phthalic acid precipitate was filtered off and the filtrate was evaporated to constant weight by an infrared lamp. The viscous brown residue was taken up in 100 cc. of ethyl alcohol and was treated slowly with a slight excess of aniline to precipitate 2-aminoethanephosphonic acid, which after recrystallization from 50% alcohol, was obtained in 50% over-all yield in the form of tiny plates which resinify at 265° and melt at 285°. Finkelstein's product[4] is reported to melt at 281–282°.

B. α-Amino-α-phenylethanephosphonic Acid.—α-Chloro-α-phenylethanephosphonic acid[7] (89.5 g.) was added, with stirring and cooling, to 500 cc. of concentrated ammonium hydroxide contained in a one-liter round bottomed flask. The stoppered flask was allowed to stand for two weeks at room temperature. The suspension was filtered by suction to yield 63 g. of crude ammonium salts of the corresponding hydroxy derivative, which were not investigated further. The mother liquor from the above was evaporated to dryness. The residue was treated with 25 cc. of water and was carefully acidified by hydrochloric acid to yield 10 g. of α-amino-α-phenylethanephosphonic acid, as tiny colorless flakes. This was dissolved in 1:1 hydrochloric acid and precipitated by 20% sodium hydroxide at congo red end-point. Yield was 10 g. (12%); m. p. 214–215° (with some decomposition).

Anal. Calcd.: N, 6.96. Found: N, 6.75, 6.92.

C. α-Aminobenzylphosphonic acid ("Phenylphosphonoglycine").—Diethyl benzoylphosphonate[8] readily yields the *p*-nitrophenylhydrazone, m. p. 126°, and the 2,4-dinitrophenylhydrazone, m. p. 171–172°, on heating with the corresponding hydrazines in alcohol.

The distillation of the ester is attended by decomposition at the end of the distillation, when appreciable amounts remain in the still; this was felt to be the reason for the rather low yield of the phosphonate. Accordingly, the crude reaction mixture, after removal of traces of residual triethylphosphite and benzoyl chloride under reduced pressure, was taken up in 300 cc. of ethanol containing an equimolar amount of *p*-nitrophenylhydrazine. The solution was refluxed for one hour and cooled, to yield 55% of the *p*-nitrophenylhydrazone in the first crop. Evaporation of the mother liquor gave 34% additional product. Recrystallization from alcohol gave 85% pure hydrazone, m. p. 126°. Ten grams of the hydrazone in 250 cc. of ethanol was treated with hydrogen, which was slowly bubbled through the solution in the presence of 2% palladium–charcoal catalyst, for two hours. The pale yellow solution was filtered, and the filtrate concentrated to 25 cc. This residue was treated with a solution of 21.4 g. of $Na_2S{\cdot}9H_2O$ in 100 cc. of water and heated to 90–95° for two hours. On cooling, 150 cc. of concentrated hydrochloric acid was added to the dark solution, the precipitated sulfur was filtered off and the mixture was refluxed for four hours, with gradual concentration to about 100 cc. Fifty cubic centimeters of concentrated hydrochloric acid was then added and the solution was evaporated to dryness by an infrared lamp. The residue was extracted with 150 cc. of warm ethanol and the extract was neutralized with aniline to yield 4 g. of α-aminobenzylphosphonic acid, which after recrystallization from 90% ethanol, formed almost colorless fine flaky crystals, which decomposed at 165°. The product was however contaminated with traces of the aniline salt, no means having been found for a satisfactory purification.

Anal. Calcd.: N, 7.5. Found: N, 7.9, 8.0.

D. ω-Aminopropanephosphonic Acid.—Forty grams of 3-bromopropanephosphonic acid was dissolved in the smallest amount of water and added slowly to ice-cold, stirred, concentrated ammonium hydroxide (1 liter). The mixture was allowed to stand for two weeks, after which it was filtered and the filtrate was evaporated to dryness. After acidification with concentrated hydrochloric acid, evaporation to dryness and extraction of the solid residue with ethanol, the extract was neutralized with aniline to yield 10 g. (36.5%) ω-aminopropanephosphonic acid, which after recrystallization from dilute ethanol, formed colorless needles, which resinified and melted at 274°.

Anal. Calcd.: N, 10.05. Found: N, 9.72, 9.65.

Summary

The available methods of synthesis of aminophosphonic acids are discussed and the examples of their applications are given.

DAYTON, OHIO RECEIVED MAY 5, 1947

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(7) Conant and Coyne, THIS JOURNAL, **44**, 2530 (1922).

(8) Kabachnik and Rossiiskaya, *Bull. Acad. Aci. U. S. S. R., cl. sci. chim.*, 364–374 (1945); *C. A.*, **40**, 4688^5 (1946).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Reaction of the Dioxane–Sulfotrioxide Reagent with Aniline. Classification of the Sulfamic Acids

BY CHARLES D. HURD AND NORMAN KHARASCH[1]

Reaction of the dioxane–sulfotrioxide reagent with aniline has been mentioned[2] as resulting in the formation of phenylsulfamic acid (C_6H_5-$NHSO_3H$). Our interest in the possible existence of this acid in the free state led us to study this reaction in some detail.

The sulfonation of aniline with one molar proportion of dioxane–sulfotrioxide was carried out in carbon tetrachloride solution at ice-bath temperatures. The product proved to be a mixture of phenylammonium phenylsulfamate with a smaller proportion of sulfanilic acid.

In accord with the work of Suter and co-workers,[2] we believe that the first product of the reaction is phenylsulfamic acid; but that this does not exist as such, and stabilizes itself by forming the phenylammonium salt. The formation of phenylammonium phenylsulfamate, under these conditions, agrees with the work of Wagner,[3] who obtained it by sulfonation of aniline with pyridine–sulfotrioxide. Willcox,[4] using dimethylaniline–sulfotrioxide, obtained analogous results. The simultaneous formation of sulfanilic acid was not reported, however, by these earlier workers. The product of reaction of aniline with dioxane–sulfo-

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[1] Present address: University of Southern California, Los Angeles, Calif.

(2) Suter, Evans and Kiefer, THIS JOURNAL, **60**, 538 (1938).

(3) Wagner, *Ber.*, **19**, 1157 (1886).

(4) Willcox, *Ann. Chem. J.*, **32**, 459 (1904).

trioxide was converted into a mixture of barium phenylsulfamate and barium sulfanilate by neutralizing with barium hydroxide, but phenylsulfamic acid, as such, could not be obtained.

In their thorough review concerning the chemistry of sulfamic acids, Audrieth and co-workers[5] point out that for an amine to react with chlorosulfonic acid to yield a substituted sulfamic acid according to the equation: $3R_2NH + ClSO_3H \rightarrow R_2NSO_3H \cdot HNR_2 + R_2NH \cdot HCl$, "the amine used must be sufficiently basic to form not only the amine salt of the desired sulfamic acid, but also the hydrochloride which is formed as a by-product of the reaction." They emphasize that "if the amine is not sufficiently basic to stabilize the sulfamic acid by salt formation, aminolysis is not effected."

Thus, it has been recognized that substituted sulfamic acids which stem from amines of low basicity (arylsulfamic acids) are not stable in acid solution, whereas sulfamic acid or alkylsulfamic acids which are derived from ammonia or alkylamines, respectively, are comparatively stable in cold aqueous solutions. Although a number of claims for the isolation of free arylsulfamic acids are made in the literature (*cf.* Table I, group II), careful analysis of these claims shows that (1) they have been definitely disproved or, (2) they have been seriously disputed by later workers, or (3) they are not in accord with accumulated evidence which indicates that the acids claimed should not be isolable under the conditions reported. Attempts in our laboratory to check such claims for the isolation of free arylsulfamic acids were not successful. These studies, as well as our recent preparation of the 2-thiazolyl sulfamic acids,[6] which are stabilized by reason of their existence as dipolar-ions, suggest a classification of sulfamic acids as illustrated in Table I, and lead to the conclusion that the thermal and hydrolytic stability of a given sulfamic acid is a function of the degree of salt formation (dipolar-ion character) in which it partakes.

Group I collects sulfamic acid and its N-alkyl derivatives. The acids of this group are readily isolable, and are fairly resistant to hydrolytic and thermal cleavage. This stability is no doubt related to the existence of such acids in dipolar-ion form, $H_3N^+SO_3^-$, *e. g.*, in the case of sulfamic acid itself.

Group II comprises phenylsulfamic acid and other arylsulfamic acids, as well as acylsulfamic acids, $RCONHSO_3H$. The free acids of this group are too unstable to permit isolation, and are known only in the form of their salts. This instability of the free aryl and acylsulfamic acids accords with prediction. It would be expected that attachment of the sulfonyl group to the amino nitrogen atom of aromatic amines (or amides), whose basicity approximates that of aniline, would so diminish its already weak basicity, that the formation of a dipolar-ion structure ($ArN^+H_2SO_3^-$) would be largely precluded.

The sulfamic acids in groups III are stable. Were it not for the additional basic positions in such molecules, these sulfamic acids would fall into group II, but internal salt formation is possible, making for stabilization. In 2-pyridylsulfamic acid, for example, it is the hetero nitrogen atom which is available for salt formation. The dipolar-

TABLE I

CLASSIFICATION OF THE SULFAMIC ACIDS ACCORDING TO THEIR STABILITIES

Acid	K_b of parent amine	Ref.
Group I. Alkylsulfamic Acids (stable)		
Sulfamic	1.4×10^{-5}	5, 7
Alkylsulfamic, alkyl =		
Methyl	5×10^{-4}	8
Isobutyl	3.1×10^{-4}	8
Isoamyl	5.0×10^{-4}	8
Benzyl	2.4×10^{-5}	9, 10
Cyclohexyl	*ca.* 10^{-5}	11
Dialkylsulfamic		
Diisoamyl	9.6×10^{-4}	12, 13
Dicyclohexyl	*ca.* 10^{-4}	11
Ethyl-*s*-butyl	*ca.* 10^{-4}	14
Group II. Aryl and Acylsulfamic Acids (unstable)		
Arylsulfamic, aryl =		
Phenyl	4.6×10^{-10}	15, 16, 17, 18
1-Naphthyl	9.9×10^{-11}	19, 20
p-Tolyl	2×10^{-9}	17, 21
p-Chlorophenyl	*ca.* 10^{-10}	22, 23
Acylsulfamic, acyl =		
Acetyl	3.1×10^{-15}	24
Group III. Sulfamic Acids Stabilized by Dipolar-Ion Formation		
2-Thiazolyl		6
4-Alkyl-2-thiazolyl		6
4-Aryl-2-thiazolyl		6
N-(4-Methyl-2-thiazolyl)-phenyl		6
p-Aminophenyl		25
2-(Aminophenyl)-phenyl		26
p-Pyridyl		6

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(6) Hurd and Kharasch, THIS JOURNAL, **68**, 653 (1946).

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(10) Paal and Lowitsch, *Ber.*, **30**, 869 (1897).

(11) Audrieth and Sveda, *J. Org. Chem.*, **9**, 89 (1944).

(12) Traube, *Ber.*, **24**, 360 (1891).

(13) Traube, *ibid.*, **46**, 2513 (1913).

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(15) Traube, *ibid.*, **23**, 1655 (1890).

(16) Hunter and Sprung, THIS JOURNAL, **53**, 1443 (1931).

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(21) Paal and Jänicke, *Ber.*, **28**, 3160 (1895).

(22) Paal, *ibid.*, **34**, 2748 (1901).

(23) Weil and Moser, *ibid.*, **55**, 732 (1922).

(24) Baumgarten and Marggraff, *ibid.*, **64**, 1582 (1931)

(25) Weil and Wassermann, *ibid.*, **55**, 2533 (1922).

(26) Spiegel, *ibid.*, **18**, 1479 (1885).

ion character of sulfamic acids of group III has been demonstrated experimentally.[6]

Experimental[27]

Reaction of the Dioxane-Sulfotrioxide Reagent with Aniline.—Twenty-two grams of dry dioxane was dissolved in 150 ml. of carbon tetrachloride in a 500 ml. three-necked flask, surrounded by an ice-bath. The solution was stirred with a mercury-sealed stirrer, while 21 g. of sulfur trioxide was passed in from an all-glass generator containing 60% oleum. To the dioxane–sulfotrioxide reagent, thus formed, there was now added, dropwise, with continued stirring and cooling, a solution containing 25 g. of aniline dissolved in 25 ml. of carbon tetrachloride. The reaction mixture was stirred for one-half hour after the addition of the aniline, stoppered, and kept at 0° for three days with occasional shaking. The pasty solid was collected by suction filtration and was washed with 200 ml. of dry ether, in several portions, to remove unreacted aniline or sulfur trioxide. After air-drying, the product weighed 47 g.

This product gave a heavy test for sulfate ions. The greater portion of it dissolved in several volumes of water at room temperature, and complete solution of 1 g. of it could be effected by gently heating with 10 ml. of water. On treatment with aqueous sodium hydroxide solution, the product dissolved, but an oil separated simultaneously. This was extracted with ether, and proved to be aniline by reason of its odor, appearance, solubility in mineral acids, and conversion to acetanilide (m. p. 114°). The product could not be recrystallized from water without decomposition (increase in sulfate ion concentration), and other solvents also were not suited for this purpose. It melted mainly between 180–190°.[28] The value for neutralization equivalent of the product varied considerably (from 118 to 181), in various runs wherein the period of exposure of the product to the air, the extent of washing with dry ether, and time of drying of the sample varied somewhat. Calcd. for sulfanilic acid, 173; for phenylammonium phenylsulfamate, 133. On the basis of the experiments described below, it is our conclusion that the product was a mixture of phenylammonium phenylsulfamate and a smaller amount of sulfanilic acid.

Isolation of Phenylammonium Sulfate.—Five grams of the product from the sulfonation of aniline was dissolved in 100 ml. of hot water, boiled for a few minutes with 2 g. of decolorizing charcoal, and filtered. After keeping the filtrate in the ice-chest for several hours no crystallization occurred, but on evaporating (100°) to smaller volume there was obtained nearly 2 g. of a white, crystalline product which was dried at 100–110°. This product did not decompose when heated to 280–300°. It was readily soluble in water, and gave a heavy test for sulfate ions. When neutralized with cold, dilute sodium hydroxide solution, aniline separated. The neutralization equivalent of the product, twice recrystallized, and dried at 110°, was 142. Calcd. for phenylammonium sulfate, 142. This accords with the report of Wagner, who isolated phenylammonium sulfate by similar hydrolysis of phenylammonium phenylsulfamate.

Isolation of Sulfanilic Acid.—Six grams of the product from the sulfonation of aniline with dioxane–sulfotrioxide reagent was dissolved in 75 ml. of cold water, and the solution was filtered to remove a small quantity of undissolved residue. To the clear filtrate, 300 ml. of acetone was added, whereupon white crystals precipitated. These were collected and dried in the vacuum desiccator (0.5 g.). The neutralization equivalent of the product was 172, and in all other respects (decomposition temperature, conversion to methyl orange, and to tribromoaniline, aqueous solubility, and solubility in sodium hydroxide solution) it resembled an authentic sample of sulfanilic acid. It tested negatively for sulfate ions, and did not release these when boiled with hydrochloric acid. Thus, it was neither aniline sulfate nor a sulfamate.

In the procedure just described, only a small proportion of sulfanilic acid was obtained from the product of sulfonation of aniline with dioxane–sulfotrioxide. It was found, however, that when 10 g. of the product was heated at 130° for twenty-four hours, then recrystallized from boiling water, there was obtained nearly 5 g. of a product which by all tests described above, was sulfanilic acid. This result was expected, since phenylammonium phenylsulfamate is converted by heating to sulfanilic acid.

Isolation of a Mixture of Barium Phenylsulfamate and Barium Sulfanilate.—Twenty grams of the product of reaction of aniline with dioxane–sulfotrioxide was added to a suspension of 31 g. of barium hydroxide crystals in 200 ml. of water, so that the reaction mixture was strongly basic to litmus. Steam-distillation of the mixture and extraction of the distillate with ether yielded 3 g. of aniline. The residue in the flask was filtered, and freed from excess barium hydroxide by passing in carbon dioxide. When the precipitation of barium carbonate was complete, the solution was made slightly basic with ammonium hydroxide, boiled with decolorizing charcoal, and refiltered. The filtrate from the last procedure was now concentrated to small volume by heating on the steam bath, the precaution taken to keep it alkaline with ammonium hydroxide to prevent hydrolysis of the sulfamate. On cooling, 8 g. of a white, crystalline, water-soluble mixture of barium salts was obtained. When a fairly concentrated aqueous solution of the latter was prepared, and the cold solution acidified with hydrochloric acid, colorless crystals of sulfanilic acid precipitated. On gentle heating of such an acidified solution, these first crystals would dissolve, and in their place there was deposited very rapidly a heavy precipitate of an inorganic (non-charring) product which was unquestionably barium sulfate. A portion of the barium salts obtained were recrystallized from dilute ammonia solution, dried *in vacuo* over phosphorus pentoxide at the temperature of boiling toluene, and analyzed for barium content. *Anal.* Calcd. for $C_{12}H_{12}O_6N_2S_2Ba$: Ba, 28.5. Found: Ba, 28.2. Prior to heating the above mixture of barium salts, the hydrolytic behavior of the barium phenylsulfamate could be detected, but after heating at 110–130° for some time, this behavior could no longer be detected. This was to be expected, since barium phenylsulfamate is converted by heat to barium sulfanilate.

Pure barium phenylsulfamate was prepared as directed by Traube,[15] and its hydrolytic behavior in acid aqueous solution was found to compare exactly to that observed with the mixture of barium salts described above. This rapid hydrolysis, even in cold solutions, precluded all attempts to isolate free phenylsulfamic acid.

Summary

The sulfamic acids have been classified into three groups on the basis of observed differences in their stabilities.

The thermal and hydrolytic stability of a given sulfamic acid is shown to be related to the degree of salt formation (dipolar-ion character) in which that acid partakes.

The reaction of the dioxane–sulfotrioxide reagent with aniline is described.

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(27) All melting points and decomposition temperatures are uncorrected.

(28) Michaelis and Petou, *Ber.*, **31**, 988 (1898), and Wagner (ref. 3) report the melting point of pure phenylammonium phenylsulfamate as 192°.