[Contribution from the Department of Chemistry and Chemical Engineering of the Polytechnic Institute of Brooklyn]

MONO-ARYLGUANIDINES. I. ALPHA-PHENYLGUANIDINE[1]

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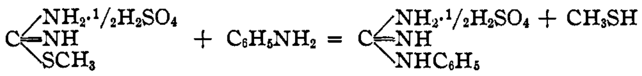
Introduction

Mono-arylguanidines have received little attention or study, while diaryl- and triarylguanidines are well known and a number are produced commercially. One method only, the ammonation of cyanamide,[4] has been suggested for the preparation of α-phenylguanidine, the simplest compound of this series.[5]

In considering possible new methods for the preparation of α-phenylguanidine, attention was directed to the synthesis of methylguanidine[6] by the reaction between methyl-isothiourea sulfate and monomethylamine. It has been found that an excess of aniline reacts with methyl-isothiourea sulfate to form α-phenylguanidine sulfate.



$$C\left\{\begin{matrix}NH_2\cdot{}^1/_2H_2SO_4\\ =NH\\ SCH_3\end{matrix}\right. + C_6H_5NH_2 = C\left\{\begin{matrix}NH_2\cdot{}^1/_2H_2SO_4\\ =NH\\ NHC_6H_5\end{matrix}\right. + CH_3SH$$

This substance is contaminated with aniline sulfate, which cannot be removed by recrystallization from water,[7] but purification may be accomplished by taking advantage of the relative insolubility of α-phenylguanidine carbonate.

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[1] A preliminary report was presented at the Philadelphia meeting of the American Chemical Society in September, 1926.

This article is respectfully dedicated by the author to Professor L. M. Dennis and will be reprinted in the Louis Monroe Dennis Quarter Century Volume to be published in commemoration of the completion by Professor Dennis of twenty-five years of service as Head of the Department of Chemistry at Cornell University.

[2] The author takes pleasure in acknowledging the assistance of his students, M. J. Goldstein, A. E. Cleghorn and E. L. Jung.

[3] With Microscopical Studies by C. W. Mason, Assistant Professor of Chemical Microscopy at Cornell University.

[4] Franklin has pointed out the relationship existing between guanidine and a number of carbon–hydrogen–nitrogen compounds, classifying them as ammono carbonic acids, and hence the arylguanidines as ammono esters; This Journal, **44**, 486 (1922); **46**, 2137 (1924); also Burdick, *ibid.*, **47**, 1485 (1925).

[5] α-Phenylguanidine, its nitrate, picrate, chloroplatinate and dibenzoyl derivatives have been described: McKee, *Am. Chem. J.*, **26**, 22 (1901); Feuerlein, *Ber.*, **26**, 1602 (1897); Prelinger, *Monatsh.*, 13, 97 (1892); Kampf, *Ber.*, **376**, 1682 (1904).

[6] Phillips and Clarke, This Journal, **45**, 1755 (1923).

[7] The author contemplates a study of the system α-phenylguanidine–aniline–sulfuric acid–water with a view to ascertaining the exact nature of the product of this side reaction with aniline.

Experimental Part

Materials.—Methyl-isothiourea sulfate was prepared by the method of Arndt,[8] using thiourea of a high grade of purity.[9]

Crude α-Phenylguanidine Sulfate.—Four moles (555 g.) of methyl-isothiourea sulfate and eight moles (740 cc.) of redistilled aniline were heated to boiling under a reflux by means of an oil-bath, and the uncondensed vapors were led through a series of three wash bottles containing a 20% solution of sodium hydroxide. The system was placed under reduced pressure and the heating was continued until the solid was completely dissolved (or melted) and there was no further evolution of methyl mercaptan. On cooling the liquid solidified and was intimately incorporated with about one liter of 95% alcohol, allowed to stand with occasional shaking for twenty-four hours, filtered and the remaining solid treated in the same manner with a second liter of alcohol. This solid material when dried was generally a pale lavender in color. Further purification may be effected by decolorizing with vegetable charcoal and recrystallizing, but the sulfuric acid content of the product varies with the concentration of sulfuric acid used in recrystallizing. One speciman recrystallized from water containing 5% of sulfuric acid gave an analysis for sulfuric acid of 29.00 and for nitrogen of 18.20, indicating the presence of about 30% of aniline sulfate.

α-Phenylguanidine Carbonate.—A solution of 50 g. of crude α-phenylguanidine sulfate was neutralized with barium hydroxide and filtered. Barium hydroxide or sulfuric acid was added to the filtrate until neither was in excess and it was filtered a second time. The volume of the solution was now about 500 cc. and carbon dioxide was passed in for about two hours while the solution was cooled in an ice-bath. A granular precipitate formed which was filtered and the filtrate concentrated to half volume and treated with carbon dioxide a second and third time; yield, 30 g.

TABLE I

ANALYTICAL AND OTHER DATA OF SALTS

Compound		Analyses Calcd., %	Found, %		M. p., °C.	Solubility	Crystal form
Base	N	31.11	31.38	31.25	66–68	Sol. in Bz, EtOH	Monoclinic
	C	62.22	61.66	61.79		Sl. sol. in H_2O,	
	H	6.67	6.58	6.88		CCl_4 and Et_2O	
Sulfate[a]	H_2SO_4	26.66	26.66	26.63	205	Sol. in H_2O. Sl. sol. in 95% EtOH	Monoclinic
	N	22.83	23.00	23.30			
Carbonate[a]	CO_2	13.20	12.72	12.77	138–140	Sl. sol. cold H_2O. Sol. hot	....
Hydrochloride[a]	HCl	21.26	21.51	21.36	...	Sl. sol. EtOAc. Sol. in all ord. solvents	Monoclinic
Nitrate	HNO_3	31.86	31.68	31.57	118–119	Sol. hot H_2O, EtOH. Sl. sol. in cold	Triclinic
Picrate	....	...	...	...	218–220	Insol. H_2O.	Orthorhombic or triclinic
Chloroplatinate	....	...	...	...	196	Sl. sol. H_2O	Triclinic

[a] Previously undescribed.

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[8] Arndt, *Ber.*, **54B**, 2236 (1921).

[9] Obtained from the American Cyanamide Company.

α-Phenylguanidine (Base).—The preparation of the base may be accomplished by treatment of a solution of one of the salts with an alkali and in general the sulfate and barium hydroxide was used. In a typical experiment 30 g. of pure α-phenylguanidine sulfate in 100 cc. of hot water was treated with crystalline barium hydroxide and digested for one hour. After the barium sulfate was filtered off, the base separated as an oil and crystallized on seeding with a crystal of previously prepared base. The crystals were separated by filtration, washed with 5 cc. of 95% alcohol and dried *in vacuo* over phosphorus pentoxide. This material melted at 67–68° and when crystallized from benzene at 66–67°.

α-Phenylguanidine when exposed to the laboratory atmosphere takes on carbon dioxide and moisture rapidly and the melting point is raised. A sample after standing for several months was analyzed for carbon dioxide and 7.94% was found. A melting point of about 125° was invariably found when the base was dried in the atmosphere or in the oven at 50–60° and such specimens always contained carbon dioxide.

Salts of α-Phenylguanidine.—Salts of α-phenylguanidine may be prepared by adding the respective acid to a solution or suspension of the base or carbonate in hot water. The salt may be isolated by chilling the concentrated solution, or in the case of the hydrochloride concentrating to crystallization in a desiccator. The picrate precipitates when picric acid is added to the solutions of any salt. The extremely hygroscopic character of the hydrochloride rendered an accurate melting point determination difficult. A statement of analytical results and properties of α-phenylguanidine and its salts is given in the accompanying table.

Microscopical Notes

Base.—When prepared from the sulfate and sodium hydroxide, droplets of liquid are first formed; these coalesce and crystallize on standing. Seeding or stirring aids the crystallization. The crystals obtained are mostly rhomb-shaped tablets and dendritic forms derived from them. The acute angle of the rhombs is about 63° and is frequently truncated by a small crystal face. The tabular views of the crystals show symmetrical extinction and fairly strong double refraction, with somewhat anomalous polarization colors. They give a biaxial interference figure, the axial plane bisecting the acute angle of the rhombs; 2V is large. Edge views of the tablets exhibit oblique extinction, dispersed at about 40°.

Sulfate.—The crystals are elongated tablets and flattened prisms, with symmetrical end faces making an angle of 150° with each other. Double refraction is moderately strong, with parallel extinction shown by tabular and edge views. The end views were not observed. The crystals showed biaxial interference figures, with the plane of the optic axes transverse of the long crystals; 2V large; optically positive; acute bisectrix is not perpendicular to the principal plane of the tablets.

Hydrochloride.—A number of crystallographic forms are represented: prisms, pinacoids, pyramids and domes, in differing degrees of development. The simpler crystals show a rhomb-shaped outline with beveled edges and terminal angles of either 70 or 85°. Double refraction is strong, with symmetrical extinction shown by the rhombs, and oblique extinction shown by edge views; biaxial, with the plane of the optic axis bisecting the acute angle of the rhombs, and the acute bisectrix inclined to the principal plane of the crystals; optically positive.

Nitrate.—Recrystallized from water, the crystals are in the form of oblique prisms with beveled edges, the ends truncated by a pinacoid at about 70° to their axis. The double refraction is strong, with oblique extinction exhibited by all views of the prisms. The extinction angle varies, depending on the orientation, but the maximum is about 35°; biaxial interference figure; 2V large, with plane of optic axis obliquely transverse of the crystals, optically positive,

Picrate.—Spherulites, crosses, dendrites, fine needles, prisms, and small tablets, six-sided in outline and having terminal angles of about 95° may be seen. Double refraction is very strong, with symmetrical extinction; biaxial interference figure; 2V large, with plane of the optic axis transverse of the crystals, optically negative.

Chloroplatinate.—The golden-yellow crystals are sparingly soluble in water and when precipitated show a marked tendency to form a supersaturated solution. The crystals are oblique bi-pyramids, with basal and clino-pinacoids. They show strong double refraction and all views show oblique extinction; biaxial; 2V large; probably optically positive.

Summary

The reaction between methyl-isothiourea sulfate and aniline resulted in the formation of a product consisting of α-phenylguanidine sulfate and aniline sulfate. Pure α-phenylguanidine and a number of its salts were prepared by first converting the α-phenylguanidine sulfate in the crude product to the carbonate. Certain physical and chemical properties of these substances have been described.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ALBERTA]

MERCURATION OF RESORCINOL AND SOME ALKYLRESORCINOLS

BY REUBEN B. SANDIN

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No trimercurated derivative of resorcinol has been described in the literature and no work has been published on the mercuation of the alkylresorcinols. Dimroth has prepared a chloromercuriresorcinol and a dichloromercuriresorcinol.[1] Leys has prepared a yellow mercury resorcinol compound to which he gives the formula $HgO_2{=}C_6H_3.HgOAc$.[2] Kharasch and Chalkley[3] have examined the reactivity of acetoxymercurire-

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[1] Dimroth, *Ber.*, **35**, 2865 (1902).

[2] Leys, *J. pharm. chim.*, (6) 21, 1388 (1905).

[3] Whitmore, "Organic Compounds of Mercury," The Chemical Catalog Co., Inc., New York, 1921, p. 59.