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[CONTRIBUTION FROM THE STAMFORD RESEARCH LABORATORIES OF THE AMERICAN CYANAMID CO.]

Cyanuric Chloride Derivatives. I. Aminochloro-*s*-triazines

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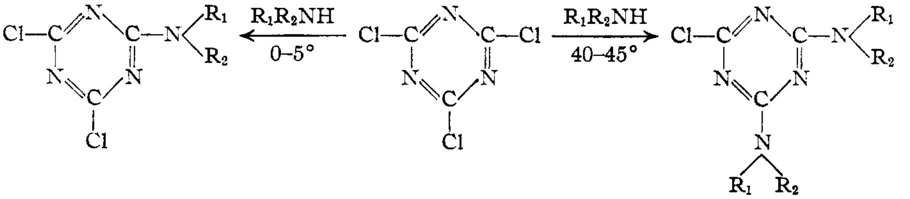
The reaction of cyanuric chloride with amines has been studied in order to provide intermediates for the preparation of substituted melamines, ammelides and ammelines. A number of new 2-amino-4,6-dichloro-*s*-triazines and 2,4-diamino-6-chloro-*s*-triazines have been prepared, and general methods for their preparation are described.

The reactions of cyanuric chloride have been summarized by Fierz-David and Matter,[1] but aside from its reaction with ammonia[2,3] and a few amines,[1,3,4] most of which were aromatic, the formation of aminochloro-*s*-triazines has not been generally studied until recently.[5] A number of these derivatives have been prepared in this Laboratory in connection with a program of investigating substituted melamines, ammelides and ammelines.

The 2-amino-4,6-dichloro-*s*-triazines and 2,4-diamino-6-chloro-*s*-triazines listed in Tables I and II were prepared by modifications of the known methods which have proven to be widely applicable.



Some of the compounds were not analyzed, and these have been identified only through the preparation of derivatives.[6] Since satisfactory analytical values were obtained for most of the compounds included in this paper, the unanalyzed substances were included here to provide continuity for the description of their derivatives.

The 2-amino-4,6-dichloro-*s*-triazines were prepared by modifications of the method of Diels.[3a] We have found, however, that it is not necessary to carry out the reaction of cyanuric chloride with ammonia or amines under anhydrous conditions. The reaction in water is incomplete unless the cyanuric chloride used is in a finely divided state, but no difficulties are experienced if the cyanuric chloride is freshly precipitated by pouring an acetone or dioxane solution into ice-water. The use of an aqueous system allows the products to be isolated easily in high yields. This modification was preferred except for the preparation of 2-amino-4,6-dichloro-*s*-triazine itself. Sodium hydroxide, sodium carbonate or sodium bicarbonate can be used to advantage in place of the amine reactant to neutralize the hydrogen chloride formed in the reaction. The 2,4-diamino-6-chloro-*s*-triazines were prepared in a similar manner in aqueous systems, the primary difference being a higher temperature requirement for complete reaction.

It is well known that the reactivity of the chlorine atoms in cyanuric chloride, 2-amino-4,6-dichloro-*s*-triazines and 2,4-diamino-6-chloro-*s*-triazines decreases from one series to the next in the order given.[3a,3c,4b] We have discovered that the reactivity of the chlorine atoms in the last two series also varies greatly with the degree of substitution of the amino nitrogen atom. 2-Amino-

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(1) H. E. Fierz-David and M. Matter, *J. Soc. Dyers Colourists*, **53**, 424 (1937).

(2) (a) J. Liebig, *Ann.*, **10**, 43 (1834); (b) M. P. Lemoult, *Compt. rend.*, **125**, 822 (1897).

(3) (a) O. Diels, *Ber.*, **32**, 691 (1899); (b) C. K. Banks, O. M. Gruhzit, E. W. Tillitson and J. Controulis, THIS JOURNAL, **66**, 1771 (1944); (c) H. S. Mosher and F. C. Whitmore, *ibid.*, **67**, 662 (1945).

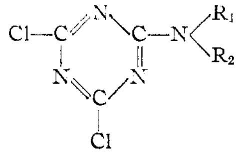
(4) (a) M. A. Laurent, *Compt. rend.*, **22**, 695 (1846); (b) H. H. Fries, *Ber.*, **19**, 242, 2055 (1886); (c) A. W. Hofmann, *ibid.*, **18**, 2755 (1886); (d) E. von Meyer and Fr. Näbe, *J. prakt. Chem.*, [2] **82**, 531 (1910); (e) H. Jensch, U. S. Patent 2,092,352 (1937); (f) A. H. Friedheim, U. S. Patent 2,295,574 (1942); A. H. Friedheim, THIS JOURNAL, **66**, 1775 (1944).

(5) W. M. Pearlman and C. K. Banks, *ibid.*, **70**, 3726 (1948).

(6) (a) D. W. Kaiser, *et al.*, *ibid.*, **73**, 2986 (1951); (b) J. R. Dudley, *et al.*, *ibid.*, **73**, 2984 (1951).

TABLE I[a]

2-AMINO-4,6-DICHLORO-*s*-TRIAZINES,

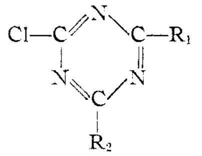


R_1	R_2	Base[b]	Yield,[c] %	Crystallized from	M.p., °C.	Formula	Analyses, %			
							Nitrogen		Chlorine	
							Calcd.	Found	Calcd.	Found
H[d]	H	NH_3	95	Water[e]	235–236	$C_3H_2Cl_2N_4$	...	...	...	...
n-Butyl	H	Na_2CO_3	92	Benzene	51–52	$C_7H_{10}Cl_2N_4$	...	...	...	...
n-Dodecyl	H	Amine	100	Heptane	65	$C_{15}H_{26}Cl_2N_4$	...	...	...	...
Cyclohexyl	H	Na_2CO_3	88	......	Oil	$C_9H_{12}Cl_2N_4$	...	...	...	...
Phenyl[f]	H	Na_2CO_3	99	Benzene	133–135	$C_9H_6Cl_2N_4$	...	...	...	...
Sodium *p*-sulfophenyl	H	NaOH	100	Water	.....	$C_9H_5Cl_2N_4O_3SNa\cdot 2H_2O$[g]	14.78	14.49	...	...
Ethyl	Ethyl	Na_2CO_3	91	Benzene	78–79	$C_7H_{10}Cl_2N_4$	25.34	24.85	...	...
Butyl	Cyanomethyl	$NaHCO_3$	73	Naphtha	80–81	$C_9H_{11}Cl_2N_5$	26.92	27.08	27.62	26.96
Cyclohexyl	Cyanomethyl	NaOH	66[h]	Methanol	145–146	$C_{11}H_{13}Cl_2N_5$	24.48	24.11	24.78	24.85
β-Cyanoethyl	β-Cyanoethyl	$NaHCO_3$	93	Naphtha	212–215	$C_9H_8Cl_2N_6$	31.00	30.62	26.16	26.63
Methyl	Phenyl	Na_2CO_3	92	Benzene	131–132	$C_{10}H_8Cl_2N_4$	...	...	27.80	27.80
Phenyl	Phenyl	$NaHCO_3$	85	Ethanol	172–174	$C_{15}H_{10}Cl_2N_4$	17.67	17.80	...	...

[a] The preparation of derivatives of these compounds is described in reference 6. [b] The base used to neutralize the hydrogen chloride formed in the reaction is listed. The listing of ammonia or amine shows that an excess of the reactant was used for this purpose. [c] Yield of product as isolated from the reaction mixture. Most of these products were essentially pure, and little improvement in purity was effected by crystallization. [d] References 3a, 3c. [e] Added to boiling water, filtered, and cooled rapidly to avoid hydrolysis. [f] References 1, 4c. [g] *Anal.* Calcd.: C, 28.51; H, 2.39. Found: C, 28.99; H, 2.42. [h] Yield of purified product.

TABLE II[a]

2,4-DIAMINO-6-CHLORO-*s*-TRIAZINES,

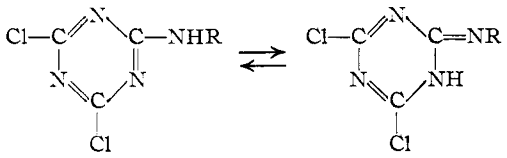


R_1	R_2	Base[b]	Yield,[c] %	Crystallized from	M.p., °C.	Formula	Analyses, %			
							Nitrogen		Chlorine	
							Calcd.	Found	Calcd.	Found
Amino[d]	Amino	NH_3	100	Water	Infusible	$C_3H_4ClN_5$[e]	...	...	24.36	24.34
Amino	*n*-Butylamino	Na_2CO_3	85	Aq. dioxane	148–150	$C_7H_{12}ClN_5$	34.73	35.22	...	...
Amino	Anilino	Amine	99	Ethanol–dioxane	213–214	$C_9H_8ClN_5$[f]	31.60	31.82	16.00	16.03
Amino	Di-*n*-butylamino	Amine	100	Methanol	119–120	$C_{11}H_{20}ClN_5$[g]	27.17	27.13	13.76	13.65
Ethylamino	Ethylamino	Na_2CO_3	97	Methyl cellosolve	226–227	$C_7H_{12}ClN_5$	34.73	34.58	...	...
n-Octadecylamino		Na_2CO_3	100	*n*-Butanol	136–137	$C_{39}H_{76}ClN_5$[h]	...	...	5.45	5.60
Cyclohexylamino		Na_2CO_3	...	Methyl ethyl ketone	228–229	$C_{15}H_{24}ClN_5$[i]	22.61	22.74	11.44	11.61
Cyanomethylamino		$NaHCO_3$	76	Aq. cellosolve	275–280	$C_7H_6ClN_7$	43.85	44.00	15.86	15.59
β-Hydroxyethylamino[d]		NaOH	93	Cellosolve	205–206	$C_7H_{12}ClN_5O_2\cdot H_2O$	27.83	27.60	...	...
γ-Hydroxypropylamino		Na_2CO_3	100	Aq. methyl cellosolve	210–212	$C_9H_{16}ClN_5$	...	...	...	...
Anilino[j]	Anilino	NaOH	100	Benzene	199–201	$C_{15}H_{12}ClN_5$	...	...	...	...
Diethylamino		NaOH	95	[k]	Oil	$C_{11}H_{20}ClN_5$	...	...	13.76	13.61
Di-β-cyanoethylamino		NaOH	90	Ethylene dichloride	162–165	$C_{15}H_{16}ClN_9$	35.24	35.20	...	...
Di-β-hydroxyethylamino		Na_2CO_3	79	Water	147–148	$C_{11}H_{20}ClN_5O_4$[l]	21.77	21.69	11.02	11.13

[a] The preparation of derivatives of these compounds is described in ref. 6. [b] The base used to neutralize the hydrogen chloride formed in the reaction is listed. The listing of ammonia or amine shows that an excess of the reactant was used for this purpose. [c] Yield of product as isolated from the reaction mixture. Most of these products were essentially pure, and little improvement in purity was effected by crystallization. [d] Reference 3b. [e] *Anal.* Calcd.: C, 24.75. Found: C, 24.70. [f] *Anal.* Calcd.: C, 48.77; H, 3.64. Found: C, 49.13; H, 3.60. [g] *Anal.* Calcd.: C, 51.25; H, 7.82. Found: C, 51.34; H, 7.78. [h] *Anal.* Calcd.: C, 72.01; H, 11.78. Found: C, 71.85; H, 11.83. [i] *Anal.* Calcd.: C, 58.14; H, 7.81. Found: C, 58.12; H, 7.80. [j] Reference 4a. [k] Purified by distillation. B.p., 132.5–134° (1.0 mm.). [l] *Anal.* Calcd.: C, 41.06; H, 6.26. Found: C, 40.72; H, 6.35.

4,6-dichloro-*s*-triazine is easily hydrolyzed, and a serious problem is encountered if an attempt is made to dry more than a few hundred grams of this compound after its preparation in water. Similarly, monosubstituted derivatives such as 2-methylamino-4,6-dichloro-*s*-triazine are difficult to dry or store without hydrolysis. On the other hand, 2-diethylamino-4,6-dichloro-*s*-triazine can be suspended in water at 50° for at least one day without perceptible attack, and 2-N-methylanilino-4,6-dichloro-*s*-triazine can be freed from an equal weight of water without detectable hydrolysis by drying in an oven at 100°. This effect is not due merely to insolubility of the triazine in water because the same relative reactivities exist in reactions with alcohols and amines in homogeneous systems.

An explanation for this striking difference in behavior may lie in the fact that those derivatives bearing hydrogen on the amino nitrogen atom can function as hydrogen donors, either in the *s*-triazine or the tautomeric dihydro-*s*-triazine form. A water molecule could be bound by hydrogen



bonding in a manner which would facilitate attack on the neighboring carbon–chlorine bond. Obviously hydrogen bonding in this way would be impossible with a disubstituted amino group.

Experimental[7,8]

2-Amino-4,6-dichloro-*s*-triazine.—Ammonia gas was introduced into a cold slurry (5–8°) of 184.4 g. (1.0 mole) of cyanuric chloride in 1000 ml. of dioxane, to which 150 ml. of diethyl cellosolve had been added to depress the freezing point, until the theoretical requirement (34 g.) had been added. Any slight excess of ammonia was removed by blowing a stream of air through the slurry. The 2-amino-4,6-dichloro-*s*-triazine was dissolved by heating the mixture to 95°, and the insoluble ammonium chloride was filtered from the hot solution. The product, which crystallized when the solution cooled to room temperature, was filtered and dried. Oven drying at 60° was necessary to completely remove the solvent. The yield of product was 45% of the theoretical, m.p. 235–236°. Through the use of saturated solvent for subsequent runs, the yields averaged 95%. The solubility of this compound in dioxane was about 54 g. per 100 ml. at 100° and 9 g. per 100 ml. at 25°.

Substituted 2-Amino-4,6-dichloro-*s*-triazines.—A fine slurry of cyanuric chloride was prepared by running a thin stream of a hot solution of one mole of cyanuric chloride in 400 ml. of hot acetone or dioxane into 600 ml. of well-stirred ice-water. Two moles of an amine, or one mole of an amine and one equivalent of sodium hydroxide, carbonate or bicarbonate was added at 0–5°, and the mixture was stirred for 0.5–1.0 hour. The product was filtered, washed free of chloride ion with cold water, and pressed as dry as possible in a pressure filter at 15 lb. pressure. The dichloro-*s*-triazines could be dried in small lots over sulfuric acid in a desiccator.

2,4-Diamino-6-chloro-*s*-triazine.—A solution of 184.4 g. (1.0 mole) of cyanuric chloride in 400 ml. of hot acetone was added with agitation to a solution of 68 g. (4.0 moles) of ammonia in 1000 ml. of water, maintaining the temperature at 40–45°. The reaction was slightly exothermic. The product was filtered after four hours, washed free of chloride ion, and oven-dried. The yield of infusible product was quantitative. This procedure yielded a more easily filterable product than one in which the temperature was raised slowly.

Substituted 2,4-Diamino-6-chloro-*s*-triazines.—For the preparation of compounds having the same substituents on both amino groups, a slurry of cyanuric chloride was prepared at 0–5° as described above. Two moles of the amine or a solution of 2 moles of the amine in acetone was added, and the reaction mixture was allowed to warm to room temperature. An aqueous solution of two equivalents of sodium hydroxide, carbonate or bicarbonate was added at such a rate that the reaction mixture remained essentially neutral. When sodium hydroxide or carbonate was used, the alkalinity could be conveniently controlled by the use of phenolphthalein in the reaction mixture. The temperature was allowed to rise to 40–45°. The product was filtered, washed with water and oven dried. The yields were over 90%.

For the preparation of compounds having substituents on one amino group only, one mole of dry 2-amino-4,6-dichloro-*s*-triazine was added to an aqueous solution of two moles of the amine or of one mole of the amine and one equivalent of sodium carbonate. The mixture was well agitated, and the temperature was allowed to rise to 40–45°. The product was filtered, washed with water, and oven-dried.

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[7] All melting points are uncorrected values for purified compounds.

[8] The triazine structure often presents a problem in analysis for nitrogen by the Dumas procedure.[3b,3c] However, satisfactory values were obtained in most cases by the micro Dumas method. Chlorine was determined by micro Carius, micro Parr bomb, or micro catalytic combustion methods. With the exception of the Van Slyke wet combustion analyses, which were carried out on 3–5 mg. samples, carbon-hydrogen values were determined by semimicro combustions on 10–12 mg. samples.