

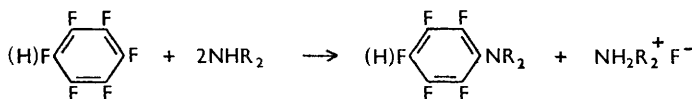
350. Aromatic Polyfluoro-compounds. Part IV.* The Reaction of Aromatic Polyfluoro-compounds with Nitrogen-containing Bases.

By G. M. BROOKE, J. BURDON, M. STACEY, and J. C. TATLOW.

Hexafluorobenzene reacts with ammonia and hydrazine to give pentafluoroaniline and pentafluorophenylhydrazine, respectively. Pentafluorobenzene reacts analogously to give the 2,3,5,6-tetrafluoro-compounds. More drastic reaction of ammonia with pentafluoroaniline affords 2,4,5,6-tetrafluoro-1,3-phenylenediamine. Methylamine gives a mono- and a di-replacement compound with hexafluorobenzene; the latter compound is believed to be the *p*-isomer.

ALTHOUGH there are several reports¹⁻⁵ of nucleophilic substitution for hexafluorobenzene, only one² describes a reaction with a nitrogen base, pentafluoroaniline having been obtained from hexafluorobenzene and sodamide in liquid ammonia. From this reaction mixture we have now isolated, besides pentafluoroaniline, a small amount of another compound, believed to be perfluorodiphenylamine, (C₆F₅)₂NH. Further, we have simplified the preparation of pentafluoroaniline and extended the scope of the process to include the reactions of several other nitrogen bases with polyfluoro-aromatic compounds.

At elevated temperatures (100—230°), in aqueous ethanol, nitrogen bases (in excess) and polyfluoro-aromatic compounds reacted easily with elimination of fluoride ions and formation of the expected nitrogen-containing derivatives in good yields:



Thus, pentafluoroaniline was formed in 59% yield when hexafluorobenzene was treated with aqueous-ethanolic ammonia at 167°.

* Part III, *Tetrahedron*, in the press.

¹ Godsell, Stacey, and Tatlow, *Nature*, 1956, **178**, 199.

² Forbes, Richardson, and Tatlow, *Chem. and Ind.*, 1958, 630.

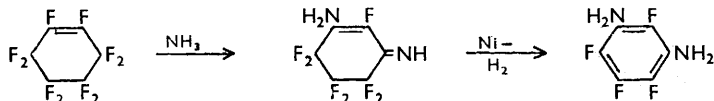
³ Forbes, Richardson, Stacey, and Tatlow, *J.*, 1959, 2019.

⁴ Pummer and Wall, *Science*, 1958, **127**, 643.

⁵ Birchall and Haszeldine, *J.*, 1959, 13.

Under similar conditions, pentafluorobenzene gave a tetrafluoroaniline. This compound is believed to be the 2,3,5,6-tetrafluoro-isomer (*i.e.*, the hydrogen and amino-groups being orientated *para*), both by analogy with the results described below for the tetrafluorophenylhydrazine prepared similarly, and from its nuclear magnetic resonance spectrum. This spectrum showed that there were only two magnetically different kinds of fluorine atoms in the molecule: if the compound had had the hydrogen and amino-groups orientated *ortho* or *meta*, then four different types of fluorine atom should have been disclosed in the spectrum.

Under more drastic conditions, at 220°, reaction of pentafluoroaniline with aqueous-ethanolic ammonia gave a small amount of a tetrafluorophenylenediamine. This diamine was identical with the *meta*-isomer which had been prepared previously⁶ in this Department as illustrated. The nuclear magnetic resonance spectrum confirmed the orientation



of this diamine. The sluggishness of the double replacement of fluorine by ammonia was not unexpected: pentafluoroaniline is powerfully deactivated towards nucleophilic attack, owing presumably to an increase of electron-density in the aromatic ring by back-conjugation of the electron pair on the nitrogen atom of the amino-group. It is well-known⁷ in aromatic chemistry that the amino-group is one of the most powerful activating substituents towards electrophilic attack. The formation of the *meta*-diamine is of considerable interest; it is the first example we have found so far of nucleophilic double replacement in the fluoro-aromatic series that did not give a *para*-isomer as the main product.

At 115°, methylamine and hexafluorobenzene gave pentafluoro-*N*-methylaniline. However, under the more drastic conditions used to prepare pentafluoroaniline from hexafluorobenzene and ammonia, methylamine and hexafluorobenzene gave a tetrafluoro-*NN'*-dimethylphenylenediamine in 61% yield. Somewhat surprisingly, in view of the *meta*-orientation of the tetrafluorophenylenediamine obtained from the pentafluoroaniline-ammonia reaction, this *NN'*-dimethyl compound appeared to be the *para*-isomer since it showed only one fluorine absorption in the nuclear magnetic resonance spectrum: the *ortho*-isomer would have shown two groups of peaks and the *meta*-isomer three. Further work is in progress to confirm the structure of this compound by chemical methods. The obvious explanation for the difference in reactivities between ammonia and methylamine is that methylamine, being a stronger base than ammonia, is a more powerful nucleophile.

Hydrazine with hexafluorobenzene gave crystalline pentafluorophenylhydrazine, and with pentafluorobenzene gave a tetrafluorophenylhydrazine, both in high yields. Both these products reacted with carbonyl compounds to give solid derivatives in the usual way. The tetrafluorophenylhydrazine was shown to be the 2,3,5,6-tetrafluoro-isomer (*i.e.*, with the hydrogen and the hydrazino-group *para*) in two ways. First, with Fehling's solution, the hydrazino-group was replaced by hydrogen to give the known 1,2,4,5-tetrafluorobenzene.⁸ This reaction, which produces an aromatic hydrocarbon from an arylhydrazine, has been applied⁹ outside fluorine chemistry but may well be particularly useful in the latter field because of the ready availability of the fluorophenylhydrazines that we have now demonstrated. The second orientation of the tetrafluorophenylhydrazine was provided by nuclear magnetic resonance spectroscopy; two magnetically different kinds of

⁶ Robson, Roylance, Stephens, and Tatlow, unpublished work.

⁷ Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 239.

⁸ Finger, Reed, Burness, Fort, and Blough, *J. Amer. Chem. Soc.*, 1951, **73**, 145; Infrared Spectral Data, American Petroleum Research Project 44, Serial No. 1018.

⁹ Chattaway and Pearce, *J.*, 1915, **107**, 32; Chattaway and Ellington, *J.*, 1916, **109**, 587.

fluorine atom were present; had the hydrogen and the hydrazino-groups been orientated *ortho* or *meta*, then four kinds of fluorine atom would have been shown.

No nucleophilic replacement occurred when hydrazine reacted³ with pentafluoroanisole. Presumably, demethylation proceeded much more readily than replacement, and the pentafluorophenoxide ion formed was too deactivated to react itself.

Both hydroxylamine and guanidine reacted with hexafluorobenzene, but no tractable products could be isolated. This may well have been due to the instability of hydroxylamine, guanidine, and their immediate substitution products at the temperature of the reaction.

Aniline reacted with hexafluorobenzene at room temperature with the formation of a white precipitate. This precipitate decomposed, however, upon filtration and appeared to be a loose addition complex, since hexafluorobenzene was recovered. At elevated temperatures aniline did not react with hexafluorobenzene except to produce small amounts of tar at the highest temperatures tried. This is not unexpected since aniline is a weaker base, and hence a weaker nucleophile, than the other bases used.

Full discussion of the orientation effects described in this and earlier papers is deferred until more results are available.

EXPERIMENTAL

Perfluorodiphenylamine.—Hexafluorobenzene (10 g.) reacted with sodamide in liquid ammonia as described before² to give, besides pentafluoroaniline, a higher-boiling material which solidified and recrystallised from light petroleum (b. p. 40–60°) to give *perfluorodiphenylamine* (0.3 g.), m. p. 81–82° (Found: C, 41.5; H, 0.3. $C_{12}HNF_{10}$ requires C, 41.3; H, 0.3%).

Pentafluoroaniline.—Hexafluorobenzene (5.0 g.), prepared by defluorination¹⁰ of octafluorocyclohexadienes, aqueous ammonia (10.4 ml.; *d* 0.88), and ethanol (20 ml.) were heated together in a sealed tube at 167° for 18 hr. The mixture was then diluted with water and extracted with methylene chloride. Distillation of the dried ($MgSO_4$) extracts afforded pentafluoroaniline (2.9 g.), b. p. 156–157°, m. p. 33.5–35.0° (lit.,² b. p. 153–154°, m. p. 33.5–34.5°). This material had an infrared spectrum identical with that of the compound prepared previously.²

2,3,5,6-Tetrafluoroaniline.—Pentafluorobenzene¹¹ (4.6 g.), aqueous ammonia (10.4 ml.; *d* 0.88), and ethanol (20 ml.) were treated as in the previous experiment, to give *2,3,5,6-tetrafluoroaniline* (2.9 g.), b. p. 158–159°, m. p. 23.5–26.5° (Found: C, 43.7; H, 2.0. $C_6H_3NF_4$ requires C, 43.7; H, 1.8%). The ^{19}F nuclear magnetic resonance spectrum of the pure, molten compound showed two multiplets of equal intensity at 65.3 and 85.9 p.p.m. with respect to trifluoroacetic acid as external reference. The multiplet pattern of these, and of the ring proton resonance,¹² is also consistent with the *2,3,5,6-tetrafluoro-structure*.

Treatment with acetic anhydride and concentrated sulphuric acid for 2 min. under reflux gave *2,3,5,6-tetrafluoroacetanilide* (57%), m. p. 138.5–139° (from aqueous ethanol) (Found: C, 46.2; H, 2.3. $C_8H_5ONF_4$ requires C, 46.4; H, 2.4%).

2,4,5,6-Tetrafluoro-1,3-phenylenediamine.—Pentafluoroaniline (4.1 g.), aqueous ammonia (7.0 ml.; *d* 0.88), and ethanol (15 ml.) were heated in a sealed tube at 223° for 24 hr. The dark red product was isolated by extraction with methylene chloride and was fractionally sublimed at 80–90° to give, initially, a mixture (0.4 g.) which was shown by infrared spectroscopy to contain about 75% of pentafluoroaniline and 25% of *2,4,5,6-tetrafluoro-phenylenediamine*, and finally, pure *2,4,5,6-tetrafluoro-1,3-phenylenediamine* (0.4 g.), m. p. 129.5–131° alone and on admixture with the material obtained by another route⁶ (Found: C, 39.8; H, 2.3. $C_6H_4N_2F_4$ requires C, 40.0; H, 2.2%). The two specimens of diamine had identical infrared spectra.

2,3,5,6-Tetrafluoro-NN'-dimethyl-1,4-phenylenediamine.—Hexafluorobenzene (5.0 g.), methylamine [distilled from methylamine hydrochloride (11.2 g.) and dilute alkali], ethanol (20 ml.), and water (5 ml.) were heated together in a sealed tube at 168–172° for 12 hr. Isolation by methylene chloride as before gave *2,3,5,6-tetrafluoro-NN'-dimethyl-1,4-phenylenediamine* (3.4 g.),

¹⁰ Gething, Patrick, Tatlow, Banks, Barbour, and Tipping, *Nature*, 1959, **133**, 586.

¹¹ Stephens and Tatlow, *Chem. and Ind.*, 1957, 821.

¹² Thomas, unpublished work.

b. p. 226—230°. This material solidified and was recrystallised from light petroleum (b. p. 80—100°), to give the pure compound, m. p. 92·5—94° (Found: C, 46·2; H, 3·8. $C_8H_9N_2F_4$ requires C, 46·2; H, 3·9%). A 3*M*-solution of this compound in acetone showed one fairly sharp ^{19}F nuclear magnetic resonance absorption at 84·2 p.p.m. from trifluoroacetic acid.

Pentafluoro-N-methylaniline.—Treated as in the previous experiment, but at 115° for 24 hr., hexafluorobenzene (5·0 g.) gave *pentafluoro-N-methylaniline* (1·6 g.), b. p. 160—177° (mainly 171°) (Found: C, 42·9; H, 2·1. $C_7H_4NF_5$ requires C, 42·7; H, 2·1%), and a higher-boiling (177—230°) fraction (1·5 g.) which solidified on cooling and was probably mainly the *NN'*-dimethyl compound described above.

Pentafluoro-*N*-methylaniline gave a liquid acetyl derivative with acetyl chloride, but with toluene-*p*-sulphonyl chloride in pyridine gave an *N-toluene-p-sulphonyl derivative* (25%), m. p. 84—85·5° (from aqueous ethanol) (Found: C, 47·7; H, 2·9. $C_{14}H_{10}O_2NSF_5$ requires C, 47·9; H, 2·9%).

Pentafluorophenylhydrazine.—Hexafluorobenzene (5·1 g.), hydrazine hydrate (14·4 g.; 100% w/w), water (10·4 ml.), and ethanol (30 ml.) were refluxed together for 12·5 hr. Dilution with water, extraction with methylene chloride, and evaporation of the dried ($MgSO_4$) extracts left a brown solid (4·0 g.), m. p. 63—70°. Recrystallisation from light petroleum (b. p. 80—100°) afforded 2,3,4,5,6-*pentafluorophenylhydrazine* (2·6 g.), m. p. 76·0—77·5° (Found: C, 36·3; H, 1·5. $C_6H_3N_2F_5$ requires C, 36·4; H, 1·5%).

Treatment of this compound in aqueous ethanol with benzaldehyde gave *benzaldehyde pentafluorophenylhydrazone* (77%), m. p. 130—131° (from aqueous ethanol) (Found: C, 54·8; H, 2·6. $C_{13}H_7N_2F_5$ requires C, 54·6; H, 2·5%). With hydrogen chloride in anhydrous ether the hydrazine gave its *hydrochloride* (99%), m. p. 239—241° (from ethanol-ether) (Found: C, 30·8; H, 1·7. $C_6H_4N_2ClF_5$ requires C, 30·7; H, 1·7%).

2,3,5,6-*Tetrafluorophenylhydrazine*.—Pentafluorobenzene (4·88 g.), hydrazine hydrate (16·7 g.; 100% w/w), water (11·6 g.), and ethanol (20 ml.) were refluxed together for 7½ hr., then poured into water and the product (4·08 g.), m. p. 87—88°, was filtered off and recrystallised from light petroleum (b. p. 80—100°) to give pure 2,3,5,6-*tetrafluorophenylhydrazine* (3·30 g.), m. p. 90—91·5° (Found: C, 40·0; H, 2·3. $C_6H_4N_2F_4$ requires C, 40·0; H, 2·2%). The ^{19}F nuclear magnetic resonance spectrum of a 3*M*-solution of this compound in acetone has two multiplets of equal intensity at 64·5 and 79·0 p.p.m. from trifluoroacetic acid.

Treatment of this phenylhydrazine with benzaldehyde in aqueous-ethanol gave *benzaldehyde 2,3,5,6-tetrafluorophenylhydrazone* (54%), m. p. 109—109·5° (from aqueous ethanol) (Found: C, 58·6; H, 3·3. $C_{13}H_8N_2F_4$ requires C, 58·2; H, 3·0%).

1,2,4,5-*Tetrafluorobenzene* from 2,3,5,6-*Tetrafluorophenylhydrazine*.—The phenylhydrazine (2·00 g.) and Fehling's solution [mixture of solution "A" (40 ml.) and solution "B" (40 ml.)] were refluxed together for 40 min., a red precipitate being formed. The product was then distilled from the reaction mixture in steam, separated from the lighter aqueous layer, and distilled *in vacuo* from phosphorus pentoxide to give 1,2,4,5-tetrafluorobenzene (0·89 g.), identified by its infrared spectrum⁸ and by its retention time on vapour-phase chromatography.

Reaction of Hexafluorobenzene with Aniline.—Hexafluorobenzene (5·0 g.) was added to a five-fold excess of aniline in aqueous ethanol at room temperature. A white precipitate was formed immediately. When an attempt was made to filter off this precipitate, it liquified and passed through the filter. The whole mixture was therefore refluxed for 27 hr., but, even after this time, only hexafluorobenzene (2·8 g.) was isolated. After being treated for 27 hr. at 165° a similar reaction mixture still contained hexafluorobenzene (gas-liquid chromatography). A small amount of tar was also isolated from this last reaction, but no 2,3,4,5,6-pentafluorodiphenylamine.

Nuclear Magnetic Resonance Measurements.—These were carried out on a Mullard SL44 Mark I instrument at 30·107 Mc./sec. Further details will be published later.¹²

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