acid solution was extracted with three 75-ml. portions of chloroform and then cautiously neutralized by the addition of a sufficient amount of 35% sodium hydroxide solution. The red oil that appeared was taken up in ethyl ether and the alkaline solution further extracted with three 75-ml. portions of ether. The ethereal extracts were combined and dried over potassium carbonate. After the ether was removed at atmospheric pressure, the residual oil was distilled *in vacuo*. There was obtained 17.8 g. (40%) of a colorless oil b.p. 104–106°/3.5 mm., n_D^{30} = 1.4544 (lit.[1] b.p. 87°/1.3 mm.; n_D^{30} = 1.4542). Picrate (from ethanol) m.p. 282° dec.

Alkaline hydrolysis of III. Ten g. (0.055 mol.) of III were added to 100 ml. of 10% aqueous sodium hydroxide and refluxed for 24 hr. The colorless oil which was present was taken up in ether and the remaining aqueous layer was saturated with sodium chloride and extracted twice with an equal volume of ether. The ether extracts were combined and dried over anhydrous sodium carbonate. After removal of the ether, distillation of the residue yielded 6.3 g. of 4-amino-4-methyl-2-pentanol, b.p. 71–72°/12 mm., n_D^{20} = 1.4345 (lit.[5] b.p. 74–75°/15 mm., n_D^{20} = 1.4335).

Acidification of the alkaline aqueous solution yielded succinic acid, m.p. 272–274° dec. Admixture with an authentic sample of succinic acid showed no depression in the melting point.

2,4,4,6-Tetramethyldihydro-1,3-oxazine. This compound was prepared according to the method of Tillmanns and Ritter.[2] B.p. 58°/25 mm., n_D^{25} = 1.4355.

2-Ethyl-4,6,6-trimethyldihydro-1,3-oxazine. Prepared in the same manner as the 2-methyl derivative. B.p. 67°/20 mm., n_D^{25} = 1.4385.

Anal. Calcd. for $C_9H_{17}ON$: C, 69.67; H, 10.96. Found: C, 69.62; H, 10.91.

Acknowledgment. The author wishes to express his gratitude to the Research Corporation and the National Institutes of Health (DGMS-6248) for funds granted to support a study of which the present work is a part. Thanks are due to Mr. R. T. O'Connor and his staff at the Southern Regional Research Laboratory, United States Department of Agriculture, for determining the infrared spectra.

DIVISION OF SCIENCES
LOUISIANA STATE UNIVERSITY IN NEW ORLEANS
NEW ORLEANS 22, LA.

Synthesis of 5-Alkyl-2-iminohexahydro-*s*-triazine-1-carbonitriles and 3,3′-Ethylenebis-(6-iminohexahydro-*s*-triazine-1-carbonitrile)

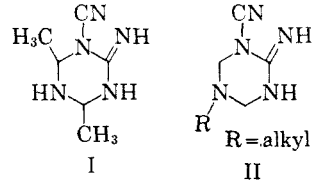
EDWARD H. SHEERS

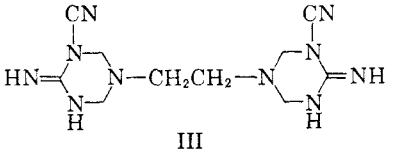
Received August 5, 1959

The condensation of primary alkylamines with one mol. of urea or thiourea and 2 mol. of formaldehyde to give 5-alkylhexahydro-*s*-triazinones and 5-alkylhexahydro-*s*-triazinethiones[1] suggested that cyanoguanidine might react in a similar fashion to form a cyclic derivative.

Pohl[2] showed that cyanoguanidine condenses with acetaldehyde-ammonia to give 2-imino-4,6-dimethylhexahydro-*s*-triazine-1-carbonitrile (I). This reaction has not been reported with any aldehyde-ammonia above C_2. This, together with the fact that the higher aliphatic aldehydes are not readily available, somewhat limits the scope of Pohl's reaction.

Cyanoguanidine reacted readily with one mol. of alkylamine and 2 mol. of formaldehyde to give high yields of 5-alkyl-2-iminohexahydro-*s*-triazine-1-carbonitriles (II), a new series of colorless, solid hexahydro-*s*-triazine derivatives. With 0.5 mol. of ethylenediamine and 1 mol. of formaldehyde cyanoguanidine yielded the expected 3,3′-ethylenebis(6-iminohexahydro-*s*-triazine-1-carbonitrile) (III). This condensation appears to be quite general in nature.





EXPERIMENTAL

The cyanoguanidine used was American Cyanamid Company's commercial grade (purity 99%+). All other compounds used were Eastman White Label grade. All melting points are uncorrected.

Typical procedure for 5-alkyl-2-iminohexahydro-s-triazine-1-carbonitriles: 5-Butyl-2-iminohexahydro-s-triazine-1-carbonitrile. To 400 ml. water, there were added 43 g. cyanoguanidine, 37 g. *n*-butylamine, and 81 ml. formalin while stirring vigorously. The temperature rose to 54°. Stirring was continued for 1 hr. after the addition was complete. A colorless oil deposited which crystallized on standing overnight. This product was collected by filtration and recrystallized from 95% ethanol. The yield was 80% of theory and consisted of colorless platelets having a melting point of 149–150°.

Anal. Calcd. for $C_8H_{15}N$: C, 53.01; H, 8.34; N, 38.64. Found: C, 52.89; H, 8.45; N, 38.80.

3,3′-Ethylenebis(6-iminohexahydro-s-triazine-1-carbonitrile). To a solution of 43 g. cyanoguanidine in 200 ml. water, there were added 20 g. ethylenediamine and 81 ml. formalin while stirring vigorously. The temperature rose to 72°. The hot, clear solution was stirred, and white crystals of the product, m.p. 225–226°, deposited within 1 hr. in 75% yield.

Anal. Calcd. for $C_{10}H_{16}N_8$: C, 48.37; H, 6.50; N, 45.13. Found: C, 48.54; H, 6.47; N, 45.11.

(1) Burke, W. J., *J. Am. Chem. Soc.*, **69**, 2136 (1947); U. S. Patent **2,304,624** (1942); *cf.* also Paquin, A. M., *Angew. Chem.*, **A60**, 267 (1948).

(2) Pohl, F., *J. prakt. Chem.*, **77**, 538–539 (1908).

TABLE I

5-ALKYL-2-IMINOHEXAHYDRO-s-TRIAZINE-1-CARBONITRILES

Alkyl	Yield, %	M.P., °C.	Analysis					
			Calculated			Found		
			% C	% H	% N	% C	% H	% N
Methyl	92	196–197	43.15	6.52	50.33	43.20	6.58	50.30
Butyl	80	149–150	53.01	8.34	38.64	52.89	8.45	38.80
Isobutyl	88	177–178	53.01	8.34	38.64	52.96	8.35	38.71
Allyl	86	172–173	50.89	6.71	42.40	51.00	6.69	42.30
Cyclohexyl	84	172–173	57.94	8.28	33.79	57.91	8.29	33.69
n-Decyl	94	160–161	63.36	10.25	26.39	63.27	10.29	26.35
n-Dodecyl	92	157–158	65.48	10.65	23.87	65.54	10.59	23.82
n-Octadecyl	92	132.3	69.97	11.48	18.55	69.94	11.42	18.51

Acknowledgment. The author wishes to thank the Microanalytical Laboratory of the Stamford Laboratories for the microanalyses and Stanley E. Polchlopek for the infrared curves and their interpretation.

INDUSTRIAL CHEMICALS DIVISION
AMERICAN CYANAMID CO.
STAMFORD, CONN.

Studies in Purine Chemistry. VII. An Improved Synthesis of Hypoxanthine[1,2]

EDWARD C. TAYLOR AND C. C. CHENG

Received August 6, 1959

The desulfurization of a mercapto or alkylmercapto substituent is often a critical step in heterocyclic synthesis, particularly in pyrimidine and purine chemistry. The most commonly employed desulfurization method is to reflux the compound with an excess of Raney nickel under what are commonly termed "Mozingo conditions,"[3] and this procedure[4] has been employed in syntheses of both hypoxanthine[5] and adenine[6–8] derivatives. Other methods for replacement of the mercapto group by hydrogen include oxidation with nitric acid[9] or with hydrogen peroxide in acidic solution.[9–11]

An attractive alternative has more recently been described which involves oxidation of the mercapto group in alkaline solution with hydrogen peroxide to a sulfinic acid, followed by decomposition with strong acid, and has been applied to the synthesis of 4,5,6-triaminopyrimidine from 2-mercapto-4,5,6-triaminopyrimidine[12,13] and of 4,6-diaminopyrimidine from 2-mercapto-4,6-diaminopyrimidine.[13] By application of this method to the preparation of 4-hydroxy 5,6-diaminopyrimidine from 2-mercapto-4-hydroxy-5,6-diaminopyrimidine, and by means of certain other modifications, we have been able to effect significant improvements in the conventional synthesis of hypoxanthine from thiourea and ethyl cyanoacetate. Details are given in the Experimental.

Evans *et al.*[13] pointed out that the decomposition of 4,6-diaminopyrimidine-2-sulfinic acid to 4,6-diaminopyrimidine required much stronger acid than the analogous decomposition of 4,5,6-triaminopyrimidine-2-sulfinic acid to 4,5,6-triaminopyrimidine and that weaker acid led predominately to the 2-hydroxy derivative. This was attributed to the weaker basicity of the former pyrimidine, coupled with the requirement that diprotonation precede heterolytic cleavage of the C—S bond. We have found that oxidation of 2-mercapto-4-hydroxy-6-aminopyrimidine, a still weaker base, leads directly to 2,4-dihydroxy-6-aminopyrimidine; the 2-sulfinic acid could not even be isolated.

(1) This investigation was supported in part by a grant (C-2551) to Princeton University from the National Cancer Institute of the National Institutes of Health, Public Health Service.

(2) For the previous paper in this series, see E. C. Taylor and C. C. Cheng, *Tetrahedron Letters*, No. 12, 9 (1959).

(3) R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, *J. Am. Chem. Soc.*, **65**, 1013 (1945).

(4) For examples of the utilization of this method, see M. P. V. Boarland, J. F. W. McOmie, and R. N. Timms, *J. Chem. Soc.*, 4691 (1952); M. P. V. Boarland and J. F. W. McOmie, *J. Chem. Soc.*, 4942 (1952); L. F. Cavalieri and A. Bendich, *J. Am. Chem. Soc.*, **72**, 2587 (1950); E. A. Falco and G. H. Hitchings, *J. Am. Chem. Soc.*, **78**, 3143 (1956); R. K. Robins and G. H. Hitchings, *J. Am. Chem. Soc.*, **78**, 973 (1956); E. C. Taylor, *J. Am. Chem. Soc.*, **74**, 2380 (1952); C. C. Cheng and R. K. Robins, *J. Org. Chem.*, **23**, 852 (1958); D. J. Brown, *J. Soc. Chem. Ind.*, **69**, 353 (1950); H. Getler, P. M. Roll, J. F. Tinker, and G. B. Brown, *J. Biol. Chem.*, **178**, 259 (1949).

(5) G. B. Elion, E. Burgi, and G. H. Hitchings, *J. Am. Chem. Soc.*, **74**, 411 (1952).

(6) A. Bendich, J. F. Tinker, and G. B. Brown, *J. Am. Chem. Soc.*, **70**, 3109 (1948).

(7) G. A. Howard, B. Lythgoe, and A. R. Todd, *J. Chem. Soc.*, 556 (1945).

(8) E. C. Taylor, O. Vogl, and C. C. Cheng, *J. Am. Chem. Soc.*, **81**, 2442 (1959).

(9) W. Traube, *Ann.*, **331**, 64 (1904).

(10) H. Andersag and K. Westphal, *Ber.*, **70**, 2035 (1937).

(11) G. W. Kenner, B. Lythgoe, A. R. Todd, and A. Topham, *J. Chem. Soc.*, 574 (1943).

(12) M. Hoffer, "Jubilee Volume Dedicated to Emil C. Barrell," Basel, 1946, p. 428.

(13) R. M. Evans, P. G. Jones, P. J. Palmer, and F. F. Stephens, *J. Chem. Soc.*, 4106 (1956).