was concentrated at diminished pressure to obtain 0.40 g. of solid matter. This was treated with 5 cc. water and after removal of unchanged trimethylisocyanuric acid by filtration, the solution was again concentrated to dryness at diminished pressure leaving *sym*-dimethylurea, m.p. 80°. It formed a characteristic nitroso compound melted at 97–98°. It showed no depression of the melting point on admixture with the authentic sample.

Hydrolysis of trimethylmelamine. A 10-cc. sample of concd. hydrochloric acid was added to a solution of 2.20 g. of distilled trimethylmelamine in 10 cc. water, and the mixture was heated at 150–160° for 5 hr. in a sealed tube. The resulting solution was allowed to cool to room temperature resulting in the separation of cyanuric acid needle crystals. The crystals were filtered, dried, and weighed 1.32 g., 79%, m.p. above 350°.

Anal. Calcd. for $C_3H_3N_3O_3$: N, 32.55. Found: N, 32.23.

Identity was further confirmed by converting them to cyanuric chloride. It melted at 145° and gave no melting point depression with the authentic sample.

The filtrate was then diluted to 300 cc; made alkaline and subjected to steam distillation. The distillate was caught into 0.1*N* hydrochloric acid. The hydrochloric acid solution was evaporated to dryness leaving 2.46 g. methylamine hydrochloride, m.p. 225–226° after recrystallization from butanol. The Nessler's test for ammonia was completely negative. Identity was further confirmed by converting it to methylguanidine hydrochloride by treating it with cyanamide. The picrate derived from the hydrochloride melted at 199°.

Ultraviolet and infrared spectrums. The ultraviolet absorption spectrum of trimethylisomelamine indicated no maxima from 250 mμ to 280 mμ. On the other hand, that of trimethylmelamine showed a weak maxima at about 235 mμ which might have been due to the conjugated double bond.

The infrared absorption spectrum of trimethylmelamine[8] indicated a very distinct absorption at 12.25 μ, pointing to the presence of triazine ring.[9] Trimethylisomelamine[10] had no absorption at the same region.

The infrared absorption spectrum of cyanuric acids[11] derived from melamine and trimethylamine was also measured. They showed the same spectrum indicating the same identity and had an absorption at 12.80 μ.

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[8] Film from ether.

[9] Same result was obtained by W. M. Padgett and W. F. Hamner, *J. Am. Chem. Soc.*, **80,** 803 (1958), for trimethylmelamine.

[10] In Nujol.

[11] Pressed into a potassium bromide disk.

[12] Present address, Nippon (Japan) Carbide Industries Inc., Uozu City, Toyama-Pref. Japan.

Cyanamide Derivatives. LVII.[1] New Route for Preparation of Biguanide[2]

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O-alkylisuorea is a substance quantitatively obtainable from crystalline cyanamide on a commercial basis.

We have discovered that biguanide can be obtained in a pure state and good yield by treating *O*-alkylisourea with guanidine in ethanol.

The reactions are indicated schematically as follows:

$$NH_2C(NH)OR + NH_2C(NH)NH_2 \longrightarrow NH_2C(NH)NHC(NH)NH_2 + ROH$$

$$NH_2C(NH)NHC(NH)NH_2 + NH_2C(NH)NH_2{\cdot}HCl \longrightarrow NH_2C(NH)NHC(NH)NH_2{\cdot}HCl + NH_2C(NH)NH_2$$

Melamine was a main by-product resulting from the reaction of *O*-alkylisourea with biguanide as well as other reactions of the former.[3] A small amount of dicyandiamide was also formed.

Although we have been able to obtain the biguanide salt by treating dicyandiamide with the ammonium salt in the fused state,[4] we do not consider it a convenient method to prepare biguanide because of the low yield and complexity of purification. Therefore, this method offers a practical route for the preparation of biguanide.

EXPERIMENTAL

A 500-cc. sample of an ethanolic solution[5] of 88.1 g. of *O*-ethylisourea, 59.1 g. of guanidine, and 191 g. of guanidine hydrochloride was placed in a four necked flask fitted with a condenser, stirrer, thermometer, and a sodium hydroxide tube. The solution was heated at 60°–65° with stirring and a precipitate formed after 2 hr. Heating was continued for 3 hr. and then allowed to cool overnight. The separated crystals were filtered and washed with ethanol, dried, and weighed 64.2 g. They were dissolved in 200 cc. of cold water and the insoluble residues were filtered. Evaporation of the filtrate at diminished pressure gave 57.0 g. of pure biguanide monohydrochloride, m.p. 224°–225°. The melting points of free base, mononitrate, and monopicrate derived from the monohydrochloride were 130°,[6] 202°,[7] and 232°,[7] respectively. The yield was 54% based on

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[1] Part LVI, *J. Org. Chem.*, **25,** 1043 (1960).

[2] This paper was prepared for delivery before the annual meeting of the Chemical Society of Japan held on April 1957.

[3] K. Sugino and K. Shirai, unpublished results. U. S. patent application, Serial No. 782675, Dec. 24, 1958.

[4] For example, K. Sugino, *J. Chem. Soc. Japan*, **60,** 351 (1939), (Part VII of this series).

[5] This solution was prepared in the following manner: Free guanidine ethanolic solution was first prepared from a solution of guanidine hydrochloride in ethanol by removing the acid with metallic sodium. It was concentrated at diminished pressure to a concentration of 3–5*N*. A quantity of *O*-ethylisourea and guanidine hydrochloride crystals was added to a certain volume of the solution and diluted to a certain concentration by ethanol.

reacted *O*-ethylisourea.[8] The insoluble residue consisted of melamine whose melting point was 349°. The yield was 6.2 g., 19% based on reacted *O*-ethylisourea. Both yields based on guanidine were almost quantitative.

Anal. (Biguanide monohydrochloride). Calcd. for $C_2H_8N_5Cl$: N, 50.91, Cl, 25.77. Found: N, 51.13, Cl, 25.53.

To the mother liquor were added 67.0 g. of *O*-ethylisourea and 39.6 g. of guanidine hydrochloride and the resulting solution was heated for 3 hr. at 60°–65° and worked up as described above. As a result, 71.1 g. of pure biguanide monohydrochloride and 6.7 g. melamine were obtained. The yields were 58% and 12%, respectively, based on reacted *O*-ethylisourea.

Another run was carried out using 400 cc. of a methanolic solution of 74.1 g. of *O*-methylisourea, 59.1 g. of guanidine, and 191 g. of guanidine hydrochloride. The solution was heated at 60°–65° for 3 hr. and worked up as described above. As a result, 54.5 g. of pure biguanide monohydrochloride, melting at 224°–225°, and 6.0 g. of melamine, melting at 349°, were obtained. The yields were 54% and 19%, respectively, based on *O*-methylisourea consumed. To the mother liquor were added 55.0 g. of *O*-methylisourea and 38.0 g. of guanidine hydrochloride; the reaction was again carried out in the same manner as described above. As a result, 69.0 g. of pure biguanide monohydrochloride and 6.5 g. of melamine were obtained. The yields were 56% and 17%, respectively, based on *O*-methylisourea consumed. Both yields based on guanidine were almost quantitative.

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(6) K. Rackman, *Ann.* **376,** 171 (1910); K. Sugino and M. Ogawa, *J. Electrochem. Assoc. Japan,* **6,** 294 (1938), (Part IV of this series).

(7) K. Sugino, *J. Chem. Soc. Japan,* **60,** 359 (1939).

(8) This was calculated as follows: The total alkalinity of the solution was determined by titration with 0.1*N* hydrochloric acid using methylorange as the indicator. The concentration of *O*-alkylisourea was then calculated by subtracting the amount of guanidine from the amount of total base.

Cyanamide Derivatives. LVIII.[1] Formation of Formoguanamine and Guanidine Salt by the Reaction of Formamidine Salt with Dicyandiamide[2]

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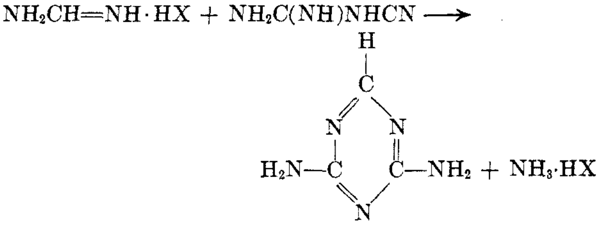
We discovered that the reaction of formamidine with dicyandiamide gave good yields of formoguanamine and guanidine salt.



$$0.5\ NH_2C(NH)NHCN + NH_3\cdot HX \longrightarrow NH_2C(NH)NH_2\cdot HX$$

As a simple method for the preparation of formamidine has been devised by us,[3] we have obtained a convenient route to prepare pure formoguanamine.

EXPERIMENTAL

A sample of 4.03 g. of formamidine hydrochloride and 6.30 g. of dicyandiamide was thoroughly mixed and heated in an oil bath at 150°–160° for 1.5 hr. The mixture melted at 70° and heat evolution was observed at about 160°. Therefore, attention is required to keep the reaction temperature at the desired region by a suitable method. Crystals of the products began to separate during the reaction and a solidification of the total mixture was observed at the end. The reaction products were pulverized, extracted with 30 cc. of water, and filtered. After the residue was washed with 5 cc. of ethanol and dried, it was recrystallized from hot water. A 4.90-g. sample (88%) of formoguanamine was obtained, m.p. 316°. It showed no depression on admixture with an authentic sample.[4] Melting point of the picrate[4] was 247°.

The water extract, combined with ethanol wash, was concentrated to dryness and then extracted with 20 cc. of ethanol.[5] Evaporation of the extract gave 3.71 g., 78% of guanidine hydrochloride, m.p. 184°; m.p. of picrate, 315°.

Better results were obtained by using phenol as a solvent. Here is an example.

An 8.05-g. sample of formamidine hydrochloride and 12.60 g. of dicyandiamide were mixed with 20 g. of phenol and the mixture was heated in an oil bath at 200° for 1 hr. After the reaction, the solvent was removed by distillation and the residue was worked up as described above. A 10.28-g. sample, 93%, of formoguanamine and 8.40 g., 89%, of guanidine hydrochloride were obtained.

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(1) Part LVII, *J. Org. Chem.,* **25,** 1045 (1960).

(2) Synthesis of *sym*-triazine system, I. This paper was prepared for delivery before the annual meeting of the Chemical Society of Japan on April 1958.

(3) K. Odo, E. Ichikawa, K. Shirai, and K. Sugino, *J. Org. Chem.,* **22,** 1715 (1957).

(4) M. Yamashita, *J. Chem. Soc. Japan (Ind. Chem. Sec.),* **54,** 786 (1951), (Part XL of this series).

(5) If a salt other than hydrochloride is used, the solvent should be changed accordingly.