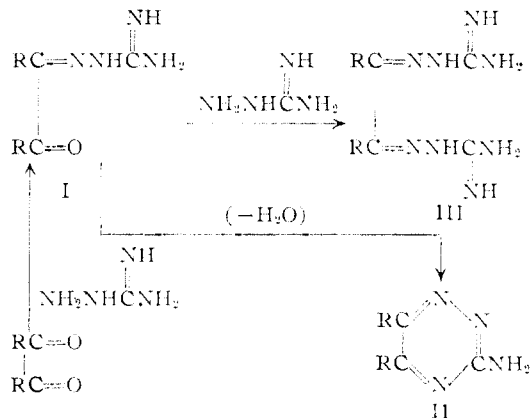


3-Amino-*as*-triazinesBY JOHN G. ERICKSON¹

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Thiele and Dralle² have studied the reactions of aliphatic 1,2-dicarbonyl compounds with certain aminoguanidine salts. Using glyoxal, biacetyl and dioxytartaric acid with aminoguanidine hydrochloride or nitrate in aqueous solution, they obtained no ring compounds. The monoguanilyhydrazones (I), rather than cyclizing to *as*-triazines (II), reacted with a second mole of aminoguanidine and only osazone-like compounds (III) were isolated.



We have found that glyoxal and biacetyl react readily with aminoguanidine bicarbonate in aqueous medium at room temperature. 3-Amino-*as*-triazine (II, R = H) and 3-amino-5,6-dimethyl-*as*-triazine (II, R = CH_3) were obtained in this manner in good yields. These successful results are no doubt due to a difference between aminoguanidine bicarbonate and the hydrochloride and nitrate. The bicarbonate is relatively insoluble in water; its solutions therefore contain much lower concentrations of aminoguanidine salt than was the case with the hydrochloride or nitrate. As a result, monoguanilyhydrazones are given a greater chance to cyclize before reacting further with aminoguanidine to form the osazones.

3-Amino-*as*-triazine appears to be the simplest *as*-triazine known.

Acknowledgment.—Analyses were performed by the Microanalytical Group of these laboratories.

Experimental

3-Amino-*as*-triazine.—Thirty per cent. glyoxal solution in water (80 g., 0.41 mole of glyoxal) was added to a suspension of aminoguanidine bicarbonate (76.5 g., 0.56 mole) in 1200 ml. of water at 25°. The evolution of carbon dioxide began almost immediately. The mixture was stirred for two hours; at the end of this period the evolution of gas had virtually ceased. After standing overnight, the mixture was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was extracted with 1 liter of cold methanol. The methanol solution was filtered, evaporated to 100 ml., chilled and filtered again, yielding 24.0 g. (60.3%) of crude product as brown crystals. Recrystallization from acetonitrile gave fine, white needles, m.p. 171.5–172.5° (cor.), soluble in water.

Anal. Calcd. for $C_3H_4N_4$: C, 37.50; H, 4.19; N, 58.31. Found: C, 38.08, 38.03; H, 4.35, 4.30; N, 58.44, 58.05.

- (1) Research Dept., General Mills, Inc., Minneapolis, Minn.
(2) J. Thiele and E. Dralle, *Ann.*, **608**, 275 (1898).

3-Amino-5,6-dimethyl-*as*-triazine.—A solution of biacetyl (64.4 g., 0.75 mole) in 250 ml. of water was added to a suspension of aminoguanidine bicarbonate (102 g., 0.75 mole) in 1250 ml. of water at 25°. The reaction was slow at first but carbon dioxide began gradually to be evolved. After standing for 22 hours at 25°, the mixture was warmed to 50° for an hour, then chilled and filtered, yielding 60.6 g. of nearly white solid, m.p. 208–210° (cor.). Concentration of the filtrate to 400 ml., followed by chilling and filtration, gave an additional 6.2 g. of product; total yield of crude product, 66.8 g. (82.6%). Recrystallization from toluene-ethanol (3:1 by volume) gave a very light yellow product, m.p. 211–212° (cor.). It is approximately 1% soluble in water at 25°.

Anal. Calcd. for $C_5H_8N_4$: C, 48.37; H, 6.50; N, 45.13. Found: C, 48.25, 48.52; H, 6.46, 6.73; N, 45.13, 45.13.

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Preparation of N-Bis-(2-cyanoethyl)-acetamide¹

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In the course of certain researches carried on in this Laboratory, a quantity of N-bis-(2-cyanoethyl)-acetamide was required. A search of the literature revealed two reports of this compound. In an attempt to characterize β, β' -iminodipropionitrile, Kost² reported the preparation of the acetyl derivative, N-bis-(2-cyanoethyl)-acetamide, and indicated a melting point of 146°. No details of the method of preparation are given, but it must be concluded from our findings that the reaction used was that between β, β' -iminodipropionitrile and acetyl chloride, inasmuch as the compound actually obtained was the hydrochloride³ and not the acetyl derivative of β, β' -iminodipropionitrile.

In a patent⁴ by McQueen, a preparation of N-bis-(2-cyanoethyl)-acetamide is described which involves the base-catalyzed reaction of acetamide and acrylonitrile.⁵ The product was isolated as a liquid boiling at 210–225° and 2 mm., but no other physical constants are given. Several attempts to repeat the reaction in this Laboratory by adding acrylonitrile dropwise to a stirred solution of acetamide and catalytic amounts of Triton B in dioxane at about 30° were unsuccessful. The acetamide was recovered and a polymer of acrylonitrile was isolated.

We have obtained N-bis-(2-cyanoethyl)-acetamide as a solid (m.p. 50°) using very slightly more than two moles of amine to one mole of acid chloride. The excess amine permits complete reaction of the acid chloride by accepting the hydrogen chloride generated in the reaction.

(1) Financial support of this research was supplied by the United States Office of Naval Research.

(2) A. N. Kost, *Vestnik, Moskov, Univ.*, No. 2, 141 (1947); *C. A.*, **42**, 3722 (1948).

(3) In a subsequent publication, the preparation of the hydrochloride of β, β' -iminodipropionitrile was reported, and its melting point was listed as 147–148°. No remark was made of the earlier erroneous report of the constants for the supposed acetyl derivative. See A. P. Terent'ev, *et al.*, *Zhur. Obshchei Khim.*, **20**, 1073 (1950); *C. A.*, **44**, 9349 (1950); **45**, 1968 (1951).

(4) D. M. McQueen, U. S. Patent 2,424,664 (1947).

(5) In the review article on "Cyanoethylation," by H. A. Bruson, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 79 *et seq.*, the reaction is represented as giving a 72% yield. However, no indication is given of the low conversion, 24%, reported by McQueen.

Experimental

N-Bis-(2-cyanoethyl)-acetamide.—A solution of 25 g. (0.203 mole) of β,β' -iminodipropionitrile in 30 ml. of chloroform was cooled and rapidly stirred during the addition of 7.85 g. (0.1 mole) of acetyl chloride. A vigorous reaction set in instantly, causing the precipitation of a white solid. After stirring for about one hour, the solid was removed by suction filtration. The solid melted at 147° , the melting point of the hydrochloride of β,β' -iminodipropionitrile, and it was obtained in 95–100% of the theoretical amount. The filtrate was a clear yellow solution, and when hydrogen chloride gas was bubbled through it, more of the hydrochloride formed. In addition, the yellow color was discharged, giving rise to a yellow gum and a water-white solution. The solid and gum were removed by filtration, and the chloroform solvent was evaporated from the clear filtrate. A solid began to crystallize out, and even before the entire product had solidified, it was poured into boiling ethyl acetate. Upon cooling, white plates crystallized slowly; a dried sample of this material melted at 50° (cor.). The yield of product was 82%.

Anal. Calcd. for $C_8H_{11}N_3O$: C, 58.16; H, 6.71; N, 25.44. Found: C, 58.32; H, 6.65; N, 25.37.

β,β' -Iminodipropionitrile Hydrochloride.—Dry hydrogen chloride was passed into a solution of β,β' -iminodipropionitrile in chloroform and a white solid precipitated immediately. The needles were filtered off, washed with chloroform and ethanol, and then dried in a vacuum desiccator. A sample of this solid melted at 147 – 148° , and recrystallization from methanol did not raise the melting point. A determination of the melting point of a mixture consisting of the pure hydrochloride and a sample of the white solid obtained during the preparation of N-bis-(2-cyanoethyl)-acetamide showed no depression.

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Preparation and Chlorinolysis of α -Mercaptodiethylacetic Acid

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A recent oxidation of thioglycolic acid to chlorosulfonylacetic acid with chlorine¹ suggested the possibility of obtaining α -chlorosulfonyldiethylacetic acid, desired for synthetic purposes, in this way. The action of chlorine on α -mercaptodiethylacetic acid resulted, however, in the formation of dichloro- α -ethylbutyric acid (apparently the α,β -isomer), α -ethylcrotonic acid and sulfuric acid as the only isolable products.² These observations may be helpful in suggesting the nature of products obtained from the chlorine oxidation of other sulfur compounds.

Experimental³

α -Bromodiethylacetic Acid (I).—A modification of the general method of Marvel⁴ was used. A mixture of 288.7 g. of diethylacetic acid, 435 g. of dry bromine and 4.4 ml. of phosphorus trichloride was heated at 70 – 80° for ten hours. Additional bromine (23 g.) was added and heating continued for six hours. Distillation using a 15-cm. Vigreux column gave 370 g. (76%) of I, b.p. 98.5 – 103.5° (0.9 mm.); m.p.

(1) J. B. Dickey, U. S. Patent 2,466,396 (1949) [C. A., **43**, 4868 (1949)].

(2) Dr. E. Campaigne of Indiana University has informed us that an attempted synthesis of ethyl α -chlorosulfonylisobutyrate by the wet chlorine oxidation of the isothiuronium salt of ethyl α -bromoisobutyrate resulted in the evolution of sulfur dioxide upon working up the product.

(3) Melting points are corrected and boiling points are uncorrected. Most of the analyses are by the Clark Microanalytical Laboratory, Urbana, Ill.

(4) C. S. Marvel, *Org. Syntheses*, **29**, 106 (1940).

20 – 21.5° ; n_D^{25} 1.4743; reported⁵ b.p. 130 – 133° (18 mm.); m.p. 20° ; Br found, 40.73 (calcd., 40.97).

I reacts rapidly with two equivalents of 0.1 *N* sodium hydroxide upon titration in the usual way. Thus, while rapidly fading end-points corresponding to neut. equiv. of 170–192 (calcd. 195) were observed, end-points stable for one-half hour corresponded to neut. equiv. 97.9 (calcd. for I/2 97.5).

This neutralization of I with two equivalents of alkali was found to involve both elimination and substitution reactions. Addition of 4.1 g. of sodium hydroxide in 23 ml. of water to 10 g. of I with cooling, followed by acidification and extraction gave solid and oil which were separated. Short-path distillation of the solid gave 0.5 g. (8%) of α -hydroxydiethylacetic acid, m.p. 78 – 79.5° (reported⁶ 80°); neut. equiv., 133 (calcd., 132). Short-path distillation of the oil gave 0.83 g. (14%) of the liquid form of α -ethylcrotonic acid (II), n_D^{25} 1.4441; neut. equiv., 112 (calcd., 114); this form of II upon heating with hydrobromic acid⁷ gave the solid form, m.p. 39.5 – 40° (reported⁸ 41 – 42°).

In order to substantiate the α -position of bromine in the presumed I, a portion of the bromo acid was converted with silver oxide in water to α -hydroxydiethylacetic acid, m.p. 78° .

α -(Ethylxantho)-diethylacetic Acid (III).—III was prepared using a procedure based on one of Billmann.⁹ A solution of 600 g. of potassium ethyl xanthate¹⁰ in 950 ml. of water containing 347 g. of I was allowed to stand for two days. Oil which separated was removed with ether and the aqueous layer was treated with 360 ml. of 30% hydrochloric acid. An ether extract of the oily product on partial evaporation and chilling gave 192.0 g. (46%) of III as white crystals, m.p. 108 – 112° (uncor.), which after recrystallization from aqueous ethanol had a constant m.p. of 114.5 – 115° .

Anal. Calcd. for $C_9H_{16}O_3S_2$: C, 45.74; H, 6.82; S, 27.13; neut. equiv., 236. Found: C, 46.07; H, 6.67; S, 27.04; neut. equiv., 236.

α -Mercaptodiethylacetic Acid (IV).¹¹—III was converted to IV by a method similar to one of Billmann.⁹ A flask completely filled with 192 g. of III, 332 ml. of 25% ammonium hydroxide and 638 ml. of absolute alcohol, was allowed to stand closed for four days. The mixture was then heated at the reflux temperature for three hours, after which excess alcohol and ammonia were removed by distillation. The residue was adjusted with concentrated ammonium hydroxide to about pH 10, extracted with ether, and then brought to about pH 3 with concentrated hydrochloric acid (137 ml.). An ether extract of the resulting oil was dried over anhydrous sodium sulfate, and the IV obtained therefrom was purified by distillation; yield 56.9 g. (47%), b.p. 85 – 118° (1 mm.). Redistillation gave IV having b.p. 113 – 117° (5 mm.); m.p. 26 – 28.5° ; n_D^{25} 1.4768; d_4^{25} 1.0718; M_D calcd. 39.14, found 39.06.

Anal. Calcd. for $C_8H_{12}O_2S$: C, 48.62; H, 8.16; S, 21.63; neut. equiv., 148. Found: C, 48.55; H, 8.04; S, 21.44; neut. equiv., 148.

Chlorinolysis of IV.—Chlorine gas was passed through a solution of 10 g. of IV in 10 ml. of water and 25 ml. of acetic acid cooled to -15° . The temperature rose initially to 15° but could soon be maintained at -15° during one hour of chlorination; 16.4 g. of chlorine was absorbed. After addition of ice-water, a benzene extract was dried and concentrated with gentle heating under reduced pressure to an oil from which 0.7 g. (6%) of a dichloro- α -ethylbutyric acid slowly separated, m.p. 99 – 103.5° . Recrystallization from petroleum ether–benzene (5:1) gave the pure dichloro acid, m.p. 111 – 112° , an aqueous solution of which was strongly acidic.

(5) K. W. Rosenmund, *Ber.*, **42**, 4472 (1909). Cf. M. S. Newman, *THIS JOURNAL*, **57**, 732 (1935).

(6) F. Tiemann and L. Friedländer, *Ber.*, **14**, 1974 (1881).

(7) E. Blaise and P. Bagard, *Ann. chim. phys.*, [8] **11**, 120–131 (1907).

(8) K. von Auwers, *Ann.*, **432**, 76 (1923).

(9) E. Billmann, *ibid.*, **343**, 128 (1906).

(10) Prepared by Frey's procedure as given by C. Bruchhold, *Eng. Mining J.*, **125**, 338 (1928).

(11) The preparation of IV by another method was reported by E. Clemmensen and A. H. C. Heitman, *Am. Chem. J.*, **40**, 298 (1908); no physical constants were given.