with ether (3 × 30 ml.), followed by sublimation at 80° *in vacuo*, yielded tetrafluoro-4-hydroxybenzonitrile (0·90 g., 47%), m.p. 128—129°.

4-*Azidotetrafluorobenzonitrile*.—Sodium azide (1·63 g., 25 mmoles) was added to pentafluorobenzonitrile (4·83 g., 25 mmoles) in acetone (25 ml.) and water (5 ml.), and an exothermic reaction occurred. The mixture was heated under reflux for 4 hr., cooled, diluted with water (75 ml.), and extracted with ether (3 × 40 ml.). Distillation of the dried ($MgSO_4$) extract gave 4-*azido*-2,3,5,6-*tetrafluorobenzonitrile* (2·93 g., 54%) (Found : C, 38·6; N, 26·2. $C_7F_4N_4$ requires

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C, 38·9; N, 25·9%), b.p. 115°/15 mm., as a colourless liquid which turned yellow on exposure to air. Analysis of the crude reaction product by g.l.c. showed the presence of only one component. The azido-compound shows $-C\equiv N$ absorption at 4·46 μm and absorption attributed to the $-N_3$ group at 4·35w, 4·62s, and 4·70vs μm (*cf.* $C_6F_5{\cdot}N_3$, 4·42w, 4·55s, and 4·70vs μm); its n.m.r. spectrum is an AA′XX′ system with δ = 57·9 and 73·8 p.p.m.

Pentafluorobenzaldehyde.—Pentafluorobenzonitrile (3·86 g., 20 mmoles), formic acid (98—100%; 60 ml.), and moist Raney nickel [prepared from the alloy (5·80 g.) and aqueous 2N-sodium hydroxide (90 ml.)] were stirred at 75—80° for 30 min. The mixture was diluted with aqueous 70% ethanol and filtered, and the residual nickel was washed with warm ethanol. The addition of a large excess of water to the filtrate gave an oil, which was extracted with ether (3 × 40 ml.), and the combined extracts were washed with dilute aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and distilled to give pentafluorobenzaldehyde (1·80 g., 46%), b.p. 166—168° (lit.,[24] b.p. 168—170°), identified by i.r. spectroscopy.

Pentafluorobenzophenone.—Pentafluorobenzonitrile (4·68 g., 24 mmoles) in dry ether (10 ml.) was added to a stirred solution of phenylmagnesium bromide in ether [made from bromobenzene (5·33 g., 34 mmoles) and magnesium (0·80 g., 33 mg.-atoms) in ether (15 ml.)] during 30 min. at room temperature. The mixture was kept overnight and then added dropwise with vigorous stirring to ammonium chloride (50 g.) and crushed ice (100 g.). The ether layer was separated and dried ($MgSO_4$), and dry hydrogen chloride was passed through it to give a precipitate of *pentafluorophenyl phenyl ketimine hydrochloride* (4·50 g., 60%) (Found: C, 50·3; H, 2·3; Cl, 11·1; N, 4·3. $C_{13}H_7ClF_5N$ requires C, 50·7; H, 2·3; Cl, 11·5; N, 4·5%), m.p. 168—173°. The hydrochloride (3·59 g.) was heated under reflux with aqueous 5N-hydrochloric acid (100 ml.) for 2·5 hr., and the oil, which separated when the mixture was cooled, was extracted with ether (3 × 30 ml.) and distilled to give pure (g.l.c.) 2,3,4,5,6-pentafluorobenzophenone (2·17 g., 68%) (Found: C, 57·4; H, 1·9. Calc. for $C_{13}H_5F_5O$: C, 57·4; H, 1·8%), b.p. 75·5°/0·2 mm. (lit.,[25] b.p. 93°/0·2 mm.). Its 2,4-dinitrophenylhydrazone (Found: C, 50·5; H, 2·3. Calc. for $C_{19}H_9F_5N_4O_4$: C, 50·5; H, 2·0%) had m.p. 203·5—204° (lit.,[25] m.p. 204—205°).

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