

Studies of Cyanamide Derivatives. Part 110. A Facile Synthesis of 2,4,6-Triureido-1,3,5-triazine and 2-Amino-4,6-diureido-1,3,5-triazine

Kokoro IIO* and Eiichi ICHIKAWA†

Industrial Products Research Institute, Yatabe-machi Higashi, Tsukuba-gun, Ibaraki 305

†Faculty of Engineering, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152

(Received December 24, 1983)

Synopsis. 2,4,6-Triureido-1,3,5-triazine and 2-amino-4,6-diureido-1,3,5-triazine were readily synthesized in high yields, 94 and 85% respectively, by the alcoholysis of 2,4,6-tris(cyanoamino)-1,3,5-triazine and 2-amino-4,6-bis(cyanoamino)-1,3,5-triazine in the presence of hydrogen chloride.

There are numerous reports¹⁻⁷⁾ on preparations and uses of ureido-1,3,5-triazines such as 2,4-diamino-6-ureido-1,3,5-triazine (**1**), 2-amino-4,6-diureido-1,3,5-triazine (**2**), and 2,4,6-triureido-1,3,5-triazine (**3**). However, there are still problems with the preparations of these compounds.^{8,9)} In our previous paper,^{10,11)} we reported the preparation of **1** and its properties. This paper will describe a facile method of synthesizing **2** and **3** from the corresponding cyanoamino-1,3,5-triazines and will clarify their properties in acidic and alkaline aqueous solutions.

An attempted cyclotrimerization of linear cyano-ureido compounds such as cyanourea and *N*-cyano-*O*-ethylisourea did not give **3**. Cyanourea, however, gave 1-carbamoyl-3-cyanoguanidine and 1-cyanobiuret,¹²⁾ and *N*-cyano-*O*-ethylisourea gave 2-amino-4-ethoxy-6-ureido-1,3,5-triazine (**4**) in the presence of hydrogen chloride, using sulfolane as a solvent. The isoureido group attached to 1,3,5-triazine ring might be converted into the ureido group by the action of hydrogen chloride. Furthermore, acid hydration of cyanoamino-1,3,5-triazines failed to give the corresponding ureido-1,3,5-triazines, except for **1**.¹⁰⁾

Alcoholysis of 2,4,6-tris(cyanoamino)-1,3,5-triazine in the presence of hydrogen chloride gave **3** hydrochloride. During the reaction, methyl chloride was evolved and identified by its mass spectrum. The free **3** was given in 94% yield by the treatment of its hydrochloride with a dilute sodium hydroxide solution. **3** was slightly soluble in water and ordinary organic solvents, but could be recrystallized from a hot dilute nitric acid solution as the nitrate.

In a similar manner, **2** was synthesized from 2-amino-4,6-bis(cyanoamino)-1,3,5-triazine in 85% yield. **2** was also slightly soluble in water and organic solvents, but could be recrystallized from a hot dilute sulfuric acid solution as the sulfate.

It was reported¹⁰⁾ that the alkaline hydrolysis of **1** gave melamine, carbon dioxide, and ammonia in high yields. The similar alkaline hydrolysis of **3**, however, gave ammeline instead of melamine, along with carbon dioxide and ammonia. In the case of **2**, melamine, ammeline, carbon dioxide, and ammonia were all obtained.

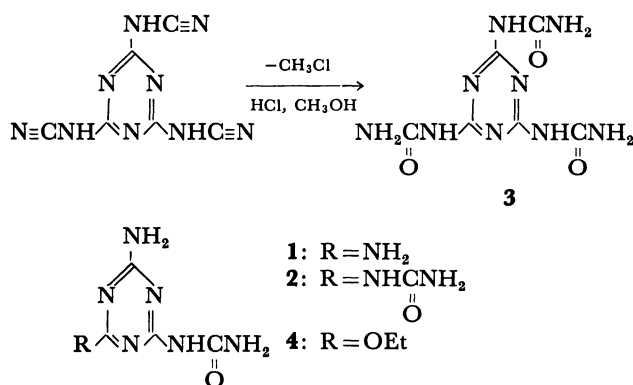
Acid hydrolyses of **2** and **3** with 2 mol dm⁻³ of hydrochloric acid were examined. The reaction was followed by the IR spectrum of the reaction mixture. Small amounts of the solution were taken out at 30 min intervals and evaporated to dryness. In the case of **3**, cyanuric acid was readily detected after 30 min refluxing the solution. Cyanuric acid and urea were obtained in 95 and 26% yields respectively after 4 h. In the case of **2**, cyanuric acid was detected after 1 h. Cyanuric acid, ammeline and urea were obtained in 74, 2 and 34% yields respectively after 2 h. These results suggest that the hydrolysis of **2** and **3** is liable to take place on the carbon atom of the 1,3,5-triazine ring attached with ureido group, and that the preparation of **2** and **3** by the acid hydration of corresponding cyanoamino-1,3,5-triazines is very difficult.

Experimental

The melting points are uncorrected. The IR spectra were taken with a Hitachi EPI-2 spectrometer. The UV spectra were taken with a Hitachi 624 spectrometer. The NMR spectra were measured with a Hitachi R-24A spectrometer using TMS as an internal standard. The mass spectra were taken with a JEOL JMS-D100 mass spectrometer.

2-Amino-4-ethoxy-6-ureido-1,3,5-triazine (4). Hydrogen chloride (1.82 g, 0.05 mol) was introduced into a stirred solution on *N*-cyano-*O*-ethylisourea (5.66 g, 0.05 mol) in 20 ml of sulfolane at room temperature. After 2 h at 70 °C, the solution was poured into a large amount of water. The precipitate of **4** was filtered and recrystallized from water. The yield was 2.52 g (51%). Mp 220 °C. Found: C, 36.10; H, 4.99; N, 42.10%; M⁺, 198. Calcd for C₆H₁₀N₆O₂: C, 36.36; H, 5.09; N, 42.42%; M⁺, 198. IR (KBr) 1700 (C=O) and 815 cm⁻¹ (1,3,5-triazine ring). UV (H₂O) 212.4 nm (log ε 4.55). NMR (DMSO-*d*₆) δ=1.24 (3H, CH₃), 4.25 (2H, CH₂), 7.10, 7.36, 8.60, and 9.67 (5H, m).

2,4,6-Triureido-1,3,5-triazine (3). Hydrogen chloride (7.29 g, 0.2 mol) was introduced into a suspension of the trisodium salt of 2,4,6-tris(cyanoamino)-1,3,5-triazine¹³⁾ (5.34 g, 166 mmol) in 40 ml of methanol under cooling below 5 °C. The reaction mixture was stirred for 2 h at room temperature, and then heated to reflux for 2 h, evolving methyl



chloride, which was identified by the mass spectrometer, MS m/z 52 and 50 (M^+). After cooling, the precipitate was filtered and washed with a dilute sodium hydroxide solution and water. The yield of **3** was 4.52 g (94%). **3** was recrystallized from a hot dilute nitric acid solution (0.50 g of **3**/4 mol dm^{-3} HNO_3 180 ml) as the nitrate: mp >360 °C; Found: C, 21.19; H, 3.56; N, 41.62; H_2O , 5.87%. Calcd for $\text{C}_6\text{H}_9\text{N}_3\text{O}_3 \cdot \text{HNO}_3 \cdot \text{H}_2\text{O}$: C, 21.43; H, 3.60; N, 41.66; H_2O , 5.36%. IR (KBr) 1720, 1700 ($\text{C}=\text{O}$), and 795 cm^{-1} (1,3,5-triazine ring). UV (H_2O) 215.5 ($\log \epsilon$ 4.86) and ca. 247.0 nm (sh, 4.08).

2-Amino-4,6-diureido-1,3,5-triazine (2). **2** was synthesized from 2-amino-4,6-bis(cyanoamino)-1,3,5-triazine¹⁴ by the same method as above, in 85% yield. **2** was recrystallized from the hot dilute sulfuric acid solution (0.50 g of **2**/10% H_2SO_4 100 ml) as the sulfate: mp >360 °C; Found: C, 19.07; H, 3.43; N, 36.40%. Calcd for $\text{C}_5\text{H}_8\text{N}_8\text{O}_2 \cdot \text{H}_2\text{SO}_4$: C, 19.36; H, 3.23; N, 36.12%. IR (KBr) 1715 ($\text{C}=\text{O}$) and 790 cm^{-1} (1,3,5-triazine ring). UV (H_2O) 216.0 ($\log \epsilon$ 4.62) and ca. 242.5 nm (sh, 3.86).

Alkaline Hydrolysis. According to the previously reported method,¹⁰ **3** gave ammeline (43%), barium carbonate (83%), and ammonia (82%).

Similarly **2** gave melamine (33%), ammeline (9%), barium carbonate (62%), and ammonia (57%).

Acid Hydrolysis. **3** (0.97 g, 1/300 mol) was refluxed in 40 ml of 2 mol dm^{-3} of hydrochloric acid for 4 h. After the reaction mixture had been evaporated to dryness under reduced pressure, the residue was washed with a small amount of water to give 3.30 g (77%) of cyanuric acid. The filtrate was neutralized with dilute sodium hydroxide solution and the saturated melamine solution was added to give 0.13 g (18%) of melamine cyanurate. The filtrate was evaporated and extracted with ethanol to give 0.32 g (26%) of urea as the nitrate. Ammonia was detected in the solution.

In a similar manner, **2** was refluxed in 2 mol dm^{-3} of

hydrochloric acid for 2 h, and gave cyanuric acid (70%), melamine cyanurate (4%), urea nitrate (34%), and ammeline (2%). Ammonia was also detected in the solution. Products were confirmed by comparing their IR spectrum and melting points with those of an authentic sample.

References

- 1) K. Muraoka, I. Sugaya, H. Noda, K. Horie, S. Suda, and Y. Ooya, Jpn. Patent 70-27835 (1970).
- 2) H. H. Grossmann, K. H. Burg, and G. Sextro, Ger. Offen. 2348808 (1975).
- 3) M. Taguchi and M. Aramaki, Jpn. Patent 69-04656 (1969).
- 4) A. Hantzsch and H. Bauer, *Chem. Ber.*, **38**, 1005, (1905).
- 5) G. F. D'Alelio, U. S. Patent 2394042 (1946).
- 6) F. L. Scott and H. Q. Smith, U. S. Dept. Com., Office Tech. Serv. PB Rept., 152012 (1960); U. S. Patent 3101335 (1963).
- 7) H. Bieling, M. Radüchel, G. Wenzel, and H. Beyer, *J. Prakt. Chem.*, **28**, 325, (1965).
- 8) E. A. Werner, *J. Chem. Soc.*, **103**, 2275, (1913).
- 9) I. Honda, A. Murata, A. Nisikawa, M. Maekawa, and Y. Oshima, *Kogyo Kagaku Zasshi*, **71**, 529, (1968); Jpn. Patent 12429 (1967).
- 10) E. Ichikawa, T. Takizawa, and K. Odo, *Yuki Gosei Kagaku Kyokai Shi*, **32**, 936, (1974).
- 11) K. Iio, E. Ichikawa, and K. Odo, *Yuki Gosei Kagaku Kyokai Shi*, **32**, 513, (1974).
- 12) K. Iio, *Bull. Chem. Soc. Jpn.*, **57**, 625, (1984).
- 13) W. Madelung and E. Kern, *Justus Liebigs Ann. Chem.*, **427**, 26, (1922).
- 14) T. Suyama and K. Odo, *Yuki Gosei Kagaku Kyokai Shi*, **29**, 298, (1971).