methylaminoethyl chloride[10] [prepared from 21.6 g. (0.15 mole) of the hydrochloride and 20% sodium hydroxide solution] was added to the sodium salt suspension. The mixture was heated at reflux temperature for six hours, and the turbid light brown solution cooled and filtered to remove sodium chloride. Benzene was evaporated from the filtrate, and 75 ml. of absolute alcohol was added. Dry hydrogen chloride gas was passed in, and upon evaporation of solvent to one-third of the original volume, 14.5 g. (40% yield) of the dihydrochloride of α-(2-dimethylaminoethylamino)-pyridine (III) was unexpectedly obtained; m.p. 223–225°.

The identity of the product was confirmed by a mixed melting point with an authentic sample[2] and by analysis.

Anal. Calcd. for $C_9H_{15}N_3 \cdot 2HCl$: C, 45.39; H, 7.20; Cl, 29.77. Found: C, 45.02; H, 7.18; Cl, 29.85.

The filtrate from which III dihydrochloride was isolated was evaporated to a viscous black liquid, which was extracted twice with hot benzene. The insoluble layer was distilled at 4 mm. to give 5.5 g. of *sym*-tetraphenylethane; m.p. 209–210.5°.[11] The benzene layer was evaporated and the residue distilled at 135–145° (2–4 mm.) to give 5 g. of benzohydryl chloride.[12] Heated gently, in accord with the literature,[5] the chloride was converted to *sym*-tetraphenylethane, m.p. 204–209°.

(10) Burckhalter, Stephens and Hall, *J. Am. Pharm. Assoc.*, **39**, 271 (1950).

(11) Anschütz found 207°.

(12) Huntress lists 135–145° (4 mm.).

DEPARTMENT OF PHARMACEUTICAL CHEMISTRY
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Preparation of Nitroaminoguanidine

BY RONALD A. HENRY, ROBERT C. MAKOSKY AND G. B. L. SMITH

The synthesis of nitroaminoguanidine reported by Phillips and Williams[1] involves the reaction of nitroguanidine with an equivalent amount of hydrazine sulfate and two equivalents of one normal ammonium hydroxide solution at 55–60°. Reduced to its simplest terms, this hydrazinolysis is represented by the equation

$$NH_2C(NH)NHNO_2 + N_2H_4 \longrightarrow NH_2NHC(NH)NHNO_2 + NH_3$$

Although these authors claimed yields of 50%, repeated duplication of their procedure, coupled with more precise methods for the analysis of nitroaminoguanidine, indicated that their yields were actually 30–35% and the purity of their product 70–80%.

In an attempt to improve the yield of nitroaminoguanidine, certain variables in the reaction of hydrazine with nitroguanidine in aqueous systems were investigated in this Laboratory.

As a result, a modified procedure has been developed which consistently yields nitroaminoguanidine of improved purity in 40–50% yield. The by-products formed in this reaction were described previously.[2]

Experimental

Typical Procedure for the Preparation of Nitroaminoguanidine.—In a two-liter, three-necked flask, equipped with a stirrer, a dropping funnel and a thermometer was placed 52 g. (0.5 mole) of nitroguanidine and one liter of distilled water at 60–65°. To the well-agitated slurry was added, dropwise, 31.9 g. (0.55 mole) of 87% hydrazine hydrate in 500 ml. of water. The temperature was maintained at 55–60°. The addition of the hydrazine required 55–60 minutes after which the solution was stirred for an additional 15 minutes. Ammonia was copiously evolved throughout the entire reaction period. When the reaction was completed, the orange-colored solution was rapidly cooled to below 45° and neutralized with concentrated hydrochloric acid to stop further reaction. The solution obtained from the reaction was chilled at 0° for several hours, after which the impure crystalline product was removed by filtration, washed with several small volumes of ice-cold water, and air-dried. The yield of impure product, containing about 96% nitroaminoguanidine, was 25–30 g. (41–49%); m. p. 186–187° (dec.). Two recrystallizations from water (30 ml. per gram) gave a white powder, decomposing at 190°. The melting point is an unsatisfactory criterion for ascertaining the purity of this compound.

Anal. Calcd. for $CH_5O_2N_5$: hydrazino nitrogen, 23.53. Found: hydrazino nitrogen, 23.51, 23.56, 23.53, 23.49.

Rapid evaporation of the original mother liquor over an open flame to one-third the original volume and cooling for 24 hours at 0° gave a second crop of crude material (12–20 g.), containing about 30% nitroaminoguanidine. Recovery of the pure nitroaminoguanidine, as such, from this crop was very difficult.

Analysis of Nitroaminoguanidine.—The purity of nitroaminoguanidine samples was determined by the following modification of the Jamieson method[3] for estimating hydrazine nitrogen: A 90- to 110-mg. sample of material is accurately weighed into a 125-ml. iodine flask; 20 ml. of water is added and the sample dissolved by heating and swirling. The solution is then cooled to 20–25°, 25 ml. of concentrated hydrochloric acid is added and the solution recooled to 25°, after which 15 ml. of chloroform is added and the solution titrated with standardized 0.1 *N* potassium iodate solution (theoretically 5.3505 g./liter) until the iodine color is completely discharged from the chloroform layer. Initially the iodate is added in increments of 5 to 6 ml., followed by shaking. As the end-point is approached (gradual fading of the iodine color), the size of the increment is progressively decreased so that ultimately the iodate solution is being added dropwise. The shaking between each addition must be maintained and must be very vigorous. If the approximate titer of the sample is known, 90 to 95% of the iodate solution can be added all at once, followed by the more careful addition. The usual precautions must be taken to prevent spurting when the stopper from the iodine flask is being removed.

$$\% \text{ nitroaminoguanidine} = \frac{(\text{ml. of } KIO_3)(\text{normality of } KIO_3)(119.09/4)}{(\text{sample weight})(10)}$$

(3) Jamieson, "Volumetric Iodate Methods," Chemical Catalog Co., Inc., New York, N. Y., 1926, p. 36.

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The Rates of Absorption of and the Formation of Liver Glycogen by L-Proline and L-Hydroxyproline[1]

BY W. C. HESS AND I. P. SHAFFRAN

L-Proline fed to chickens, as the half sodium salt, was found by Kratzer[2] to be adsorbed at the rate of 49.8 mg. per 100 g. body weight per hour. No previous reports upon the rate of absorption of L-hydroxyproline were found in the literature. Dakin[3] fed L-proline to phlorhizinized dogs and noted the production of extra urinary glucose. Stöhr[4] reported that feeding L-proline and L-

(1) Presented in part before the Division of Biological Chemistry of the American Chemical Society, Phila., April, 1950.

(2) Kratzer, *J. Biol. Chem.*, **153**, 237 (1944).

(3) Dakin, *ibid.*, **14**, 321 (1913).

(4) Stöhr, *Biochem. Z.*, **299**, 242 (1938).

(1) Phillips and Williams, THIS JOURNAL, **50**, 2469 (1928).

(2) Henry, Lewis and Smith, *ibid.*, **72**, 2015 (1950).