Preparation and Reactions of N-Cyanoamidines

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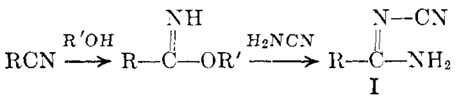
Several N-cyanoamidines were prepared by the reaction of imidates with cyanamide or of amidine hydrochlorides with monosodium cyanamide. Various methods were examined for the conversion of simple N-cyanoamidines to *s*-triazines and other heterocyclic products. Some related reactions of N-carbamoylamidines are reported also.

N-Cyanoamidines (I) rarely have been examined as synthetic intermediates, despite their close structural similarity to cyanoguanidine (I. R = NH_2), a compound which has been extensively studied for over a century.[1] The reaction of N-cyanoformamidine with guanidine to give a good yield of 2,4-diamino-*s*-triazine is apparently the only reported direct conversion of an N-cyanoamidine to a heterocyclic product.[2] The present paper contains the results of an exploratory survey of the preparation of these compounds and their utility as intermediates for the synthesis of nitrogen heterocycles.

Compounds of structure I have been obtained previously from the action of cyanide ion upon N-haloamidines[3] or by treatment of an amidine with cyanogen bromide.[3] N-Cyanoformamidine has been prepared in high yield from the reaction of cyanamide with formamidine[2] or *s*-triazine.[4]

We have prepared several N-cyanoamidines in good yields by the reaction of imidates with cyanamide, a method which has heretofore been reported only for isolated examples of N′-substituted-N-cyanoamidines.[5,6] Simplification of this procedure was possible when R contained an appropriately situated electron-withdrawing group, in that the imidate could then be prepared from the corresponding nitrile by base-catalyzed addition of alcohol.[7] Addition of cyanamide to this solution produced the N-cyanoamidine directly. In addition to the simple N-cyanoamidines (I. R = CH_3, C_6H_5) employed in the synthetic studies, several other compounds were obtained by this procedure, as shown in Table I.

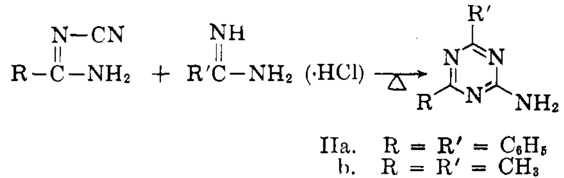


$$\mathrm{RCN} \xrightarrow{R'OH} R-\overset{\overset{\displaystyle NH}{\|}}{C}-OR' \xrightarrow{H_2NCN} \underset{\displaystyle \mathrm{I}}{R-\overset{\overset{\displaystyle N-CN}{\|}}{C}-NH_2}$$

N-Cyanoacetamidine and N-cyanobenzamidine were also prepared in good yields by the interaction of monosodium cyanamide with the corresponding amidine hydrochloride in aqueous solution. This appears to be an equally good preparative method, notably for cases in which the first procedure would require preparation and isolation of an imidate by the Pinner method.[8]

The N-cyanoamidines were characterized by analyses and infrared absorption spectra. The products showed three strong bands attributed to the amino group at 2.9–3.0, 3.1–3.2, and near 6.0 μ; carbon–nitrogen double bond absorption at 6.3–6.5 μ; and strong nitrile absorption, usually in the form of a doublet centered near 4.55 μ.

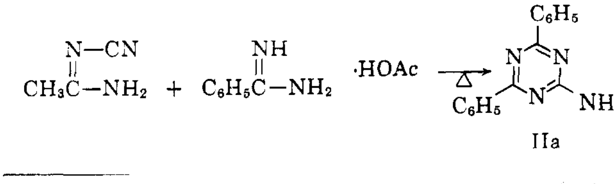
A convenient route to 2,4-diamino-*s*-triazines involves the reaction of cyanoguanidine with nitriles or amidine salts.[9] By analogy, it appeared that N-cyanoamidines might similarly function as useful intermediates for the preparation of monoamino-*s*-triazines. These reactions did occur as anticipated, although isolation of pure products was sometimes difficult.



IIa. R = R′ = C_6H_5
b. R = R′ = CH_3
c. R = CH_3, R′ = C_6H_5
d. R = H, R′ = C_6H_5
e. R = CH_3, R′ = NH_2
f. R = C_6H_5, R′ = NH_2

2-Amino-4,6-diphenyl-*s*-triazine (IIa) was obtained by treating N-cyanobenzamidine with benzonitrile in the presence of sodium hydroxide in refluxing 1-butanol, benzamidine in hot ethanol, or benzamidine hydrochloride at 175° in the absence of solvent, but yields in all three cases were around 15%. Compounds IIb, IIc, and IId were obtained in better yields (25–40%) from reactions using the appropriate combination of an N-cyanoamidine with an amidine hydrochloride at 150–175°. This procedure was found to be the most generally applicable for the conversion of I to monoamino-*s*-triazines, whereas diamino-*s*-triazines (IIe and IIf) were obtained conveniently from N-cyanoamidines with free guanidine in alcoholic solution.

Substitution of benzamidine acetate for benzamidine hydrochloride in the reaction with N-cyanoacetamidine resulted in formation of 2-amino-4,6-diphenyl-*s*-triazine (IIa), rather than the expected 4-methyl-6-phenyl analog. Although there are several possible mechanisms for this transformation, it is evident that the elements of cyanamide must have been lost from the starting N-cyanoamidine at some point.



IIa

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(1) See "*The Chemistry of Dicyandiamide*," American Cyanamid Company, New York, N. Y., 1949.

(2) K. Shirai, K. Odo, and K. Sugino, *J. Org. Chem.*, **23**, 100 (1958).

(3) J. Goerdeler and D. Loevenich, *Ber.*, **86**, 890 (1953).

(4) Unpublished results obtained in this laboratory by I. Hechenbleikner.

(5) W. J. Comstock and H. L. Wheeler, *Am. Chem. J.*, **13**, 514 (1891).

(6) G. Pellizzari, *Gazz. chim. ital.*, **41**, 93 (1911).

(7) F. C. Schaefer and G. A. Peters, *J. Org. Chem.*, **26**, 412 (1961).

(8) A. Pinner, "Die Imidoäther und ihre Derivate," Robert Oppenheim (Gustav Schmidt), Berlin, 1892.

(9) (a) E. M. Smolin and L. Rapoport, "*s*-Triazines and Derivatives," Interscience Publishers, Inc., New York, N. Y., 1959, p. 229; (b) E. J. Modest, "Heterocyclic Compounds," Vol. 7, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1961, p. 650.

TABLE I

PREPARATION OF N-CYANOAMIDINES FROM IMIDATES AND CYANAMIDE

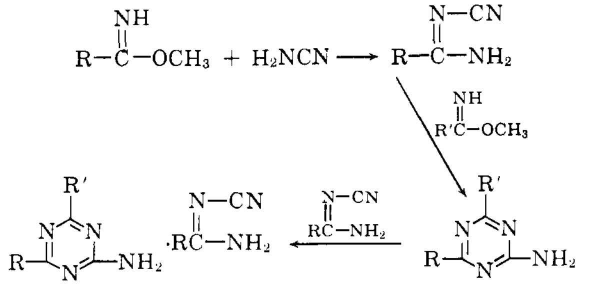
$$\overset{NH}{\overset{\|}{RC}}-OCH_3 + H_2NCN \longrightarrow \overset{N-CN}{\overset{\|}{RC}}-NH_2$$

R	Time at 25°	Yield, %	M.p., °C.	Recrystallization solvent	Formula	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
CH_3	15 min.	72	135–137	C_2H_5OH	$C_3H_5N_3$	43.36	6.07	50.57	43.59	5.96	50.59
C_6H_5	12 hr.	72	142–142.5[a]	C_2H_5OH/H_2O	$C_8H_7N_3$						
C_2H_5	30 min.	53	78.5–80	C_2H_5OAc	$C_4H_7N_3$	49.46	7.27	43.27	49.27	7.50	42.88
$ClCH_2$	4 hr.	59[b]	110.5–111.5	CH_3CN	$C_3H_4N_3Cl$	30.65	3.43	35.75	31.14	3.40	35.99
Cl_3C	3 hr.	43[b]	166.5–168	CH_3CN	$C_3H_2N_3Cl_3$	19.33	1.08	22.54	19.44	1.38	22.94
p-NO_2–C_6H_5	15 min.[c]	52[b]	233–234 dec.[d]	. . .	$C_8H_6N_4O_2$						
2-C_5H_4N	16 hr.	83[b]	224–226	CH_3OH	$C_7H_6N_4$	57.52	4.14	38.34	57.52	4.04	38.38

[a] Ref. 3 gives m.p. 142.5°. [b] Yield calculated on basis of nitrile. Imidate was not isolated. [c] At 50°. [d] Ref. 3 reports m.p. 243° dec.

Reaction of N-cyanoacetamidine with methyl acetimidate in refluxing methanol gave a product, $C_8H_{13}N_7$, which upon treatment with hydrochloric acid and subsequent neutralization afforded 2-amino-4,6-dimethyl-*s*-triazine (IIb). This same material was formed in high yield upon recrystallization of an equimolar mixture of N-cyanoacetamidine and 2-amino-4,6-dimethyl-*s*-triazine, thus establishing the structure as IIIa. The reaction of N-cyanoacetamidine with methyl propionimidate gave the homolog IIIb containing one ethyl group in the ring.

Since the N-cyanoamidines were originally prepared by treatment of imidates with cyanamide, it appeared that interaction of cyanamide with an excess of an imidate under more strenuous conditions would convert the initially formed N-cyanoamidine to the aminotriazine.



IIIa. R = R′ = CH_3
b. R = CH_3, R′ = C_2H_5

II
IIg. R = R′ = CCl_3

This reaction sequence occurred as predicted with methyl acetimidate and a 42% yield of IIIa was obtained. With methyl benzimidate, however, the reaction did not proceed beyond the first step, since N-cyanobenzamidine was the only product found. On the other hand, when methyl trichloroacetimidate was used as the starting material, the reaction proceeded to give a 29% yield of 2-amino-4,6-bis(trichloromethyl)-*s*-triazine (IIg). Apparently, the amino group in this compound is not basic enough to form a salt with the N-cyanoamidine. It should be pointed out that this synthesis of IIg is essentially a cotrimerization of cyanamide with trichloroacetonitrile as the imidate was prepared and used *in situ*.

Other methods of ring closure to form the *s*-triazine system were investigated briefly using N-cyanobenzamidine as the cyanoamidine component and acetic anhydride, formamide, and thioacetamide[10] as cyclizing agents. These are shown in Chart 1.

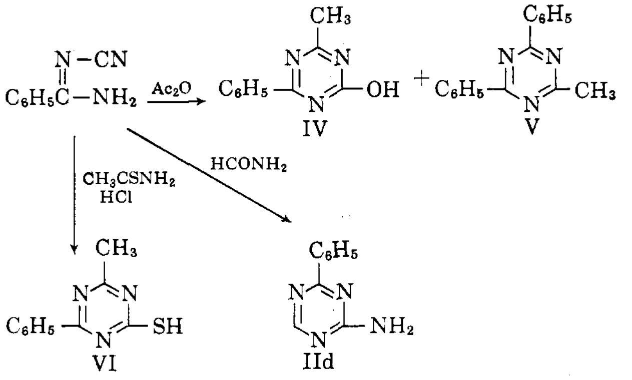
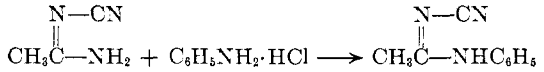


CHART 1

Although the expected product was obtained in each case, yields were again rather low (<20%). 2-Methyl-4,6-diphenyl-*s*-triazine was the major product from N-cyanobenzamidine and acetic anhydride, again demonstrating loss of cyanamide from an N-cyanoamidine during the course of a reaction. This tendency to lose cyanamide, either through dissociation or displacement, together with the somewhat lower reactivity of the nitrile groups in the N-cyanoamidines, may account for the inferior yields in many of these reactions when compared to the corresponding reactions of cyanoguanidine.

A striking example of this difference in reactivity was observed in the attempted reaction of N-cyanoamidines with aniline hydrochloride in hot aqueous solution. Although cyanoguanidine readily affords phenylbiguanide in high yield,[11] N-cyanobenzamidine did not react under these conditions, while N-cyanoacetamidine gave only a small yield of N-cyano-N′-phenylacetamidine (VII) rather than undergoing addition at the nitrile group.



$$\overset{N-CN}{\overset{\|}{CH_3C}}-NH_2 + C_6H_5NH_2{\cdot}HCl \longrightarrow \overset{N-CN}{\overset{\|}{CH_3C}}-NHC_6H_5$$

VII

As is the case with cyanoguanidine, the nitrile groups of N-cyanoamidines are readily hydrolyzed under strongly acidic conditions.[3,6,12] In the present work, N-carbamoylamidine hydrochlorides (VIII) were isolated in good yields upon addition of N-cyanoami-

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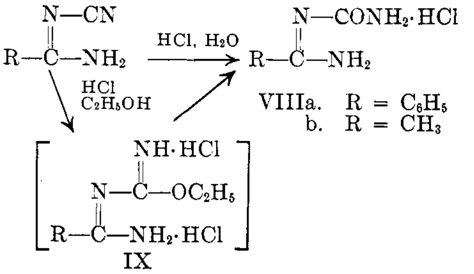
(10) *Cf.* E. C. Taylor and J. A. Zoltewicz, *J. Am. Chem. Soc.*, **83**, 248 (1961).

(11) G. Cohn, *J. prakt. Chem.*, [2] **84**, 394 (1911).

(12) G. Palazzo and G. Strani, *Gazz. chim. ital.*, **91**, 216 (1916).

dines to cold concentrated hydrochloric acid or treatment of the cyano compounds with excess dry hydrogen chloride in ethanol. The latter conditions presumably involve formation of an intermediate such as IX, which then loses ethyl chloride to give VIII.



Attempts to convert N-carbamoylbenzamidine (VIIIa) to 2-hydroxy-s-triazines by various methods were unsuccessful. The only products isolated were those from which the carbamoyl group had been lost (Chart 2). Presumably, the manner of decomposition of these compounds is similar to, but easier than, that occasionally found with the N-cyanoamidines, although mechanisms have not been established for these reactions.

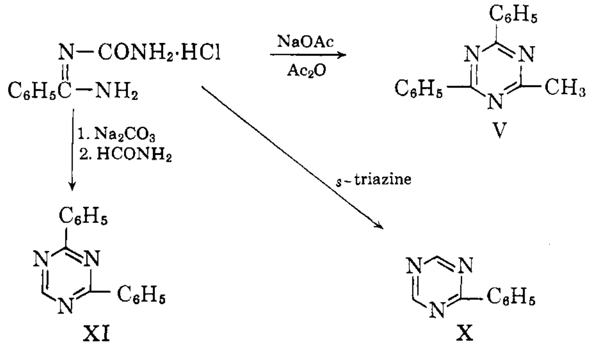
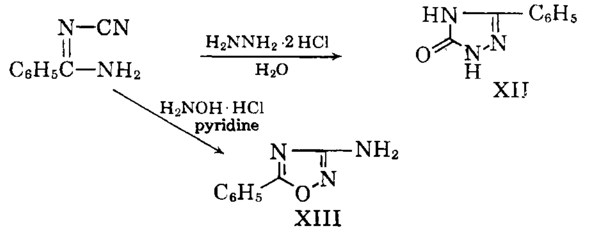


CHART 2

Recently, the preparation of N-carbamoylbenzamidine and its reaction with benzoyl chloride to give 2-hydroxy-4,6-diphenyl-s-triazine was reported.[12]

The use of N-cyanoamidines for the synthesis of five-membered heterocycles was demonstrated by formation of compounds XII and XIII from N-cyanobenzamidine with hydrazine dihydrochloride and hydroxylamine hydrochloride, respectively.



It is interesting that the reaction of hydroxylamine with the related methyl N-cyanobenzimidate leads to the isomer of XIII in which the positions of the amino and phenyl groups are reversed.[13]

Experimental[14]

Reagents.—Crystalline cyanamide was obtained by evaporation of the commercially available 50% aqueous solution. It was purified before each reaction by dissolution in ether, filtration of the insoluble cyanoguanidine, and evaporation of the filtrate.

All imidates and amidines were prepared by standard methods.[7,8,15]

Reaction of Imidates with Cyanamide. General.—N-Cyanoamidines listed in Table I were prepared by the following general procedure. To 0.1 mole of imidate was added slowly with swirling a solution of 0.1 mole of freshly purified cyanamide in 20 ml. of methanol. The reaction mixture was cooled in an ice bath if necessary to keep the temperature below 50°. After the specified length of time, the product was isolated by filtration or by evaporation of the methanol and crystallization of the residue from the appropriate solvent.

When the imidate could be prepared *in situ*, the following procedure was effective. A solution of 0.1 mole of the nitrile in 25 ml. of methanol was treated with 0.005 mole of sodium methoxide using the previously described conditions.[7] After imidate formation was essentially complete, the solution was neutralized with 0.005 mole of acetic acid and then treated with cyanamide and worked up as before.

N-Cyanobenzamidine.—A mixture of 25.0 g. of benzamidine hydrochloride dihydrate (0.13 mole) and 11.0 g. of 75% monosodium cyanamide[16] (0.13 mole) in 75 ml. of water was stirred until the starting materials had dissolved and the product began to crystallize. After 2 hr. it was filtered to give 11.6 g. of white crystalline product, m.p. 135–137.5°. Another 2.2 g., m.p. 139–141°, crystallized from the filtrate after several more hours, for a total of 13.8 g. (74%). Recrystallization from ethanol-water raised the m.p. to 141–142° (lit.[3] m.p. 142.5°).

N-Cyanoacetamidine.—Acetamidine hydrochloride, 94.5 g., 1.0 mole, was mixed with 69.5 g. of 92% monosodium cyanamide (1.0 mole) in 100 ml. of water. After 2 hr., the mixture was chilled and filtered, and the resulting white solid was extracted with hot acetone. Sodium chloride was removed by filtration and the acetone solution was concentrated and chilled to give 38.5 g. of white crystals, m.p. 134–136°, and a second crop of 6.0 g., m.p. 125–133°. The original aqueous filtrate was evaporated and worked up as before to give another 7.7 g., m.p. 125–130°, for a total of 52.2 g. (63%). This material was identical with that described in Table I.

2-Amino-4,6-diphenyl-s-triazine (IIa). A.—A mixture of 1.05 g. (0.0072 mole) of N-cyanobenzamidine and 1.15 g. (0.0074 mole) of benzamidine hydrochloride was fused at 175° for 2.5 hr. Crystallization of the resulting mixture from ethanol–water afforded 0.30 g. (17%) of the triazine, m.p. 167–169° (lit.[17,18] m.p. 172° and 168–170°.

B.—A solution of 0.016 mole of benzamidine, prepared from 2.50 g. of benzamidine hydrochloride and 0.85 g. of sodium methoxide in 10 ml. of ethanol, was filtered and mixed with 2.30 g. (0.016 mole) of N-cyanobenzamidine. The resulting solution was refluxed for 2 hr. and stored overnight. The product was collected by filtration. The yield was 0.60 g. (15%), m.p. 168–170°.

C.—A solution of 2.0 g. (0.014 mole) of N-cyanobenzamidine, 1.4 g. (0.014 mole) of benzonitrile, and 20 mg. of powdered sodium hydroxide in 10 ml. of 1-butanol was refluxed for 4 hr. The mixture was filtered to remove traces of solid and evaporated to an oily residue which was crystallized from ethanol–water yielding 0.60 g. (17%) of crude IIa, m.p. 135–160°. Two recrystallizations from ethanol afforded pure material, m.p. 167–170°.

D.—Fusion of a mixture of 1.0 g. of N-cyanoacetamidine (0.012 mole) and 2.2 g. of benzamidine acetate (0.012 mole) at 160–165° for 3.5 hr. yielded an oil which was partially crystallized from water. Several recrystallizations from aqueous ethanol gave pure IIa, m.p. 169–171°, identical with the samples described previously.

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[13] K. R. Huffman and F. C. Schaefer, *J. Org. Chem.*, **28**, 1816 (1963).

[14] Melting points are uncorrected. N. B. Colthup aided in interpretation of the infrared spectra.

[15] F. C. Schaefer and G. A. Peters, *J. Org. Chem.*, **26**, 2778 (1961).

[16] R. A. Vingee and L. J. Christmann, U. S. Patent 2,656,256 (October 20, 1953); *Chem. Abstr.*, **48**, 2996 (1954).

[17] J. Ephraim, *Ber.*, **26**, 2226 (1893).

[18] P. B. Russell and G. H. Hitchings, *J. Am. Chem. Soc.*, **72**, 4922 (1950).

2-Amino-4,6-dimethyl-*s*-triazine (IIb).—A mixture of 4.15 g. (0.050 mole) of N-cyanoacetamidine and 4.8 g. (0.051 mole) of acetamidine hydrochloride in 6 ml. of 2-methoxyethanol was heated at a bath temperature of 155° for 4 hr. The solid which separated on cooling was filtered and recrystallized from water to give 2.55 g. (41%) of IIb, m.p. 160–166°. After one additional recrystallization from acetonitrile the m.p. was 167–169° (lit.[19,20] m.p. 170° and 171°.

2-Amino-4-methyl-6-phenyl-*s*-triazine (IIc).—A mixture of 1.6 g. of benzamidine hydrochloride dihydrate (0.0083 mole) and 0.85 g. of N-cyanoacetamidine (0.010 mole) was fused at 150° for 3 hr. The resulting oil was cooled and treated with 10 ml. of water which caused crystallization of a tan solid, 0.40 g. (26%), m.p. 148–152°. This crude material was identified by infrared comparison with pure IIc, m.p. 155–156°, obtained as described in the following paper.[13]

2-Amino-4-phenyl-*s*-triazine (IId). **A.**—A solution of 2.0 g. of N-cyanobenzamidine in 5 ml. of formamide was heated at 180° for 2 hr. Upon cooling, a tan solid separated. It was recrystallized from ethanol to give 0.35 g. (15%) of crude material, m.p. 187–195°. Two additional recrystallizations afforded white flakes, m.p. 203–204°.

Anal. Calcd. for $C_9H_8N_4$: C, 62.77; H, 4.68; N, 32.54. Found: C, 62.39; H, 4.63; N, 32.44.

B.—A mixture of 1.0 g. (0.0145 mole) of N-cyanoformamidine[2] and 2.3 g. of benzamidine hydrochloride (0.015 mole) was fused at 160° for 30 min. The resulting solid was triturated successively with water and hot ethanol to give 0.70 g. of IId as tan crystals, m.p. 201–204°. The ethanol solution yielded another 0.07 g., m.p. 195–198°, for a total of 0.77 g. (31%).

2,4-Diamino-6-methyl-*s*-triazine (IIe).—A solution of guanidine was prepared from 3.1 g. of guanidine hydrochloride and 1.75 g. of sodium methoxide in 20 ml. of methanol. This was filtered and 2.5 g. of N-cyanoacetamidine was added. After refluxing for 6 hr., the solution was chilled and filtered to give 2.0 g. (53%), m.p. 275–276°, identical with an authentic sample.

2,4-Diamino-6-phenyl-*s*-triazine (IIf).—Application of the above procedure to N-cyanobenzamidine afforded a 19% yield of IIf, m.p. 219–223°, compared with an authentic sample.

2-Amino-4,6-dimethyl-*s*-triazine, N-Cyanoacetamidine Salt (IIIa). **A.**—A solution of 2.1 g. (0.050 mole) of cyanamide in 10 ml. of ethanol was added slowly with swirling to 7.4 g. (0.10 mole) of methyl acetimidate. The resulting warm solution was refluxed for 6 hr. and stored at room temperature overnight, during which time the product crystallized. The yield was 2.2 g. (42%), m.p. 179–182°. Two recrystallizations from methanol gave an analytical sample, m.p. 182–183.5°.

Anal. Calcd. for $C_8H_{13}N_7$: C, 46.36; H, 6.32; N, 47.32. Found: C, 46.68; H, 5.90; N, 47.38.

This compound was converted to the hydrochloride of 2-amino-4,6-dimethyl-*s*-triazine by treatment with excess dry hydrogen chloride in ethanol. Addition of the salt to aqueous bicarbonate gave the free base, m.p. 166–167°, identical with the sample prepared earlier.

B.—A solution of 1.65 g. (0.020 mole) of N-cyanoacetamidine and 1.50 g. (0.020 mole) of methyl acetimidate in 5 ml. of methanol was refluxed for 6 hr. and chilled. The crystalline IIIa was filtered; yield, 1.05 g. (51%), m.p. 182–184°.

C.—Recrystallization of a mixture of 0.30 g. (0.0024 mole) of 2-amino-4,6-dimethyl-*s*-triazine and 0.20 g. (0.0024 mole) of N-cyanoacetamidine from methanol afforded 0.35 g. (70%) of pure IIIa, m.p. 183–184.5°, identical with the samples described previously.

2-Amino-4-ethyl-6-methyl-*s*-triazine, N-Cyanoacetamidine Salt (IIIb).—A solution of 2.5 g. of N-cyanoacetamidine (0.030 mole) and 2.85 g. of 94% methyl propionimidate (0.031 mole) in 5 ml. of ethanol was refluxed for 5.5 hr. and chilled to give 1.50 g. (45%) of white solid, m.p. 148–155°. An analytical sample, m.p. 158–159°, was obtained after three recrystallizations from methanol.

Anal. Calcd. for $C_9H_{15}N_7$: C, 48.85; H, 6.83; N, 44.32. Found: C, 48.97; H, 6.72; N, 44.08.

2-Amino-4,6-bis(trichloromethyl)-*s*-triazine (IIg).—A cold solution of 7.4 g. (0.051 mole) of trichloroacetonitrile in 20 ml. of methanol was treated with 0.15 g. of sodium methoxide and kept at room temperature for 30 min. It was then treated successively with 0.20 g. of acetic acid and 1.05 g. (0.025 mole) of cyanamide and then refluxed for 4.5 hr. The resulting solution was evaporated to a dark oil from which there was obtained, by crystallization and recrystallization from ethanol–water, 2.4 g. (29%) of the triazine as dirty white prisms, m.p. 163–165.5°. Further recrystallization raised the m.p. to 165–167° (lit.[21] m.p. 165–166°). A mixture melting point with N-cyano-2,2,2-trichloroacetamidine, m.p. 166.5–168°, was strongly depressed. No nitrile band was apparent in the infrared spectrum.

Reaction of N-Cyanobenzamidine with Acetic Anhydride.—A solution of 1.0 g. of N-cyanobenzamidine in 4 ml. of acetic anhydride was refluxed for an hour. The resulting yellow solid was recrystallized from acetonitrile to give 0.18 g. (14%) of **2-hydroxy-4-methyl-6-phenyl-*s*-triazine** (IV), m.p. 239–241°. Another recrystallization afforded material, m.p. 243–245°.

Anal. Calcd. for $C_{10}H_9N_3O$: C, 64.16; H, 4.85; N, 22.45. Found: C, 64.13; H, 4.58; N, 22.79.

The acetic anhydride solution was then distilled and the oily residue was crystallized from water and recrystallized from ethanol–water yielding 0.25 g. (29%) of **2-methyl-4,6-diphenyl-*s*-triazine** (V), m.p. 94–102°. After another recrystallization the m.p. was 107–108°. The structure was confirmed by comparison with an authentic sample.[22]

2-Mercapto-4-methyl-6-phenyl-*s*-triazine (VI).—A solution of 0.75 g. (0.0052 mole) of N-cyanobenzamidine and 0.40 g. (0.0053 mole) of thioacetamide in 5 ml. of acetone was treated with excess dry hydrogen chloride. An orange gum was quickly formed. The acetone was decanted and 5 ml. of water was added, causing crystallization of a bright yellow solid. The yield was 0.20 g. (19%), m.p. 208–213°. Two recrystallizations from ethanol raised the m.p. to 230.5–233°.

Anal. Calcd. for $C_{10}H_9N_3S$: C, 59.09; H, 4.46; N, 20.68; S, 15.77. Found: C, 59.46; H, 4.54; N, 20.75; S, 16.07.

N-Cyano-N′-phenylacetamidine (VII).—A solution of 0.85 g. (0.010 mole) of N-cyanoacetamidine and 1.3 g. (0.010 mole) of aniline hydrochloride in 5 ml. of water was heated on the steam bath for 3 hr. Addition of dilute sodium hydroxide to the cooled solution caused separation of an oil which partially crystallized on standing. Recrystallization from ethanol gave 0.08 g. of VII, m.p. 190–192° (lit.[6] m.p. 193°).

N-Carbamoylbenzamidine Hydrochloride (VIIIa).—Addition of excess dry hydrogen chloride to 1.0 g. of N-cyanobenzamidine in 10 ml. of absolute ethanol, while cooling in an ice bath, produced a white crystalline solid which was filtered and washed with ether. The yield of VIIIa was 1.2 g. (87%), m.p. 192–194°, in agreement with the lit.[12] m.p. 192–194°.

N-Carbamoylacetamidine Hydrochloride (VIIIb). **A.**—Application of the previous procedure to 0.40 g. of N-cyanoacetamidine gave 0.40 g. (60%) of VIIIb, m.p. 167–170°. The melting point was raised to 170–172° by recrystallization from ethanol.

Anal. Calcd. for $C_3H_7N_3O \cdot HCl$: C, 26.18; H, 5.86; N, 30.54. Found: C, 26.41; H, 5.83; N, 30.79.

B.—When 0.50 g. of N-cyanoacetamidine was mixed with 3 ml. of cold concentrated hydrochloric acid a vigorous reaction occurred with formation of a clear solution. Evaporation to dryness and crystallization from ethanol afforded 0.65 g. (78%) of VIIIb, m.p. 163–165° dec. Further recrystallization gave a sample identical with that described earlier.

Reaction of N-carbamoylbenzamidine with Acetic Anhydride.—A mixture of 1.0 g. of VIIIa and 0.41 g. of sodium acetate in 5 ml. of acetic anhydride was refluxed for an hour. The cooled solution was poured into water and neutralized with sodium bicarbonate. Extraction with ether gave a dark oil which slowly crystallized on drying under vacuum. Recrystallization from ethanol–water gave 0.30 g. (48%) of **2-methyl-4,6-diphenyl-*s*-triazine** (V), m.p. > 100°, in two crops. Further recrystallization from ethanol gave pure material, m.p. 108–108.5°, identical with an authentic sample.[22]

2-Phenyl-*s*-triazine (X).—A solution of 1.0 g. of N-carbamoylbenzamidine hydrochloride (0.0050 mole) and 0.43 g. of *s*-triazine[15] (0.0053 mole) in 10 ml. of absolute ethanol was refluxed for 2.5 hr. Removal of the ethanol left a colorless oil which was partially crystallized from methanol–acetonitrile to give 0.25 g. of an unidentified hydrochloride, m.p. 77–79°. The mother liquor was evaporated to dryness leaving an oil which crystallized upon addition of water. This material, 0.47 g., m.p. 62–63°, was identified as 2-phenyl-*s*-triazine (X) by comparison with an authentic sample[23]; yield, 59%.

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2,4-Diphenyl-s-triazine (XI).—A solution of 1.1 g. of N-carbamoylbenzamidine,[12] m.p. 130–132°, in 3 ml. of formamide was heated at 180–185° for an hour. The white solid which crystallized on cooling was extracted into petroleum ether. This solution was decanted from some insoluble oil and evaporated to give 0.10 g. (13%) of XI, m.p. 68–72°. Recrystallization from aqueous ethanol gave a sample which had m.p. 73–75° and an infrared spectrum identical with that of an authentic sample.[23]

3-Phenyl-1,2,4-triazolin-5-one (XII).—A mixture of 1.0 g. (0.007 mole) of N-cyanobenzamidine and 0.75 g. (0.007 mole) of hydrazine dihydrochloride in 15 ml. of 50% aqueous methanol and was refluxed for 3 hr. Most of the methanol was distilled. Upon cooling 0.30 g. (30%) of the starting material crystallized. A little sodium bicarbonate was added to the aqueous filtrate, from which XII slowly crystallized during 24 hr. The yield was 0.25 g. (23%), m.p. > 300°. It was recrystallized from 50% aqueous ethanol; m.p. 322–325° (lit.[24,25] m.p. 321° and 324°).

In another run, under slightly more strenuous conditions, a 15% yield of **benzoylurea,**[3] m.p. 210–212°, was isolated in addition to a lesser amount of XII.

3-Amino-5-phenyl-1,2,4-oxadiazole (XIII).—A solution composed of 1.0 g. of N-cyanobenzamidine, 0.50 g. of hydroxylamine hydrochloride, 3 ml. of ethanol, and 2 ml. of pyridine was refluxed for 30 min. and filtered hot to remove ammonium chloride. The filtrate was chilled to give 0.35 g. (31%) of XIII, m.p. 156–160°. One recrystallization from ethanol raised the m.p. to 164–165.5° (lit.[26,27] m.p. 164° and 164–165°).

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N-Cyanoimidates

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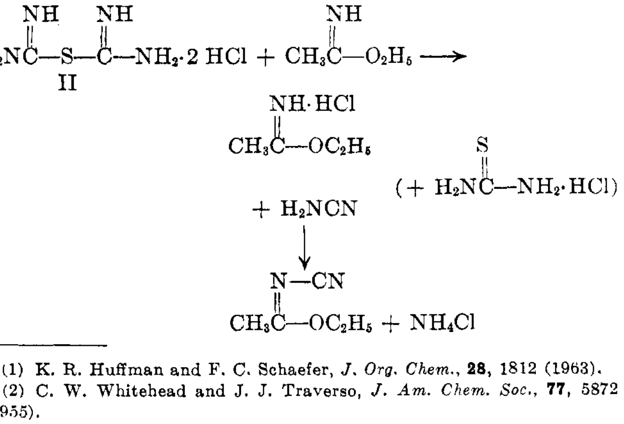
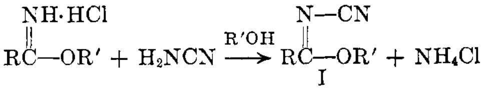
Alkyl N-cyanoimidates, a new class of reactive intermediates, have been prepared by reaction of cyanamide with ortho esters or imidate hydrochlorides. The N-cyanoimidates react with amidines to give 2-amino-s-triazines, with amidoximes to give 2-amino-s-triazine 1-oxides, with hydroxylamine to give 5-amino-1,2,4-oxadiazoles, and with hydrazine to give 3-amino-1,2,4-triazoles. Interaction of monosodium cyanamide with N-cyanoimidates gives N,N'-dicyanoamidine salts, which cyclize to 2-amino-s-triazines upon treatment with dry hydrogen chloride.

As an extension of the work reported in the previous paper[1] concerning the use of N-cyanoamidines as intermediates for the synthesis of certain nitrogen heterocycles, we have investigated the chemistry of the related N-cyanoimidates (I), with the expectation that the more easily displaceable alkoxy group would allow more efficient reactions with nucleophilic reagents. Although N-cyanoimidates have apparently not been reported in the literature, various N-carbamoylimidates[2] and N-acylimidates[3,4] are known. Moreover, they have been reported to react well with amines to give N-acylamidines.[2,5] An N-cyanopseudourea (I. $R = NH_2$) has also been prepared,[6] but its reactions were apparently not investigated.

We first obtain ethyl N-cyanoacetimidate as an unexpected product from attempted cotrimerization[7a] of ethyl acetimidate with thiodiformamidine dihydrochloride (II). Consideration of the probable mechanism of this reaction suggested that this N-cyanoimidate resulted from reaction of the imidate hydrochloride with cyanamide, the latter arising from dissociation of the starting material. Although imidates generally react with amino compounds with displacement of alcohol to give amidines, in many cases use of the imidate hydrochloride shifts the reaction to give formation of the N-substituted imidate by loss of ammonium chloride.[8] Thus, while reaction of cyanamide with imidates rapidly gave N-cyanoamidines,[1] it appeared that the corresponding reaction of the imidate salt might lead to N-cyanoimidates.



$$\underset{\text{II}}{\mathrm{H_2N\overset{NH}{\overset{\|}{C}}{-}S{-}\overset{NH}{\overset{\|}{C}}{-}NH_2\cdot 2\,HCl}} + \mathrm{CH_3\overset{NH}{\overset{\|}{C}}{-}O_2H_5} \longrightarrow \mathrm{CH_3\overset{NH\cdot HCl}{\overset{\|}{C}}{-}OC_2H_5} + \mathrm{H_2NCN}\ \left(+\ \mathrm{H_2N\overset{S}{\overset{\|}{C}}{-}NH_2\cdot HCl}\right) \longrightarrow \mathrm{CH_3\overset{N-CN}{\overset{\|}{C}}{-}OC_2H_5} + \mathrm{NH_4Cl}$$



$$\mathrm{R\overset{NH\cdot HCl}{\overset{\|}{C}}{-}OR'} + \mathrm{H_2NCN} \xrightarrow{\mathrm{R'OH}} \underset{\text{I}}{\mathrm{R\overset{N-CN}{\overset{\|}{C}}{-}OR'}} + \mathrm{NH_4Cl}$$

The first results were immediately encouraging when it was found that ethyl and methyl N-cyanoacetimidates (I. $R = CH_3$, $R' = C_2H_5$ or CH_3) could be prepared in 60–65% yields according to the equation shown. The procedure consisted simply of mixing the imidate hydrochloride with cyanamide in alcoholic solution, filtering the ammonium chloride after a few hours, and isolating the product by distillation. The somewhat slower reaction of imidate hydrochlorides with alcohols to give ortho esters[8] did not appear to be interfering to any appreciable extent.

Unfortunately, this method failed to give pure isolable N-cyanoimidates when the group R was made more complex than alkyl. The use in this reaction of alkyl imidates containing α- or β-chloro, α-hydroxy, or α-cyano groups led to complex mixtures or different products.

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