was obtained by one recrystallization from 95% ethanol; m.p. 263–264° dec. The infrared spectrum of VI showed absorption at 2220 (C≡N) and 1685 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{11}H_4N_2OS$: C, 62.25; H, 1.89; N, 13.20; S, 15.10. Found: C, 62.15; H, 1.81; N, 13.04; S, 15.49.

Diels-Alder Adduct of VI (VIII).—A solution of 0.5 g. of VI, 0.02 g. of hydroquinone, and 4.5 ml. of 2,3-dimethylbutadiene in 50 ml. of ethyl alcohol was refluxed for 48 hr. The solvent was removed under vacuum on a hot water bath. The residue was recrystallized from ethanol–water. The yield of VIII was 0.65 g. (93.8%). The white needles were recrystallized twice from ethanol–water to give an analytical sample; m.p. 157–158°.

Anal. Calcd. for $C_{17}H_{14}N_2OS$: C, 69.35; H, 4.79; N, 9.52. Found: C, 69.57; H, 4.97; N, 9.52.

The Preparation of *s*-Triazine Derivatives Containing the N—O Bond. I. Mono-*N*-oxides of Amino-substituted *s*-Triazine Derivatives[1]

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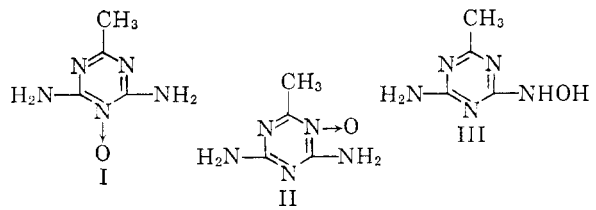
The preparation of mono-*N*-oxides of amino-substituted *s*-triazine derivatives by two methods is reported: peracetic acid oxidation of aminotriazines and cyclization of dicyanoamidine salts with hydroxylamine hydrochloride. Both methods give the same *N*-oxide. The dicyanoamidine salts were obtained by reaction of alkyl imidate hydrochlorides with sodium acid cyanamide (limited to lower alkyl) or by reaction of alkyl- or arylamidines with cyanogen chloride. The latter method appears to be general.

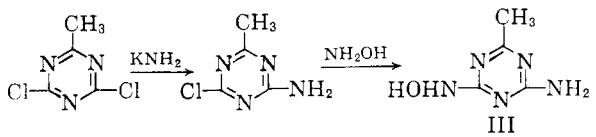
The objective of this investigation was the preparation of mono-*N*-oxides of amino-substituted *s*-triazine derivatives. A review of the literature uncovered only one reference to the preparation of an *s*-triazine mono-*N*-oxide. In this work, by Kaiser and Roemer,[2] a good yield of melamine *N*-oxide was obtained by slurrying an equimolar mixture of potassium dicyanoguanidine and hydroxylamine hydrochloride in Cellosolve. This cyclization method was not chosen initially primarily because the dicyanoamidines required in the reaction were themselves unknown. An alternative route to the *N*-oxides was an oxidative procedure. Grundmann and Schroeder[3] had shown that Caro's acid oxidation of 2-amino-4,6-bis-*p*-chlorophenyl-*s*-triazine gave a tris-*N*-oxide. It was hoped that the use of a milder peracid like peracetic acid under the proper reaction conditions would lead to mono-*N*-oxide formation.

The Peracetic Acid Oxidation of Amino-substituted *s*-Triazines.—The reaction of acetoguanamine (1 mole) with peracetic acid (1.5 moles) was carried out in acetic acid at 40–45° for about twenty-four hours. The compound isolated was a white crystalline solid, whose elemental analysis gave the empirical formula $C_4H_7N_5O$; no water present. The material was soluble in dilute acid and base and gave a deep red color with ferric chloride. To confirm the assumption that the triazine ring was still intact, the oxidized product was treated with phosphorus trichloride in chloroform to deoxygenate it. Acetoguanamine was identified as the resulting product by melting point, elemental analysis, and infrared comparisons with an authentic sample.

With the previous data in mind, the structural possibilities $C_4H_7N_5O$ appeared to be I, II, or III



and tautomers thereof. The normal triazine *N*-oxide structures are shown for sake of simplicity. The other triazine isomer of $C_4H_7N_5O$, 2,4-diamino-6-hydroxymethyl-*s*-triazine (which was not really expected), was eliminated on the basis of recovering acetoguanamine from the phosphorus trichloride reaction.



In the synthesis of III, freshly prepared potassium amide was added in the cold to 2,4-dichloro-6-methyl-*s*-triazine[4] in ether, followed by the addition of an intimate mixture of hydroxylamine hydrochloride and sodium carbonate. The usual physical properties of melting point, infrared, and solubility of III did not agree with those of the peracetic acid–acetoguanamine oxidation product. Furthermore, III gave a blue color with ferric chloride in contrast to the red color of the acetoguanamine product.

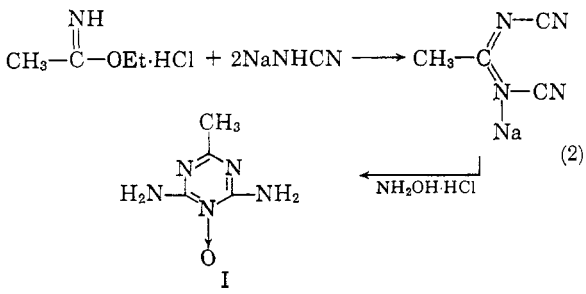
(1) Presented in part before the Division of Organic Chemistry at the 140th National Meeting of the American Chemical Society, Chicago, Ill., September, 1961.

(2) D. W. Kaiser and J. J. Roemer, U. S. Patent 2,729,640 (January 3, 1956).

(3) C. Grundmann and H. Schroeder, *Chem. Ber.*, **87**, 747 (1954).

(4) R. Hirt, H. Nidecker, and R. Berchtold, *Helv. Chim. Acta*, **33**, 1365 (1950).

With compound III eliminated, only the synthesis of either I or II was necessary to complete the proof of structure. After several unsuccessful attempts to prepare II, we turned our attention to the preparation of I.



(2)

Here ethyl acetimidate hydrochloride was treated with two moles of monosodium cyanamide to give sodium dicyanoacetamidine; the dicyano derivative was then treated with hydroxylamine hydrochloride to give I. I was found to agree precisely with the peracetic acid–acetoguanamine reaction product in the usual physical properties such as melting point, infrared, solubility, and ferric chloride reaction.

Table I shows the results obtained when the peracetic acid oxidation was carried out with other guanamines and a few miscellaneous aminotriazines. The reaction conditions unless otherwise noted were, in general, the same as given before: namely 1.5 moles peracetic acid/1 mole of triazine for twenty-four hours at about 40°.

Although the oxidation reaction appears to be quite general, yields were very low (2–16%) in nine of the fifteen cases where any *N*-oxide was isolated. The reaction is of greatest synthetic value when one electron-withdrawing group is on the ring (compounds 5, 6, 7, and 18 of Table I).

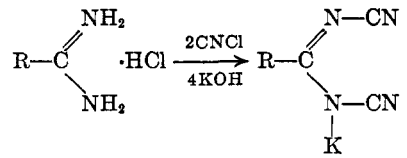
A steric factor appeared to operate whenever two of the three carbon positions in the *s*-triazine system were occupied by bulky groups (compounds 4 and 19 of Table I). Attempts to force these reactions at elevated temperatures were of no avail; the bistrichloromethyl compound gave only unchanged starting material while with the bisdimethylamino compound, cleavage of one of the dimethylamino groups took place.

Hydrolysis of amino groups was observed in two cases (although it possibly took place in others but was undetected due to the nature of the work-up). Thus, in the case of acetoguanamine, in addition to the desired *N*-oxide, a product was isolated in which the elementary analysis and infrared suggested that not only had oxidation of one of the ring nitrogens taken place but also one of the amino groups had been hydrolyzed to hydroxy. A similar product was isolated in a stearoguanamine oxidation when the temperature inadvertently rose to 80° for a few minutes.

Since we had only proved the structure of one *N*-oxide (in melamine *N*-oxide the symmetry of the molecule eliminates the problem of the location of the oxygen) the question arose whether the location of the oxygen in the other guanamine *N*-oxides was the same. The cyclization reactions with hydroxylamine hydrochloride shown in equation 2 required alkyl- or aryldicyanoamidines. A search of the literature showed these compounds to be undescribed.

The Preparation of Alkyl- and Aryldicyanoamidine Salts.—In the preparation of the dicyanoamidine salts, two methods were investigated. The first method involved the reaction of imidates with sodium acid cyanamide as shown in equation 2 and was successful only with the lower alkyl imidates. Longer chain alkyl imidates like ethyl lauryl imidate gave no characterizable products, while the only aryl imidate tried, methyl benzimidate hydrochloride, gave a small amount of benzoguanamine as the only characterizable new product.

The difficulties involved in extending the imidate–acid cyanamide method to longer alkyl chains and to the aryl types led to an investigation of the second method: the reaction of cyanogen chloride with amidines. This synthesis worked



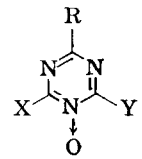
(3)

nicely for alkyl-, alkylenebis-, and arylamidines. The compounds prepared by these two methods are shown in Table II. The stability of the free acids was found to vary since potassium dicyanobenzamidine was converted easily to the free acid using concentrated hydrochloric acid while attempts to convert potassium dicyanoacetamidine to the free acid either directly using hydrochloric acid or by conversion to the copper salt followed by reaction with hydrogen sulfide were not successful.

All of the alkali metal dicyanoamidines were high-melting solids which gave green precipitates with copper sulfate. Only in the case of potassium dicyanoacetamidine was an attempt made to isolate the copper complex; microanalysis indicated two moles of dicyanoacetamidine associated with each copper atom. The infrared spectra showed several characteristic bands: in the alkyl dicyanoamidines, a strong nitrile band about 4.6–4.68 μ and another strong band around 6.65 μ, which may be due to —C≡N— conjugated with —C=N; in the aryldicyanoamidines, a nitrile doublet around 4.63 and 4.72 μ; both of these bands are associated with carbodiimides. Again, a very strong band around 6.65 μ associated with conjugated nitrile. Resonance forms of the dicyanoamidines can be written which make the

TABLE I

AMINOTRIAZINE *N*-OXIDES

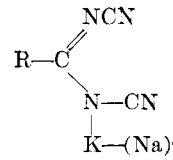


Compound	X	R	Y	M.p., °C.	Yield,[a] %	Method[b]	S[c]	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1	NH_2	CH_3	NH_2	>310	20	A	H–W	34.1	4.98	49.7	34.1	5.02	49.4
					52	B					34.4	5.18	49.5
2	NHC_6H_5	CH_3	NH_2	258 dec.	16	A	A	55.3	5.07	32.3	55.2	4.87	32.3
3	$NHCH_3$	CH_3	$NHCH_3$	204–207 dec.	8	A	K	42.6	6.50	41.4	42.8	6.54	41.5
4	$H(CH_3)_2$	CH_3	$N(CH_3)_2$	...	0	A							
5	NH_2	CCl_3	NH_2	>330	91	A	...	19.7	1.64	28.6	19.8	1.85	28.8
6	NH_2	CF_3	NH_2	330 dec.	61	A	...	24.6	2.05	35.9	24.6	2.15	36.1
7	NH_2	$CF_3(CF_2)_6$	NH_2	193–196 dec.	54	A	T	24.2	0.81	14.2	24.0	0.91	14.4
8	NH_2	C_2H_5	NH_2	304–305 dec.	16	A	C–W	38.7	5.86	45.2	38.5	5.86	45.0
					25	B					39.0	6.14	...
9	NH_2	$(CH_3)_2CH$	NH_2	317 dec.	35	A	H–W	42.6	6.54	41.4	42.5	6.60	41.7
10	NH_2	n-C_4H_7	NH_2	282–283 dec.	44	B	W	42.6	6.54	41.4	42.6	6.63	41.5
11	NH_2	n-$C_{11}H_{23}$	NH_2	249–251 dec.	15	A	M	59.8	9.66	24.9	59.7	9.08	25.2
					53	B					60.1	10.0	24.6
12	NH_2	n-$C_{17}H_{35}$	NH_2	234–236 dec.	2	A[d]	H	65.6	10.2	19.2	65.6	11.1	19.0
13	NH_2	$-(CH_2)_4-$	NH_2	255–257 dec.	4	A[e]	W	38.9	5.19	45.4	38.6	5.17	45.3
14	NH_2	C_6H_5	NH_2	280–282 dec.	2.5	A[f]	C–W	53.2	4.44	34.5	52.9	5.05	34.1
					24	B					53.4	4.74	34.6
15	NH_2	p-$NO_2C_6H_5$	NH_2	247–249 dec.	4	A	C–W	43.6	3.23	33.8	43.6	3.11	33.8
16	NH_2	p-ClC_6H_5	NH_2	272–274 dec.	42	B	C–W	45.6	3.37	29.5	45.4	3.33	29.3
17	NH_2	NH_2	NH_2	>310	24[g]	A	W	25.4	4.23	59.2	25.5	4.28	59.4
				>310	69	B					25.3	3.91	59.0
18	NH_2	CH_3	CCl_3	187–189 dec.	47	A	M	24.7	2.06	23.1	24.8	2.29	23.3
19	NH_2	CCl_3	CCl_3	...	0	A							

[a] Crude yield. [b] Method A: peracetic acid oxidation; method B: ring closure of a dicyanoamidine salt with hydroxylamine hydrochloride. [c] Solvent used for recrystallization: A, ethyl alcohol; C, Cellosolve; E, ether; H, acetic acid; I, isopropyl alcohol; K, monochlorobenzene; M, methanol; T, acetone; W, water. If none given (–), none required. [d] A reaction in which the temp. inadvertently rose to 80° for 5 min. gave a small yield of what appears to be 2-amino-1-hydroxy-4-heptadecyl-6(1H)-one. *Anal.* Calcd. for $C_{20}H_{38}N_4O_2$: C, 65.3; H, 10.4; N, 15.3. Found: C, 65.4; H, 10.4; N, 15.4. [e] 700 ml. of glacial acetic acid used for 0.038 *M* adipoguanamine. [f] Reaction conditions: 70–75° for 6 hr after an initial exotherm; major product was a compound which gave a deep red color with ferric chloride and appeared to be a molecular complex composed of 1 mole each of benzoguanamine and benzoguanamine *N*-oxide, m.p. 234–236°. The small amount of desired *N*-oxide was isolated as the last fraction of a repeated fractional crystallization. [g] No reaction at 40°; reaction conditions: 78–80° for 6 hr.

TABLE II

DICYANOAMIDINE SALTS



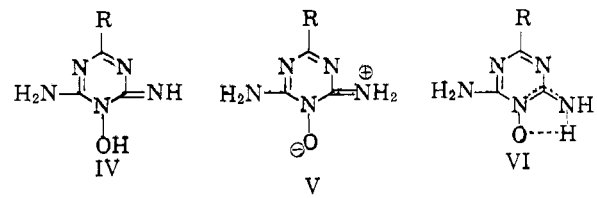
Compound	R	M.p. °C.	Yield,[b] %	Method[a]	S[c]	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1	CH_3	262–263 dec.	87	C	A–E	36.9	2.31	43.3	36.8	2.45	43.3
	CH_3	225–227	59	D	A	32.8	2.07	38.4	32.5	2.20	38.7
2	C_2H_5	201–202	75	C	I	41.8	3.48	39.1	41.8	3.67	38.7
3	C_3H_7	194–195	77	D	I	41.3	4.06	32.2	41.7	4.12	32.2
4	$C_{11}H_{23}$	196	25[d]	D[e]	W[f]	58.6	8.11	19.6	58.8	8.04	19.4
5	$-(CH_2)_4-$	260–262 dec.	49	D[e]	A–E	37.7	2.54	35.2	38.0	2.54	35.2
6	C_6H_5	245–247	54	D[g]	I	51.9	2.42	26.9	51.8	2.68	26.8
7	*p*-ClC_6H_5[h]	308–310	62	D	I	44.6	1.60	22.0	44.8	1.58	22.7

[a] Method C employing imidate hydrochlorides and sodium acid cyanamide gave the sodium salt; method D, the cyanogen chloride–amidine–potassium hydroxide route gave the potassium salt. [b] Crude yield; product suitable for further reaction. [c] Solvent used for recryst.; see Table I, footnote *c*. [d] Recryst. yield. [e] Method C not successful. [f] Potassium chloride cake obtained from filtering the reaction mixture contained the dicyanoamidine. Two recrystallizations from water gave the product. [g] Method C gave a small amount of benzoguanamine as the only isolable product. [h] Calcd.: Cl, 14.6; Found: Cl, 14.6.

carbodiimide wave length reasonable. The ultraviolet curves of dicyanoacetamidine and dicyanobenzamidine gave λ_{max} close to each other: 263 and 275 mμ, respectively.

Cyclization of the dicyanoamidine salts with hydroxylamine hydrochloride to the corresponding guanamine *N*-oxides was carried out simply by stirring the components in β-ethoxyethanol at room temperature for several days (equation 2). While no attempt was made to study the effect of temperature, solvent, and concentration of reactants on yields, it appears at this juncture that where the dicyanoamidine salts are available the preparation of guanamine *N*-oxides *via* cyclization of dicyanoamidines with hydroxylamine in general affords better yields and a more easily isolable product than the peracetic acid method. In all cases tried, the melting points, the infrared curves, ferric chloride tests, and other physical properties of the compounds obtained by cyclization matched those obtained by the peracetic acid route. Since for the most part no attempt was made to achieve a material balance, there is a possibility that oxidation at the nitrogen *ortho* to the guanamine R substituent took place and was missed in the isolation procedure.

For ease of discussion throughout this paper, we have been treating the aminotriazine peracetic acid oxidation products as *N*-oxides. Of course, other tautomeric forms are possible. Which form actually exists has not been unequivocally established; however, from the spectra obtained the following can be said. The ultraviolet spectra of the oxidized materials with the exception of a slight bathochromic shift, in general, resemble the spectra of the starting materials, that is "three-conjugated" systems. In the infrared the oxidized materials show weak to medium bands around 5.9 μ which together with new strong bands around 12.9 to 13.2 μ suggest an isotriazine system, that is a "three-conjugated" system with one double bond "exo" to the triazine ring. Tautomeric structures like IV or V as well as the hydrogen bonded structure



VI probably could account for these data. The only other new absorption consistently present in the oxidized structures was a medium to strong band in the range 8.2–8.3 μ presumably due to the *N*-oxide function. Koelsch and Gumbrecht[5] assigned the band at 7.55 to 8.13 μ found in various diazine *N*-oxides to the *N*-oxide function.

Experimental[6]

Materials.—With the exception of acetoguanamine, benzoquanamine, stearoguanamine, melamine, monosodium cyanamide, and cyanogen chloride which were supplied by the American Cyanamid Co., the various aminotriazines[7]

(5) C. F. Koelsch and W. H. Gumprecht, *J. Org. Chem.*, **23**, 1603 (1958).

(6) All melting points are uncorrected. Microanalyses by John Kobliska and the late Oliver Sundberg and their staff. Infrared interpretation by Dr. Jesse Gove and Mr. Norman Colthup.

(7) E. M. Smolin and L. Rapoport, "*s*-Triazines and Derivatives," Interscience Publishers, Inc., New York, N. Y., 1959, pp. 242–245.

and amidines,[8,9] were prepared by methods given in the literature.

Aminotriazine *N*-Oxides from Peracetic Acid Oxidation *via* Method A.—All compound numbers given in this section refer to those shown in Table I. A few general comments concerning the oxidative procedure will be helpful inasmuch as a detailed description will be given only in two cases. The general procedure was to add dropwise a solution of 40% peracetic acid (1.5 moles of peracetic acid per mole of triazine) to a stirring slurry or solution of the triazine derivative in acetic acid (approx. 6 ml. of acetic acid per gram of triazine unless otherwise noted) at about 30.–40°. The mixture was then stirred for 20–24 hr. at 40–45°. The work-up procedure depended upon the solubility of the starting material and *N*-oxide in acetic acid. When the starting material was soluble or at some time during the reaction went completely into solution and the *N*-oxide was insoluble, the isolation involved simply filtering off the product at 40–45° and in many cases no recrystallization was necessary; compounds 1, 5, 6, and 12 were processed in this fashion. When the *N*-oxide was soluble, two procedures were found suitable: water was added to precipitate the product (compounds 7 and 11); or the solution was allowed to evaporate at room temperature in the hood under a good draft until a thick slurry formed, then filtered and the cake tested with aqueous ferric chloride. A deep red coloration (sometimes heating or ferric chloride in dimethylformamide was required for the more insoluble *N*-oxides) developed if the *N*-oxide were present. If no color except a light orange formed, the filtrate was further evaporated, filtered, etc., until the *N*-oxide was isolated. This procedure was used for compounds 2, 3, 8, 9, 13, 14, and 18 of Table I and in all these cases the material was recrystallized before analysis. It turned out that in the one case, compound 15, where the mixture remained a slurry throughout the entire reaction, that the insoluble material was largely starting material, which was filtered and the filtrate worked up as in the previous case.

2,6-Diamino-4-methyl-*s*-triazine 1-Oxide (Acetoguanamine *N*-Oxide) *via* Method A.—Acetoguanamine, 125.1 g. (1 mole), was added in portions to 750 ml. of glacial acetic acid with stirring; an exotherm ensued with the formation of a thick slurry. Then, 271 g. of 42% peracetic acid (1.5 moles) was added dropwise over a period of 5 hr. at 38–43°. After two thirds of the peracetic acid had been added an almost clear solution formed, but on completion of the addition, a moderate amount of precipitate appeared. During the latter two thirds of the addition, a mild exotherm took place which kept the temperature at 42–43° without the aid of a heating mantle. The mixture was stirred at 40–45° for an additional 19 hr. and then filtered at this temperature. The filtrate, I, was separated and the cake washed with 50% aqueous acetic acid followed by acetone and then allowed to air-dry, 29 g. (20.5%), m.p. > 330°. This product, II, a white crystalline solid was later proved to be the *N*-oxide. It gave a deep red color with ferric chloride, and was soluble in 1 *N* hydrochloric acid and 1 *N* sodium hydroxide, the latter with warming. Neutralization of the caustic solution with acetic acid gave II unchanged. Recrystallization of 5 g. of II from 500 ml. of 50% aqueous acetic acid gave 2.8 g., m.p. > 330.

Anal. Calcd. for $C_4H_7N_5O$: C, 34.1; H, 4.98; N, 49.7. Found: C, 34.1; H, 5.02; N, 49.4.

Filtrate I, after standing 4 days, deposited 16.9 g. of large colorless crystals, III, m.p. 215–216°, which when crushed gave the odor of acetic acid. A portion of III was made alkaline to pH 10 by slurrying with 1 *N* caustic and then filtered; the cake was recrystallized in hot water and gave a white solid, m.p. 221–222. This solid gave only a light orange color with ferric chloride; microanalysis and a new medium band at 5.75 μ in the infrared suggested that not only had oxidation taken place but also one of the amino groups had been hydrolyzed which then presumably tautomerized to the keto form (the tautomer usually observed in amino hydroxy triazines).

Anal. Calcd. for $C_4H_6N_4O_2$: 2-amino-1-hydroxy-4-methyl-*s*-triazine-6-(1*H*)-one. C, 33.8; H, 4.24; N, 39.4; O, 22.4. Found: C, 33.9; H, 4.35; N, 39.3; O, 22.7.

Melamine *N*-Oxide *via* Method A.—Reaction at 40–45° following the general procedure as outlined above gave only unreacted starting material. The reaction was then investigated at higher temperatures. To a very thick stirred slurry of 25.2 g. (0.2 mole) of melamine and 300 ml. of glacial acetic acid was added at 28–30°, 56.6 g. of 41% peracetic acid (0.3 mole). The mixture was heated to 80° at which temperature a mild exotherm occurred. After 5 min. the exotherm was spent and the thin slurry was heated for an additional 6 hr. at 78–80° and then filtered at 80°. The cake gave a negative ferric chloride test. The filtrate on cooling deposited a white solid which after filtering, washing with ether, and air-drying weighed 23.1 g., m.p. > 310°. This material gave a deep red color with ferric chloride and appeared to be the acetic acid salt of the desired product and a portion of it was neutralized by slurrying with 1 *N* sodium hydroxide to pH 7.5–8, filtering, and recrystallizing twice from hot water. From the second recrystallization two crops were obtained: I, the first crop was deposited while the solution was still hot, m.p. < 310°; II, the crystals were obtained on cooling and chilling m.p. 305° dec. Both I and II possessed identical infrareds and are identical to the product[2] obtained from potassium dicyanoguanidine and hydroxylamine hydrochloride, m.p. > 310; I and II are apparently polymorphs.

Anal. Calcd. for $C_3H_6N_6O$: C, 25.4; H, 4.23; N, 59.2. Found: (I) C, 25.5; H, 4.28; N, 59.4. (II) C, 25.5; H, 4.45; N, 59.1.

Aminotriazine *N*-Oxides *via* Hydroxylamine Cyclization of Dicyanoamidine Salts. Method B.—The general procedure consisted in slurrying the dicyanoamidine salts and hydroxylamine hydrochloride (moles hydroxylamine hydrochloride/moles dicyanoamidine salt = 1–1.5) in β-ethoxyethanol (10–15 ml. of β-ethoxyethanol 0.01 mole of dicyanoamidine salt) at 25–35° for 3–5 days in a closed system, followed by isolation of products. The product which was usually insoluble was filtered, slurried in water to remove salts, and then recrystallized. Compounds 1, 8, 10, 11, 16, and 17 of Table I were handled in this fashion. The only exception to this general procedure occurred with benzoguanamine *N*-oxide, which after reaction, evaporation and slurrying with water gave a product whose infrared indicated the presence of the starting dicyanoamidine, probably as a salt of the desired *N*-oxide (since the free acid is a fairly strong acid). The compound (0.5 g. in 50 ml. of water) was made alkaline to pH 10 with 5 *N* caustic, heated to boiling, filtered, and the desired product isolated on cooling and chilling; 0.2 g., m.p. 278–279° dec.; deep red color with ferric chloride. All the compounds prepared by procedure B were identical to the corresponding compound prepared by Procedure A.

2,6-Diamino-4-methyl-*s*-triazine 1-Oxide (Acetoguanamine *N*-Oxide) *via* Method B.—A stirred solution of 4.38 g. (0.03 mole) of potassum dicyanoacetamidine in 30 ml. of Cellosolve was treated with 2.09 g. (0.03 mole) of hydroxylamine hydrochloride in one portion. The mixture was stirred at room temperature for 3 days, chilled, and filtered and the damp cake slurried in 25 ml. of water for 2.5 hr. Filtration, followed by air and then oven drying at 60° gave 2.2 g. of a white solid which gave a deep red color with ferric chloride and melted higher than 330°. The infrared spectrum of this compound was identical to that of the compound prepared by the peracetic acid oxidation of acetoguanamine.

Anal. Calcd. for $C_4H_7N_5O$: C, 34.1; H, 4.98; N, 49.7. Found: C, 34.4; H, 5.18; N, 49.5.

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Sodium Dicyanoacetamidine *via* Method C.—The preparation of sodium dicyanoacetamidine from sodium acid cyanamide and ethyl acetimidate hydrochloride will serve to illustrate method C. A stirred solution of 123.4 g. (1 mole) of ethyl acetimidate hydrochloride in 500 ml. of absolute methanol was treated with 168.5 g. (2.2 moles) of powdered 83.5% sodium acid cyanamide and the mixture heated to reflux. A gentle stream of nitrogen was passed through the system to aid in the removal of ammonia which was liberated in the reaction. After refluxing for 27 hr., the mixture was cooled to room temperature and filtered. The filtrate was allowed to evaporate at room temperature for 5 days and then in a 60° oven to constant weight. There was obtained 114.5 g. of a light yellow solid which melted at 233–235° with decomposition and which gave a green precipitate with aqueous copper sulfate. This material was of suitable purity for further reactions. An analytical sample was obtained as follows: An amount of 8.6 g. was warmed with 10 ml. of water, and after refrigerating overnight was filtered; the filtrate was evaporated to dryness, 7.5 g., m.p. 240–242°. After this material was recrystallized twice from ethanol–ether, there was obtained 1.5 g. of a white solid, m.p. 262–263° dec.; green precipitate with aqueous copper sulfate.

Anal. Calcd. for $C_4H_3N_4Na$: C, 36.9; H, 2.31; N, 43.3. Found: C, 36.8; H, 2.45; N, 43.3.

A similar preparation using dimethyl sulfoxide as solvent gave a 55% crude yield.

Dicyanoamidines *via* Cyanogen Chloride and Amidines. Method D.—The cyanogen chloride used in these reactions was obtained from the liquid outlet of a cyanogen chloride cylinder and collected in a chilled (0 to 5°) graduate cylinder. It was allowed to vaporize from this cylinder (a porous plate chip added greatly in vaporization) and was conducted *via* Tygon and glass tubing to the reaction flask and added as a gas just above the surface of the stirred mixture. Cessation of the gas flow was easily achieved by cooling the graduate cylinder to 0–5°. Compound numbers in this section refer to those in Table II.

The general procedure consisted in treating a slurry of amidine hydrochloride in acetone with 2 equivalents of powdered potassium hydroxide, stirring for 15–20 min. at −15 to −20° and then adding 1 equivalent of cyanogen chloride gas at 7 to 11°. Completion of the reaction in most cases was evident by cessation of the exotherm and the fall in pH from about 11 to 8–9. The mixture was then chilled to −15 to −20° and the addition of 2 equivalents of potassium hydroxide and 1 equivalent of cyanogen chloride was repeated as before. After completion of reaction, the mixture was stirred for 30–45 min. at 5 to 15°, filtered and the filtrate adjusted to pH 5–6 with acetic acid. The filtrate was distilled *in vacuo* (pot temperature ≤ to 25°) first on the water aspirator and then under high vacuum (1 mm.) until it was evident that all of the acetone and most of the water formed in the reaction has been removed. The residue which was usually a sirup or a thick slurry was treated with isopropyl alcohol (compounds 1 and 5), or ether (compounds 3, 6, and 7) to induce crystallization. The crude material was then recrystallized where necessary although in many cases it was of sufficient purity to use as isolated.

Potassium Dicyanoacetamidine *via* Method D.—A stirred slurry of 47.2 g. (0.5 mole) of acetamidine hydrochloride in 500 ml. of acetone was cooled to −20 to −30° and 66 g. (1.0 mole) of 85% powdered potassium hydroxide was added in one portion, the temperature being held at −20° or lower. After stirring for 20 min. at −20 to −5°, cyanogen chloride gas was added through a tube just above the surface of the agitated slurry, the temperature being held at 7 to 9°. Addition of 30.7 g. (0.5 mole) of cyanogen chloride required about 50 min., the pH of the mixture by this time had fallen from 10 to about 8 and the exotherm also ceased. The flow of cyanogen chloride was interrupted and the reaction flask cooled to −20° and 66 g. (1 mole) of 85% powdered potassium hydroxide was added. The solids tended to agglomerate so 200 ml. of additional acetone was added. After stirring for 15–20 min. at −20 to −5°, cyanogen chloride gas was added as above. The temperature was held at 7–9° and the addition of 30.7 g. (0.5 mole) required 1 hr. and 10 min. The mixture was stirred at 5 to 15° for 35 min., cooled to 5°, filtered and the filtrate acidified to pH 6 with acetic acid. The filtrate was allowed to stand overnight and then distilled *in vacuo* (Dry Ice on the receiver) first at the aspirator and then at 1–2 mm.; a smooth paste remained. This was treated with 200 ml. of isopropyl alcohol, stirred for 1 hr., chilled, and filtered, the cake being washed with ether; 43.3 g. of a white solid, m.p. 208–210° (turbid melt). An infrared spectrum of this sample was essentially identical with that of sodium dicyanoacetamidine prepared *via* method C, and gave a good precipitate with copper sulfate. Analysis of this unrecrystallized material showed a high degree of purity.

Anal. Calcd. for $C_4H_3N_4K$: C, 32.8; H, 2.07. Found: C, 31.5; H, 1.94.

Copper(II) Dicyanoacetamidine.—A solution of 16.8 g. (0.1 mole) of sodium dicyanoacetamidine (77.2% real) in 15 ml. of water was treated with a solution of 24.8 g. (0.1 mole) of copper sulfate pentahydrate in 50 ml. of water. The green precipitate which formed immediately was stirred for 1 hr. at room temperature and filtered, 12 g., m.p. >300°. Elemental analysis indicated that two dicyanoacetamidine groups are associated with each copper atom.

Anal. Calcd. for $C_8H_6N_8Cu \cdot 2H_2O$: C, 30.7; H, 3.19; N, 35.7. Found: C, 30.4; H, 2.83; N, 35.4.

An attempt to convert the copper salt to the free acid with hydrogen sulfide was not successful. Also, an attempt to convert sodium dicyanoacetamidine to the free acid with concentrated hydrochloric acid did not lead to any product suitable for analysis.

Dicyanobenzamidine from the Potassium Salt.—A solution of 5 g. of potassium dicyanobenzamidine in 50 ml. of water was chilled to 10° and treated dropwise at 10 to 15° with concentrated hydrochloric acid to maximum precipitation. The mixture was stirred at 10 to 15° for 5 min., filtered and the cake washed with a small amount of water. After drying *in vacuo* over phosphorus pentoxide and potassium hydroxide pellets at room temperature, the material weighed 4 g., m.p. 102° dec. Dicyanobenzamidine appears to be a very strong acid and gave a pea-green precipitate with copper sulfate solution.

Anal. Calcd. for $C_9H_6N_4 \cdot H_2O$: C, 57.5; H, 4.26; N, 29.7; H_2O, 9.56. Found: C, 57.4; H, 4.12; N, 29.7; H_2O, 10.1.

Deoxygenation of Acetoguanamine *N*-Oxide with Phosphorus Trichloride.—A mixture of 2 g. of acetoguanamine *N*-oxide, 12.6 g. of phosphorus trichloride, and 40 ml. of chloroform was refluxed for 5 hr. The suspension after cooling was collected and the dry material added to 7 ml. of water with stirring and chilling (mild exotherm). The precipitate which formed was filtered and the damp cake was slurried in 5 ml. of water. After making the mixture alkaline to pH 8 with solid sodium carbonate, it was heated to boiling and filtered; the precipitate which formed on chilling was collected (0.7 g.) and recrystallized from 5 ml. of water. A white solid melting 267–269° and possessing an identical infrared spectrum with an authentic sample of acetoguanamine was obtained.

Anal. Calcd. for $C_4H_7N_5$: C, 38.4; H, 5.63; N, 56.0. Found: C, 38.4; H, 5.39; N, 56.1.

2-Amino-4-hydroxyamino-6-methyl-*s*-triazine.—To a stirred solution of 16.4 g. (0.1 mole) of 2,4-dichloro-6-methyl-*s*-triazine in 250 ml. of ether at 0–2° was added in portions 5.5 g. (0.1 mole) of potassium amide. After 0.5 hr., there still appeared to be no reaction so ten $^3/_8$-in. diameter steel balls were added to the reaction mixture. The character of the solids gradually changed and a fine white granular material formed. Stirring at 2 to 5° was then carried out for 1 hr., followed by 20 hr. at room tem-

perature. To this thin slurry was added in one portion an intimate mixture of 9.04 g. (0.13 mole) of hydroxylamine hydrochloride and 12.1 g. (0.115 mole) of anhydrous sodium carbonate followed by dropwise addition of 8 ml. of water. After stirring for 4 days at room temperature, the ether was decanted and the gummy residue triturated with 200 ml. of ice water, the pH (7.5) being adjusted to 6 with acetic acid. Filtration followed by air drying for 10 hr. and then oven-drying (60°) to constant weight gave 13.2 g. of a light gray solid, m.p. 230, partial decomposition, with no further melting after 300°. This material gave a violet color with aqueous ferric chloride. Recrystallization of 2 g. from 100 ml. of distilled water (not all dissolved) gave 0.8 g. of an off-white solid with an indeterminate melting point, violet color with ferric chloride, and an infrared spectrum different from the peracetic acid oxidation product of acetoguanamine.

Anal. Calcd. for $C_4H_7N_5O$: C, 34.1; H, 4.98; N, 49.7. Found: C, 34.3; H, 5.09; N, 49.6.

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Preparation of Several Methyl D-Pentothiapyranosides[1]

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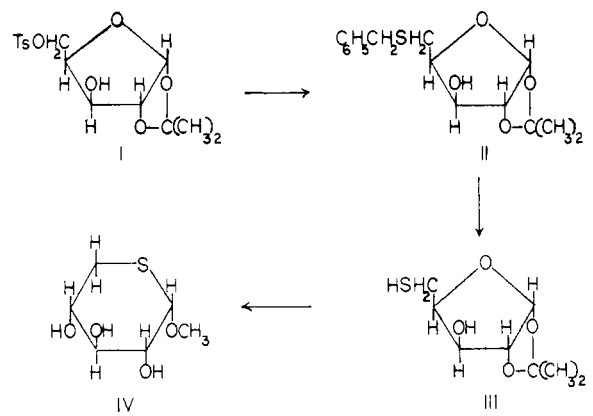
The preparation of D-xylothiapyranose is described. The synthesis and certain properties of methyl-D-xylothiapyranoside, methyl D-ribothiapyranoside, and methyl 2-deoxy-D-ribothiapyranoside are given.

The possibility of producing analogs of sugars in which the ring oxygen is replaced by sulfur or nitrogen is intriguing, not only from the point of view of the chemistry involved but from the possibility that analogs of important metabolic sugars such as D-glucose, D-ribose and 2-deoxy-D-ribose may be of biochemical and medical interest. Consequently, work was initiated here to produce sugars wherein the ring oxygen atoms are suitably replaced, initially with sulfur. To obtain such sugars in which sulfur is positively located in a stable sugar ring, several methyl D-pentothiapyranosides were first prepared.

Previous work involved analogs of methyl D-xylopyranoside in which sufur replaced the ring oxygen.[2] Ring size was determined by periodate oxidation and isolation of the expected amount of formic acid. Shortly before the announcement of the synthesis of methyl α-D-xylothiapyranoside, two other reports[3,4] appeared on the synthesis of D-xylose and L-idose with sulfur as the ring hetero atom as indicated mainly by spectral data. However, production of crystalline methyl α-D-xylothiapyranoside made it easy to obtain definite chemical evidence that sulfur was a part of a stable ring. This initial work is now extended to D-ribose and 2-deoxy-D-ribose.

Synthesis of the two latter pentothiapyranosides is somewhat more difficult than the synthesis of methyl α-D-xylothiapyranoside. This sugar derivative is prepared by displacement of the tosyloxy group in 1,2-O-isopropylidene-5-O-tosyl-α-D-xylofuranose[5] (I) with the thiobenzyl nucleophile, reduction to the mercapto derivative (III), and methanolysis. The methyl α-D-xylothiapyranoside (IV) has the expected molecular weight and liberates one mole of formic acid on treatment with periodate. During oxidation, excess periodate is consumed, probably in the formation of a sulfoxide or sulfone.[6] The alpha configuration at the anomeric carbon is suggested by the high positive specific rotation of the glycoside which mutarotates downward on acid hydrolysis.



Somewhat similar reactions are possible for the introduction of sulfur into D-ribose. Methyl 2,3-O-isopropylidene-D-ribofuranoside is converted to the crystalline 5-O-tosyl derivative[7] (V) and thence by tosyloxy displacement, to the 5-deoxy-5-thiobenzyl derivative (VI) which on reduction results in the

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