

HALOGENATION: PART XXIII. HALOGENATION OF FLUOROBENZENE, o-, m-, AND p-FLUOROTOLUENES

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Fluorobenzene, o-, m- and p-fluorotoluenes have been chlorinated, brominated and iodinated under different conditions as a result of which mixed halogen derivatives have been obtained by direct halogenation.

The majority of the mixed halogen derivatives of fluorobenzene have been generally obtained either from fluoroanilines or other halogenated anilines, through the Sandmeyer's reaction. By passing chlorine into fluoro-benzene in presence of iron, Wallach and Hensler (*Annalen*, 1905, **243**, 225) obtained p-fluorochlorobenzene and a dichloro product, considered to be either 2:4- or 3:4-dichlorofluorobenzene or a mixture of both, as separation is not possible due to the close boiling point (Van De Laude, *Rec. trav. chim.*, 1932, **51**, 98; Kraay, *ibid.*, 1929, **48**, 1055). By a similar method Wallach and Hensler (*loc. cit.*) obtained p-bromofluorobenzene and two isomeric dibromofluorobenzenes, one a liquid boiling at 109-12°/30 mm. and a solid, m.p. 69°, which is also obtained during the bromination of fluorobenzene (Schieman and Pelarsky, *Ber.*, 1931, **64B**, 1340) and described as 2:4- or 3:4-dibromofluorobenzene. The liquid dibromo product has been obtained from 2:4-dibromoaniline, through the diazonium fluoroborate and hence, the solid product is obviously 3:4-dibromofluorobenzene.

Very little work has been done on the halogen derivatives of o-, m- and p-fluorotoluenes. By the direct action of chlorine, bromine and iodine in presence of catalyst, many mixed halogen derivatives have now been prepared. The constitution of the compounds, so prepared, has been determined in as many cases as possible either by referring them to compounds already known or by oxidising them to known derivatives of fluorobenzoic acids, or synthesising them from the corresponding amino compounds by replacing the amino group by Sandmeyer's reaction by the suitable halogen atom. In a few cases the position of the entering halogen has been assigned from analogy.

The action of chlorine and bromine on o-, m-, and p-fluorotoluenes has been tried either in the presence of iron or iodine as catalyst and the iodination generally effected in presence of a mixture of nitric and sulphuric acids or in presence of sodium nitrite and strong sulphuric acid (Varma and Panickar, *J. Indian Chem. Soc.*, 1926, **3**, 342; Varma and Narayan, *ibid.*, 1927, **4**, 283). o-Fluorotoluene on chlorination gives, 2-fluoro-5-chloro- (obtained in larger quantities) and 2-fluoro-6-chlorotoluene, the former is obtained from 2-fluoro-5-aminotoluene and the latter oxidised to 2-fluoro-6-chlorobenzoic acid, m.p. 190° (Lock, *Ber.*, 1936, **69B**, 2253). The corresponding bromo compounds are also described and their constitution assigned from analogy. 2-Fluoro- and 5-fluoro-5-iodo-, and 2-fluoro-6-iodo-toluenes are obtained from the iodination and they have also been prepared from the corresponding fluoro-amino-toluenes. In a similar way from m-fluoro-toluene, 3-fluoro-1-bromo-, 3-fluoro-6-bromo-, 3-fluoro-4-iodo- and 3-fluoro-6-iodo-toluenes have been obtained. The constitutions have been assigned only from analogy and the compound obtained in larger proportion being taken to be the 6-substituted derivative. Some of the compounds have been oxidised to the corresponding benzoic acids. p-Fluorotoluene yields 4-fluoro-3-bromo-toluene, which has been oxidised to the corresponding

acid; 4-fluoro-iodo- and the already known 4-fluoro-3-iodotoluene, obtained previously from 3-iodo-4-aminotoluene (Yaun and Adams, *J. Amer. Chem. Soc.*, 1932, **54**, 4426), have also been oxidised to the corresponding acids.

Only a few simple sidechain halogen derivatives of *o*-, *m*-, and *p*-fluorotoluenes are described in the literature. The fluorotoluenes, fluorobenzyl and -benzal halogen derivatives have been halogenated under varying conditions and many mixed halogen compounds have been obtained. The constitution of all these compounds has been determined by oxidising them to the corresponding fluorobenzoic acids.

EXPERIMENTAL

p-Chlorofluorobenzene.—Fluorobenzene (10 c.c.) and iron powder (0.5 g.) were taken in a flask with a reflux condenser and chlorine (1 mol.) was passed into it in a slow current with occasional shaking. The liquid was filtered, washed with a very dilute solution of sodium hydroxide and with water, dried over calcium chloride and distilled. The fraction (10.3 g.) distilling at 125–34° was collected separately and on redistillation gave a clear liquid boiling at 130°.

Dichlorofluorobenzene. (i) *From fluorobenzene.*—Chlorine (2 mols.) was passed into fluorobenzene (10 c.c.) and iron powder (0.5 g.) and the product worked up as above. The fraction (3.5 g.) distilling at 125–35° was found to be *p*-chlorofluorobenzene while the fraction distilling at 165–75° (11.8 g.) on redistillation gave a liquid boiling at 169–75°. This fraction seems to be a mixture of 2:4- and 3:4-dichlorofluorobenzene. Since the boiling points of the two liquids are very close together it was not possible to separate the two constituents by fractional distillation.

(ii) *From p-chlorofluorobenzene.*—*p*-Chlorofluorobenzene (10 c.c.) under similar conditions with chlorine (1 mol.) gave the mixture of dichlorofluoro derivatives (9.9 g.).

3:4-Dibromofluorobenzene.—To *p*-fluorobromobenzene (15 g.) and iron powder (1 g.) in a flask, bromine (4.5 c.c.) was added slowly and the solution refluxed on a water-bath for about 8 hours. After this period the product was washed as before and distilled under reduced pressure. The distillate (5.8 g.) solidified and was crystallised from rectified spirit as needles, m.p. 69°. (Found: Br, 64.12. $C_6H_3Br_2F$ requires Br, 62.96 per cent).

2:4-Dibromofluorobenzene. (i) *From p-bromofluorobenzene.*—The liquid product (11.8 g.) from the preceding experiment was redistilled under reduced pressure and a pure product, b.p. 109–12°/38 mm. was obtained. (Found: Br, 63.33. $C_6H_3Br_2F$ requires Br, 62.96 per cent).

(ii) *From 2:4-Dibromoaniline.*—2:4-Dibromoaniline (25 g.) (Chattaway and Clemo, *J. Chem. Soc.*, 1916, 109, 91) was diazotised in the usual way at 0° to -5° and to the diazo solution 40% of hydrofluoboric acid (50 c.c.) added gradually with stirring and the precipitated fluoborate was washed with alcohol and ether, mixed with water (100 c.c.) and refluxed for about 6 hours when on cooling a dark brown liquid separated out. It was extracted with chloroform, washed, dried and distilled under reduced pressure. The fraction distilling at 75–90°/9 mm. was collected and it gave on redistillation a pure product, b.p. 103–105°/32 mm. or 114–16°/756 mm. It is a heavy oily liquid, colourless when pure. (Found: Br, 62.13. $C_6H_3Br_2F$ requires Br, 62.96 per cent).

p-Iodo-fluorobenzene.—Fluorobenzene (5 c.c.), iodine (6.5 g.), sodium nitrite (8 g.) and carbon tetrachloride (20 c.c.) were refluxed on a water-bath. Fuming sulphuric acid (20 c.c.)

was added drop by drop during an hour and the solution refluxed for 4 hours more, allowed to cool, poured into a large volume of water, dried and distilled. The fraction (9 g.) between 175-80° was collected and on redistillation it gave a light brown oil. b.p. 178-81°/758 mm. Its constitution was established by converting it into 4:4-difluorodiphenyl in the following way.

p-Iodofluorobenzene (2 g.) and copper bronze (1 g.) were refluxed on a sand-bath at 200-20° for 6 hours. The product was extracted with ether, filtered and allowed to stand for some days when 4:4-difluorodiphenyl, m.p. 89°, separated out.

2-Fluoro-5-chlorotoluene.—Chlorine (1.3 mols.) was passed slowly into a flask containing *o*-fluorotoluene (15 c.c.) and iron powder (0.3 g.) during a period of 5 to 6 hours with shaking. The products were washed repeatedly with water, dilute alkali solution, finally again with water, dried over calcium chloride and distilled. Unacted *o*-fluorotoluene distills at first at 95-125° and then two distinct fractions one (3.5 g.) distilling at 145-55° and the other (11.5 g.) at 155-60° were obtained. These fractions gave pure samples on redistillation. The first fraction was found to be 2-fluoro-6-chlorotoluene, b. p. 151-52°/752 mm. It gives on oxidation 2-fluoro-6-chlorobenzoic acid, m.p. 159° (Hock, *Ber.*, 1936, 69B, 2253). The second fraction on repeated distillation gives a pure product, b. p. 157-59°/752 mm. (Found: Cl, 24.6. C₇H₅ClF requires Cl, 24.56 per cent). The same compound was prepared from 2-fluoro-5-aminotoluene by diazotising with sodium nitrite and hydrochloric acid at 0° and treating the diazo product with cuprous chloride and concentrated hydrochloric acid. Both of these compounds give on oxidation the same 2-fluoro-5-chlorobenzoic acid, m. p. 168°. (Found: Cl, 20.30. C₇H₄O₂ClF requires Cl, 20.34 per cent).

3-Fluoro-6-bromotoluene.—To a solution of *m*-fluorotoluene (15 c.c.) in carbon tetrachloride (20 c. c.) a solution of bromine (8 c. c.) in carbon tetrachloride (20 c. c.) was added in the presence of iron powder (0.5 g.) drop by drop under cooling and the solution allowed to stand overnight. The product was washed free of bromine, dried and distilled. Two fractions, one (5.2 g.) distilling between 160-75°/756 mm. and the other (18.7 g.) distilling between 175-85°/756 mm. were obtained. The latter fraction on repeated distillation gave 3-fluoro-6-bromotoluene, a colourless liquid, b. p. 177°/756 mm. (Found: Br, 42.43. C₇H₅BrF requires Br, 42.35 per cent). It is oxidised in the usual way by alkaline potassium permanganate to 3-fluoro-6-bromobenzoic acid, m. p. 151°, needle-shaped crystals, soluble in ether and alcohol. (Found: Br, 37.58. C₇H₄O₂BrF requires Br, 36.51 per cent).

3-Fluoro-4-bromotoluene.—The first fraction in the above experiment distilling at 160-75° on redistillation gave pure 3-fluoro-4-bromotoluene, b. p. 169°/756 mm. (Found: Br, 42.13. C₇H₅BrF requires Br, 42.35 per cent).

3-Fluoro-6-iodotoluene.—To *m*-fluorotoluene (10 c. c.), iodine (1.3 g.) carbon tetrachloride (30 c. c.) and sodium nitrite (10 g.) in a flask, heated in a paraffin bath at 120-30° under reflux, fuming H₂SO₄ (20 c. c.) was added drop by drop for 2 hours, under shaking and the temperature of the bath raised to 160-70° and maintained for about 3 hours after the addition of the acid. The product was poured into water, washed, dried and distilled when the main product (12.5 g.) distilled at 135-45°/9 mm. On redistillation it gave 3-fluoro-6-iodotoluene, b. p. 138-39°/9 mm. (Found: I, 52.35. C₇H₅IF requires I, 53.80 per cent).

3-Fluoro-4-iodotoluene.—In the previous experiment the fraction distilling at 125-35° on repeated distillation yielded 3-fluoro-4-iodotoluene (2.3 g.), b. p. 138-39°/9 mm. Found: I, 52.98. C₇H₅IF requires I, 53.80 per cent).

4-Fluoro-3-bromotoluene.—To a solution of *p*-fluorotoluene (10 c. c.) in carbon tetrachloride (15 c. c.) in a flask, iron powder (1 g.) and bromine (5 c. c.) in carbon tetrachloride (15 c. c.) were added when a vigorous reaction set in with evolution of hydrogen bromide. After the addition the product was allowed to stand for 24 hours, washed free of bromine and distilled. The fraction distilling at 174–80° (11 g.) was redistilled thrice when a colourless liquid, boiling at 174°–177°/757 mm. was obtained. (Found: Br, 42.46. C_7H_6BrF requires Br, 42.35 per cent).

4-Fluoro-3-bromobenzoic Acid.—4-Fluoro-3-bromotoluene (1 c. c.), potassium permanganate (0.8 g.) water and potassium hydroxide (10% solution, 2 c. c.) were heated under reflux for 30 hours and the acid formed isolated in the usual way. White crystalline solid, m. p. 156°, sparingly soluble in cold water, was obtained. (Found: Br, 36.42. $C_7H_4O_2BrF$ requires Br, 36.51 per cent).

2-Fluoro-5-iodotoluene.—(i) From 2-fluorotoluene.—*o*-Fluorotoluene (15 c. c.), carbon tetrachloride (40 c. c.), powdered iodine (20 g.) and sodium nitrite (15 g.) were refluxed on a paraffin-bath at 120°, while fuming sulphuric acid (25 c. c.) was added slowly in 2 hours. After this period, the temperature was raised and maintained at 150–60° for 2 hours. The product was cooled, washed free of iodine, dried and distilled when one fraction at 75–95°/8 mm. (13.8 g.) and another fraction (5.3 g.) at 105–25°/8 mm. were obtained. The first fraction when purified boils at 85°/8 mm. and is a light yellowish liquid. (Found: I, 53.28. C_7H_6IF requires I, 53.80 per cent).

2-Fluoro-6-iodotoluene.—The second fraction in the above experiment gives on repeated distillation a pure product boiling at 114–16°/8 mm. (Found: I, 53.28. C_7H_6IF requires I, 53.80 per cent).

2-Fluoro-5-aminotoluene.—Nitration of *o*-fluorotoluene (80 g.) with fuming nitric acid (88 c. c.) according to Schiemann (*Ber.*, 1929, 62 B, 1795), gave 2-fluoro-5-nitrotoluene (52 g.) and 2-fluoro-6-nitrotoluene (16 g.). 2-Fluoro-5-nitrotoluene was reduced (Hock, *loc. cit.*) when brownish black liquid, b. p. 85–86°/9 mm. was obtained. (Found: N, 11.11. C_7H_6NF requires N, 11.20 per cent). The hydrochloride melts at 220° with decomposition.

(ii) From 2-fluoro-5-aminotoluene.—2-Fluoro-5-aminotoluene (10 g.) was diazotised and treated with potassium iodide (15 g.) in water (25 c. c.). The dark heavy oil was washed free of iodine and distilled at 80–90°/9 mm. On redistillation it gave 2-fluoro-5-iodotoluene, b. p. 86–87°/9 mm.

2-Fluoro-6-iodotoluene from 2-fluoro-6-aminotoluene.—2-Fluoro-6-aminotoluene (7 g.) was diazotised and treated with potassium iodide (10 g.) dissolved in water (20 c. c.) and the oily product separated was purified and distilled at 117°/9 mm. as a heavy oily liquid.

o-, *m*- and *p*-Fluorobenzyl iodides.—These compounds were obtained by boiling the corresponding benzyl chlorides or bromides (5 g.) with potassium iodide (8 g.) and acetone (50 c. c.) under reflux for 4 to 5 hours. The product was then cooled, diluted with water, extracted with carbon tetrachloride, washed with sodium carbonate solution, filtered and distilled under reduced pressure. The benzyl iodides are brownish coloured liquids which distil under ordinary pressure with partial decomposition and have lachrymatory properties.

o-Fluorobenzyl iodide, b. p. 91°/8 mm. (Found: I, 54.36. C_7H_6IF requires I, 53.73 per cent).

m-Fluorobenzyl iodide, b. p. 98°/12 mm. (Found: I, 54.10. C_7H_6IF requires I, 53.73 per cent).

p-Fluorobenzyl iodide, b. p. 102-103°/9 mm. (Found : I, 54.76. C_7H_6IF requires I, 53.73 per cent).

These compounds on oxidation with potassium permanganate gave the corresponding fluorobenzoic acids.

m-Fluorobenzal Chloride.—Chlorine (2 mols.) was passed through *m*-fluorotoluene (10 c. c.) heated on a sand-bath and after 6 hours the product was extracted with carbon tetrachloride, washed, dried and distilled when one fraction at 170-85° and another at 185-200° were obtained. The former on redistillation gave *m*-fluorobenzyl chloride, b. p. 176°/756 mm. and the latter on repeated distillation gave *m*-fluorobenzal chloride, a colourless liquid with pronounced lachrymatory properties boiling at 195-97°/756 mm. (Found : Cl, 39.09. $C_7H_5Cl_2F$ requires Cl, 39.64 per cent).

m-Fluorobenzal Bromide.—It was obtained by adding bromine (1 mol.) to *m*-fluorobenzyl bromide or bromine (2 mols.) to *m*-fluorotoluene heated on a sand-bath and separated as before. Slightly brownish liquid, b. p. 108-10°/8 mm. was obtained. (Found : Br, 59.80. $C_7H_5Br_2F$ requires Br, 59.68 per cent).

o- and *m*-Fluorobenzyl Chlorobromides.—These compounds were prepared by adding bromine (1 mol.) to *o*- or *m*-fluorobenzyl chloride heated on a sand-bath or by passing a slow current of chlorine (1 mol.) through the corresponding bromides under the same conditions and the products isolated in the usual way.

o-Fluorobenzal Chlorobromide.—The fraction distilling at 100-20° was subjected to repeated distillation when brownish heavy liquid, b. p. 109-10°/7 mm. was obtained. (Found: total halogen, 51.76. C_7H_5BrClF requires total halogen, 51.65 per cent).

m-Fluorobenzalchlorobromide.—The fraction at 105-25° on repeated distillation gave a pure product, boiling at 111-13°/9 mm. It boils at 228-30°/756 mm. with slight decomposition. (Found : total halogen, 51.05. C_7H_5BrClF requires total halogen, 51.65 per cent).