[CONTRIBUTION FROM THE STAMFORD RESEARCH LABORATORIES OF THE AMERICAN CYANAMID COMPANY]

Cyanuric Chloride Derivatives. II. Substituted Melamines

BY DONALD W. KAISER, JACK T. THURSTON, JAMES R. DUDLEY, FREDERIC C. SCHAEFER, INGENUIN HECHENBLEIKNER AND DAGFRID HOLM-HANSEN

In the course of investigating the reactions of cyanuric chloride, a series of substituted melamines has been prepared for investigation of their utility in synthetic resins and in other applications. A number of new derivatives have been prepared, and a general method for their synthesis is described.

In the reaction of cyanuric chloride with ammonia or with amines, one, two or all of the chlorine atoms may be replaced by amino groups, depending upon the temperature of the reaction.[1] Although these reactions offer a convenient route for the preparation of substituted melamines, these derivatives have received little attention. A few simple aliphatic[1a,2] and aromatic[1a,2b,3] melamines have long been known, but recent attention has been directed to more complex derivatives.[4]

It was found in the present work that the reaction of chlorotriazines with amines generally proceeds readily in aqueous medium to give substituted melamines in good yields, and the derivatives listed in Tables I, II and III were prepared by a general procedure which was useful for the preparation of a wide variety of substituted melamines.

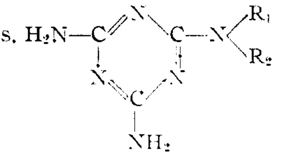
The use of water as a reaction medium does not cause noticeable hydrolysis of the chlorotriazine, and it greatly simplifies the isolation of the product. Ordinarily the formation of the substituted melamine occurs readily at 80–100°, but we have found that the reactivity of the intermediate aminochloro-*s*-triazines varies with the degree of substitution of the amino nitrogen atoms.[5] In spite of its volatility, it was possible to condense ammonia with several 2-alkylamino-4,6-dichloro-*s*-triazines at atmospheric pressure. On the other hand, tetrasubstituted 2,4-diamino-6-chloro-*s*-triazines required temperatures above 100° or relatively long reaction periods at 100° for conversion to the melamine.

Since the alkylmelamines are weaker bases than the amines from which they are made, an excess of the amine reactant or the use of a base is required for neutralizing the hydrogen chloride formed in the reaction, and sodium hydroxide was the preferred base for this purpose. This general requirement was illustrated in the preparation of *n*-butylmelamine. The condensation of equimolar quantities of *n*-butylamine and 2,4-diamino-6-chloro-*s*-triazine gave a 49% yield of the melamine, whereas yields of 90, 90 and 82% were obtained when the reaction was carried out in the presence of equivalent quantities of *n*-butylamine, sodium hydroxide and calcium hydroxide, respectively.

The monoarylmelamines, on the other hand, are stronger bases than the amines from which they are made, and their preparation does not require

TABLE I[a]

2-N-SUBSTITUTED MELAMINES,



R_1	R_2	Yield,[b] %	Crystallized from	M.p., °C.	Formula	Analyses, % Carbon Calcd.	 Found	 Hydrogen Calcd.	 Found	 Nitrogen Calcd.	 Found
Ethyl	H	96	Aq. ethanol	171–172	$C_5H_{10}N_6$[c]	38.95	39.27	6.54	6.35	54.51	54.29
n-Butyl	H	90	Isopropyl alc.	167–169	$C_7H_{14}N_6$	46.13	46.02	7.74	7.24	...	...
Phenyl	H	96	Methanol	204–205[d]	$C_9H_{10}N_6$	53.45	53.35	4.98	5.00	41.56	41.30
o-Phenylphenyl[e]	H	98	Acetic acid[f]	191–193	$C_{15}H_{14}N_6$	64.73	64.86	5.07	5.04	30.20	30.19
p-Sulfophenyl[g]	H	95	Water	Infusible	$C_9H_{10}N_6O_3S \cdot H_2O$	35.99	36.04	4.03	4.07	27.99	27.94
Ethyl	Ethyl	93	Isopropyl alc.	168–170	$C_7H_{14}N_6$[h]	46.13	46.27	7.74	7.38	46.12	46.28
Ethylene(bis)[i]	H	90	Water[j]	314–316	$C_8H_{14}N_{12}$[k]	34.52	34.33	5.07	4.84	60.41	60.39
Ethylene(bis)[i]	Cyclohexyl	91	Aq. cellosolve	338–340	$C_{20}H_{34}N_{12}$	54.28	54.27	7.74	7.17	...	...

[a] With one exception, all compounds were prepared from 2,4-diamino-6-chloro-*s*-triazine (ref. 5). [b] Yield of product as isolated from the reaction mixture. [c] *Anal.* Calcd.: neut. equiv., 154.2. Found: neut. equiv., 154.4. [d] Klason (ref. 2b) recorded the m.p. as 284°. This is actually the m.p. of the hydrochloride. Our hydrochloride melted at 274°. *Anal.* Calcd. for $C_9H_{11}ClN_6$: N, 35.21; Cl, 14.86. Found: N, 34.81; Cl, 14.93. [e] Prepared in Cellosolve solution at 110°. [f] Crystallized as the triacetate, m.p. 150–151°. *Anal.* Calcd. for $C_{15}H_{14}N_6 \cdot 3CH_3COOH$: N, 18.02. Found: N, 18.11. This was converted to the free base by heating 2 days at 120° and 1 day at 140°. [g] Prepared from 2-*p*-sodium sulfoanilino-4,6-dichloro-*s*-triazine. [h] *Anal.* Calcd.: neut. equiv., 182.2. Found: neut. equiv., 185.5. [i] Structure is $(H_2N)_2C_3N_3N(R)CH_2CH_2N(R)C_3N_3(NH_2)_2$, where R is H or cyclohexyl. [j] Crystallized as the hydrochloride and reconverted to the free base. [k] *Anal.* Calcd.: neut. equiv., 278.3. Found: neut. equiv., 283.

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(1) (a) H. H. Fries, *Ber.*, **19**, 242, 2055 (1886); (b) O. Diels, *Ber.*, **32**, 691 (1899).

(2) (a) A. W. Hofmann, *Ber.*, **18**, 2755 (1885); (b) P. Klason, *J. prakt. Chem.*, [2] **33**, 290 (1886).

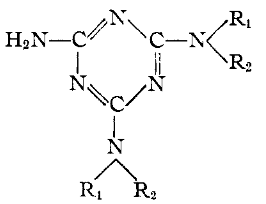
(3) E. von Meyer and Fr. Näbe, *J. prakt. Chem.*, [2] **82**, 531 (1910).

(4) (a) H. E. Fierz-David and M. Matter, *J. Soc. Dyers Colourists*, **53**, 424 (1937); (b) H. Jensch, U. S. Patent 2,092,352 (1937); (c) E. Friedheim, THIS JOURNAL, **66**, 1775 (1944); E. Friedheim, U. S. Patent 2,295,574 (1942); (d) C. K. Banks, THIS JOURNAL, **66**, 1127 (1944); C. K. Banks, O. M. Gruhzit, E. W. Tillitson and J. Controulis, *ibid.*, **66**, 1771 (1944); (e) H. S. Mosher and F. C. Whitmore, *ibid.*, **67**, 662 (1945); (f) D. F. Walker, Y. J. L'Italien, W. Pearlman and C. Banks, *J. Am. Pharm. Assn.*, **39**, 393 (1950).

(5) J. T. Thurston, *et al.*, THIS JOURNAL, **73**, 2981 (1951).

TABLE II[a]

2-N,4-N-SUBSTITUTED MELAMINES,

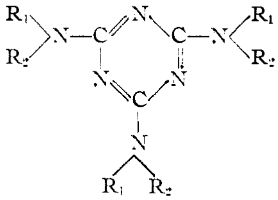


R₁	R₂	Yield,[b] %	Crystallized from	M.p., °C.	Formula	Analyses, %					
						Carbon		Hydrogen		Nitrogen	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
Ethyl	H	91	Aq. ethanol	156–158	$C_7H_{14}N_6$[c]	46.13	46.44	7.74	7.63	46.12	46.10
Cyanomethyl[d]	H	80	Water	220	$C_7H_8N_8$	41.17	40.62	3.95	3.79	54.88	55.26
2-Hydroxyethyl	H	86	Methanol	160–161	$C_7H_{14}N_6O_2$[e]	39.24	39.73	6.59	6.45	39.23	39.62
3-Hydroxypropyl[f]	H	..	Methanol	110–112	$C_9H_{18}N_6O_2$	44.62	44.83	7.49	7.65	34.69	34.29
Phenyl[g]	H	96	Isopropyl alc.	219–220	$C_{15}H_{14}N_6$	64.73	64.68	5.07	4.59		
p-Ethoxyphenyl	H	87[h]	Aq. acetic acid	269–270[h]	$C_{19}H_{22}N_6O_2 \cdot HCl$	56.64	56.73	5.75	5.43	20.86	21.03
Phenyl	Methyl	98	Isopropyl alc.	166–167	$C_{17}H_{18}N_6$	66.64	66.82	5.92	5.29	27.44	27.15
Ethyl	Ethyl	97	Aq. methanol	71–72	$C_{11}H_{22}N_6$[i]	55.43	55.65	9.31	8.98	35.26	35.27
2-Hydroxyethyl	2-Hydroxyethyl	100	Methanol	128–129	$C_{11}H_{22}N_6O_4$[j]	...	...	..	..	27.80	27.53
2-Amino-4,6-dimorpholino-*s*-triazine		100	Aq. ethanol	170–172	$C_{11}H_{16}N_6O_2$	...	...	..	..	31.56	31.28

[a] With two exceptions, all compounds were prepared from 2-amino-4,6-dichloro-*s*-triazine. Reference 5 gives details of the preparation of the intermediates. [b] Yield of product as isolated from the reaction mixture. [c] *Anal.* Calcd.: neut. equiv., 182.2. Found: neut. equiv., 183.3. [d] Prepared from 2,4-bis-(cyanomethylamino)-6-chloro-*s*-triazine by heating with aqueous ammonia at 100° under pressure. [e] *Anal.* Calcd.: neut. equiv., 214.2. Found: neut. equiv., 215.9. [f] Prepared from 2,4-bis-(γ-hydroxypropylamino)-6-chloro-*s*-triazine. [g] B. Rathke, *Ber.*, **21**, 867 (1888). [h] Isolated as the hydrochloride, for which the m.p. is given. [i] *Anal.* Calcd.: neut. equiv., 238.3. Found: neut. equiv., 240.3. [j] *Anal.* Calcd.: neut. equiv., 302.3. Found: neut. equiv., 300.9.

TABLE III

2-N,4-N,6-N-SUBSTITUTED MELAMINES,



-*s*-Triazine	Yield,[a] %	Crystallized from	M.p., °C.	Formula	Analyses, %					
					Carbon		Hydrogen		Nitrogen	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
2,4,6-Tris-(ethylamino)-[b]	91	Aq. ethanol	72–75	$C_9H_{18}N_6 \cdot {}^1/_2H_2O$[c]	49.29	49.92	8.73	8.64	38.33	38.01
2,4,6-Tris-(β-hydroxyethylamino)-[d]	100	Butanol	100–101	$C_9H_{18}N_6O_3$[e]					32.54	32.11
2,4,6-Tris-(γ-hydroxypropylamino)-[f]	87	Ethyl acetate	113–114	$C_{12}H_{24}N_6O_3$[g]	47.98	48.09	8.05	8.02	27.98	28.10
2,4-Bis-(β-hydroxyethylamino)-6-phenylamino-[d]	94	Methanol	134–135	$C_{13}H_{18}N_6O_2$	54.16	54.17	5.59	6.18	29.15	29.17
2-Bis-(β-cyanoethyl)-amino-4,6-dianilino-[h]	84	Aq. acetone	181–183	$C_{21}H_{20}N_8$					29.15	29.07
2,4,6-Tris-(di-β-hydroxyethylamino)-[i]	65	Butanol	169–170	$C_{15}H_{30}N_6O_6$[j]	46.14	45.89	7.74	7.40	21.53	21.52
2,4,6-Tris-(N-cyanomethyl-N-cyclohexylamino)-[i]	82	Methanol	165–167	$C_{27}H_{39}N_9$	...	...	..	..	25.75	25.63
2,4,6-Tris-(N-carbomethoxymethyl-N-cyclohexylamino)-[k]	91	Methanol	136–137	$C_{30}H_{48}N_6O_6$	...	...	..	..	14.28	14.00
2,4,6-Tris-(N-cyanomethyl-N-*n*-dodecylamino)-[i]	67	Methanol	46–48	$C_{45}H_{82}N_9$	...	...	..	..	16.83	16.80

[a] Yield of product as isolated from the reaction mixture. [b] Prepared from 2,4-bis-(ethylamino)-6-chloro-*s*-triazine. [c] *Anal.* Calcd.: neut. equiv., 219.3. Found: neut. equiv., 222.4. [d] Prepared from 2,4-bis-(β-hydroxyethylamino-6-chloro-*s*-triazine. [e] *Anal.* Calcd.: neut. equiv., 258.3. Found: neut. equiv., 263.3. [f] Prepared from 2,4-bis-(γ-hydroxypropylamino)-6-chloro-*s*-triazine. [g] *Anal.* Calcd.: neut. equiv., 300.4. Found: neut. equiv., 300.4. [h] Prepared from 2-bis-(β-cyanoethyl)-amino-4,6-dichloro-*s*-triazine. [i] Prepared directly from cyanuric chloride. [j] *Anal.* Calcd.: neut. equiv., 390.4. Found: neut. equiv., 393.9. [k] Prepared by methanolysis of the preceding compound in the table.

the use of a base to neutralize the hydrogen chloride formed in the reaction. Our preferred procedure consisted of condensation of equimolar quantities of the arylamine and the 2,4-diamino-6-chloro-*s*-triazine and subsequent conversion of the arylmelamine hydrochloride to the free base. The more highly substituted arylmelamines, however, are weaker bases, and the use of a base is required for their preparation in good yields in aqueous systems. This procedure was satisfactory for the preparation of the diarylmelamines, but N^2,N^4,N^6-triphenylmelamine was obtained in 50% yield. While it may have been possible to improve the yield, the direct fusion[2b] of 2-chloro-4,6-bis-anilino-*s*-triazine with two moles of aniline at 160–180° was more satisfactory, the melamine being obtained in 91% yield. It was found, however, that neither the excess of aniline nor the preparation of the intermediate is required, and our preferred procedure consisted of the direct fusion of cyanuric chloride and three moles of aniline at about 300°. Hydrogen chloride was evolved and N^2,N^4,N^6-triphenylmelamine was formed in good yield. The use of benzene as a dilute in the initial reaction mixture served to moderate the exothermic reaction and to facilitate mixing of the reactants before the reaction mixture was heated.

Experimental[6,7]

General Procedure.—One mole of the appropriate chlorotriazine was slurried in water (600–1000 ml.), and the amine was added. The molar quantity of the latter was such that there was one equivalent of amine for each chloro group to be replaced on the triazine. The mixture was slowly heated to reflux, and the refluxing temperature was maintained for one to two hours. During this time an aqueous solution of one equivalent of sodium hydroxide, carbonate or bicarbonate was added at such a rate that the reaction mixture remained neutral or slightly alkaline. The alkalinity could be conveniently controlled by the use of phenolphthalein in the reaction mixture. After cooling, the product was filtered from the reaction mixture, washed free of chloride ion with water and oven-dried. Purification was effected by crystallization from appropriate solvents.

Alternatively, twice the theoretical quantity of the amine was initially added to the reaction mixture, and no base was subsequently added. This variation was not preferred.

Monoarylmelamines.—The preparation of these compounds differed from the above procedure only in that the caustic was not added until the reaction was complete. Conversion of the hydrochloride of the product to the free base was effected with aqueous sodium hydroxide at 50–60° or at room temperature.

N^2,N^4,N^6-Triphenylmelamine.[8]—A gentle reaction occurred when 301 g. (3.2 moles) of aniline was added to 184.4 g. (1.0 mole) of cyanuric chloride in 400 ml. of benzene over a period of two hours. The benzene was distilled as the bath temperature was then raised to 290–310° over a period of 1.5 hours. Hydrogen chloride was smoothly evolved in this temperature range, and the reaction was complete in 1.5 hours. After cooling, the solid cake was digested with methyl cellosolve. The yield was 92%, m.p. 229–231°. Recrystallization from methyl cellosolve gave m.p. 232–234°.

Pentaethylmelamine.—One mole of 2-chloro-4,6-bis-(diethylamino)-*s*-triazine and 2.4 moles of 70% aqueous ethylamine were heated for five hours at 110° under pressure in dioxane solution. One mole of aqueous sodium hydroxide was added, and the mixture was evaporated on a steam-bath. The yield of product, after extraction of the residue with benzene and removal of the solvent, was 95%. Purification of the liquid product was effected by distillation; b.p. 120–121° (0.4 mm.).

Anal. Calcd. for $C_{13}H_{28}N_6$: C, 58.61; H, 9.84; N, 31.55; neut. equiv., 266.4. Found: C, 58.62; H, 9.82; N, 30.84; neut. equiv., 267.6.

Hexaethylmelamine.—A solution of one mole of 2-chloro-4,6-bis-(diethylamino)-*s*-triazine in toluene was heated to reflux, and 2.2 moles of anhydrous diethylamine was added slowly to prevent flooding in the condenser. The addition required six hours. The product was isolated as described above; yield 93%. Purification was first effected by distillation, b.p. 151–154° (2–3 mm.), and then by crystallization from methanol, m.p. 46–47°.

Anal. Calcd. for $C_{15}H_{30}N_6$: C, 61.18; H, 10.27; N, 28.55. Found: C, 61.26; H, 10.25; N, 28.62.

Hexamethylmelamine.—A 26% aqueous solution of 3.3 moles of dimethylamine was added to one mole of cyanuric chloride in 800 ml. of acetone, maintaining the temperature at about 50° by intermittent cooling. One mole of aqueous sodium hydroxide was added, and the mixture was heated under reflux for one hour. The water and acetone were removed by distillation, finally adding xylene to completely remove the water by azeotropic distillation. Two moles of powdered sodium hydroxide were added, and the mixture was heated for three hours at 100°. Fractional crystallization of the product from methanol gave a 37% yield of hexamethylmelamine, m.p. 172–174°, and a 26% yield of 2-chloro-4,6-bis-(dimethylamino)-*s*-triazine, m.p. 62–63°.

Anal. Calcd. for $C_9H_{18}N_6$: N, 39.97. Found: N, 39.72.

Acknowledgment.—We are indebted to Dr. Clarence J. Hull and Mr. Lennart A. Lundberg for aid in the preparative work. Microanalyses were carried out in these laboratories under the direction of Dr. J. A. Kuck.

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

[7] Comments on analytical procedures are given in footnote 8, reference 5.

[8] Also prepared according to Klason's method (ref. 2b). The direct method avoids the preparation of an intermediate and the use of excess aniline in the final step.

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Cyanuric Chloride Derivatives. III. Alkoxy-*s*-triazines

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A series of new trialkyl cyanurates, 2,4-dialkoxy-6-amino-*s*-triazines, and 2-alkoxy-4,6-diamino-*s*-triazines have been prepared for investigation of their use in a number of applications. Modifications in procedure have been developed, and a general method for the preparation of alkoxy-*s*-triazines from the corresponding chloro-*s*-triazines has been reported.

Trialkyl cyanurates,[1] I, and alkyl ethers of ammelide[2] and ammeline derivatives,[3] II and III, have long been known. However, the only reported work on the development of a general and practical preparative method is that of Controulis and Banks,[3b] who prepared an extensive series of 2-alkoxy-4,6-diamino-*s*-triazines. Their method, which gave acceptable yields in most cases, was similar to that used by Hofmann[3a] to prepare cyanurates, *i.e.*, reaction of the chloro-*s*-triazine with the appropriate sodium alkoxide, generally in excess alcohol. They also mentioned the use of potassium carbonate or dry hydrogen chloride as condensing agents for reaction of the chloro-*s*-triazine with the alcohol, but these methods were considered inferior.

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[1] (a) F. S. Cloez, *Compt. rend.*, **44**, 482 (1857); (b) E. Mulder, *Ber.*, **15**, 69 (1882); **16**, 390, 2763 (1883); *Rec. trav. chim.*, **1**, 63, 191 (1882); **2**, 133 (1883); **3**, 287 (1884); (c) J. Ponomareff, *Ber.*, **15**, 513 (1882); **18**, 3261 (1885); (d) P. Klason, *J. prakt. Chem.*, (2) **33**, 116 (1886); (e) A. Hantzsch and L. Mai, *Ber.*, **28**, 2466 (1895); (f) E. Bülmann and J. Bjerrum, *Ber.*, **50**, 503 (1917); W. Hentrick, U. S. Patent 2,306,440 (1942).

[2] A. W. Hofmann and O. Olshausen, *Ber.*, **3**, 269 (1870).

[3] (a) A. W. Hofmann, *Ber.*, **19**, 2061 (1886); (b) J. Controulis and C. K. Banks, THIS JOURNAL, **67**, 1946 (1945); (c) W. Pearlman and C. K. Banks, *ibid.*, **71**, 1128 (1949); (d) W. Pearlman, J. D. Mitulski and C. K. Banks, *ibid.*, **71**, 3248 (1949).