SOME REACTIONS OF 1,2,3,4-TETRAFLUOROBENZENE AND DERIVED COMPOUNDS

L. J. BELF, M. W. BUXTON, and J. F. TILNEY-BASSETT*

Imperial Smelting Corporation Limited, St. Andrew's Road, Avonmouth, Bristol

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Abstract The preparation of 2,3,4,5-tetrafluoro-nitrobenzene and -bromobenzene and their use for the synthesis of other tetrafluorophenyl compounds and octafluoro-2,2'-disubstituted biphenyls is described.

As PART of a programme on the evaluation of the biocidal properties of fluorinated aromatic compounds we wished to prepare various 1.2-disubstituted tetrafluorobenzenes and 2.2'-disubstituted octafluorobiphenyls. Because of the known fungistatic activity of mono- and di-fluoronitrobenzenes¹ we were particularly interested in highly fluorinated benzenes and biphenyls containing a nitro group or another electron withdrawing group. This paper describes syntheses for the compounds listed in Fig. 1, which are based on 1.2.3.4-tetrafluorobenzene as starting material. Some of the compounds are useful as intermediates in the synthesis of octafluorophenothiazine, which we described recently.²



Fig.1

* Present address : Unilever Research Laboratory, Port Sunlight, Cheshire.

¹ Fluorine Chemistry (Edited by J. H. Simons), Vol. III; p. 48. Academic Press (1963).

² L. J. Belf, M. W. Buxton, and D. E. M. Wotton, Chem & Ind. 238 (1966).

Compounds derived from 2,3,4,5-tetrafluoronitrobenzene. 1,2,3,4-Tetrafluorobenzene (1) reacts under mild conditions with nitrating mixture to give 2,3,4,5-tetrafluoronitrobenzene (11). Reduction of this nitrocompound gives 2,3,4,5-tetrafluoroaniline (11) which reacts with bromine in boiling acetic acid giving 2-bromo-3,4,5,6-tetrafluoroacetanilide (IV); it may be possible to brominate the amine (111) without concurrent acetylation by carrying out the reaction at a lower temperature. Acidic hydrolysis of the anilide (IV) affords 2-bromo-3,4,5,6-tetrafluoroaniline (V).

The mononitro compound (II) proved resistant to further nitration, but 3,4,5,6-tetrafluorodinitrobenzene (VI) was prepared by the sequence: nitration of 2,3,4,5-tetrafluoracetanilide (VII) under mild conditions with nitrating mixture, and hydrolysis of the 2,3,4,5-tetrafluoro-6-nitroacetanilide (VIII) so formed to give 2-amino-3,4,5,6-tetrafluoronitrobenzene (IX), which was oxidized with peroxy-trifluoroacetic acid under similar conditions to those used by Tatlow³ for the oxidation of pentafluoroaniline to pentafluoronitrobenzene. Reduction of the nitroamine (IX) gives 1,2-diamino-3,4,5,6-tetrafluorobenzene (X). These reactions are shown in Fig. 2.

Compounds derived from 1-bromo-2,3,4,5-tetrafluorobenzene. The benzene (I) reacts at 15° with an equimolar quantity of bromine in 65% oleum giving a mixture of 1-bromo-2,3,4,5-tetrafluorobenzene (XI). 43% yield, and 1,2-dibromotetrafluorobenzene (XII), 20% yield. It has been reported recently that at 0° this reaction gives



Reagents: 1, H_2SO_4/HNO_3 ; 2, Sn/HC1; 3, Br/AcOH; 4, 50% H_2SO_4 ; 5, Ac_2O ; 6, $H_2/Raney Ni$; 7, CF_3CO_3H

FIG. 2.

³ G. M. Brooke, J. Burdon, and J. C. Tatlow, J. Chem. Soc. 802 (1961).

predominantly (>95%) the monobromo compound.⁴ We did not attempt to optimise the yield of the monobromo compound since we subsequently found that it is conveniently prepared by reduction of 1,2-dibromotetrafluorobenzene with zinc dust in boiling acetic acid.⁵

The monobromo compound (XI) reacts similarly to bromopentafluorobenzene.^{6–8} Thus, with cuprous cyanide in dimethylformamide it gives 2,3,4,5-tetrafluorobenzonitrile (XIII), with copper bronze it gives octafluoro-2,2'-dihydrobiphenyl (XV), and it forms a Grignard reagent which reacts with N-methylformanilide to give 2,3,4,5tetrafluorobenzaldehyde (XVI). Application of the Knoevenagel reaction to this aldehyde gave 2,3,4,5-tetrafluorocinnamic acid (XVII) and oxidation of the aldehyde gave 2,3,4,5-tetrafluorobenzoic acid (XVIII), identical with a sample prepared by hydrolysis of the nitrile (XIII).

The bromo compound (XI) reacts at 10 20° with nitrating mixture giving 2-bromo-3,4,5,6-tetrafluoronitrobenzene (XIX) in 62% yield. This compound was also formed (75% yield) by treatment of the nitro compound (II) with bromine and oleum, and this is the preferred synthesis. Compound (XIX) undergoes an Ullmann reaction giving octafluoro-2,2'-dinitrobiphenyl (XX). These reactions are shown in Fig. 3.



Reagents: 1, Zn. AcOH; 2, CuCN/DMF; 3, Cu; 4, Mg; 5, Ph(Me)CHO; 6, CH₂(CO₂H)₂/Pyr; 7, Na₂Cr₂O₂, H₂SO₄; 8, H₂SO₄; HNO₃; 9, Br₂/SO₃; 10, 36N; H₂SO₄; 11, HNO₂

FIG. 3.

- ⁴ J. Burdon, D. R. King, and J. C. Tatlow, Tetrahedron 22, 2541 (1966).
- ³ J. F. Tilney-Bassett, Chem. & Ind. 693 (1965).
- ⁶ L. J. Belf, M. W. Buxton, and G. Fuller, J. Chem. Soc. 3372 (1965).
- ⁷ E. Nield, R. Stephens, and J. C. Tatlow, J. Chem. Soc. 166 (1959).
- A. K. Barbour, M. W. Buxton, P. L. Coe, R. Stephens, and J. C. Tatlow, J. Chem. Soc. 808 (1961).

Compounds derived from 2-bromo-3,4,5,6-tetrafluoroaniline. 2-Bromo-3,4,5,6-tetrafluoroaniline (V) reacts with cuprous cyanide in boiling dimethylformamide to give 2-amino-3,4,5,6-tetrafluorobenzonitrile (XXI). Heating the aminonitrile (XXI) with $36N H_2SO_4$ gave the amino-amide (XXII), but an attempt to hydrolyse this amide with boiling 50% sulphuric acid gave 2,3,4,5-tetrafluoroaniline. Presumably, 3,4,5,6tetrafluoroanthranilic acid (XXIII) is formed but undergoes decarboxylation under these conditions. The occurrence of decarboxylation of fluorinated aromatic amino acids under alkaline conditions has been observed before^{9,10} but this appears to be the first report of decarboxylation of a fluorinated aromatic aminoacid in an aqueous acidic medium. The acid (XXIII) is, however, stable to boiling aqueous alkali since we found that it is formed in 92% yield by heating the amide (XXII) with boiling 10% sodium hydroxide solution. The acid had virtually the same m.p. and IR spectrum as the sample prepared by Tatlow et al.¹¹ The acid (XXIII) is more directly prepared (19% yield) by metalation and carbonation of 2,3,4,5-tetrafluoroaniline, a method used by Tamborski¹² for preparing 4-aminotetrafluorobenzoic acid from 2.3.5.6-tetrafluoroaniline.

Attempts to prepare 2-bromo-3.4,5.6-tetrafluorobenzonitrile (XXIV) either by (a) treating 2,3,4,5-tetrafluorobenzonitrile (XIII) with bromine in oleum at 10° , or (b) heating the nitrile (XIII) with bromine in the presence of aluminium bromide, were unsuccessful. However, by diazotization of the aminonitrile (XXI) in anhydrous hydrofluoric acid and addition of cuprous bromide, the bromonitrile (XXIV) was obtained in 55° yield. Partial acidic hydrolysis of the bromonitrile gave 2-bromo-3,4,5,6-tetrafluorobenzamide (XXV) but the further acidic hydrolysis of the amide to give 2-bromo-3,4,5,6-tetrafluorobenzoic acid (XXVI) was only achieved by prolonged (32 hr) contact with hot 50° sulphuric acid. The acid was identical with a sample prepared by carbonation of 2-bromotetrafluorobenylmagnesium bromide. An Ullmann reaction with the bromonitrile (XXIV) gave 2,2'-dicyano-octafluorobiphenyl (XXVII).

The reaction of 2-bromotetrafluoronitrobenzene (XIX) with cuprous cyanide in boiling dimethylformamide gave a complex mixture which appeared to contain tetrafluoro-2-nitrobenzonitrile (XXVIII) but this compound could not be isolated in pure form. However, it was prepared by oxidation of the aminonitrile (XXI) with peroxytrifluoroacetic acid. Partial acidic hydrolysis of the nitronitrile (XXVIII) gave the nitro amide (XXIX) and prolonged (16 hr) acid hydrolysis gave the nitro acid (XXX).

These reactions are shown in Fig. 4.

Miscellaneous 2,2'-disubstituted octafluorobiphenyls. 2,2'-Diamino-octatluorobiphenyl (XXXI) was prepared by hydrogenation of the dinitrobiphenyl XX. Octafluoro-2,2'-diphenamide (XXXII) was prepared by partial acidic hydrolysis of the dinitrile (XXVII) and octafluoro-2,2'-diphenic acid (XXXIII) was obtained by metalation and carbonation of octafluoro-2,2'-dihydrobiphenyl (XV), a method previously used by Tamborski to prepare the 4,4'-isomer.¹³ Octafluoro-2,2'-dimethylbiphenyl (XXXIV)

⁹ B.P. 915,587 1963.

¹⁰ J. Burdon, W. B. Hollyhead, and J. C. Tatlow, J. Chem. Soc. 6336 (1965).

¹¹ B. Gething, C. R. Patrick, and J. C. Tatlow, J. Chem. Soc. 1574 (1961).

¹² C. Tamborski and E. J. Soloski, J. Org. Chem. 31, 746 (1966).

¹³ R. J. Harper, E. J. Soloski, and C. Tamborski, J. Org. Chem. 29, 2385 (1964).



then Cu_2Br_2 ; 6, 50 % H_2SO_4 ; 7, Mg/CO_2 ; 8, Cu; 9, CF_3CO_3H

FIG. 4.

was prepared by means of an Ullmann reaction with 2-bromo-3,4,5,6-tetrafluorotoluene (XXXV) which was obtained by treating 2-bromotetrafluorophenylmagnesium bromide with dimethyl sulphate in tetrahydrofuran.

Some of these compounds are being examined for molluscicidal activity at The Tropical Pesticides Research Headquarters and Information Unit. The results of these tests will be published elsewhere.

EXPERIMENTAL

2,3,4,5-Tetrafluoronitrobenzene (II)

To 1,2,3,4-tetrafluorobenzene (300 g) kept at 25-30° was added a mixture of 36N H₂SO₄ (500 ml) and 16N HNO₃ (350 ml), with stirring, during 2 hr. After 4 hr longer, water (1 l.) was added. The organic layer was washed with NaOHaq, with water, and distilled to give 2,3,4,5-tetrafluoronitrobenzene (309 g), b.p. 80°/24 mm, ht.¹⁴ b.p. 179°; n_{0}^{25} 1.4710. (Found: C, 369; H, 0-7; F, 38-4. Calc. for C₆HF₄NO₂: C, 369; H, 0-5; F, 38-95°, .) v_{max} 1355 and 1560 (NO₂) and 1520 cm⁻¹ (fluorinated aromatic nucleus).

2,3,4,5-Tetrafluoroaniline (111)

11N HCl (800 ml) was added in 4 hr to a stirred mixture of 2,3,4,5-tetrafluoronitrobenzene (390 g) and granulated tin (447 g) at 100°. The mixture was made alkaline (NaOH) and steam distilled to give 2,3,4,5-tetrafluoroaniline (276 g), b.p. 65–66°/13 mm, m.p. 27°, lit.¹⁴ m.p. 27-28°. (Found: C, 43·1; H, 19. Calc. for $C_6H_3F_4N$: C, 43·6; H, 1·8°,) v_{max} 3370, 3450 (NH₂); 1495, 1525 cm⁻¹ (fluorinated aromatic nucleus).

¹⁴ P. L. Coe, A. E. Jukes, and J. C. Tatlow, J. Chem. Soc. (C), 2323 (1966).

Treatment of the amine with Ac₂O in the presence of H_2SO_4 gave (90°, yield) 2,3,4,5-tetrafluoroacetanilide (VII), m.p. 106-107.5° from aqueous EtOH. (Found: C, 46.5; H, 2.5; F, 36.2. C_BH₃F₄NO requires: C, 46.4; H, 2.4; F, 36.7°,)

2- Bromo-3,4,5,6-tetrafluoroaniline (V)

Bromine (78:6 g) was added to a stirred mixture of 2,3,4,5-tetrafluoroaniline (80:0 g) and AcOH (250 ml), causing an exothermic reaction. The mixture was boiled for 2 hr, then poured into water (11). The ppt (1119 g) was recrystallized from benzene to give 2-bromo-3,4,5,6-tetrafluoroacetanilide (IV; 56:0 g), m.p. 160 161 5 (Found: C, 34:2; H, 15; Br, 28:2; F, 26:6. $C_8H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 14; Br, 27:9; F, 26:6. $C_9H_4BrF_4NO$ requires: C, 33:6; H, 30:0 P, 20:0 P, 20:0

The anilide (56.0 g) was hydrolysed by boiling with 50°_{\circ} H₂SO₄ (200 ml) for 1 hr giving 2-bromo-3,4,5,6- tetrafluoroaniline (32.7 g), b.p. 65° 1 mm, m.p. 50–52°. (Found: C, 29.5; H, 0.9; Br, 32.1; F, 31.2, C₆H₂BrF₄N requires: C, 29.5; H, 0.8; Br, 32.75; F, 31.1.°_o.) v_{max} 3380, 3480 (NH₂); 1495, 1505 cm⁻¹ (fluorinated aromatic nucleus).

2,3,4,5-Tetrafluoro-6-nitroacetanilide (VIII)

16N HNO₃ acid (140 ml) was added to a soln of 2,3,4,5-tetrafluoroacetanilide (50 g) in 36N H₂SO₄ (150 ml) at 10° during 65 min. The mixture was stirred at 10° 15° for 2 hr longer, then added to ice to give the *nitroanilide* (48 g), m p° 150° 151°5° from aqueous EtOH. (Found: C, 37'8; H, 20; F, 29'6; C₈H₄F₄N₂O₃ requires: C, 38'1; H, 16; F, 30'1°₀.)

2,3,4.5-Tetrafluoro-6-nitroaniline (IX)

The anilide VIII (50 g) was stirred for 1 hr in boiling 50°_{o} H₂SO₂ (200 ml) to give 2-amino-3,4,5,6-tetrafluoronitrobenzene (42 g), m.p. 43-44⁻ (lit.³ 42·5 43·5) after sublimation at 100-120⁻/0.1 mm then crystallization from light petroleum, b.p. 60-80⁻ (Found: C, 33·8; H, 1·3; F, 35·4. Calc. for C₆H₂F₄N₂O₂: C, 34-3; H, 1·0; F, 36·2^{\circ}₀.)

3,4,5,6-Tetrafluorodinitrobenzene (VI)

A soln of 2.3.4,5-tetrafluoro-6-nitroaniline (10.5 g) in CH_2Cl_2 (30 ml) was added in 45 min to a stirred mixture of 85% H_2O_2 (19 ml), trifluoroacetic anhydride (39 g) and CH_2Cl_2 (60 ml). The mixture was boiled for 4 hr. Water (100 ml) was added. The organic layer was washed with water, dried and distilled to give the dinitro compound (9.2 g), b.p. 89°/0-9 mm, m.p. 31-33°. (Found: C, 30-1; F, 31-5. $C_6F_4N_2O_4$ requires: C, 30-0; F, 31-7%) v_{max} 1355, 1570 (NO₂) and 1505, 1530 cm⁻¹ (fluorinated aromatic nucleus).

1,2-Diamino-3,4,5,6-tetrafluorobenzene (X)

A soln of IX (10.5 g) in EtOH (100 ml) was shaken with H₂ in the presence of Raney Ni W4 until uptake of H₂ was complete. The catalyst was filtered off and the solvent evaporated from the filtrate. The residue was sublimed at 100° 0.2 mm to give the diamine (6.7 g), m.p. 131.5 132.5°; lit.³ 131-131.5. (Found: C, 39.9; H, 2.4; F, 41.9. Calc. for $C_6H_4F_4N_2$; C, 40.0; H, 2.2; F, 42.2°c.)

1-Bromo-2.3,4,5-tetrafluorobenzene (X1)

(a) Oleum (266 g, 65% SO₃) was added to a stirred mixture of 1,2,3,4-tetrafluorobenzene (320 g) and Br₂ (336 g) at 0. The mixture was stirred at 15 for 15 hr then poured into ice and worked up in the usual way to give 1-bromo-2,3,4,5-tetrafluorobenzene (208 g), b.p. 140–142°, n_D^{22} 14650. (Found: C, 31.6; H, 0.5; F, 33.6. Calc for C₆HBrF₄: C, 31.4; H, 0.4; F, 33.2°_o) and 1,2-dibromotetrafluorobenzene (134 g), b.p. 93–96–25 mm.

(b) A mixture of 1,2-dibromotetrafluorobenzene (154 g), Zn powder (40 g), and A_cOH (500 ml) was boiled under reflux for 2 hr, then steam distilled to give the mono-bromocompound (89 g), identical with the sample described above.

1-Bromo-2.3.4.5-tetrafluorobenzene (186 g) was heated with copper bronze (57 g) in boiling DMF (800 ml) for 7 hr. Octafluoro-2,2'-dihydrobiphenyl (XV) (88-5 g), m.p. 79–81° (from MeOH) (lit¹⁵, 80-5–81-5°) was isolated by steam distillation of the mixture. (Found: C, 48-4; H, 0-7; F, 51-0. Calc. for $C_{12}H_2F_8$: C, 48-3; H, 0-7; F, 51-0.)

2.3.4.5-Tetrafluorobenzonitrile (XIII)

A mixture of 1-bromo-2.3.4,5-tetrafluorobenzene (91.6 g), cuprous cyanide (39.5 g) and DMF (250 ml) was stirred and boiled for 3 hr then worked up² to give 2,3,4,5-*tetrafluorobenzonitrile* (50.0 g), b.p. 164-165, n_0^{21} 1/4557. (Found: C, 47.8; H, 0.9; F, 43.0. C₇HF₄N requires: C, 48.0; H, 0.6; F, 43.4°_o.) v_{max} 2240 (CN) and 1498, 1522 cm⁻¹ (fluorinated aromatic ring).

Heating the nitrile with 36N H₂SO₄ at 100° for 30 min gave (77°_o yield) 2,3,4,5-*tetrafluorobenzamide* (XIV), m.p. 135:5-137:5° (Found : C, 43:1; H, 1:7; F, 39:5. C₇H₃F₄NO requires: C, 43:5; H, 1:6; F, 39:4°_o.)

Treatment of the amide (0.6 g) with nitrous acid gave 2,3,4,5-tetrafluorobenzoic acid (0.3 g), identical with the sample obtained by oxidizing 2,3,4,5-tetrafluorobenzaldehyde.

2,3,4,5-Tetrafluorobenzaldehyde (XVI)

To the Grignard reagent, prepared from 2.3,4,5-tetrafluorobromobenzene (45.8 g) and Mg (5.2 g) in ether (100 ml) at 0°, was added N-methylformanilide (30.0 g). The mixture was boiled for 1 hr then hydrolysed at 0° with 10°_o H₂SO₄ and steam distilled to give 2.3,4,5-tetrafluorobenzaldehyde (28.9 g), b p. 80–82° (62 mm, n_D^{22} 1.4613. (Found: C, 47.0; H, 1.3; F, 42.0; C-H₂F₄O requires: C, 47.2; H, 1.1; F, 42.7°_o) v_{max} 1700 (carbonyl) and 1485, 1520 cm⁻¹ (fluorinated aromatic nucleus).

The aldehyde gave an oxime, m.p. 79:5-80:5". (Found: C, 43:3; H, 1:7; F, 39:4. $C_7H_3F_4NO$ requires: C, 43:5; H, 1:6; F, 39:4 °₀) and a semicarbazone, m.p. 251 252" (Found: C, 40:8; H, 2:2; F, 32:4. $C_9H_3F_4N_3O$ requires: C, 40:9; H, 2:1; F, 32:3 °₀.)

2,3,4,5-Tetrafluorocinnamic acid (XVII)

A mixture of 2,3,4,5-tetrafluorobenzaldehyde (1.0 g), malonic acid (1.3 g), pyridine (2.5 ml), and piperidine (0.1 ml) was kept at 110 for 30 min, then poured into 2N HCl (25 ml). The ppt was recrystallized from water giving 2,3,4,5-tetrafluorocinnamic acid (0.7 g), m.p. 153 154°. (Found: C, 49.3; H, 1.8; F, 34.3, $C_9H_3F_4O_2$ requires: C, 49.3; H, 1.4; F, 34.8°.)

2.3,4,5-Tetrafluorobenzoic acid (XVIII)

A mixture of 2.3,4,5-tetrafluorobenzaldehyde (1-0 g), sodium dichromate (0-8 g), 36N H₂SO₄ (1 ml), and water (2 ml) was kept at 100° for 10 min. 2,3,4,5-Tetrafluorobenzoic acid (0-64 g) crystallized when the mixture was cooled, m.p. 85:5-87° (from light petroleum, b.p. 60-80°), lit.¹³ 92:92:5° (Found: C, 43:2; H, 0-7; F, 39:2. Calc. for $C_7H_2F_4O_2$: C, 43:3; H, 1-0; F, 39:2°₀).

2-Bromo-3,4,5,6-tetrafluoronitrobenzene (XIX)

(a) 1-Bromo-2.3,4,5-tetrafluorobenzene (184 g) was added during 90 min to a stirred mixture of 36N H_2SO_4 (350 ml) and 16N HNO₃ (250 ml) at 0.10. The mixture was stirred at 15° for 5 hr longer, then poured into ice and worked up to give 2-bromo-3,4,5,6-tetrafluoronitrobenzene (130 g), b.p. 94°/20 mm, (ht.¹⁴ 200°), n_D^{28} 14970. (Found: C, 26°1; Br, 29°6; F, 27°5. Calc. for C₆BrF₄NO₂: C, 26°3; Br, 29°2; F, 27°7°₀) v_{max} 1375. 1560 (NO₂) and 1485, 1515 cm⁻¹ (fluorinated aromatic nucleus).

(b) Oleum (76 ml, 65°_{\circ} , SO₃) was added to a mixture of 2,3,4,5-tetrafluoronitrobenzene (180 g) and Br₂ (76.5 g). The mixture was boiled for 5 hr then worked up to give the bromonitro compound (115 g), identical with the sample described above.

Heating the bromonitro compound (27.4 g) with copper bronze (7.5 g) in boiling dimethylformamide (100 ml) for 1 hr gave octafluoro-2,2'-dinitrobiphenyl (XX; 11.0 g), m.p. 120-122° (from light petroleum, b.p. 60-80. (Found: C, 37.0; F, 39.0. $C_{12}F_8N_2O_4$ requires: C, 37.1; F, 39.2°,) v_{max} (CCl₄) 1350, 1545 (NO₂) and 1480, 1545 cm⁻¹ (fluorinated aromatic nucleus).

2-Amino-3,4,5,6-tetrafluorobenzonitrile (XXI)

2-Bromotetrafluoroaniline (610 g) was stirred with cuprous cyanide (247 g) in boiling DMF (11) for 2 hr, then a soln of FeCl₃ (1 kg) in 3N HCl (2250 ml) was added. The product, isolated by steam distillation, was recrystallized from benzene to give the *aminonitrile* (273 g), b.p. 115^o/14 mm, m.p. 89-90^o. (Found: C, 44·3; H, 0·9; F, 39·6. C₇H₂F₄N₂ requires: C, 44·2; H, 1·1; F, 40·0%) v_{max} (KBr disc) 1510 (fluorinated aromatic ring), 3300, 3410 (NH₂) and 2260 cm⁻¹ (CN).

Heating the aminonitrile (4.75 g) with 36N H₂SO₄ (10 ml) at 100° for 1 hr gave 2-amino-3,4,5,6-tetrafluorobenzamide (XXII; 4.3 g), m.p. 140–141° from water. (Found: C, 39.8; H, 2.0; F, 37.0. $C_7H_4F_4N_2O$ requires: C, 40.4; H, 1.9; F, 36.5°,) Treatment of the aminoamide (31.2 g) with boiling 50°_{\circ} H₂SO₄ (75 ml) for 2 hr gave 2,3,4,5-tetra-fluoroaniline (29.0 g), with the expected IR spectrum.

3,4,5,6-Tetrafluoroanthranilic acid (XXIII)

(a) Treatment of 2-amino-3,4,5,6-tetrafluorobenzamide (10-8 g) with boiling 10°_{\circ} NaOH aq (5 ml) for 2 hr gave 3,4,5,6-tetrafluoroanthranilic acid (10-0 g), m.p. 143-144^{\circ} from water (lit.,¹¹ 141-142^{\circ}), with the expected IR spectrum. (Found: C, 40-1; H, 1-2; F, 36-2. Calc. for C₂H₃F₄NO₂: C, 40-2; H, 1-4; F, 36-3^{\circ}_{\circ})

(b) A soln of BuLi in hexane (150 ml, 0.3 mole) was added to a soln of 2,3,4,5-tetrafluoroaniline (16.5 g) in THF (150 ml) at -70° in 90 min. After 2 hr longer at this temp, CO₂ was bubbled into the mixture while it warmed to room temp. The usual work-up gave XXIII (4 g), m.p. and mixed m.p. 143-144°.

2-Bromo-3,4,5,6-tetrafluorobenzonitrile (XXIV)

Sodium nitrite (7.5 g) was added in portions during 30 min to a soln of 2-aminotetrafluorobenzonitrile (19.0 g) in anhyd HF (50 ml) at 0.5°. A soln of cuprous bromide (14.5 g) in 47°_{0} HBr (50 ml) was added and the mixture allowed to warm to room temp. Borax (75 g) was added. Extraction of the mixture with CH₂Cl₂ and distillation of the extract gave the 2-bromonitrile (14.0 g), b.p. 84.85°/10 mm. (Found: C, 33.0; Br, 31.0; C₇BrF₄N requires: C, 33.1; Br, 31.5°₀.) v_{max} 1480, 1510 (fluorinated aromatic nucleus) and 2255 cm⁻¹ (CN).

Heating the bromonitrile (5:1 g) with 36N H_2SO_4 (10 ml) at 100° for 1 hr gave 2-bromo-3,4,5,6-*tetra-fluorobenzamide* (XXV; 4:3 g), m.p. 118–119° from water. (Found: C, 31:3; H, 0:8; Br, 29:5. C- H_2BrF_4NO requires C, 30:9; H, 0:7; Br, 29:4%.)

2-Bromo-3,4,5,6-tetrafluorobenzoic acid (XXVI)

(a) The bromoamide (XXV; 12:0 g) was heated in 18N H₂SO₄ (100 ml) at 120-130° for 32 hr to give 2-bromo-3,4,5,6-*tetrafluorobenzoic acid* (7:5 g), m.p. 108–109° from light petroleum, b.p. 60-80°. (Found: C, 30-6; H, 0-3; F, 27:9; Equiv. 277. C₂HBrF₄O₂ requires: C, 30-7; H, 0-4; F, 27:8%; Equiv. 273.) v_{max} (KBr disc) 1705 (carbonyl), 1465, 1505 (fluorinated aromatic nucleus) and 2800, 3100 cm⁻¹ (OH in carboxyl).

(b) The Grignard reagent, prepared at 0° from 1.2-dibromotetrafluorobenzene (15.4 g) and Mg (1.2 g) in THF (100 ml), was carbonated while the mixture warmed to room temp. Acidification and ether extraction of the mixture gave a solid which, after 4 recrystallizations from light petroleum, b.p. 60-80°, gave (XXVI; 5.5 g), m.p. and mixed m.p. 108-109°.

2.2'-Dicyano-octafluorobiphenyl (XXVII)

2-Bromotetrafluorobenzonitrile (7.6 g) was heated with copper bronze (2.1 g) in boiling DMF (20 ml) for 1 hr to give 2,2'-dicyano-octafluorobiphenyl (4.0 g), m.p. 142-143° from aqueous EtOH. (Found: C, 48.3; F, 43.3. $C_{14}F_{0}N_{2}$ requires: C, 48.3; F, 43.7°,) v_{max} (KBr disc) 1465, 1510 (fluorinated aromatic nucleus) and 2240 cm⁻¹ (CN).

2,3,4,5-Tetrafluoro-6-nitrobenzonitrile (XXVIII)

A soln of 2-aminotetrafluorobenzonitrile (40 g) in CH₂Cl₂ (125 ml) was added during 80 min to a mixture of trifluoroacetic anhydride (155 g), 85°_{\circ} , H_2O_2 (102 g) and CH₂Cl₂ (250 ml) at 0°, then the mixture was boiled for 5 hr. Water (500 mi) was added, the organic layer washed with water, dried and distilled to give 2,3,4,5-*tetrafluoro-6-nitrobenzonitrile* (24-9 g), b.p. 75 76°/0-7 mm. (Found: C, 38-0; F, 34-35°), ν_{max} 1490, 1515 (fluorinated aromatic nucleus), 1345, 1560 (NO₂) and 2240 cm⁻³ (CN).

Treatment of the nitronitrile (2·2 g) with 36N H_2SO_4 at 100° for 1 hr gave 2,3,4,5-tetrafluoro-6-nitrobenzamide (XXIX) (1·6 g), m.p. 124–125° from chloroform. (Found: C, 35·1; H, 0·9; F, 32·0. $C_7H_2F_4N_2O_3$ requires: C, 35·3; H, 0·8; F, 31·9°.)

2,3,4,5-Tetrafluoro-6-nitrobenzoic acid (XXX)

Hydrolysis of 2,3,4,5-tetrafluoro-6-nitrobenzamide (23.8 g) with $18N-H_2SO_4$ acid (80 ml) at 130 140° for 16 hr gave 2,3,4,5-tetrafluoro-6-nitrobenzoic acid (17.5 g), m.p. 137 138° after sublimation at 130° /0.2 mm. (Found : C, 35.2; H, 0.8; F, 31.1; Equiv. 230. C₂HF₄NO₄ requires: C, 35.2; H, 0.4; F, 31.8°°; Equiv. 239.) v_{max} (KBr disc) 1485, 1515 (fluorinated aromatic nucleus), 1740 (carbonyl), 2800, 3200 (OH in carboxyl), and 1360, 1560 cm⁻¹ (NO₂).

2-Bromo-3,4,5,6-tetrafluorotoluene (XXXV)

A soln of 1,2-dibromotetrafluorobenzene (92 g) in dry THF (250 ml) was added to Mg turnings (7.6 g) in THF (250 ml) at 0-5° during 45 min. After 1 hr longer at this temp, Me_2SO_4 (760 g) was added and the mixture allowed to warm to 15°. The solvent was removed, the residue washed with water and distilled to give the *bromotoluene* (120 g), b.p. 76-78°/28 mm. (Found : C, 34.2; H, 14; Br, 32.4. $C_7H_3BrF_4$ requires : C, 34.6; H, 1/2; Br, 32.9°₀.) v_{max} 1480, 1500 (fluorinated aromatic nucleus) and 2940 cm⁻¹ (C—H stretching).

Heating the bromotoluene (5.4 g) with copper bronze (1.6 g) in DMF (25 ml) at 150–160° for 2 hr gave octafluoro-2,2'-dimethylbiphenyl (XXXIV; 2.2 g), m.p. 110–111°. (Found : C, 51.4; H, 20. $C_{14}H_6F_8$ requires : C, 51.6; H, 1.9%)

Octafluoro-2,2'-diphenic acid (XXXIII)

BuLi (46 ml) of a soln in hexane, 0-1 mole) was added during 45 min to a soln of octafluoro-2,2'dihydrobiphenyl (149 g) in THF (75 ml) at -70° . After 30 min, CO₂ was passed into the soln while it warmed to room temp. Acidification and ether extraction of the mixture gave a solid which was continuously extracted (Soxhlet) with light petroleum (b.p. 60-80') to give octafluoro-2,2'-diphenic acid (13·0 g), m.p. 230-231°. (Found: C, 43·4; H, 0·6; F, 39·2; Equiv. 198. C₁₄H₂F₈O₄ requires: C, 43·3; H, 0·5; F, 39·7, Equiv. 193.) v_{max} (KBr disc) 1750 (carbonyl), 1480, 1505 (fluorinated aromatic nucleus) and 2800, 3200 cm⁻¹ (OH in carboxyl).

Octafluoro-2,2'-diphenamide (XXXII)

Heating 2,2'-dicyano-octafluorobiphenyl (2.5 g) with 36N H₂SO₄ (10 ml) at 90° for 1 hr gave the diamide (1.4 g), m.p. 240-241° from aqueous EtOH. (Found: C, 43.8; H, 1.2; F, 39.7. $C_{14}H_4F_8N_2O_2$ requires: C, 43.5; H, 1.0; F, 39.9°,)

2,2'-Diamino-octafluorobiphenyl (XXXI).

Octafluoro-2,2'-dinitrobiphenyl (12·1 g) in EtOH (200 ml) containing Raney Ni was hydrogenated with H₂ at room temp and press. The product was sublimed at 14030-5 mm and recrystallized from light petroleum (b.p. 60-80°) to give the *diamine* (50 g), m.p. 108 110°. (Found: C, 44·1; H, 1·1; F, 46·2. C₁₂H₄F₈N₂ requires: C, 43·9; H, 1·2; F, 46·3%) v_{max} (CCl₄) 1490 (fluorinated aromatic nucleus) and 3380, 3540 cm⁻¹ (NH₂).

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