stant r in Goldschmidt's equation is independent either of the nature of the organic acid or of its concentration. It is also demonstrated that, in agreement with esterification studies made with 0.5 N acid concentrations, the activation energy is constant throughout the normal series, having a value of 10,000 cal./mole.

Bethlehem, Penna. Received September 13, 1940

[Contribution from the Department of Chemistry of the Pennsylvania State College]

Hydrogen Fluoride as a Condensing Agent. XIII. Sulfonation[1]

By J. H. Simons, H. J. Passino and S. Archer

The use of hydrogen fluoride to promote a condensation between carboxylic acids and hydrocarbons[2] and also its use to rearrange *p*-cresyl benzenesulfonate to 2 hydroxy-5-methyl diphenyl sulfone[3] indicate that this reagent would be useful in reactions for the preparation of sulfonic acids and sulfones.

It was found that a mixture of hydrogen fluoride and sulfuric acid would react with an aromatic compound to form either the sulfonic acid or the symmetrical sulfone depending on the temperature. The sulfone was formed at higher temperatures. Unsymmetrical sulfones were formed by the treatment of either a sulfonic acid or sulfonyl chloride with an aromatic compound in the presence of hydrogen fluoride. It is believed that sulfuric acid reacts with hydrogen fluoride to form fluorosulfonic acid and water,[4] and fluorosulfonic acid is an effective sulfonating agent.[5] We have found it more reactive than chlorosulfonic acid. It reacts with chloroform but not carbon tetrachloride at room temperature and it also reacts with normal pentane at room temperature.

Experiments using hydrogen fluoride as an aid in nitration were also investigated. It was found that benzene in the presence of hydrogen fluoride was rapidly nitrated by nitric acid at 0° but that nitrobenzene did not nitrate at this temperature. Patents[6] have indicated the use of potassium nitrate to nitrate benzene and phenol in the presence of hydrogen fluoride.

Experimental

Benzene and Sulfuric Acid.—A mixture of 75 g. of hydrogen fluoride, 25 g. of sulfuric acid, and 100 cc. of benzene was heated for sixteen hours at 85 to 95° in a copper bomb. Less than 1 g. of diphenyl sulfone was formed but a yield of 75% of benzene sulfonic acid was obtained as the calcium salt. This was analyzed for calcium: found 11.2% calculated 11.3%.

A mixture of 9.8 g. of sulfuric acid, 118 g. of hydrogen fluoride, and 110 g. of benzene was heated in a bomb for eighteen hours at 140–150°. From the reaction products 8.9 g. of diphenyl sulfone melting at 127–128° was obtained. This represented a yield of 40%. A dinitro derivative[7] was prepared which after one recrystallization melted at 196–197°.

Benzene and Fluorosulfonic Acid.—A mixture of 25 g. of fluorosulfonic acid and 88 g. of benzene was heated at 160° for sixteen hours. A yield of 14% of diphenyl sulfone, melting at 127–128°, was obtained. It was identified by the melting point, 195.5–196.5°, of its dinitro derivative.

At 60–70° a mixture of benzene and fluorosulfonic acid gave a 53% yield of benzene sulfonic acid.

***p*-Toluene Sulfonic Acid and Benzene.**—A mixture of 20 g. of the acid, 70 g. of hydrogen fluoride, and 250 cc. of benzene was heated at 85–95° for twenty-four hours. From the reaction mixture 2 g. of *p*-tolyl phenyl sulfone was obtained. It melted at 119–122°.

Benzenesulfonyl Chloride and Toluene.—A mixture of 17 g. benzenesulfonyl chloride, 200 cc. of toluene, and 200 g. of hydrogen fluoride was first allowed to stand for twenty-four hours at 0° and then heated for twenty-four hours at 85–95°. A small amount of *p*-tolyl phenyl sulfone, m. p. 120–122°, was obtained.

Benzene and Nitric Acid.—A mixture of 44 g. of benzene and 47 g. of hydrogen fluoride was placed in a copper vessel which was coated on the inside with a high melting wax. This was placed in a salt–ice mixture and one-eighth mole of nitric acid was added with stirring in a fifteen-minute period. An 83% yield of nitrobenzene was obtained. No dinitrobenzene nor fluorobenzene was detected. A portion of the nitrobenzene was further nitrated to give *m*-dinitrobenzene, m. p. 89–90°. A similar experiment using nitrobenzene instead of benzene failed to produce any detectable amount of dinitrobenzene.

Summary

Hydrogen fluoride has been shown to be effective in promoting sulfonation and nitration. Benzene sulfonic acid and diphenyl sulfone were

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[1] For the previous paper of this series see Simons and Passino, This Journal, **62**, 1624 (1940).

[2] Simons, Randall and Archer, *ibid.*, **61**, 1795 (1939).

[3] Simons, Archer and Randall, *ibid.*, **62**, 485 (1940).

[4] Simons, *Chem. Rev.*, **8**, 213 (1931).

[5] Meyer and Schramm, *Z. anorg. allgem. Chem.*, **206**, 24 (1932).

[6] Fredenhagen, German Patent 529,538, Aug. 2, 1930; Gleich, Russian Patent 39,775, Nov. 30, 1934.

[7] Buehler and Masters, *J. Org. Chem.*, **4**, 262 (1939).

made from benzene both with a mixture of hydrogen fluoride and sulfuric acid and with fluorosulfonic acid. *p*-Tolyl phenyl sulfone was made both from benzenesulfonyl chloride and toluene and *p*-toluenesulfonic acid and benzene by the action of hydrogen fluoride. Benzene was nitrated at a temperature below 0° by nitric acid aided with hydrogen fluoride.

STATE COLLEGE, PENNSYLVANIA

RECEIVED DECEMBER 19, 1940

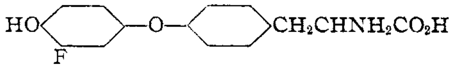
[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 800]

The Synthesis of 3′-Fluoro-*dl*-thyronine and Some of its Iodinated Derivatives

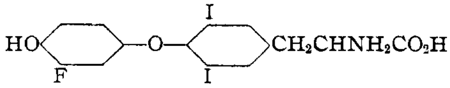
BY CARL NIEMANN, JAMES F. MEAD AND ANDREW A. BENSON

In continuation of our investigations upon the halogenated tyrosines and thyronines,[1,2] we now wish to report the synthesis of 3′-fluoro-*dl*-thyronine (I), 3′-fluoro-3,5-diiodo-*dl*-thyronine (II), and 3′-fluoro-5′-iodo-3,5-diiodo-*dl*-thyronine (III).

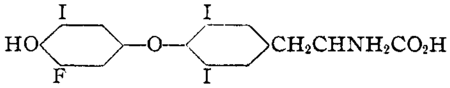
I



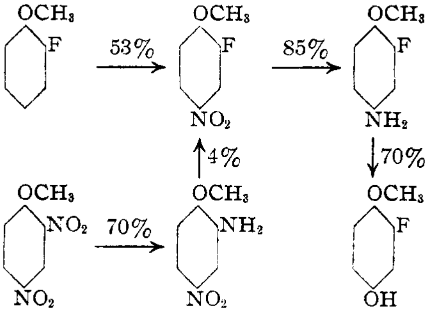
II



III



The synthesis of these three compounds demanded as an intermediate 3-fluoro-4-methoxyphenol which was prepared by the following series of reactions



This phenol was condensed with triiodonitrobenzene and the resulting substituted diphenyl ether was converted into 3′-fluoro-3,5-diiodo-*dl*-thyronine (II) by following the general procedure used by Harington and Barger[3] for the synthesis of 3,5-diiodo-*dl*-thyronine. Partial dehalogenation of 3′-fluoro-3,5-diiodo-*dl*-thyronine (II) gave 3′-fluoro-*dl*-thyronine (I); 3′-fluoro-5′-iodo-3,5-diiodo-*dl*-thyronine (III) was obtained by the direct iodination of 3′-fluoro-3,5-diiodo-*dl*-thyronine (II). The authors wish to express their indebtedness to Messrs. H. Lanz, Jr., and G. A. Swinehart for the microanalyses reported in this paper.

Experimental

2-Amino-4-nitroanisole.[4]—To a mechanically stirred suspension of 189 g. of 2,4-dinitroanisole[5] in one l. of water, maintained at 80–85°, was added, in the course of twenty minutes, 389 g. of sodium sulfide and 141 g. of sodium bicarbonate dissolved in 2.9 l. of water. After forty minutes the reaction mixture was cooled, the solid recovered and dissolved in dilute hydrochloric acid. The addition of ammonium hydroxide to this solution gave 70–80% of crude 2-amino-4-nitroanisole, m. p. 107–111°. Upon repeated recrystallization from aqueous methanol the m. p. was raised to the maximum value of 117–118°.

2-Fluoro-4-nitroanisole.[1,6]—(A) Diazotization of crude 2-amino-4-nitroanisole, m. p. 111°, and precipitation of the diazonium fluoborate as described by Schiemann and Miau[6a] gave 70–75% of the diazonium fluoborate. This salt was mixed with two volumes of fine sand and decomposed by dry distillation at 30 mm. pressure. The distillate was taken up in ether, the ethereal phase washed with aqueous sodium carbonate solution and the crude fluoronitroanisole (10–14%, based on diazonium fluoborate), recovered from the ethereal extract, purified by steam distillation. Recrystallization of this product from a 1:1 methanol–ethanol mixture and finally from isopropyl ether gave pure 2-fluoro-4-nitroanisole, m. p. 104.0–104.5°. The over-all average yield from amine to pure fluoro compound was approximately 4%.

(B)[1,6] To a vigorously stirred solution of 250 g. of *o*-fluoroanisole[1] in 825 ml. of acetic anhydride was added, over a period of four hours, a solution of 87 ml. of nitric

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[1] J. English, Jr., J. F. Mead and C. Niemann, THIS JOURNAL, **62**, 350 (1940).

[2] This research is being conducted as a coöperative project with Professor Paul Phillips of the University of Wisconsin who has undertaken a pharmacological investigation of the compounds reported in this and a previous communication.[1]

[3] C. R. Harington and G. Barger, *Biochem. J.*, **21**, 169 (1927).

[4] I. I. Vorontzov, *J. Chem. Ind.* (Moscow), **7**, 2145 (1930).

[5] H. Vermeulen, *Rec. trav. chim.*, **25**, 12 (1906).

[6] (a) G. Schiemann and T. Miau, *Ber.*, **66**, 1179 (1933); (b) G. Schiemann, *J. prakt. Chem.*, **140**, 97 (1934); (c) E. L. Holmes and C. K. Ingold, *J. Chem. Soc.*, **129**, 1938 (1926); H. H. Hodgson and D. E. Nicholson, *ibid.*, 810 (1940).