

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF VERMONT]

**PARA-AMINOPHENYLGUANIDINE: THE PREPARATION OF THE NITRATE, HYDROCHLORIDE AND SULFATE SALTS, AND ATTEMPTED PREPARATION OF THE FREE BASE**

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RECEIVED OCTOBER 27, 1931

PUBLISHED APRIL 6, 1932

**Introduction**

It was considered advisable in the course of a physiological investigation of the hypoglycemic properties of *p*-aminophenylguanidine to prepare salts of this base other than the hydroiodide in order to eliminate the possibility of thyroid complications. Therefore the nitrate, hydrochloride and sulfate salts were prepared, and the hypoglycemic properties of the last two were investigated. Since the results of the physiological work have been reported,<sup>1</sup> this paper will treat only the methods of synthesis of these compounds, and some observations noted during the attempted preparation of the free base.

**Experimental**

***p*-Aminophenylguanidine Nitrate.**—To 26 g. (0.0935 mole) of *p*-aminophenylguanidine hydroiodide<sup>2</sup> in 700 cc. of cold water was added 16 g. (0.0940 mole) of silver nitrate in 500 cc. of water. After adding 5 g. of charcoal (*norite*) the mixture was agitated for five days at room temperature and filtered. The filtrate was treated with hydrogen sulfide, concentrated to about 75 cc., boneblackened and refiltered. Upon cooling, the concentrate set to an almost solid mass of crystals. These were washed with cold absolute alcohol and cold absolute ether, and dried at room temperature *in vacuo*. The crude yield (m. p. 183–186°) was 13.0 g. or 65.3%.

The crude salt was purified by three recrystallizations from water under an atmosphere of hydrogen sulfide. The purified nitrate was white, crystalline, and melted at 189–190°. It was stable when dry, but discolored upon standing in aqueous solution. Its solubilities in weight per cent. at 25° were: water, 1.81; absolute methyl alcohol, 1.55. The final yield (purified salt) was 6.0 g. or 30.1%.

*Anal.* Calcd. for C<sub>7</sub>H<sub>11</sub>N<sub>5</sub>O<sub>3</sub>: N, 32.86. Found: N, 32.73 (by modified Kjeldahl), 33.09 (by micro Dumas).

***p*-Aminophenylguanidine Hydrochloride.**—Equivalent quantities (0.32 mole) of *p*-phenylenediamine (Eastman product recrystallized from benzene, m. p. 140.5–141°) and S-ethyl isothiurea hydrochloride (prepared according to Stevens, m. p. 95–97°)<sup>3</sup> in 25 cc. of cold water were heated under reflux on a boiling water-bath for two and one-half hours, during which time air was blown over but not through the reaction mass to facilitate the removal of the ethyl mercaptan evolved during the condensation. The volume of the reaction mass was then reduced by heating under reduced pressure. Upon cooling the concentrate set to a semi-solid mass of crystals, which were disintegrated by grinding under absolute alcohol. This solvent removed almost completely the purple mother liquor, leaving behind, after filtration, a grayish white material,

<sup>1</sup> T. B. Parks and C. E. Braun, *J. Biol. Chem.*, **91**, 629 (1931).

<sup>2</sup> C. E. Braun, *ibid.*, **89**, 97 (1930).

<sup>3</sup> H. P. Stevens, *J. Chem. Soc.*, **81**, 80 (1902).

which, after washing with cold absolute alcohol and absolute ether, was dried at room temperature *in vacuo*. The crude yield (m. p. 165–167°) was 25 g. or 41.9%.

The crude compound was purified by two reprecipitations from alcohol–water solution by the addition of ether, and one recrystallization from absolute alcohol. The purified hydrochloride, not absolutely white but having a slight yellowish tint, was crystalline and melted at 167–168.5°. It was stable when dry but quickly discolored in aqueous or alcoholic solution. Its solubilities in weight per cent. at 25° were: water, 49.11; absolute methyl alcohol, 24.78. The final yield (purified salt) was 9 g. or 15.08%.

*Anal.* Calcd. for  $C_7H_{11}N_4Cl$ : Cl, 19.00. Found: Cl, 19.02 (as AgCl).

***p*-Aminophenylguanidine Sulfate.**—Equal weights (56 g.) of *S*-methyl isothioureia sulfate (prepared according to Arndt, m. p. 245°)<sup>4</sup> and *p*-phenylenediamine (m. p. 140.5–141°) in 60 cc. of water were heated under reflux on a boiling water-bath for two hours. The reaction mass was then transferred to a beaker and chilled. Upon cooling the entire mass set to a crystalline paste. The latter, after the addition of 50 cc. of alcohol was filtered, washed on the funnel with alcohol and dried at room temperature *in vacuo*. The crude sulfate was almost white and had a decomposition range of 260–276° when heated at a rate of 1° per second. The crude yield was 71 g. or 88.56%.

The crude salt was purified by two reprecipitations from aqueous solution by the addition of alcohol, keeping the solution saturated with hydrogen sulfide to prevent discoloration. The purified sulfate was white, crystalline and decomposed at 279° when heated at the rate of 1° per second. It was stable when dry but discolored very slowly in aqueous solution. Its solubilities in weight per cent. at 25° were: water, 10.23; absolute methyl alcohol, 0.10. The final yield (purified salt) was 45.0 g. or 56.1%.

*Anal.* Calcd. for  $C_7H_{10}N_4 \cdot 0.5H_2SO_4$ : S, 8.04. Found: S, 8.09 (as  $BaSO_4$ ).

**Attempted Preparation of *p*-Aminophenylguanidine.**—A solution containing 3.7 g. of barium hydroxide and 8.6 g. of sulfate salt in 150 cc. of water was agitated for twenty-four hours, the precipitated barium sulfate filtered off, and the filtrate evaporated to dryness under vacuum on a warm water-bath. The brown pasty residue was taken up in boiling absolute alcohol, the solution filtered hot, and a small amount of insoluble residue discarded. Upon slow evaporation of the alcohol an amorphous material deposited. This was filtered off, washed with ether and dried at room temperature *in vacuo*. The dry compound was light brown in color, readily soluble in cold water, and melted with decomposition at 174–178°.

In attempted purification the brown material was extracted for five days with absolute alcohol, in which only a small amount dissolved. This was surprising as the compound originally had been recovered from an alcoholic solution. The insoluble residue, after washing with ether, and drying at room temperature under vacuum, was light brown, amorphous, appeared very uniform and melted with decomposition at 182°. A second alcoholic extraction failed to raise the melting point. The brown compound (m. p. 182°) showed a strong alkaline reaction in aqueous solution, and was free of sulfate and barium.

*Anal.* Calcd. for  $C_7H_{10}N_4$ : N, 37.33;  $C_7H_{10}N_4 \cdot 2H_2O$ : N, 30.11. Found: N (Kjeldahl), 29.88.

The analytical data agreed with the theoretical nitrogen content of *p*-aminophenylguanidine dihydrate. The dry base when heated above 100° even *in vacuo* readily decomposed into ammonia and *p*-phenylenediamine.

The author wishes to thank Professor H. A. Iddles of the Department of Chemistry, The University of New Hampshire, who carried out the

<sup>4</sup> F. Arndt, *Ber.*, 54, 2236 (1921).

micro analyses on the nitrate salt, and acknowledges the technical assistance of Mr. C. E. Fisher of The Lyndon Institute, Lyndon Center, Vermont. The author also thanks the American Cyanamid Company for the thiourea used in this work.

### Summary

1. The preparation of the nitrate, hydrochloride and sulfate salts of *p*-aminophenylguanidine has been described.

2. Some experimental evidence has been presented which indicates that the free base, *p*-aminophenylguanidine, has been obtained as a dihydrate.

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[CONTRIBUTION NO. 84 FROM THE EXPERIMENTAL STATION OF E. I. DU PONT DE NEMOURS AND COMPANY]

## POLYMERS FROM BENZYL CHLORIDE AND RELATED COMPOUNDS

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RECEIVED OCTOBER 27, 1931

PUBLISHED APRIL 6, 1932

The formation of an insoluble hydrocarbon by the action of aluminum chloride on benzyl chloride was observed many years ago by Friedel and Crafts.<sup>1</sup> In the same year Gladstone and Tribe<sup>2</sup> obtained related materials from benzyl chloride by the action of a copper-zinc couple, and previous to these observations a similar product had been obtained by means of copper.<sup>3</sup> Although the formation of polymeric substances from benzyl chloride has since been referred to in a number of instances,<sup>4</sup> little information is available concerning the nature or properties of the polymers. Insoluble amorphous products have sometimes been obtained while in other instances the polymers have been soluble resins, yet the experimental conditions pertinent to the formation of one or the other have not been defined. In view of this situation and as part of a general study of polymeric substances, the earlier work has been repeated and extended. The study has also included the polymerization of *p*-bromobenzyl chloride

<sup>1</sup> Friedel and Crafts, *Bull. soc. chim.*, **43**, 53 (1885).

<sup>2</sup> Gladstone and Tribe, *J. Chem. Soc.*, **47**, 448 (1885).

<sup>3</sup> Zincke, *Ber.*, **2**, 739 (1869).

<sup>4</sup> Schramm, *ibid.*, **26**, 1706 (1893); Radziewanowski, *ibid.*, **27**, 3237 (1894); Auger, *Bull. soc. chim.*, [3] **21**, 562 (1899); Mailhe, *Chem. Z.*, **29**, 464 (1905); Lavaux and Lombard, *Bull. soc. chim.*, [4] **7**, 541 (1910); Lavaux, *Ann. chim.*, [8] **20**, 488 (1910); von Braun and Deutsch, *Ber.*, **45**, 1267 (1912); Badische Anilin und Soda-Fabrik, German Patent 280,595, Issued November 21, 1914, *Chem. Zentr.*, **86**, 71 (1915); Korczynski, Reinholz and Schmidt, *Roczniki Chem.*, **9**, 731 (1929); *Chem. Abstracts*, **24**, 1858 (1930); Ushakov and Kon, *Zhur. Prikladnoi Khim.*, **3**, 69 (1930); *Chem. Abstracts*, **24**, 3796 (1930).