

572. Aromatic Polyfluoro-compounds. Part XVIII.¹ Some Replacement Reactions of Perfluoro-*o*- and -*p*-xylene.

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Perfluoro-*p*-xylene has been treated with a range of nucleophilic reagents. The reactions were vigorous, and in many cases multiple substitution products were obtained in addition to the primary one. Orientation studies on four disubstituted perfluoro-*p*-xylenes show replacement of the fluorine atom *para* to the first substituent. Perfluoro-*o*-xylene has been treated with sodium hydrogen sulphide, hydrazine, and ammonia, and the major product shown to arise by replacement of the 4-fluorine atom in each case.

THIS Paper describes the reactions of perfluoroxylenes^{2,3} with nucleophilic reagents of the type studied with other aromatic polyfluoro-compounds.⁴⁻⁶ A feature of all the substitutions was the noticeable increase in the vigour of the reaction, as compared with those of most of the earlier studies; this is consistent with the expected activation to nucleophilic attack by two trifluoromethyl groups. There was an enhanced tendency to produce higher degrees of substitution.

Reaction of perfluoro-*p*-xylene with 1.8 mol. of methyl-lithium gave mainly 2,4,5-trifluoro-3,6-bistrifluoromethyltoluene and a difluorobistrifluoromethylxylene of uncertain structure. The former was hydrolysed with concentrated sulphuric acid to the terephthalic acid.

Treatment of perfluoro-*p*-xylene with 1.05 mol. of phenyl-lithium gave no monosubstitution product, only the terphenyl and unchanged perfluoro-*p*-xylene. The terphenyl was not oriented, but its high melting point and low solubility are consistent with a *para*-system, *i.e.*, 2'5'-difluoro-3',6'-bistrifluoromethyl-*p*-terphenyl.

With sodium methoxide in methanol, 2,4,5-trifluoro-3,6-bistrifluoromethylanisole was formed, together with 2,5-difluoro-1,4-dimethoxy-3,6-bistrifluoromethylbenzene. The latter structure was deduced from its ¹⁹F nuclear magnetic resonance (n.m.r.) spectrum, which displayed two groups of resonances, centred at 20.1 and 55.6, corresponding to trifluoromethyl and aromatic-ring fluorine, respectively. This spectrum was fully interpreted as an eight-spin system consisting of two non-equivalent sets of fluorine atoms.⁷

Ammoniation of perfluoro-*p*-xylene in the usual way gave largely 2,4,5-trifluoro-3,6-bistrifluoromethylaniline, together with a small amount of supposed diamine which could not be purified. The monoamine was characterised as the acetanilide, and was recovered unchanged after treatment with hydrogen chloride in ether. The latter observation is consistent with its high fluorine content. Attempts to prepare 2,4,5-trifluoro-3,6-bis(trifluoromethyl)phenylhydrazine from perfluoro-*p*-xylene, using the standard procedure⁸ of refluxing with hydrazine in aqueous ethanol, failed; a liquid product was formed with spectroscopic properties indicative of a mixture of amines. This effect is thought to result partly from the higher reactivity of perfluoro-*p*-xylene to hydrazine, producing disubstitution products, and partly from a lower thermal stability of the derived hydrazines (pentafluorophenylhydrazine begins to decompose to pentafluoroaniline at 180°⁹). However, with hydrazine hydrate in dimethylformamide at 0° a vigorous reaction occurred, to give the crystalline phenylhydrazine.

¹ Burdon, Coe, Fulton, and Tatlow, *J.*, 1964, 2673.

² Gething, Patrick, and Tatlow, *J.*, 1961, 1574.

³ Patrick, Pedler, Seabra, Stephens, and Tatlow, *Chem. and Ind.*, 1963, 1557.

⁴ Brooke, Burdon, and Tatlow, *J.*, 1961, 802.

⁵ Alsop, Burdon, and Tatlow, *J.*, 1962, 1801.

⁶ Tatlow, *Endeavour*, 1963, 22, 89.

⁷ Ayanbadejo and Thomas, unpublished work.

⁸ Brooke, Burdon, Stacey, and Tatlow, *J.*, 1960, 1768.

⁹ Birchall, Haszeldine, and Parkinson, *J.*, 1962, 4966.

The high reactivity of perfluoro-*p*-xylene was further demonstrated with potassium phenyl sulphide which gave only the tetrakisphenylthiobenzene, readily characterised by desulphurisation to 1,4-bistrifluoromethylbenzene.

Treatment of perfluoro-*p*-xylene with sodium hydrogen sulphide in dimethylformamide at 0° gave not only the expected thiophenol but also a dithiol. It is known that pentafluorothiophenol is resistant to attack by sodium hydrogen sulphide.¹⁰ The dithiol obtained here, and from the thiol and sodium hydrogen sulphide, must reflect not only the activating effect of the trifluoromethyl groups but also the compensating influence on the deactivating effect of the thiol group. Both thiols were characterised in the usual way. The thiophenol gave a hydrated potassium salt, and there was no evidence for hydrolysis of the trifluoromethyl group *ortho* to the thiol group under the strongly alkaline conditions;¹¹ an observation in agreement with the failure of the thiol group to deactivate the system to further nucleophilic substitution. As with potassium phenyl sulphide,¹² strong heating liberated fluoride ion and gave an intractable solid with an infrared (i.r.) spectrum indicative of a fluorinated polysulphide system.¹² Diazomethane in ether gave methyl 2,4,5-trifluoro-3,6-bistrifluoromethylphenyl sulphide, which was oxidised by hydrogen peroxide to the sulphone. The latter gave a trimethoxy-derivative with sodium in methanol, providing another example of the activating influence of the trifluoromethyl group in replacement reactions. The disulphide was prepared using 1 mol. of bromine in acetic acid, and the sulphonyl chloride using an excess of chlorine in acetic acid containing hydrogen peroxide.¹⁰ Desulphuration with Raney nickel was normal¹² (cf. $\text{CF}_3\cdot\text{C}_6\text{F}_4\cdot\text{SH}^5$) and gave 1,2,4-trifluoro-3,6-bistrifluoromethylbenzene. The thiol was oxidised to the disulphide by concentrated sulphuric acid at 170°, thus confirming the earlier observation that the SH group does not facilitate hydrolysis of the *ortho*-trifluoromethyl group.¹¹

The dithiol was shown to be 2,5-difluoro-3,6-bistrifluoromethylbenzene-1,4-dithiol from its ¹⁹F n.m.r. spectrum, which displayed absorptions centred at 20·7 and 29·6, arising from the trifluoromethyl groups and ring fluorines, respectively. The CF₃ portion of the spectrum was roughly a doublet ($J = 29\cdot5$ c./sec.). The ring-fluorine signal was not well resolved but a structural correlation of the chemical shifts, established with related compounds,⁷ was unambiguous. Confirmation of the structure was sought using the sequence: Raney nickel desulphuration, hydrolysis with concentrated sulphuric acid to 2,5-difluoro-terephthalic acid, and decarboxylation with soda-lime to *p*-difluorobenzene. However, the last stage gave no volatile products. Presumably processes may occur of the type observed with *ortho*-halogeno-benzoates,^{13,14} in which decarboxylation is accompanied by loss of fluoride ion to give benzyne intermediates which react with unchanged halogeno-benzoate to give comparatively involatile xanthenes. Tetrafluoro-phthalic and -terephthalic acid² are readily decarboxylated, under identical conditions, to 1,2,3,4- and 1,2,4,5-tetrafluorobenzene; likewise 2,3,5,6-tetrafluorobenzoic acid gives 1,2,4,5-tetrafluorobenzene.⁵ Assuming an ionic process to operate, this difference in behaviour might well result from the relative stabilities of the intermediate carbanions; a higher fluorine content inhibiting the loss of fluoride ion to give a benzyne system (cf. stabilities of pentafluorophenyl-lithium¹⁵ and *o*-fluorophenyl-lithium¹⁶ in ether). Consistent with this, 3,4,6-trifluorophthalic acid (see later) and soda-lime gave 1,2,4-trifluorobenzene in very small yield.

Methyl 2,5-difluoro-3,6-bistrifluoromethylphenyl sulphide readily reacted with sodium hydrogen sulphide, the fluorine atom *para* to the methylthio-group being replaced to give a mercapto-sulphide which was desulphurised to 1,4-difluoro-2,5-bistrifluoromethylbenzene.

¹⁰ Robson, Smith, Stephens, and Tatlow, *J.*, 1963, 3692.

¹¹ Filler and Novar, *Chem. and Ind.*, 1960, 1273.

¹² Robson, Stacey, Stephens, and Tatlow, *J.*, 1960, 4754.

¹³ Kochi, *J. Org. Chem.*, 1961, **26**, 932.

¹⁴ McNelis, *J. Org. Chem.*, 1963, **28**, 3188.

¹⁵ Coe, Stephens, and Tatlow, *J.*, 1962, 3227.

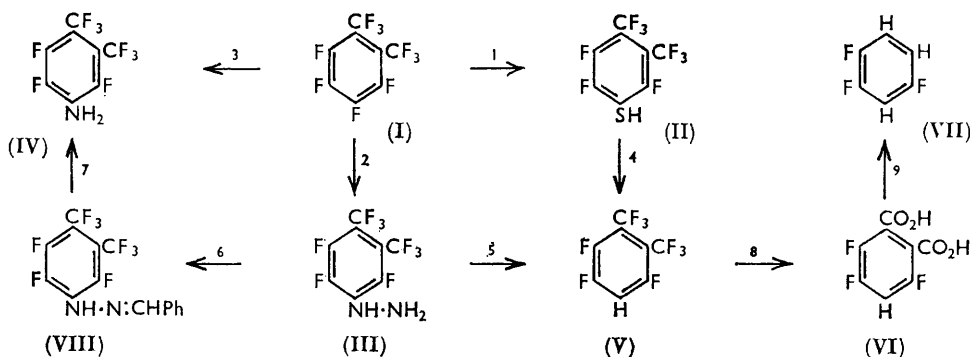
¹⁶ Wittig and Ludwig, *Angew. Chem.*, 1956, **68**, 40.

[1964]

2977

The latter compound was also the only product isolated from the reaction of perfluoro-*p*-xylene with lithium aluminium hydride in ether; this reaction was very vigorous, and the monosubstitution product was not detected.

An extension of the arguments of earlier Papers,^{4,5} which considered the orienting influence of fluorine⁴ and trifluoromethyl⁵ in C_6F_5X and $CF_3 \cdot C_6F_4 \cdot X$, indicate that the fluorine *para* to the substituent (X) in $p-(CF_3)_2 \cdot C_6F_3 \cdot X$ should be the most susceptible to nucleophilic substitution, in agreement with the experimental results. Thus, perfluoro-*o*-xylene (I) reacted with sodium hydrogen sulphide, hydrazine, and ammonia to give monosubstitution products, (II), (III), and (IV), respectively. This was established chemically by desulphuration of the thiol (II), hydrolysis with concentrated sulphuric acid, and decarboxylation of the resulting trifluorophthalic acid (VI) to give 1,2,4-trifluorobenzene (VII) in very small yield (cf. 2,5-difluoroterephthalic acid above). The orientation of the hydrazine (III) was established by its conversion into the trifluorobistrifluoromethylbenzene (V). In turn this established the orientation of the amine (IV), since reductive cleavage of the benzaldehyde



Reagents: 1, NaSH. 2, $NH_2 \cdot NH_2$. 3, NH_3 . 4, Ni. 5, Fehling's solution. 6, $Ph \cdot CHO$. 7, $Zn \cdot AcOH$. 8, H_2SO_4 . 9, soda-lime.

hydrazine (VIII) gave an amine identical with that obtained by ammoniation of perfluoro-*o*-xylene. The orientation effect so established was supported by the proton n.m.r. spectra of suitable derivatives of the thiol (II) and the amine (IV). Thus, the hydrogen-fluorine coupling effects observed in the spectra of the methyl sulphide, the sulphone, and the *NN*-dimethylamine clearly indicated the presence of two *ortho*-fluorine atoms.¹⁷

As with perfluoro-*p*-xylene, the *ortho*-isomer and sodium hydrogen sulphide gave the thiol (II) accompanied by a small amount of a dithiol of unknown orientation. Again, the deactivating influence¹⁰ of the thiol group is presumably compensated by the activating trifluoromethyl groups. 2,3,6-Trifluoro-4,5-bis(trifluoromethyl)thiophenol (II) also gave the usual series of derivatives. Thus, diazomethane in ether gave the methyl sulphide which was oxidised to the sulphone. Mild oxidation of the thiol with bromine gave the disulphide.

As with the previously described isomeric hydrazine, 2,3,6-trifluoro-4,5-bis(trifluoromethyl)phenylhydrazine (III) could not be prepared in the usual way. Hydrazine in refluxing aqueous ethanol gave a liquid with spectroscopic properties consistent with the presence of fluoroaromatic amines. Again, this would be compatible with a low thermal stability for the phenylhydrazine.

The replacement of the 4-fluorine atom observed in the above reactions of perfluoro-*o*-xylene is consistent with the orienting influences of fluorine and trifluoromethyl discussed earlier.

¹⁷ Burdon, unpublished work.

EXPERIMENTAL

Gas Chromatography.—Two preparative columns were used, both 488 cm. long \times 75 mm. diam., one packed with silicone gum-kieselguhr (1 : 2) (column A) and the other with dinonyl phthalate-kieselguhr (1 : 2) (column B).

Nuclear Magnetic Resonance Measurements.—The ^{19}F spectra were measured with a Mullard SL 44 mark I instrument at 30.107 Mc./sec. The figures quoted are fluorine chemical shifts and are in p.p.m. from trifluoroacetic acid as external reference. The proton spectra were measured with a Varian instrument at 60 Mc./sec., and the figures quoted are chemical shifts in p.p.m. from tetramethylsilane as external reference.

*Reaction of Perfluoro-*p*-xylene with Methyl-lithium.*—Methyl-lithium (8.0 g.) in ether (160 c.c.) was slowly added to a stirred solution of perfluoro-*p*-xylene 2 (57.0 g.) in dry ether (100 c.c.) during 2 hr. Stirring was maintained for a further 2 hr. and water (150 c.c.) was added. The ether layer was removed, combined with ether extracts (3×25 c.c.) of the aqueous phase, dried (MgSO_4), and evaporated. The dark brown liquid (39.0 g.) was distilled, to give a fraction (34.0 g.), b. p. 122–160°, which was separated by gas chromatography (column A, 160°, N_2 44 l./hr.), to give: (i) perfluoro-*p*-xylene (6.2 g.) with a correct i.r. spectrum; (ii) 2,4,5-trifluoro-3,6-bistrifluoromethyltoluene (21.1 g.), b. p. 130–132° (Found: C, 38.2; H, 1.0. $\text{C}_9\text{H}_3\text{F}_9$ requires C, 38.3; H, 1.1%), ν_{max} 2925–3000 (CH_3), 1620, 1565, and 1475 (fluorinated benzene ring), and 1380–1120 cm^{-1} ($\geq\text{CF}$); (iii) suspected 2,5-difluoro-3,6-bistrifluoromethyl-*p*-xylene (2.2 g.), b. p. 158–160° (Found: C, 43.2; H, 2.1. $\text{C}_{10}\text{H}_6\text{F}_8$ requires C, 43.2; H, 2.1%), ν_{max} 2950 (CH_3), 1630 and 1575 (aromatic ring), and 1380–1030 cm^{-1} ($\geq\text{CF}$), λ_{max} (in EtOH) 2830 Å (ϵ 3.62 \times 10³).

The bistrifluoromethyltoluene (7.0 g.) and concentrated sulphuric acid (6 c.c.) were heated at 170° for 16 hr. in a sealed tube, to afford a crude acid (4.5 g.), m. p. 223–225°, which was recrystallised from *p*-xylene and sublimed, to give 2,3,5-trifluoro-6-methylterephthalic acid (4.1 g.), m. p. 226° (Found: C, 46.0; H, 2.0. $\text{C}_9\text{H}_5\text{F}_3\text{O}_4$ requires C, 46.1; H, 2.1%). A portion of this acid (0.2 g.) was converted into the *di*-(*S*-benzylthiuronium) salt (0.3 g.), m. p. 222–223° (Found: C, 53.2; H, 4.4. $\text{C}_{25}\text{H}_{25}\text{F}_3\text{N}_4\text{O}_4\text{S}_2$ requires C, 53.0; H, 4.4%).

*Reaction of Perfluoro-*p*-xylene with Phenyl-lithium.*—Phenyl-lithium (8.0 g.) in ether (160 c.c.) was added to a stirred solution of perfluoro-*p*-xylene (29.0 g.) in dry ether (220 c.c.) at such a rate that the ether gently refluxed. The mixture was stirred for 4 hr. at 15°, washed with water (400 c.c.), and the ethereal layer separated. The aqueous phase, together with the precipitate, was continuously extracted with ether for 16 hr. The combined ether solutions were dried (MgSO_4), filtered, and evaporated, to leave a liquid (9.4 g.) and a solid (14.0 g.). The former was distilled, to give perfluoro-*p*-xylene (8.3 g.) with a correct i.r. spectrum. The latter gave 2',5'-difluoro-3',6'-bistrifluoromethyl-*p*-terphenyl (12.4 g.), m. p. 234–235° [from light petroleum (b. p. 100–120°)] (Found: C, 59.7; H, 2.3. $\text{C}_{20}\text{H}_{10}\text{F}_8$ requires C, 59.7; H, 2.4%), ν_{max} 1590 and 1490 (aromatic rings), and 700 and 690 cm^{-1} ($\text{C}_6\text{H}_5\text{X}$), λ_{max} (in EtOH) 2920 and 2400 Å (ϵ 1.53 \times 10⁴ and 9.17 \times 10³).

*Reaction of Perfluoro-*p*-xylene with Sodium Methoxide.*—Perfluoro-*p*-xylene (11.0 g.) and a solution from sodium (0.92 g.) in methanol (100 c.c.) were refluxed for 4 hr., poured into water (400 c.c.), and extracted with ether (3×75 c.c.). The dried (MgSO_4) extracts were filtered and evaporated to leave a liquid (9.0 g.) which was separated by gas chromatography (column A, 130°, N_2 70 l./hr.), to give: (i) 2,4,5-trifluoro-3,6-bistrifluoromethylanisole (6.1 g.), b. p. 64–66°/25 mm. (Found: C, 36.5; H, 1.1. $\text{C}_9\text{H}_3\text{F}_9\text{O}$ requires C, 36.3; H, 1.0%), ν_{max} 2950, 1450, and 1375 (CH_3), and 1480 cm^{-1} (aromatic ring), λ_{max} (in ethanol) 2900 Å (ϵ 4.42 \times 10³); (ii) 2,5-difluoro-3,6-bis(trifluoromethyl)dimethoxybenzene (1.9 g.), m. p. 20° (Found: C, 38.7; H, 2.3. $\text{C}_{10}\text{H}_6\text{F}_8\text{O}_2$ requires C, 38.7; H, 2.0%), ν_{max} 2950, 1450, and 1375 (CH_3), and 1480 cm^{-1} (aromatic ring), λ_{max} (in ethanol) 2940 Å (ϵ 5.47 \times 10³). The ^{19}F n.m.r. spectrum was consistent with the suggested structure.⁷

*Reaction of Perfluoro-*p*-xylene with Aqueous Ammonia.*—Perfluoro-*p*-xylene (30.0 g.), aqueous ammonia (d 0.88; 20 c.c.), and ethanol (100 c.c.) were kept at 145–150° for 16 hr. in a rocking autoclave. The mixture was diluted with water and extracted with ether (150 c.c.). The dried (MgSO_4) extract was filtered and evaporated, to leave a liquid (25.0 g.) which was separated by gas chromatography (column A, 160°, N_2 66 l./hr.) to give: (i) 2,4,5-trifluoro-3,6-bistrifluoromethylaniline (16.0 g.), b. p. 44–47°/0.1 mm. (Found: C, 34.2; H, 1.0. $\text{C}_8\text{H}_2\text{F}_9\text{N}$ requires C, 34.0; H, 0.7%), ν_{max} 3500 and 3400 (NH_2), 1600, 1520, and 1490 cm^{-1} (aromatic ring); (ii) an impure diamine (2.4 g.).

Treatment of the monoamine (0.5 g.) with acetic anhydride (1 c.c.) and concentrated sulphuric acid (2 drops) gave 2,4,5-trifluoro-3,6-bistrifluoromethylacetanilide (0.3 g.), m. p. 139—140° (Found: C, 37.0; H, 1.5. $C_{10}H_4F_9NO$ requires C, 36.9; H, 1.2%).

2,4,5-Trifluoro-3,6-bis(trifluoromethyl)phenylhydrazine.—Perfluoro-*p*-xylene (11.0 g.) in dimethylformamide (20 c.c.) was slowly added to hydrazine hydrate (20 g.; 100% w/w) in dimethylformamide (30 c.c.) at 0°. The mixture was stirred for 1 hr. at 15° and the brown solution extracted several times with light petroleum (b. p. 40—60°). The extract was evaporated, to leave a liquid (10.0 g.) which gave the phenylhydrazine (8.0 g.), m. p. 43° [from light petroleum (b. p. 40—60°)] (Found: C, 32.2; H, 1.0. $C_8H_5F_9N_2$ requires C, 32.2; H, 1.1%), ν_{\max} 3300 (NH·NH₂), 1630, 1600, and 1490 cm⁻¹ (aromatic ring). Treatment of this compound (0.20 g.) in aqueous ethanol with benzaldehyde (0.5 g.) gave the benzaldehyde hydrazone (0.23 g.), m. p. 98° (from aqueous ethanol) (Found: C, 46.6; H, 1.8. $C_{15}H_7F_9N_2$ requires C, 46.6; H, 1.8%).

Tetrakisphenylthio-1,4-bistrifluoromethylbenzene.—Perfluoro-*p*-xylene (18.0 g.) in pyridine (45 c.c.) was quickly added to a refluxing solution of potassium phenyl sulphide (32.0 g.) in ethylene glycol (30 c.c.). The mixture was refluxed for 20 min., poured on ice, and acidified with 8N-hydrochloric acid, to give the tetrakis-sulphide (30.0 g.), m. p. 195—196° (from ethanol) (Found: C, 58.9; H, 3.4. $C_{32}H_{26}F_6S_4$ requires C, 59.4; H, 3.1%). The tetrakis-sulphide (24.0 g.) and Raney nickel (grade W4; 120 g.) in methanol (140 c.c.) gave, in the usual way, benzene (2.5 g.) and 1,4-bistrifluoromethylbenzene (1.5 g.); both had correct i.r. spectra.

Reaction of Perfluoro-*p*-xylene with Sodium Hydrogen Sulphide.—Perfluoro-*p*-xylene (40.0 g.) in dimethylformamide (50 c.c.) was slowly added to a stirred suspension of sodium hydrogen sulphide (25 g.) in dimethylformamide (100 c.c.) at 0°, stirred for 20 min., poured into an excess of 16N-hydrochloric acid at 0°, and extracted with ether. The ether extract was dried (MgSO₄), filtered, and evaporated, and the liquid residue distilled, to give: (i) 2,4,5-trifluoro-3,6-bis(trifluoromethyl)thiophenol (13.5 g.), b. p. 68—70°/16 mm. (Found: C, 31.9; H, 0.3. C_8HF_9S requires C, 32.0; H, 0.3%), ν_{\max} 2600 (SH), 1640 and 1490 cm⁻¹ (aromatic ring), λ_{\max} (in ethanol) 2350, 2790, and 3750 Å (ϵ 9.4 × 10³, 5.8 × 10³, and 3.8 × 10³); (ii) 2,5-difluoro-3,6-bistrifluoromethylbenzene-1,4-dithiol (13.2 g.), b. p. 115—116°/16 mm., m. p. 66—68° [from light petroleum (b. p. 40—60°)] (Found: C, 30.4; H, 0.8. $C_8H_2F_8S_2$ requires C, 30.6; H, 0.6%), ν_{\max} 2600 (SH) and 1480—1470 cm⁻¹ (aromatic ring), λ_{\max} 2170, 2360, 2610, and 3330 Å (in *n*-hexane) (ϵ 4.4 × 10⁴, 3.7 × 10⁴, 5.1 × 10⁴, and 1.2 × 10⁴). The ¹⁹F n.m.r. spectrum was consistent with the assigned structure.⁷

Reactions of 2,4,5-Trifluoro-3,6-bis(trifluoromethyl)thiophenol.—(a) An aqueous solution of potassium hydroxide (50% w/v; 15 c.c.) and the thiol (3.0 g.) gave a clear solution when heated, and on cooling this gave crystals of the potassium aryl sulphide dihydrate (2.9 g.), m. p. >350°, which developed a red colour within a few hours (Found: C, 25.9; H, 0.8. $C_8F_9KS, 2H_2O$ requires C, 25.7; H, 1.1%). A broad band at 1650 cm⁻¹ was consistent with the presence of "bound" water,¹² λ_{\max} (in EtOH) 2870 Å (ϵ 8.8 × 10³). Treatment of this salt with an excess of 16N-hydrochloric acid gave back the thiol with a correct i.r. spectrum.

(b) Methylnitrosourea (10.0 g.) was slowly added to 40% (w/v) aqueous potassium hydroxide (25 c.c.) and ether (40 c.c.) at 0°. The ether layer was separated, and to it was slowly added a solution of the thiol (6.0 g.) in ether (10 c.c.). After 1 hr. at 15° the mixture was dried (MgSO₄), filtered, and evaporated. Distillation of the residual liquid gave methyl 2,4,5-trifluoro-3,6-bistrifluoromethylphenyl sulphide (4.5 g.), b. p. 73—76°/25 mm. (Found: C, 34.2; H, 0.8. $C_9H_3F_9S$ requires C, 34.4; H, 0.9%), λ_{\max} (in EtOH) 3050 and 2360 Å (ϵ 6.1 × 10³ and 7.2 × 10³). The sulphide (2.0 g.), 30% (w/v) hydrogen peroxide (15 c.c.), and acetic acid (10 c.c.) when heated at 100° for 2 hr. gave the sulphone (1.6 g.), m. p. 111—112° (from ethanol) (Found: C, 30.9; H, 0.6. $C_9H_3F_9O_2S$ requires C, 31.2; H, 0.8%). The sulphone (0.5 g.) was refluxed with sodium (0.2 g.) in methanol (25 c.c.) for 3 hr., and poured into water (60 c.c.), to give methyl 2,4,5-trimethoxy-3,6-bistrifluoromethylphenyl sulphone (0.4 g.), m. p. 90—91° (from ethanol) (Found: C, 38.0; H, 3.5. $C_{12}H_{12}F_6O_5S$ requires C, 37.7; H, 3.2%).

(c) Bromine (1.0 g.), the thiol (2.0 g.), and acetic acid (13 c.c.), treated in the usual way,¹² gave the disulphide (0.5 g.), m. p. 54—55° (from ethanol) (Found: C, 32.0; H, 0.1. $C_{16}F_{18}S_2$ requires C, 32.1; H, 0.0%), ν_{\max} 1630 and 1490 cm⁻¹ (aromatic ring), λ_{\max} (in EtOH) 2330, 2570, and 2900 Å (ϵ 3.4 × 10⁴, 2.2 × 10⁴, and 1.8 × 10⁴).

(d) The thiol (2.0 g.) and concentrated sulphuric acid (3 c.c.) were kept at 170° for 16 hr. in

a sealed tube. The oily product was distilled *in vacuo*, to give the disulphide (1.0 g.), m. p. 54—55° (from ethanol), with a correct i.r. spectrum.

(e) The thiol (6.0 g.) was added to a suspension of Raney nickel (Grade W4; 30.0 g.) in methanol (40 c.c.), refluxed for 6 hr., filtered, and separated by gas chromatography (column B, 110°, N₂ 38 l./hr.), to give methanol (32 c.c.) and 1,2,4-trifluoro-3,6-bistrifluoromethylbenzene (2.2 g.), b. p. 124° (Found: C, 36.0; H, 0.3. C₈H₄F₆ requires C, 35.8; H, 0.4%), ν_{\max} 3100 (=CH-), 1660, 1625, 1510, and 1490 cm.⁻¹ (aromatic ring).

(f) Sodium hydrogen sulphide (12.0 g.) in ethylene glycol (18 c.c.) was quickly added to a boiling solution of the thiol (6.0 g.) in pyridine (60 c.c.), and the mixture refluxed for 15 min. In the usual way this gave unchanged thiol (3.9 g.) and 2,5-difluoro-3,6-bistrifluoromethylbenzene-1,4-dithiol (0.7 g.); both had correct i.r. spectra.

(g) Chlorine was bubbled through a solution of the thiol (10.0 g.) in acetic acid (50 c.c.) containing 30% (w/v) hydrogen peroxide (5 c.c.) for 1 hr. The usual procedure¹⁰ gave the *sulphonyl chloride* (7.5 g.), b. p. 80—92°/0.2 mm. (Found: C, 26.5. C₈ClF₆O₂S requires C, 26.2%), ν_{\max} 1640, 1610, and 1480 (aromatic ring), and 1375 cm.⁻¹ (=SO₂), λ_{\max} 2870, 2580 (i), and 2250 Å (ϵ 8.8 × 10³, 7.6 × 10³, and 17.4 × 10⁴).

Desulphuration of the Benzenedithiol.—The dithiol (12.0 g.) and Raney nickel (100 g.) in methanol (150 c.c.), treated in the usual way, gave 1,4-difluoro-2,5-bistrifluoromethylbenzene (4.2 g.), b. p. 121—122° (Found: C, 38.4; H, 0.8. C₈H₂F₈ requires C, 38.4; H, 0.8%), ν_{\max} 3090 (=CH₂), 1600 and 1515 cm.⁻¹ (aromatic ring).

The difluorobistrifluoromethylbenzene (3.6 g.) and concentrated sulphuric acid (6 c.c.) were kept at 165° for 20 hr. in a sealed tube, to give 2,5-difluoroterephthalic acid (1.5 g.), subliming above 275° (Found: C, 47.5; H, 2.2. C₈H₄F₂O₄ requires C, 47.5; H, 2.0%), ν_{\max} 1710 cm.⁻¹ (CO). The acid (0.23 g.) gave a *di-(S-benzylthiouronium) salt* (0.35 g.), m. p. 209—211° (decomp.) (from aqueous ethanol) (Found: C, 53.7; H, 4.9. C₂₄H₂₄F₂N₄O₄S₂ requires C, 53.9; H, 4.5%).

Methyl 2,5-Difluoro-3,6-bistrifluoromethyl-4-mercaptophenyl Sulphide.—Sodium hydrogen sulphide (1.8 g.) in dimethylformamide (20 c.c.) was slowly added to methyl 2,4,5-trifluoro-3,6-bistrifluoromethylphenyl sulphide (6.0 g.) in dimethylformamide, and the mixture stirred at 15° for ½ hr. The normal isolation procedure gave the *mercapto-sulphide* (3.1 g.), m. p. 41—42° [from light petroleum (b. p. 40—60°)] (Found: C, 32.9; H, 1.2. C₉H₄F₆S₂ requires C, 32.8; H, 1.2%), ν_{\max} 2610 (SH), 1600, 1550, and 1470 cm.⁻¹ (aromatic ring).

The mercapto-sulphide (3.0 g.) was desulphurised in the usual way with Raney nickel (20 g.) in methanol (150 c.c.), to give 1,4-difluoro-2,5-bistrifluoromethylbenzene (0.6 g.), with a correct i.r. spectrum.

Reaction of Perfluoro-p-xylene with Lithium Aluminium Hydride.—Perfluoro-*p*-xylene (10.0 g.) in ether (10 c.c.) was slowly added to lithium aluminium hydride (2.0 g.) in ether (100 c.c.). After the initial vigorous reaction, the mixture was refluxed for 72 hr., and the usual procedure¹⁸ gave only 1,4-difluoro-2,5-bistrifluoromethylbenzene (5.2 g.), with a correct i.r. spectrum.

Reaction of Perfluoro-o-xylene with Sodium Hydrogen Sulphide.—Sodium hydrogen sulphide (12.0 g.) in ethylene glycol (18 c.c.) was slowly added to perfluoro-*o*-xylene (12.0 g.) in pyridine (100 c.c.) at 15°. After 1 hr. at 60—65° the mixture was poured on ice, acidified, and extracted with ether. The dried (MgSO₄) extract was evaporated and the liquid residue distilled, to give (i) 2,3,6-trifluoro-4,5-bis(trifluoromethyl)thiophenol (II) (8.5 g.), b. p. 69—74°/25 mm. (Found: C, 32.2; H, 0.5. C₈H₄F₆S requires C, 32.0; H, 0.3%), ν_{\max} 2600 (SH), 1625, 1595, and 1495 cm.⁻¹ (aromatic ring), λ_{\max} (in EtOH) 2340 and 3000 Å (ϵ 2.37 × 10⁴ and 1.36 × 10⁴); (ii) a difluoro-*o*-bis(trifluoromethyl)dimercaptobenzene (0.5 g.), b. p. 75—105°/25 mm., m. p. 32—33° (after two sublimations) (Found: C, 30.9; H, 0.6. C₈H₂F₆S₂ requires C, 30.6; H, 0.6%), ν_{\max} 2600 (SH), 1595, 1550, and 1490 cm.⁻¹ (aromatic ring), λ_{\max} 2340 and 3230 Å (ϵ 5.75 × 10⁴ and 16.5 × 10⁴).

Reactions of 2,3,6-Trifluoro-4,5-bis(trifluoromethyl)thiophenol (II).—(a) The thiol (6.0 g.) reacted vigorously with diazomethane, in the manner described previously, to give the *methyl sulphide* (5.4 g.), b. p. 100—105°/25 mm. (Found: C, 34.5; H, 1.2. C₉H₃F₆S requires C, 34.4; H, 1.0%). The proton n.m.r. spectrum displayed a doublet of triplets ($J = 1.1$ c/sec.) centred at 2.45. The sulphide (2.0 g.), 30% (w/v) hydrogen peroxide (15 c.c.), and acetic acid (10 c.c.) when heated at 100° for 2 hr. gave the *sulphone* (1.7 g.), m. p. 95—97° (from ethanol) (Found: C, 31.4; H, 1.0. C₉H₃F₆O₂S requires C, 31.2; H, 0.9%). The proton n.m.r. spectrum showed a triplet ($J = 1.0$ c./sec.) centred at 3.04.

(b) In the usual way, bromine in acetic acid converted the thiol (2.0 g.) into the *disulphide* (0.3 g.), m. p. 55—56° (from ethanol) (Found: C, 32.1. $C_{16}F_{18}S_2$ requires C, 32.1%).

(c) The thiol (8.0 g.) was desulphurised in the usual way with Raney nickel (40 g.) in methanol (40 c.c.), to give *1,2,5-trifluoro-3,4-bistrifluoromethylbenzene* (2.5 g.), b. p. 129—130° (Found: C, 36.1; H, 0.6. C_8HF_9 requires C, 35.8; H, 0.4%), ν_{\max} . 3100 (=CH-), 1630 and 1500 cm^{-1} (aromatic ring), λ_{\max} . (in EtOH) 2010, 2370, and 2740 Å (ϵ 2.4×10^4 , 2×10^3 , and 3.5×10^3). The trifluorobistrifluoromethylbenzene (2.0 g.) and concentrated sulphuric acid (4 c.c.) were kept in a sealed tube at 170° for 16 hr., cooled, and poured on ice (50 g.). The usual isolation procedure gave a *3,4,6-trifluorophthalic acid hydrate* (1.4 g.), m. p. 157—158° (from *o*-xylene) (Found: C, 42.4; H, 1.5. $C_8H_3F_3O_4 \cdot 0.33H_2O$ requires C, 42.5; H, 1.6%), ν_{\max} . 3100—2500 and 1720 cm^{-1} (CO_2H).

The acid (0.2 g.) gave, in the usual way, *di-(S-benzylthiouronium) 3,4,6-trifluorophthalate monohydrate* (0.35 g.), m. p. 210—211° (Found: C, 50.7; H, 4.7. $C_{21}H_{25}F_3N_4O_5S_2$ requires C, 50.5; H, 4.4%). An intimate mixture of the acid (0.8 g.) and soda-lime (2.0 g.) was slowly heated to 300°. The distillate was dried (P_2O_5) and redistilled, to give *1,2,4-trifluorobenzene* (0.1 g.) with a correct i.r. spectrum.

2,3,6-Trifluoro-4,5-bis(trifluoromethyl)phenylhydrazine.—Perfluoro-*o*-xylene (4.0 g.) in dimethylformamide (10 c.c.) was treated with 100% (w/w) hydrazine hydrate (10.0 g.) in dimethylformamide (15 c.c.), as described previously, to give *the phenylhydrazine* (2.5 g.), m. p. 70—71° [from light petroleum (b. p. 60—80°)] (Found: C, 32.5; H, 0.9. $C_8H_3F_9N_2$ requires C, 32.2; H, 1.0%). The phenylhydrazine (1.5 g.) and Fehling's solution were refluxed for 2 hr. and distilled. The distillate separated into two layers; the lower layer was dried ($MgSO_4$) and filtered, to give *1,2,5-trifluoro-3,4-bistrifluoromethylbenzene* with a correct i.r. spectrum.

The phenylhydrazine (0.20 g.) with benzaldehyde (0.2 g.) in ethanol (2 c.c.) gave the *phenylhydrazone* (0.22 g.), m. p. 112—113° (from aqueous ethanol) (Found: C, 46.4; H, 1.8. $C_{15}H_7F_9N_2$ requires C, 46.6; H, 1.8%). The hydrazone (2.0 g.) was refluxed with zinc powder (4.0 g.) in acetic acid (20 c.c.) for 3 hr. The mixture was poured into water (200 c.c.) and *2,3,6-trifluoro-4,5-bistrifluoromethylaniline* (0.6 g.) was isolated by ether extraction; its i.r. spectrum was identical with that of the ammoniation product of perfluoro-*o*-xylene.

*Reaction of Perfluoro-*o*-xylene with Aqueous Ammonia*.—Perfluoro-*o*-xylene (15.0 g.), ammonia (*d* 0.88; 12 c.c.), and ethanol were heated together in a rocking autoclave at 145—150° for 16 hr. The usual isolation procedure (column A, 140°, N_2 66 l./hr.) gave: (i) *2,3,6-trifluoro-4,5-bistrifluoromethylaniline* (6.5 g.), b. p. 208—209° (Found: C, 34.0; H, 0.7. $C_8H_2F_9N$ requires C, 33.9; H, 0.7%), ν_{\max} . 3500 and 3400 (NH_2), 1600, 1520, and 1490 cm^{-1} (aromatic ring); (ii) a mixture (1.4 g.) containing (i), which was not examined.

The amine (0.5 g.), acetic anhydride (1 c.c.), and concentrated sulphuric acid (2 drops) were refluxed for 10 min., to give *the acetanilide* (0.35 g.), m. p. 110—111° [from light petroleum (b. p. 60—80°)] (Found: C, 36.9; H, 1.3. $C_{10}H_4F_9NO$ requires C, 36.9; H, 1.2%).

The amine (1.5 g.), formaldehyde (40% w/v; 2 c.c.), and formic acid (90% w/v; 13 c.c.) were refluxed for 18 hr. The mixture was poured into water (100 c.c.), and extraction with ether gave *the NN-dimethylaniline* (1.5 g.), b. p. 203—204° (Found: C, 38.7; H, 1.9. $C_{10}H_6F_9N$ requires C, 38.6; H, 1.9%). The proton n.m.r. spectrum consisted of a triplet ($J = 2.8$ c./sec.) centred at 2.8.

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