

359. Preparation of Some Fluoronitro- and Amino-fluoro-benzoic Acids, and of Fluoronitro-benzenes, -toluenes, and -xylenes.

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Fluoronitrotoluenes containing the fluoro- and nitro-substituents in *meta*-relation to each other are oxidised by 15% nitric acid at 180—200°/ >1 atm. to the corresponding fluoronitro-benzoic acids. Thermal decomposition of diazonium fluoroborates containing nitro-substituents is best effected in an inert solvent.

NITRATION of fluorobenzoic acids¹ gives a mixture of isomers which is difficult to separate. Oxidation by nitric acid at elevated temperature and pressure has been proved a specific method for preparation of fluoro-mono- and -di-carboxylic acids from fluorotoluenes² and fluoroxylenes.³ We have applied this method to fluoronitrotoluenes.⁴

Fluoronitrotoluenes, when heated in an autoclave with 15—20% nitric acid, are oxidised at 150—160°, as the increase of pressure indicates, and care must be taken to control the temperature for the exothermic reaction. The products, however, are carboxylic acids only when the nitro- and fluoro-substituents are in *meta*-relation to one another. 4-Fluoro-2- and 2-fluoro-4-nitrotoluene were thus oxidised at 180—190° by 15% nitric acid to the corresponding pure benzoic acids. With most of the isomers oxidation was followed by hydrolysis to hydroxynitrobenzoic acids, but 3-fluoro-4-nitrotoluene gave a mixture of polynitrocresols and polynitrophenols and no carboxylic acid. 2-Fluoro-5-nitro-*p*-xylene gave a mixture of fluorine-free hydroxynitro-terephthalic and -toluic acids. 2-Fluoro-6-nitrotoluene with concentrated nitric acid at 100° has been reported⁵ to yield some 2-fluoro-6-nitrobenzoic acid.

In this way 4-fluoro-2- and 2-fluoro-4-nitrobenzoic acid were obtained in yields of 70—80%. They have been prepared previously in 19—26% yield by permanganate oxidation of the corresponding fluoronitrotoluenes.⁶ The amino-acids were obtained by boiling the fluoronitrobenzoic acids with ferrous sulphate in concentrated aqueous ammonia.⁶

Attempts to prepare some fluoronitro-toluenes and -xylenes by thermal decomposition of the diazonium fluoroborates gave low yields. Yields of 28—40% reported⁷ are unsatisfactory when compared with 70—90% in Schiemann reactions in the absence of nitro-groups. Modifications such as dilution of the fluoroborates with sand and decomposition in small portions⁶ were not useful. The thermal decomposition was also

¹ Slothouwer, *Rec. Trav. chim.*, 1914, **33**, 337; Goldstein and Urvater, *Helv. Chim. Acta*, 1951, **34**, 1350.

² Hopff and Valkanas, *J. Org. Chem.*, 1962, **27**, 2923.

³ Valkanas and Hopff, unpublished work.

⁴ Schiemann, *Chem. Ber.*, 1929, **62**, 1799.

⁵ Van Loon and Meyer, *Chem. Ber.*, 1896, **29**, 841.

⁶ Schmelkes and Rubin, *J. Amer. Chem. Soc.*, 1944, **66**, 1632; Volkani, Sicher, Bergmann, and Bendas, *J. Biol. Chem.*, 1954, **207**, 411; Adlerová *et al.*, *Czech. Chem. Comm.*, 1960, **25**, 784.

⁷ Roe, *Org. Reactions*, 1949, **5**, 193.

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tried as a modified Gattermann reaction.⁸ Bergmann *et al.*,⁸ reported that, when an acetone or aqueous acetone solution of a fluoroborate was treated with copper powder or better with cuprous chloride, 60–90% of the fluorocarbon was obtained. We found that nitro-groups promoted deamination: decomposition of 3-nitrotoluene-4-diazonium fluoroborate gave almost 100% of fluorine-free product. Barben and Suschitzky⁹ have reported that carboxyl groups similarly accelerate deamination and, when working with cuprous chloride, also observed a chlorine substitution.

Nitro-diazonium fluoroborates decompose smoothly when heated in suspension in an inert solvent,¹⁰ such as chlorobenzene. Yields are better when the salt is added in small portions to the solvent which is stirred at a temperature a little higher than the decomposition temperature. Under these conditions no deamination occurs, and no hydroxy-derivatives, the usual by-products of the Schiemann reaction, are formed. The fluoramines were easily prepared by boiling the aromatic fluoronitro-hydrocarbon in 0.1N-ammonium chloride containing powdered iron, this method being particularly satisfactory for multisubstituted aromatic derivatives.

EXPERIMENTAL

4-Fluoro-2-nitrobenzoic Acid.—4-Fluoro-2-nitrotoluene (15 g.) and 15% nitric acid (82 ml.) were heated in a glass vessel in a 500-ml. autoclave during 1.5 hr. to 180–190°. Heating was continued at that temperature for 4 hr. On cooling, 4-fluoro-2-nitrobenzoic acid separated. It was filtered off and washed with cold water until the washings were colourless, and then dried (yield, 12.3 g., 69%). Recrystallisation from 1:1 v/v water-methanol gave acid of m. p. 140–141° (Found: C, 45.35; H, 2.1; F, 10.3. Calc. for C₇H₄FNO₄: C, 45.4; H, 2.2; F, 10.3%).

2-Amino-4-fluorobenzoic Acid.—4-Fluoro-2-nitrobenzoic acid (10 g.) was boiled for 3 hr. with aqueous ammonia (*d* 0.88; 100 ml.) and ferrous sulphate (80 g.) in water (300 ml.). The mixture was filtered hot and evaporated to 40 ml., then diluted with water and acidified with acetic acid to give the grey 2-amino-4-fluorobenzoic acid (5.2 g., 62%), m. p. 190–191° (Found: C, 54.05; H, 3.9; N, 9.0; F, 12.3, 12.3. C₇H₆FNO₂ requires C, 54.2; H, 3.9; N, 9.0; F, 12.25%).

2-Fluoro-4-nitrobenzoic Acid.—By reaction as above, 2-fluoro-4-nitrotoluene (15 g.) gave the acid (14 g., 78%) which, recrystallised as above, had m. p. 166–167° (Found: C, 45.3; H, 2.2; N, 7.55; F, 10.15. Calc. for C₇H₄FNO₄: C, 45.4; H, 2.2; N, 7.6; F, 10.3%).

4-Amino-2-fluorobenzoic Acid.—As in the preceding case, 2-fluoro-4-nitrobenzoic acid (10 g.) gave 4-amino-2-fluorobenzoic acid (5.27 g., 63%), m. p. 209–210° (from water) (Found: N, 9.05; F, 12.25%).

4-Fluoro-2-nitrotoluene.—3-Nitro-*p*-toluidine (100 g.) was diazotised in concentrated hydrochloric acid (200 ml.) by sodium nitrite (45 g.) in water (100 ml.) at –5° to 0°. Addition of 40% fluoroboric acid (150 ml.) gave a heavy precipitate which was filtered off, washed with water, and dried (yield, 127 g., 72%; decomp. 131–132°). This fluoroborate was added in small portions to boiling chlorobenzene (500 ml.) with stirring during 1 hr. The resulting black solution was boiled for 15 min. with carbon, filtered hot, and distilled, and by fractionation of the high-boiling residue 4-fluoro-2-nitrotoluene was obtained as a yellow liquid at 89–90°/14 mm. (53 g., 51%) (Found: F, 12.3. C₇H₆FNO₂ requires F, 12.3%).

The diazonium fluoroborates and aryl fluorides listed in the Table were prepared similarly. Satisfactory analyses were obtained for the fluorides.

5-Fluoro-*o*-toluidine.—4-Fluoro-2-nitrotoluene (20 g.) was suspended, with stirring, in 0.1N-ammonium chloride (500 ml.) and powdered iron (50 g.) was added. The whole was boiled for 5 hr., then steam-distilled. The distillate was extracted with ether and fractionated, to yield 13 g. (81%), of 5-fluoro-*o*-toluidine, b. p. 82–83°/14 mm. (Found: N, 11.2. C₇H₈FN requires N, 11.2%).

⁸ Bergmann, Berkovic, and Ikan, *J. Amer. Chem. Soc.*, 1956, **78**, 6037.

⁹ Barben and Suschitzky, *Chem. and Ind.*, 1957, 1039.

¹⁰ Britton and Keil, U.S.P. 2,854,479; *Chem. Abs.*, 1959, **53**, 7095; French P. 1,250,130.

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Diazonium fluoroborates.

Base (NH ₂ = 1)	Yield (%)	Decomp.
4-Nitro- <i>o</i> -toluidine	79	118—119°
3-Nitro <i>p</i> -toluidine	75	131—132
5-Nitro- <i>o</i> -toluidine	81	128—129
4-Nitro-3,5-xylydine	74	121—122

Fluorides.

Compound	Yield (%) *	B. p./14 mm.
2-Fluoro-5-nitrotoluene	68	103—104°
4-Fluoro-2-nitrotoluene	51	89—90
2-Fluoro-4-nitrotoluene	66	99—100
5-Fluoro-2-nitro-1,3-xylene	61	(m. p. 51—52°)

* Calc. on the amine used.

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[Received, June 13th, 1962.]