[CONTRIBUTON FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CONNECTICUT]

Certain Arylsulfonyl Derivatives of Ethylenediamine[1]

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This paper deals with the preparation of the mono-, di- and tetrabenzenesulfonyl derivatives and the corresponding *p*-toluenesulfonyl derivatives of ethylenediamine. Our attempts to prepare the triarylsulfonyl derivatives have not been successful.

Moore, Boyle and Thorn[3] prepared N-*p*-toluenesulfonylethylenediamine (compound no. 2). More recently Peacock and Dutta[4] have prepared this compound by another method. Both of these syntheses are accomplished by three successive reactions, starting with ethylenediamine in the former method and with ethylenechlorohydrin in the latter. We have been able to prepare it directly from ethylenediamine in one step, thus effecting a notable simplification. Several attempts to extend this method to the preparation of the hitherto unknown N-benzenesulfonylethylenediamine (compound no. 1) have failed. It now seems probable that the failures were caused by the greater solubility in water of the benzenesulfonyl derivative. We finally obtained it in the form of its hydrochloride from monoacetylethylenediamine, which was prepared according to the method of Hill and Aspinall.[5] Before the publication of the paper of Hill and Aspinall we had made several unsuccessful attempts to prepare monoacetylethylenediamine by the method of Rosenmund[6] and by the method of Mignonac.[7]

The N,N′-diarylsulfonyl derivatives have long been known. Hinsberg and Strupler[8] prepared dibenzenesulfonylethylenediamine (compound no. 3) by warming a mixture of benzenesulfonamide, concentrated aqueous potassium hydroxide and ethylene dibromide. Although they were the first to describe this compound, Hinsberg[9] must have prepared it previously for he mentions the reaction of ethylenediamine with alkali and benzenesulfonyl chloride, a reaction later shown by Schneider[10] to yield this compound. Di-*p*-toluenesulfonylethylenediamine (compound no. 4) was mentioned but not described in 1891.[11] The first description was given by Howard and Marckwald[12] who prepared it by the method used by Hinsberg and Strupler[8] for the corresponding benzenesulfonyl derivative. Peacock and Dutta[4] have made it from N-*p*-toluenesulfonylethylenediamine.

Neither of the trisubstituted or tetrasubstituted derivatives have been reported in the literature. We have never obtained the former although we have made several attempts; the latter (compounds 5 and 6) we prepared without difficulty.

Experimental

N-Benzenesulfonylethylenediamine Hydrochloride (Cpd. 1).—A mixture of 94 g. of N-acetyl-N′-benzenesulfonylethylenediamine and 470 cc. of 20% hydrochloric acid was heated to boiling under a reflux condenser for twenty-six hours and then concentrated to dryness.

The product was crystallized from nitrobenzene, in which ethylenediamine hydrochloride, which apparently was present as an impurity, is extremely insoluble. Even after repeated crystallizations the analyses indicated that some of the impurity remained. Because of the easy solubility of the free base in water, attempts to isolate it were abandoned.

N-Acetyl-N′-benzenesulfonylethylenediamine (Cpd. 7).—A mixture of 50 g. of monoacetylethylenediamine,[5] 104 g. of benzenesulfonyl chloride, 60 g. of sodium bicarbonate and 540 cc. of water was shaken for two hours. The solid product was filtered off and crystallized from water in which dibenzenesulfonylethylenediamine is very insoluble. The latter compound contaminated the product because the monoacetylethylenediamine contained ethylenediamine, from which it cannot be separated easily by distillation.

N-Acetyl-N′-*p*-toluenesulfonylethylenediamine (Cpd. 8).—This compound was prepared in a manner similar to the previous one. Benzene was added to dissolve partially the *p*-toluenesulfonyl chloride and the period of shaking was six and one-half hours. The benzene was boiled off and the solution cooled before the solid was filtered off.

N-*p*-Toluenesulfonylethylenediamine (Cpd. 2).—A solution of 25 cc. of 60% ethylenediamine and 50 cc. of water was treated with 12 *N* hydrochloric acid until the mixture was just acid to methyl red. To this a solution of 38 g. of *p*-toluenesulfonyl chloride in 200 cc. of ether was added.

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(3) Moore, Boyle and Thorn, *J. Chem. Soc.*, 39 (1929).

(4) Peacock and Dutta, *ibid.*, 1303 (1934).

(5) Hill and Aspinall, THIS JOURNAL, **61**, 822 (1939).

(6) Rosenmund, U. S. Patent 1,926,015.

(7) Mignonac, French Patent 702,715.

(8) Hinsberg and Strupler, *Ann.*, **265**, 178 (1895).

(9) Hinsberg, *Ber.*, **23**, 2962 (1890).

(10) Schneider, *ibid.*, **28**, 3074 (1895).

(11) Schering, German Patent 70,055 (1891).

(12) Howard and Marckwald, *Ber.*. **32**, 2038 (1899).

TABLE I

Solvents from which the compounds were crystallized: A, water; B, benzene; C, 95% ethyl alcohol; D, nitrobenzene.

Cpd.	Name[a]	Yield, %	Cryst. from	M. p., °C.[b]	Formula	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
1	N-(β-Aminoethyl)-benzenesulfonamide hydrochloride	88	D	172.1–173.6	$C_8H_{13}ClN_2O_2S$	11.83	12.00	13.52	12.73
2	N-(β-Aminoethyl)-*p*-toluenesulfonamide[f]	23–30	A, B	123–124[c]	$C_9H_{14}N_2O_2S_2$				
3	N,N'-Ethylene-bis-benzenesulfonamide[f]	79	C	168.6–169.3[d]	$C_{14}H_{16}N_2O_4S_2$				
4	N,N'-Ethylene-bis-*p*-toluenesulfonamide[f]	75	C	162.6–163.6[e]	$C_{16}H_{20}N_2O_4S_2$				
5	N,N'-Ethylene-bis-(dibenzenesulfonamide)	51	D	209.0–209.7	$C_{26}H_{24}N_2O_8S_4$	4.52	4.41	20.6	20.3
6	N,N'-Ethylene-bis-(di-*p*-toluenesulfonamide)	31	D	248.5–249.7	$C_{30}H_{32}N_2O_8S_4$	4.14	4.06	18.9	18.7
7	N-(β-Acetamidoethyl)-benzenesulfonamide	80	A	104.9–105.2	$C_{10}H_{14}N_2O_3S$	11.56	11.44	13.32	13.09
8	N-(β-Acetamidoethyl)-*p*-toluenesulfonamide	63	A	109.5–109.9	$C_{11}H_{16}N_2O_3S$	10.93	10.88	12.50	12.28

[a] Other names are given in the text. [b] All melting points were taken with completely immersed short stem thermometers calibrated by the National Bureau of Standards. [c] Moore, Boyle and Thorn[3] reported 124°; Peacock and Dutta,[4] 121°. [d] Hinsberg and Strupler[8] reported 168°; Schneider,[10] 168–169°. [e] Howard and Marckwald[12] reported 159.5–160.5°; Peacock and Dutta,[4] 155°. [f] The identities of these compounds were established by comparison with samples prepared according to previously published methods.

The mixture was stirred rapidly with a motor while a solution of 20 cc. of 60% ethylenediamine in 300 cc. of water was added at such a rate that the solution remained faintly acid to the indicator. The addition was complete at the end of four hours. The solution was made slightly acidic and evaporated to 200 cc. It was cooled and the precipitate of di-*p*-toluenesulfonylethylenediamine (Cpd. 4) was filtered off. Thirteen grams (35% yield) of this compound was obtained. The filtrate was made basic with 50 cc. of 15 *N* ammonium hydroxide and cooled in a refrigerator. The desired product precipitated. At times difficulty was encountered in isolating the product. This was probably due to its amphoteric nature and its moderate solubility in water.

Although many modifications of this method were tried in the hope of increasing the yield, in no instance was a better yield obtained than by the simple procedure outlined above. Acetone was substituted for ether, the mixture was heated during the reaction and the effect of hydrogen ion concentration was studied. Indicators were often used but twice the *p*H was followed by means of a Beckmann *p*H meter. The electrodes were kept in the solution throughout the addition, the rate of which was so regulated that the *p*H was maintained at approximately 5. When the *p*H fell below 4.5, the reaction ceased or became extremely slow and above *p*H 5 the yields of the N,N'-di-*p*-toluenesulfonyl derivative increased.

N,N'-Dibenzenesulfonylethylenediamine (Cpd. 3).—**A.** By Schneider's[10] method we secured only a 40% yield,[13] about half the yield given by the following procedure. **B.** A solution of 17.5 g. of benzenesulfonyl chloride in 200 cc. of benzene was stirred while 13 cc. of 60% ethylenediamine was added over a period of thirty minutes. The mixture then was boiled and stirred for ten minutes to ensure complete reaction. Most of the benzene was removed by this process, but that which remained did not interfere with the isolation of the compound, which is quite insoluble in cold benzene. After 100 cc. of water was added, the solution was cooled and the insoluble product separated by filtration.

N,N'-Di-*p*-toluenesulfonylethylenediamine (Cpd. 4).—**A.** We obtained a 40% yield[13] of this substance by employing the method used by Schneider[10] for the corresponding benzenesulfonyl derivative. **B.** By substituting an additional molecular proportion of ethylenediamine for the alkali and boiling the mixture for one hour under a reflux condenser the yield was increased to 65% but the best yield (75%) was obtained by following the procedure given above for the benzenesulfonyl derivative.

N,N,N',N'-Tetrabenzenesulfonylethylenediamine (Cpd. 5).—A solution of 16 g. of the sodium salt[15] of dibenzenesulfonylethylenediamine and 16.5 g. of benzenesulfonyl chloride in 75 cc. of nitrobenzene was boiled under a reflux condenser for fifteen minutes. The product precipitated when the solution cooled. This compound was insoluble in practically all solvents even at their boiling points. It was purified by washing with boiling acetic acid, alcohol and ether and then by crystallization from nitrobenzene.

N,N,N',N'-Tetra-*p*-toluenesulfonylethylenediamine (Cpd. 6).—**A.** The method of preparation and purification was the same as that used for the corresponding benzenesulfonyl derivative. **B.** In two other instances the reactants were heated together on a water-bath for one hour without the addition of solvent; the yields were 17 and 30%, respectively. The greater yield was obtained by using 40% more than the calculated quantity of *p*-toluenesulfonyl chloride.

Summary

A study has been made of the preparation of the mono-, di- and tetrasubstituted benzenesulfonyl and *p*-toluenesulfonyl derivatives of ethylenediamine. Several new methods of preparation have been developed and several new compounds have been prepared.

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[13] A trace of the corresponding diarylsulfonylpiperazine also was obtained. It was separated by its insolubility in sodium hydroxide solution and identified by mixed melting point determinations with an authentic sample.[4,14] Apparently there is a small amount of piperazine in the commercial ethylenediamine, which was obtained from the Carbide and Carbon Chemicals Corporation, 30 East 42d Street, New York, N. Y.

[14] "Beilstein," 4th ed., Vol. XXIII, p. 14.

[15] Prepared by cooling a saturated solution of the diarylsulfonylethylenediamine in hot 40% sodium hydroxide. The sodium salt which precipitated was filtered, washed with alcohol and then with ether and dried for one day in an oven at 110°.