

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

STUDIES IN THE DIPHENYL ETHER SERIES.
II. PREPARATION AND STRUCTURE OF SOME SULFONIC
ACIDS AND RELATED DERIVATIVES¹

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The sulfonation of diphenyl ether and its derivatives has been very little investigated. Hoffmeister² found that the action of concentrated sulfuric acid on diphenyl ether gave a disulfonic acid, but the positions occupied by the acid groups were not determined. The same acid³ had been made previously but was considered to be a derivative of diphenyl. It has recently been found⁴ that aminosulfonic acid sulfonates diphenyl ether to the ammonium 4-phenoxybenzenesulfonate. A number of sulfinic acids have been used as intermediates in the preparation of phenothioxin derivatives.⁵ Apparently no thiol substitution products have been previously investigated.

The structure of the disulfonic acid was determined by bromination of its barium salt in water solution, the bromo-monosulfonate first formed giving upon further bromination the 4,4'-dibromodiphenyl ether of known⁶ structure. Since this method of determining structures has been employed previously with sulfonic acids of certain aromatic hydrocarbons,⁷ phenols,⁸ and amines^{9,8b} without any inconsistencies becoming evident, the two sulfo groups occupy the 4,4'-positions.

The acid obtained by monosulfonation of diphenyl ether was found to give derivatives with properties which did not correspond to those reported by Quilico⁴ for the compound obtained by him. However, upon repetition of his work, the products obtained by the various sulfonation methods were found to be identical.

An attempt to prepare 4-hydroxydiphenyl ether by fusion of the sodium sulfonate with sodium hydroxide was unsuccessful, as the ether linkage is broken during the reaction.

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² Hoffmeister, *Ber.*, **3**, 747 (1870); *Ann.*, **159**, 191 (1871).

³ Fittig, *ibid.*, **125**, 330 (1863).

⁴ Quilico, *Atti accad. Lincei*, [6] **6**, 512 (1927).

⁵ Krishna, *J. Chem. Soc.*, **123**, 2782 (1923).

⁶ LeFèvre, Saunders and Turner *ibid.*, 1168 (1927).

⁷ Kelbe, *Ann.*, **210**, 49 (1881); *Ber.*, **15**, 39 (1882); Kelbe and Pathe, *ibid.*, **19**, 1546 (1886); Kelbe and Koschnitzky, *ibid.*, **19**, 1730 (1886); Kelbe and Stein, *ibid.*, **19**, 2137 (1886); Baur, *ibid.*, **27**, 1619 (1894).

⁸ (a) Datta, *THIS JOURNAL*, **41**, 2028 (1919); (b) Datta and Bhoumik, *ibid.*, **43**, 303 (1921); (c) Sakellarios, *Ber.*, **55**, 2846 (1922).

⁹ Limpricht, *Ann.*, **181**, 193 (1876); Blanksma, *Rec. trav. chim.*, **29**, 377 (1910); Sudborough and Lakhmalani, *J. Chem. Soc.*, **111**, 41 (1910).

Bromination of sodium 4-phenoxybenzenesulfonate might conceivably result either in replacement of the sulfo group or substitution in the second benzene ring. Actually the latter takes place to the apparent exclusion of the former, as no 4-bromodiphenyl ether was found. A small amount of 4,4'-dibromodiphenyl ether was formed due to the further reaction with bromine of the bromosulfonic acid which is the primary product. Since this acid is also formed by sulfonation of 4-bromodiphenyl ether, the position of the bromine is evident. Its sodium and ammonium salts are only slightly soluble in water, as little as 12 mg. of sodium or ammonium ion in 10 cc. of solution giving a heavy crystalline precipitate with 1 cc. of a one molar solution of the acid. As much as 50 mg. of potassium gave no precipitate under similar conditions.

The action of excess chlorosulfonic acid upon diphenyl ether gives the 4,4'-disulfonyl chloride. It is apparently not possible to make the monosulfonyl chloride in this way, further sulfonation always occurring. 4-Bromodiphenyl ether reacts to give the 4'-sulfonyl chloride under the proper conditions, an excess of chlorosulfonic acid or a temperature higher than 25 or 30° leading to further sulfonation. The structure of this sulfonyl chloride is indicated by its formation from 4-phenoxybenzenesulfonyl chloride by bromination.

The 4-phenoxybenzenesulfonic acid prepared by reduction of the corresponding sulfonyl chloride was found to be quite unstable and could not be obtained in the pure state. Titration of the freshly prepared acid required 80% of the theoretical amount of alkali, while in three days this had dropped to about 50% of that calculated. The decomposition products have not been investigated.

The 4-thioldiphenyl ether when first distilled was odorless but developed the smell of hydrogen sulfide in a few hours. This was due to the decomposition of a trace of some impurity present since after standing for six months the evolution of hydrogen sulfide had ceased and the product had practically the same melting point as at first. A water solution of its sodium salt is rapidly oxidized by the oxygen of the air, crystals of the disulfide being deposited. This is also formed by oxidation of an alcohol solution of the thiol with iodine.

The sulfur analyses were made with a Parr bomb, and nitrogen was determined by the Kjeldahl method. All temperatures are corrected unless otherwise specified.

Experimental

Bromination of Barium Phenoxybenzene-4,4'-disulfonate.—To a solution of 11.8 g. (0.025 mole) of the salt 2 in 1 liter of water at 50° was added with stirring 4 g. (0.025 mole) of bromine. When the color of the bromine had disappeared, the precipitate which contained the sulfonic acid and sulfuric acid as a mixed salt was filtered off and treated with two 500-cc. portions of 0.5 normal sodium carbonate solution. The com-

bined filtrates upon cooling deposited the slightly soluble sodium 4-bromophenoxybenzene-4'-sulfonate as thin colorless plates. The yield was 5 g., which is 57% of the theoretical.

Anal. Calcd. for $C_{12}H_8BrO_4SNa$: S, 9.12. Found: S, 8.92, 8.90.

The *p*-toluidine salt was obtained as small colorless plates melting at 245–247°.

Anal. Calcd. for $C_{13}H_{13}BrNO_3S$: N, 3.21. Found: N, 3.06, 3.02.

Bromination of Sodium 4-Bromophenoxybenzene-4'-sulfonate.—A bromination similar to the above gave an 84% yield of 4,4'-dibromodiphenyl ether which melted at 55–56°. By recrystallizing from petroleum ether, it was obtained as large colorless needles melting at 59–60°. The value reported in the literature⁶ is 60.5°.

Monosulfonation of Diphenyl Ether.—This was carried out in various ways. Sulfonation in acetic acid solution with chlorosulfonic acid or in acetic anhydride with concentrated sulfuric acid was found to be better than the direct action of concentrated sulfuric acid without a solvent because this latter method gives considerable quantities of the disulfonic acid. This occurs because the monosulfonic acid first formed is soluble in concentrated sulfuric acid and is further sulfonated before the almost insoluble diphenyl ether has all reacted.

To a mixture of 170 g. (1 mole) of diphenyl ether and 100 cc. of acetic anhydride was added gradually with shaking 69 cc. (1.2 mole) of 95% sulfuric acid. After an hour on the steam-bath, the solution was poured into 1 liter of ice water. The unchanged ether (27 g.) was filtered off and the sodium sulfonate precipitated by adding 80 g. of sodium hydroxide in 250 cc. of water. There was obtained 212 g. of the dry salt, which is 93% of the theoretical based upon the diphenyl ether actually used. This product has the same characteristics as that obtained by Quilico⁴ from his sulfonation product. The *p*-toluidine salt was obtained from dilute methanol as colorless needles melting at 221–222°.

Anal. Calcd. for $C_{13}H_{13}NO_4S$: N, 3.92. Found: N, 3.93, 3.87.

Bromination of Sodium 4-Phenoxybenzenesulfonate.—To a solution of 27 g. (0.1 mole) of the salt in 1 liter of water at 50° was added 16 g. (0.1 mole) of bromine. Separation of a precipitate began at once. After an hour the reaction mixture was heated to boiling to dissolve all water-soluble material and the solution decanted from a small amount of oil which solidified upon cooling. This, after crystallizing from petroleum ether, gave 5 g. of 4,4'-dibromodiphenyl ether. No monobromodiphenyl ether was found. Upon cooling the water solution, there separated 19.5 g. of sodium 4-bromophenoxybenzene-4'-sulfonate.

Fusion of Sodium 4-Phenoxybenzenesulfonate with Sodium Hydroxide.—This was carried out under different conditions, none of which gave an appreciable yield of 4-hydroxydiphenyl ether. A mixture of 27 g. of the sodium salt and 100 g. of sodium hydroxide was heated at 260° for fifteen minutes and then dissolved in water. There was recovered 10 g. of unchanged sodium salt and upon acidifying with hydrochloric acid a small amount of a flocculent precipitate separated. This was too small in quantity for examination. Phenol and sodium sulfite were present in considerable amounts in the solution. A similar fusion carried out at 300° gave no products insoluble in water when the reaction products were treated like the above.

4-Phenoxybenzenesulfonyl Chloride.—Heating a mixture of 181 g. (0.66 mole) of the sodium sulfonate with 70 g. (0.33 mole) of phosphorus pentachloride under reflux at 170–180° for ten hours gave 125 g. of an oil of which upon fractionation 95 g. or 54% of the theoretical amount boiled at 205–207° (uncorr.) under 12 mm. pressure. This solidified upon cooling and crystallized from petroleum ether as colorless needles melting at 45–46°. Treatment of the sodium salt of the acid obtained by Quilico's method in the same manner gave the same sulfonyl chloride, although he reports it to be an oil.

Anal. Calcd. for $C_{12}H_9ClO_2S$: S, 11.92. Found: S, 12.09.

The amide was made by treatment of the sulfonyl chloride with a mixture of ammonium hydroxide and alcohol. It was purified by crystallizing its sodium salt from water, redissolving in water and acidifying with acetic acid. It melted at 128–129°; previously⁴ reported, 88°.

Anal. Calcd. for $C_{12}H_{11}NO_2S$: N, 5.62. Found: N, 5.59, 5.79.

The anilide obtained from a mixture of the sulfonyl chloride with aniline and 10% sodium hydroxide solution melted at 86–88°.

Anal. Calcd. for $C_{13}H_{15}NO_2S$: N, 4.31. Found: N, 4.26.

Sulfonation of 4-Bromodiphenyl Ether. (a) **With Sulfuric Acid.**—A mixture of 25 g. (0.1 mole) of 4-bromodiphenyl ether and 11 cc. (0.2 mole) of 95% sulfuric acid was warmed on the steam-bath until it was homogeneous, poured into 400 cc. of water, and sodium hydroxide added to precipitate the sodium salt. There was obtained the theoretical yield of the 4'-sulfonate identical with that from bromination of the mono- and di-sulfonic acid salts. For precipitation tests with sodium, potassium, and ammonium ions, a reaction mixture similar to the above was diluted to 100 cc. with water and 1-cc. portions of this solution added to 10 cc. of the solution to be tested. As little as 12 mg. of sodium as sodium nitrate gave a precipitate within a few minutes, while 9 mg. gave a slight precipitate after standing for twelve hours; 10 mg. of ammonium also gave a slight precipitate after twelve hours; 100 mg. of potassium gave a precipitate within half an hour, 75 mg. after twelve hours, and 50 mg. gave no precipitate.

(b) **With Chlorosulfonic Acid.**—To 25 g. (0.1 mole) of 4-bromodiphenyl ether was added with shaking 15 cc. (0.22 mole) of chlorosulfonic acid. The thick oily mixture was poured into ice water and the solid acid chloride filtered off. The yield was 16 g. of product which crystallized from petroleum ether as plates melting at 81–82°. The water-soluble sulfonation products did not include the monosulfonic acid, as they gave no insoluble sodium salt.

The same sulfonyl chloride was obtained in 91% yield by bromination of 4-phenoxybenzenesulfonyl chloride in carbon tetrachloride solution.

Anal. Calcd. for $C_{12}H_8BrClO_2S$: S, 9.23. Found: S, 9.35.

The amide was obtained from dilute methanol as colorless plates melting at 131–132°.

Anal. Calcd. for $C_{12}H_{10}BrNO_2S$: N, 4.25. Found: N, 4.20.

The corresponding anilide after crystallizing from dilute methanol several times melted at 108–109°.

Anal. Calcd. for $C_{13}H_{12}BrNO_2S$: N, 3.47. Found: N, 3.52.

Phenoxybenzene-4,4'-disulfonyl Chloride.—To 85 g. (0.5 mole) of diphenyl ether was added with shaking 200 cc. of chlorosulfonic acid. After two hours the mixture was poured into 2 liters of water and the crude disulfonyl chloride filtered off. The yield was 160 g. or 88% of the theoretical of material which crystallized from petroleum (90–120°) as colorless needles melting at 128–129°.

Anal. Calcd. for $C_{12}H_8Cl_2O_2S_2$: S, 17.45. Found: S, 17.35.

The diamide crystallized from hot water, in which it is somewhat soluble, as shiny plates melting at 158–160°.

Anal. Calcd. for $C_{12}H_{12}N_2O_2S_2$: N, 8.53. Found: N, 8.56, 8.75.

4-Phenoxybenzenesulfonic Acid.—A mixture of 13.5 g. (0.05 mole) of the sulfonyl chloride, 6.5 g. (0.05 mole) of sodium sulfite, and 6 g. of sodium carbonate in 75 cc. of water was refluxed for half an hour to complete the reaction. The mixture was filtered to remove a small amount of water-insoluble material and the solution cooled. There

separated 9.8 g. of colorless needles of the sodium sulfinate. This was recrystallized once from hot water.

Anal. Calcd. for $C_{12}H_9O_3SNa$: Na, 8.97. Found: Na, 8.98, 8.97.

By acidifying the filtrate after removal of the sodium sulfinate, there was obtained a chalky white precipitate which was not the sulfinic acid. When heated, it darkened above 180° with no definite melting point. Titration with standard alkali gave an equivalent weight approximately twice that of the sulfinic acid. It is planned to investigate this and similar products further.

Adding acid to a water solution of the sodium sulfinate precipitated an oil which soon solidified. After drying for several hours, a sample of this was titrated with standard alkali.

Anal. Calcd. for $C_{12}H_{10}O_3S$: 0.5049 g. requires 21.8 cc. of 0.099 *N* NaOH. Found: 17.6 cc. After standing for three days in a desiccator, another sample was titrated. 0.1973 g. requires 8.43 cc. of 0.011 *N* NaOH. Found: 4.11 cc.

Another similar sample showed a drop in melting point from $100-101^\circ$ to $91-93^\circ$ in forty-eight hours. Because of this instability, further attempts to obtain the acid in a pure condition were not made.

4-Thioldiphenyl Ether.—To a mixture of 70 g. of concentrated sulfuric acid and 210 g. of crushed ice was added with stirring 27 g. (0.1 mole) of the sulfonyl chloride and then 35 g. of zinc dust, the temperature being kept below 0° . After standing for two hours, the mixture was refluxed for two and one-half hours, filtered from a little unchanged zinc, and extracted with benzene. The benzene was evaporated and the residue distilled under reduced pressure. The yield was 12 g. or 60% of the theoretical of a colorless oil boiling at $178-180^\circ$ at 20 mm., which solidified upon cooling and melted at $19-22^\circ$. The product thus obtained always gave a low sulfur analysis even after repeated distillation. Recrystallizing from petroleum ether by cooling the solution to -10° gave colorless plates of a pure product melting at $21-22^\circ$.

Anal. Calcd. for $C_{12}H_{10}OS$: S, 15.86. Found: S, 15.67.

A sample was also titrated in alcohol solution with standard sodium hydroxide using phenolphthalein as the indicator.

Anal. Calcd. for $C_{12}H_{10}OS$: 0.2132 g. requires 10.7 cc. of 0.099 *N* alkali. Found: 10.5 cc.

The disulfide was formed by oxidation of a water solution of the sodium salt of the thiol by air, or by treatment of an alcoholic solution of the thiol with iodine. It crystallized from methanol as colorless plates which melted at $47-48^\circ$.

Anal. Calcd. for $C_{24}H_{18}O_2S_2$: S, 15.95. Found: S, 15.90.

Summary

The sulfonation of diphenyl ether with both sulfuric acid and chlorosulfonic acid has been studied and the structures of the products formed have been determined by replacement of the sulfo groups with bromine. In all cases, sulfonation occurs in the para positions when these are unoccupied by other groups.

The sulfinic acid and thiol have been obtained by reduction of 4-phenoxybenzenesulfonyl chloride. The sulfinic acid was found to be very unstable.