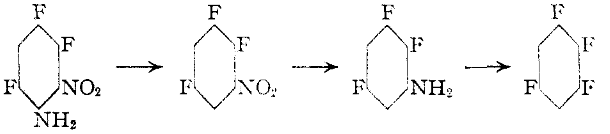
[CONTRIBUTION FROM THE GEOCHEMICAL SECTION OF THE ILLINOIS STATE GEOLOGICAL SURVEY]

# Aromatic Fluorine Compounds. IV. 1,2,3,5-Tetrafluorobenzene[1]

BY G. C. FINGER, F. H. REED AND R. E. OESTERLING

As a result of the availability of 3-nitro-4-amino-1,2,5-trifluorobenzene[2] in this Laboratory, the synthesis of 1,2,3,5-tetrafluorobenzene has been accomplished, and a study made of some of its properties and derivatives.

The first step in the synthesis involved the deamination of 3-nitro-4-amino-1,2,5-trifluorobenzene (I) to 3-nitro-1,2,5-trifluorobenzene (II). Since I is a weakly basic amine, it was diazotized by the nitrosylsulfuric phosphoric acid procedure.[3,4] Reduction of the diazonium salt by the usual hypophosphorous acid method[5] was unsuccessful until it was discovered that cuprous oxide catalyzed the reaction to give a 60–70% yield of 3-nitro-1,2,5-trifluorobenzene. The catalyst not only changed failure to success, but also effected the reduction in minutes rather than hours as is usually the case. The reductive power of the hypophosphorous acid–cuprous oxide combination was reflected also in the formation of some 3-amino-1,2,5-trifluorobenzene (III) as a secondary reduction product. This catalyst was used effectively in another instance which will appear in a later publication. In spite of the general application of cuprous oxide in ethanol deaminations, it is only recently that this catalyst had been used in the hypophosphorous acid method by Kornblum and co-workers.[6]



I II III IV

An iron reduction of II readily gave a 90% yield of 3-amino-1,2,5-trifluorobenzene (III), and a subsequent diazotization–Schiemann transformation gave a 40% yield of 1,2,3,5-tetrafluorobenzene (IV).

1,2,3,5-Tetrafluorobenzene in contrast to the 1,2,4,5-isomer[2] boils lower, 83° *versus* 87°, and can be converted readily to a nitro derivative, 4-nitro-1,2,3,5-tetrafluorobenzene. An iron reduction of the nitro compound gave 4-amino-1,2,3,5-tetrafluorobenzene.

## Experimental[7,8]

**3-Nitro-1,2,5-trifluorobenzene** (II).—Approximately 96 g. of 3-nitro-4-amino-1,2,5-trifluorobenzene[2] was dissolved in 250 cc. of concd. sulfuric acid with stirring. The clear orange solution was allowed to stand 2–3 hours to come to room temperature. A prolonged time interval appears to be necessary to complete the formation of the amine hydrosulfate, otherwise diazotization will be quite unsatisfactory. Nitrosylsulfuric acid solution was prepared by adding 40 g. of sodium nitrite to 200 g. of concd. sulfuric acid (precooled to 0°) with stirring, and then cooled to 20°. The amine salt was diazotized at 0° with vigorous stirring by adding the nitrosylsulfuric acid followed by the dropwise addition of 450 cc. of sirupy phosphoric acid (85%). Stirring was continued for thirty minutes at 0–10°.

To the diazonium solution, a slurry of 71 g. of cuprous oxide, 169 g. of sodium hypophosphite and 200 cc. of water was added at such a rate as to control the foaming due to nitrogen evolution. In order to minimize the formation of amine (III) from the nitro (II) compound by a secondary reaction, the exothermic reaction was kept below 50°. After completion of the reaction, within five minutes after the slurry had been added, the reaction mixture was diluted with an equal volume of water and immediately steam distilled. The crude nitro distillate, contaminated with amine, gave a yield of 55–61 g. or 62–67%. An ether extraction of the aqueous distillate increased the yield by 10–15%. Vacuum distillation gave pure 3-nitro-1,2,5-trifluorobenzene, f.p. *ca.* −20°, b.p. 187° (micro cap.), $n^{20}_D$ 1.4873.

*Anal.* Calcd. for $C_6H_2O_2NF_3$: C, 40.69; H, 1.14; N, 7.91. Found: C, 40.71; H, 1.38; N, 8.10.

**3-Amino-1,2,5-trifluorobenzene** (III).—This compound was prepared by the usual reduction with iron filings in ammonium chloride solution (0.78 *N*)[9] and the amine was removed by steam distillation. Vacuum distillation gave a yield of 95–100 g. or 89–92% of pure 3-amino-1,2,5-trifluorobenzene as a colorless liquid, b.p. 76° (20 mm.), $n^{20}_D$ 1.4899.

*Anal.* Calcd. for $C_6H_4NF_3$: C, 48.99; H, 2.74; N, 9.52. Found: C, 49.08; H, 2.49; N, 9.69.

The acetyl derivative was recrystallized from ether as white granular crystals, m.p. 120–121°.

*Anal.* Calcd. for $C_8H_6ONF_3$: N, 7.41. Found: N, 7.69.

**1,2,3,5-Tetrafluorobenzene** (IV).—To 20 cc. of concd. hydrochloric acid in 10 cc. of water, 14.7 g. of 3-amino-1,2,5-trifluorobenzene was added slowly with rapid stirring, and the amine hydrochloride was formed as a very insoluble salt.

In order to avoid undesirable side reactions and a low yield, diazotization and diazonium fluoborate precipitation were effected concurrently. To a solution of 20 cc. of concd. hydrochloric acid in 10 cc. of water, there were added, simultaneously but separately, three reactants, (1) the amine hydrochloride slurry, (2) 7.6 g. of sodium nitrite in 10 cc. of water, and (3) 40 g. of sodium fluoborate in 60 cc. of water. The additions required 30 minutes, and the reaction temperature was maintained at 0°. Stirring was continued for one hour at 0–10°. The diazonium fluoborate was removed by filtration at −10°, dried and a yield of 22 g. or 89% was obtained. Thermal decomposition of the salt and a subsequent steam distillation gave the crude tetrafluorobenzene, yield 6.5 g. or 43% based on the amine. 1,2,3,5-Tetrafluorobenzene is a colorless liquid with a faint sweet odor, f.p. *ca.* −48°, b.p. 83°, $d^{20}_4$ 1.393, $n^{20}_D$ 1.40381, $\gamma^{20}$ 23.99.

*Anal.* Calcd. for $C_6H_2F_4$: C, 48.01; H, 1.35; F, 50.64. Found: C, 48.21; H, 1.43; F, 50.43.

---

(1) Presented before the Organic Division at the 117th Meeting of the American Chemical Society, Philadelphia, Pa., April, 1950. The authors wish to acknowledge the financial assistance of the Office of Naval Research provided by coöperative research contract N6ori-71; Task XIV. Published with the permission of the Chief of the Illinois State Geological Survey.

(2) Finger, Reed, Burness, Fort and Blough, THIS JOURNAL, **73**, 145 (1951).

(3) Schoutissen, *ibid.*, **55**, 4531 (1933).

(4) C. Weygand, "Organic Preparations," Interscience Publishers, Inc., New York, N. Y., 1945, Ch. 2, p. 110.

(5) "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1944, Vol. II, Ch. 7, p. 277.

(6) Kornblum and Cooper, Abstracts of the 116th Meeting, American Chemical Society, Atlantic City, N. J., Sept. 1949, p. 50M

(7) Analyses by Mr. H. S. Clark, microanalyst for the Illinois Geological Survey.

(8) All melting and boiling points are uncorrected, and freezing points were determined with a toluene thermometer.

(9) Finger and Reed, THIS JOURNAL, **66**, 1972 (1944).

**3-Chloro-1,2,5-trifluorobenzene.**—This compound was obtained as a by-product from IV. It is a colorless liquid, b.p. 121° (micro cap.), $n^{20}\mathrm{D}$ 1.4550.

*Anal.* Calcd. for $C_6H_2ClF_3$: C, 43.27; H, 1.21. Found: C, 43.57; H, 1.24.

**4-Nitro-1,2,3,5-tetrafluorobenzene.**—To a mixture of 25 g. of 1,2,3,5-tetrafluorobenzene and 30 cc. of concd. sulfuric acid, a solution of 12 cc. of concd. nitric acid in 10 cc. of concd. sulfuric acid was added at 0–10°, followed by stirring, for two hours at 10°. The yield of crude steam distilled nitro compound was 23 g. or 72%. Vacuum distilatlion gave pure 4-nitro-1,2,3,5-tetrafluorobenzene, b.p. 78.5° (20 mm.), $n^{20}\mathrm{D}$ 1.46507, f.p. *ca.* −5°.

*Anal.* Calcd. for $C_6HO_2NF_4$: C, 36.94; H, 0.52; N, 7.18. Found: C, 37.17; H, 0.65; N, 7.24.

**4-Amino-1,2,3,5-tetrafluorobenzene.**—This amine was obtained from the preceding nitro compound by the usual iron reduction[9] in an 86% crude yield. It is a steam distillable liquid, b.p. 65° (20 mm.), $n^{20}\mathrm{D}$ 1.46228.

*Anal.* Calcd. for $C_6H_3NF_4$: C, 43.65; H, 1.83; N, 8.49. Found: C, 43.65; H, 1.79; N, 8.35.

The acetyl derivative was obtained as white, granular crystals from ethanol, m.p. 140–141°.

*Anal.* Calcd. for $C_8H_5ONF_4$: N, 6.76. Found: N, 6.78.

## Summary

The preparation of 1,2,3,5-tetrafluorobenzene and some of its intermediates is described.

Cuprous oxide as a catalyst was used to advantage in the hypophosphorous acid deamination method.

URBANA, ILLINOIS RECEIVED JUNE 9, 1950

---

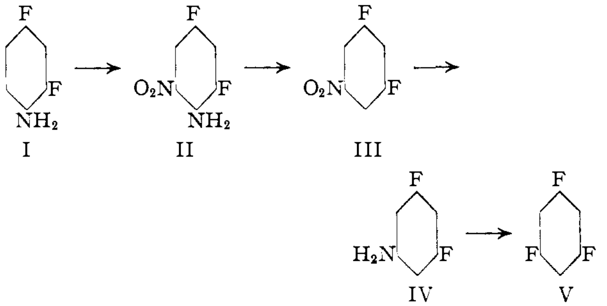
[CONTRIBUTION FROM THE GEOCHEMICAL SECTION OF THE ILLINOIS STATE GEOLOGICAL SURVEY]

# Aromatic Fluorine Compounds. V. 1,3,5-Trifluorobenzene[1]

BY G. C. FINGER, F. H. REED AND J. L. FINNERTY

Among the polyfluorobenzenes there has been considerable speculation as to the probable physical and chemical properties of symmetrical trifluorobenzene. This compound has now been synthesized and some of its properties and derivatives have been studied.

The nitration of the acetyl derivative of 4-amino-1,3-difluorobenzene (I) gave 4-amino-5-nitro-1,3-difluorobenzene (II). Reduction of the nitroamine to the diamine, followed by the formation of 2,3-diphenyl-5,7-difluoroquinoxaline proved the adjacency of the nitro and amine groups. A modified hypophosphorous acid deamination procedure[2] gave an average yield of 50% of 5-nitro-1,3-difluorobenzene (III), and a subsequent iron reduction gave 5-amino-1,3-difluorobenzene (IV).



A diazotization–Schiemann transformation on the amine gave a 60% yield of 1,3,5-trifluorobenzene (V).

The boiling point of 1,3,5-trifluorobenzene is 75.5°, thus making it the only fluorinated benzene boiling lower than benzene, 80°. It is odorless, whereas its isomer 1,2,4-trifluorobenzene, and the next higher homolog, 1,2,4,5-tetrafluorobenzene have a faint, sweet odor.

Chlorination and bromination gave the mono, di and trihalo derivatives. The trichloro derivative was identical with 2,4,6-trichloro-1,3,5-trifluorobenzene obtained by the chlorinolysis of trifluoromesitylene.[3]

Symmetrical trifluorobenzene was readily nitrated to 2-nitro-1,3,5-trifluorobenzene, and an iron reduction gave the corresponding 2-amino-1,3,5-trifluorobenzene. The amine reacted readily with hydrochloric or sulfuric acids to form the amine salts. The hydrosulfate salt was surprisingly soluble.

Nitration of the acetyl derivative of IV gave 4-nitro-5-amino-1,3-difluorobenzene; the nitro group entered an ortho position to the amino rather than the expected para. The structure of the nitroamine was proven by deamination to the known 4-nitro-1,3-difluorobenzene.

## Experimental[4,5]

**4-Amino-5-nitro-1,3-difluorobenzene (II).**—In a mixture of 400 cc. of concd. sulfuric acid and 140 cc. of acetic acid, 340 g. of 4-acetylamino-1,3-difluorobenzene[6,7] was dissolved with stirring. After cooling to 20°, a mixture containing equal volumes (140 cc. each) of concd. nitric and sulfuric acids was added in fifteen minutes, and the temperature allowed to rise to 40°. Stirring was continued for 90 minutes at 40–50°. The reaction mixture was poured over ice, and the crude nitroacetylamino compound after drying weighed 400 g. The crude product was hydrolyzed to the nitroamine in 350 cc. of concd. sulfuric acid by heating for two hours on a steam-bath, and then poured over ice. The yield of dry crude product was 228 g. or 65%. The nitroamine is steam distillable, but the purest product was obtained by recrystallization from ethanol followed by sublimation. No tangible evidence was obtained for the existence of other nitroamine isomers. Pure 4-amino-5-nitro-1,3-difluorobenzene is a yellow solid, m.p. 85.5–86.5°.

*Anal.* Calcd. for $C_6H_4O_2N_2F_2$: C, 41.39; H, 2.31; N, 16.08. Found: C, 41.48; H, 2.14; N, 15.91.

The acetyl derivative was recrystallized as cream colored

---

[1] Presented before the Organic Division at the 117th Meeting of the American Chemical Society, Philadelphia, Pennsylvania, April 1950. The authors wish to acknowledge the financial assistance of the Office of Naval Research provided by coöperative research Contract N6ori-71: Task XIV. Published with the permission of the Chief of the Illinois State Geological Survey.

[2] Finger, Reed and Oesterling, THIS JOURNAL, **73**, 152 (1951).

[3] Finger, Reed, Maynert and Weiner, *ibid.*, **73**, 149 (1951).

[4] Analyses, densities and surface tension measurements by H. S. Clark, microanalyst for the Illinois Geological Survey.

[5] Melting and boiling points are uncorrected, and the freezing points were determined with a toluene thermometer.

[6] Swarts, *Rec. trav. chim.*, **35**, 154 (1915).

[7] Schiemann, *J. prakt. Chem.*, **140**, 97 (1934).