

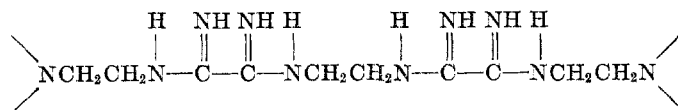
# THE REACTION OF CYANOGEN WITH ORGANIC COMPOUNDS. VI. ETHYLENEDIAMINE AND ITS ALKYL DERIVATIVES<sup>1, 2, 3</sup>

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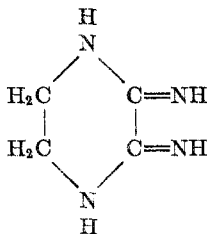
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Several years ago work in this laboratory established the fact that primary aliphatic amines react with cyanogen to yield symmetrically disubstituted oxamidines (1) whereas secondary amines normally give only cyanoformamidines (2). In the light of these results it was interesting to speculate on the possible behavior of ethylenediamine and its alkyl derivatives, since these compounds contain vicinal amino or alkylamino groups, which could react separately or in conjunction.

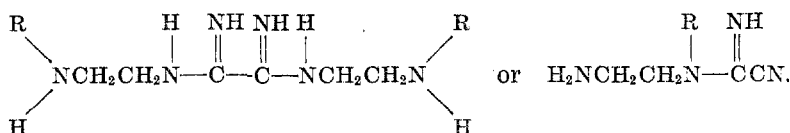
Thus a possible product of the interaction of cyanogen with ethylenediamine might be a long chain polymer with a recurring oxamidine structure,



or a cyclic compound such as



Presumably if both primary and secondary amino groups were present in the starting compound conditions might favor the rapid reaction of one group to the exclusion of the other forming either



N-Dialkylethylenediamines would undoubtedly react at the primary amino group to produce oxamidines since the tertiary amino group carries no reactive hydrogen.

<sup>1</sup> Presented at the Buffalo meeting of the American Chemical Society, March 1952.

<sup>2</sup> This work was supported in part by the Office of Naval Research under Contract N 8-onr-69200.

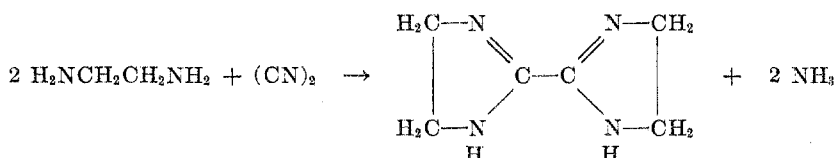
<sup>3</sup> From the thesis presented by Russell C. O'Gee in partial fulfillment of the requirements for the Ph.D. degree, June 1951.

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This paper describes our investigation of the interaction of cyanogen with various types of ethylenediamines as follows:

- (a) Ethylenediamine and C-alkylethylenediamines (2 primary amino groups).
- (b) N-alkylethylenediamines (1 primary, 1 secondary amino group).
- (c) N,N'-dialkylethylenediamines (2 secondary amino groups).
- (d) N-dialkylethylenediamines (1 primary, 1 tertiary amino group).

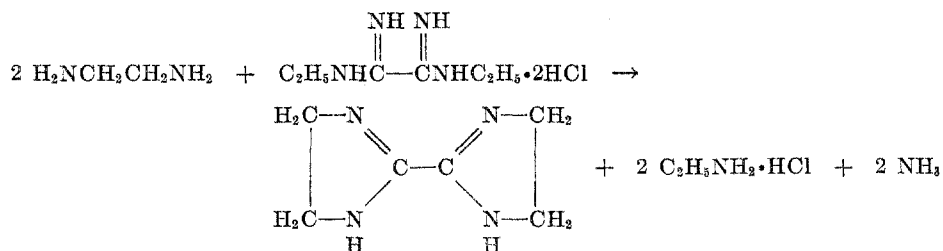
Contrary to our speculations, ethylenediamine produced neither the long chain polymer nor the diiminopiperazine predicted but instead a bicyclic compound, bis-( $\Delta^2$ -2-imidazoliny1).



The structure of this compound, first prepared by Forrsell in 1892 from dithio-oxamide and ethylenediamine (3), was finally elucidated 50 years later by Lehr and Erlenmeyer (4). It is white solid, crystallizing in needles and melting with decomposition between  $289^\circ$  and  $291^\circ$ , soluble in water and alcohol but insoluble in a wide variety of organic solvents. Its aqueous solution is alkaline and when refluxed with 10% aqueous sodium hydroxide it hydrolyzes to sodium oxalate and ethylenediamine.

Propylenediamine,  $\text{H}_2\text{NCH}(\text{CH}_3)\text{CH}_2\text{NH}_2$ , likewise reacted with cyanogen to give a bicyclic compound, bis-[ $\Delta^2$ -2-(4-methylimidazoliny1)], with properties similar to those described above.

In a separate investigation we have discovered that the two compounds can also be made by the interaction of *sym*-diethyloxamidine hydrochloride with ethylenediamine and propylenediamine (5).



While ethylene- and propylene-diamine were best cyanogenated in the pure state, N-alkylethylenediamines required aqueous solutions buffered to pH 7-8 with acetic acid. Under these conditions the primary amino group evidently was more reactive than the secondary since the products were symmetrically disubstituted oxamidines. The five compounds listed in Table I are colorless, viscous, fuming liquids, soluble in water, alcohol, and ether. They possess a strong odor of ammonia, react alkaline in aqueous solution, and rapidly absorb water and carbon dioxide from the atmosphere giving solid products. Mineral

acids do not form salts but the dipicrates are easily prepared and are stable on storage. Hydrolysis with 10% aqueous sodium hydroxide produces ammonia, sodium oxalate, and the N-alkylethylenediamine.

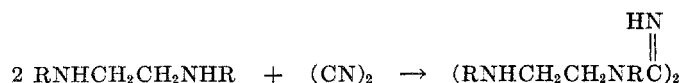
The infrared absorption curves of two of the compounds were compared with that of *sym*-diethyloxamidine (Figure 1). All three showed strong absorption in the region characteristic of C=N, 6.05–6.15 microns, and absence of absorption in the region characteristic of C≡N, 4.50–4.65 microns. The conclusion that the structure of the oxamidine was (RNHCH<sub>2</sub>CH<sub>2</sub>NHC=NH)<sub>2</sub> rather than (H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NRC=NH)<sub>2</sub> was drawn from the results of Rimini and Simon tests for primary and secondary amino groups (6) run on these compounds and selected controls. Attempts to form other disubstituted or tetrasubstituted oxamidines by exchange reactions (7) were unsuccessful.

Since N,N'-dialkylethylenediamines contain only secondary amino groups, it was logical on the basis of previous experience (2) to expect cyanoforamidine products. This, however, was not the case. Aqueous solutions of the compounds,

TABLE I

$\text{sym-BIS-(2-ALKYLAMINOETHYL)OXAMIDINES (RNHCH}_2\text{CH}_2\text{NHC=NH)}_2$			
R	B.P., °C.	MM.	DIPICRATE M.P., °C.
CH <sub>3</sub> .....	149	5	144-145 dec.
C <sub>2</sub> H <sub>5</sub> .....	166-167	5	81 dec.
<i>n</i> -C <sub>3</sub> H <sub>7</sub> .....	135-137	4	148 dec.
iso-C <sub>3</sub> H <sub>7</sub> .....	133-134	4	153-154 dec.
<i>n</i> -C <sub>4</sub> H <sub>9</sub> .....	135	4	150

buffered to pH 7-8, reacted with cyanogen to produce N,N'-dialkyl-N,N'-bis-(2-alkylaminoethyl)oxamidines (Table II) in 27-55% yield.



These again were colorless, fuming liquids with chemical properties similar to those of the oxamidines described above. Their infrared curves showed the absorption characteristic of oxamidines (Figure 2). Except for one isolated example (2) this is the first instance of oxamidine production from secondary amines.

N-Dimethyl- and N-diethyl-ethylenediamines gave no isolable product when treated with cyanogen in buffered aqueous solutions. Ether solutions, however, produced solids sufficiently stable to allow separation before tarring occurred. These could be recrystallized from ether and were then white and apparently stable.

Analysis and molecular weight determinations indicated that the solids were formed from a 1:1 molar combination of cyanogen and amine. This indicated

a cyanoformamidine structure and although such a result was considered unlikely for primary aliphatic amine reactions, it had previously been observed under certain conditions with aminopyridines (8).

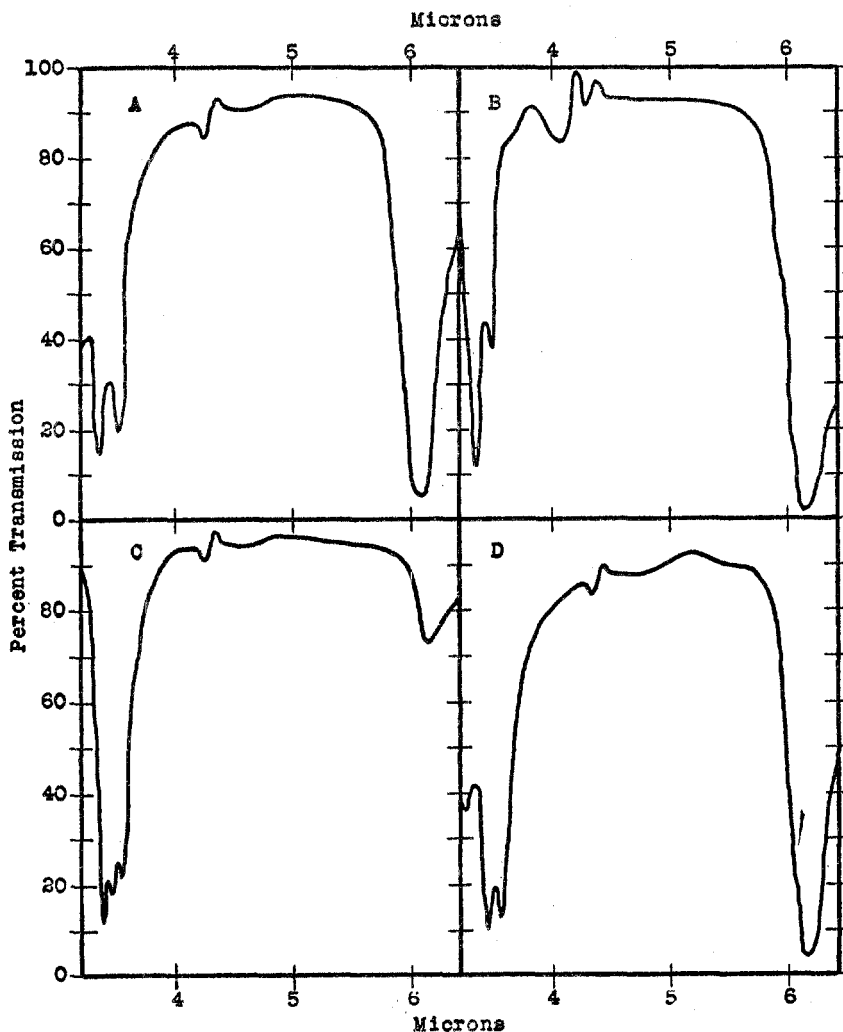


FIG. 1. INFRARED SPECTRA. A, *sym*-bis-(2-isopropylaminoethyl)oxamidine; B, *sym*-diethyloxamidine; C, *N*-*n*-propylethylenediamine; D, *sym*-bis-(2-*n*-propylaminoethyl)-oxamidine.

Accordingly infrared curves were obtained on the two products and compared with that of a known cyanoformamidine (Figure 3). It was immediately apparent that the new substances lacked the strong  $C\equiv N$  absorption in the region 4.55 microns which characterized the known material. We are, therefore, left with the problem of reconciling analytical data and chemical properties consistent

TABLE II

$$\begin{array}{c} \text{HN} \\ || \\ \text{N,N'-DIALKYL-N,N'-BIS-(2-ALKYLAMINOETHYL)OXAMIDINES (RNHCH}_2\text{CH}_2\text{NRC)}_2 \end{array}$$

R	B.P., °C.	MM.	DIPICRATE M.P., °C.
CH <sub>3</sub> .....	84-85	5	181
C <sub>2</sub> H <sub>5</sub> .....	125-126	4	138-139
<i>n</i> -C <sub>3</sub> H <sub>7</sub> .....	117	5	84-85
<i>iso</i> -C <sub>3</sub> H <sub>7</sub> .....	109-110	4	134
<i>n</i> -C <sub>4</sub> H <sub>9</sub> .....	134-135	4	>200 dec.

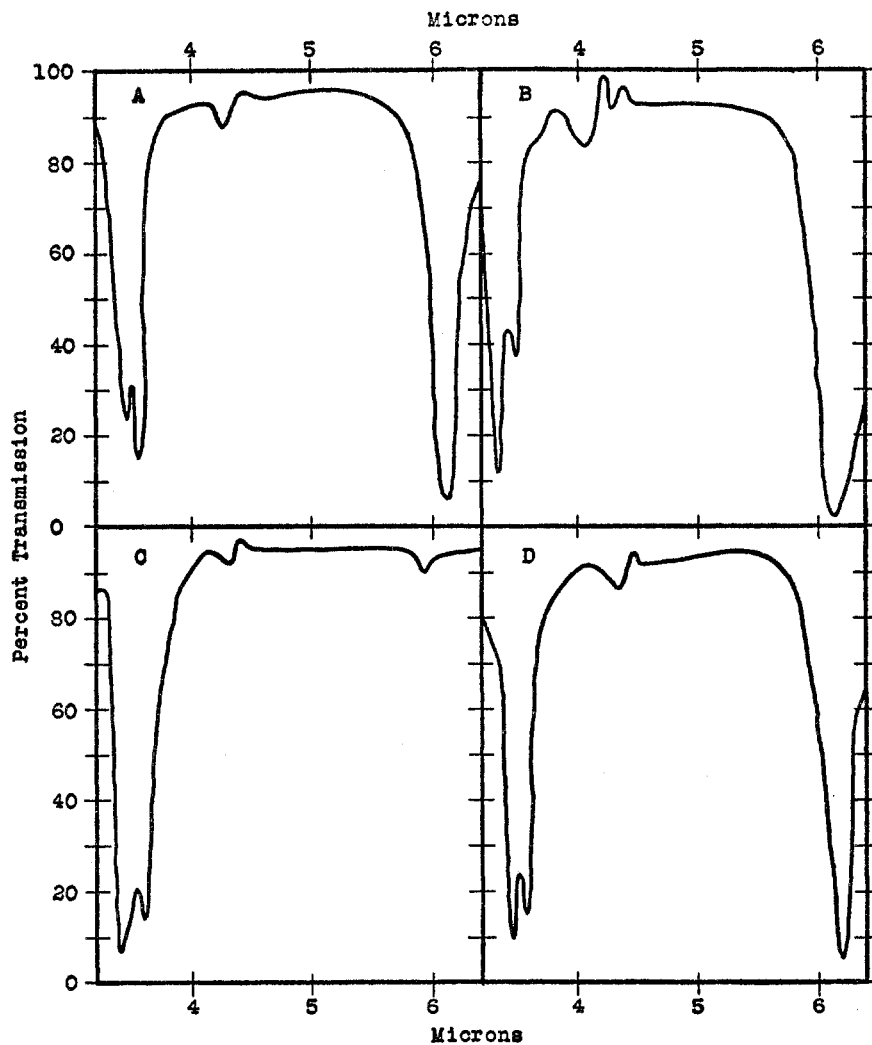


FIG. 2. INFRARED SPECTRA. A, *N,N'*-dimethyl-*N,N'*-bis-(2-methylaminoethyl)oxamidine; B, *sym*-diethyloxamidine; C, *sym*-di-*n*-propylethylenediamine; D, *N,N'*-di-*n*-butyl-*N,N'*-bis-(2-*n*-butylaminoethyl)oxamidine.

with a cyanoformamidine structure and absorption curves that seemingly are not. No solution to the problem has been reached.

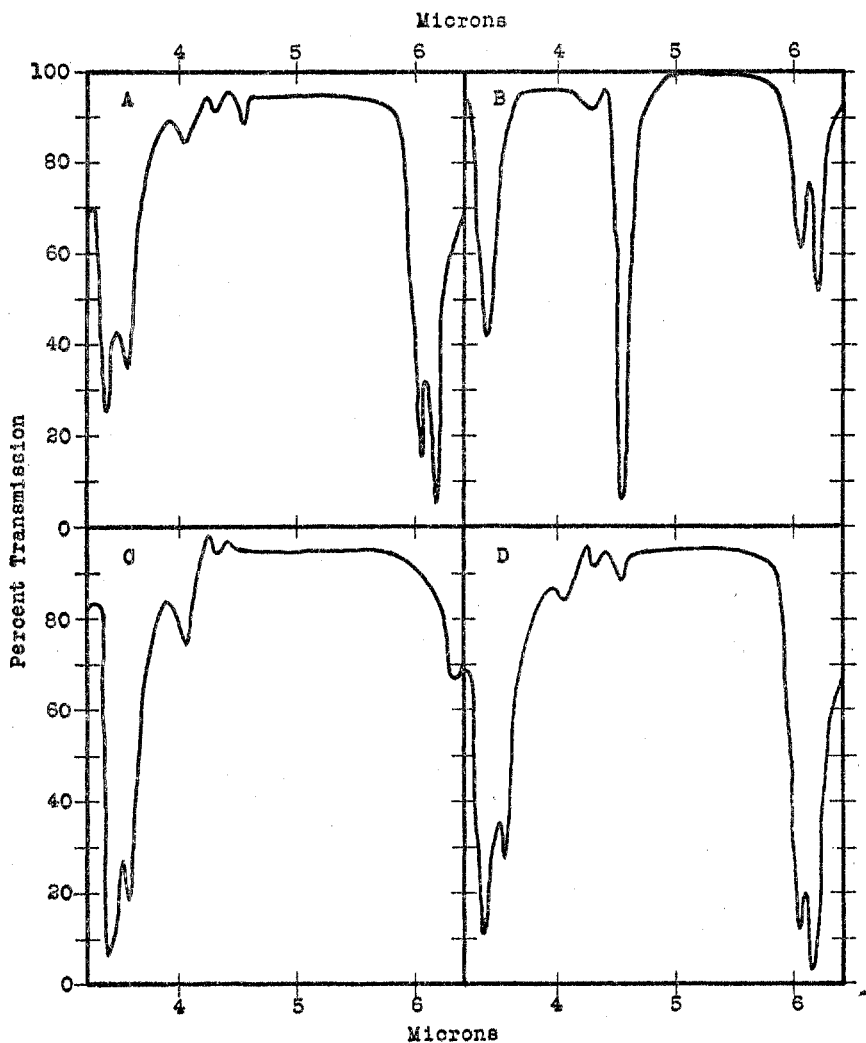


FIG. 3. INFRARED SPECTRA. A, Product from  $(\text{CN})_2$  + N-dimethylethylenediamine; B, N-dimethylecyanoformamidine; C, N-Diethylethylenediamine; D, Product from  $(\text{CN})_2$  + N-diethylethylenediamine.

#### EXPERIMENTAL

##### REAGENTS

*Ethylenediamine* and *propylenediamine* were Eastman Kodak Co. products used without further purification.

*N*-Alkylethylenediamines were prepared by the reaction of 2-bromoethylamine hydrobromide with alkylamines (9).

*N*-Dimethylethylenediamine was made by an adaptation of the same process. From a solution of 0.5 mole of 2-bromoethylamine hydrobromide in 100 ml. of water and a 25% aqueous solution containing 1 mole of dimethylamine was obtained a 54% yield of colorless liquid, b.p. 105–108°.

*N*-Diethylethylenediamine was obtained from Carbon and Carbide Chemicals Co.

*N,N'*-Dialkylethylenediamines. Modifications of a method reported by Boon (10) were used for the preparation of these compounds.

(a). To a 25% aqueous solution of methylamine containing 2.5 moles of the amine and an equal volume of alcohol was added slowly 96 g. (0.5 mole) of ethylene dibromide. The mixture was refluxed gently for three hours at which time it had become homogeneous. After cooling it was treated with solid sodium hydroxide as long as the base would dissolve. The upper of the two layers which formed as the mixture became alkaline was removed and combined later with ether extracts of the lower layer. After drying over potassium carbonate, fractionation through a 12" column packed with glass helices gave 25 g. (55% yield) of colorless liquid *N,N'*-dimethylethylenediamine boiling at 105–15°.

*N,N'*-Diethylethylenediamine was obtained by the same procedure in 32% yield as a colorless liquid which boiled at 55–60°/35 mm. or 153–154°/758 mm.

*N,N'*-Di-*n*-propylethylenediamine was obtained in 25% yield as a colorless liquid, b.p. 184–187°.

*N,N'*-Diisopropylethylenediamine was obtained in 71% yield as a colorless liquid, b.p. 165–168°.

(b). *N,N'*-Di-*n*-butylethylenediamine was prepared without the use of solvents since it forms an insoluble monohydrate. Ethylene dibromide (96 g., 0.5 mole) was added slowly, with stirring, to 183 g. (2.5 moles) of *n*-butylamine. After standing 24 hours the mixture was heated cautiously on a steam-bath for 10 hours. No difficulties were encountered although it is reported (11) that refluxing this mixture causes a highly exothermal, often explosive reaction.

The cooled solution was worked up as in (a) giving 57 g. (33% yield) of a colorless liquid which boiled at 110–111°/8 mm.

The preparation and purification of cyanogen is described in Paper IV of this series (8).

#### REACTIONS OF CYANOGEN WITH ETHYLENEDIAMINES

*Bis*-( $\Delta^2$ -2-imidazoliny). The following reaction conditions were the result of a large number of cyanogenations in which the relative proportions of reactants and the nature and quantity of solvent were changed.

The cyanogen resulting from 100 g. of sodium cyanide and 300 g. of copper sulfate was bubbled through 60 g. (1.0 mole) of pure ethylenediamine contained in a 125-ml. gas-absorption bottle and cooled to 0°. The rate of cyanogen evolution was controlled so that the complete reaction required 10–15 minutes.

The reaction mixture gradually became orange and finally red. Shortly thereafter a precipitate began to appear and increased as cyanogenation continued.

After standing overnight in the ice chest the precipitate was filtered, washed several times by stirring in cold alcohol to remove tar, and recrystallized from alcohol. Pure white needles melting with decomposition from 289–291° (sealed tube) were obtained. They gave no melting point depression when mixed with material prepared from dithiooxamide and ethylenediamine (3).

From the original filtrate there was recovered 58 g. of ethylenediamine by distillation. The yield of crude product was 2 g.

*Anal.* Calc'd for  $C_4H_{10}N_4$ : C, 52.2; H, 7.3; N, 40.5; M. W., 138.

Found: C, 52.5; H, 7.8; N, 40.4; M. W. (ebullioscopic), 135.

The *picric acid* salt was prepared by adding an excess of a hot, saturated alcoholic solution of picric acid to a hot alcoholic solution of bis-( $\Delta^2$ -2-imidazoliny). Recrystallization from alcohol gave a yellow powder melting with decomposition at 272–273°.

Hydrolysis of the free base was accomplished by refluxing in 10% aqueous sodium hydroxide for four hours. No ammonia was evolved. The white solid which precipitated was identified as sodium oxalate. Treatment of the ether extract with hydrogen chloride gave ethylenediamine dihydrochloride, identified by mixed melting point technique using a known sample as reference.

*Bis*-[ $\Delta^2$ -2-(4-methylimidazolyl)]. Cyanogenation of pure propylenediamine under conditions similar to the above gave no precipitate until the mixture had remained in the ice chest for two days. This precipitate was filtered and partially purified by stirring with ether and decanting the solid from tar which adhered to the bottom of the container. Recrystallization from alcohol gave white crystals which melted at 246–250° dec. and showed no melting point depression with material prepared from the reaction of *sym*-diethyloxamine hydrochloride and propylenediamine (5). Because of the difficult purification process the yield was not determined.

*Anal.* Calc'd for  $C_8H_{14}N_4$ : C, 57.8; H, 8.4; N, 33.8.

Found: C, 57.8; H, 8.7; N, 33.5.

#### REACTIONS OF CYANOGEN WITH N-ALKYLETHYLENEDIAMINES

*sym-Bis*-(2-methylaminoethyl)oxamidine. A solution (pH 7–8) of 10.9 g. (0.15 mole) of N-methylethylenediamine in 450 ml. of water and 9.0 ml. of glacial acetic acid was placed in a gas-absorption bottle and treated at room temperature with cyanogen until the mixture changed from colorless to orange. Solid potassium hydroxide was added as long as the base would dissolve, then the two layers were separated and the lower one extracted with ether. The combination of the extracts and the upper layer was dried over potassium carbonate and fractionated through a 12" column packed with glass helices. A fraction weighing 2.4 g. of the original amine was recovered and a yield of 3.6 g. (32% based on the amine consumed) of *sym-bis*-(2-methylaminoethyl)oxamidine boiling at 149°/5 mm. was obtained.

The *picric acid salt*, prepared for analysis from hot concentrated aqueous solutions of picric acid and the oxamidine, was recovered from water as yellow crystals, m.p. 144–145° with decomposition.

*Anal.* Calc'd for  $C_8H_{20}N_6 \cdot 2C_6H_3N_3O_7$ : C, 36.5; H, 4.0; N, 25.6; O, 33.9.

Found: C, 36.9; H, 3.7; N, 25.8; O (by difference), 33.6.

Hydrolysis of the free base brought about by refluxing for six hours with 10% aqueous sodium hydroxide produced ammonia, sodium oxalate, and N-methylethylenediamine (recovered as the dihydrochloride).

The following oxamidines were made in a manner similar to the above, all solutions of the diamines being adjusted to pH 7–8 with acetic acid before cyanogenation. Yields reported are based on the diamine consumed in the reaction.

*sym-Bis*-(2-ethylaminoethyl)oxamidine, from N-ethylethylenediamine in 40% yield; liquid, b.p. 166–167°/5 mm.

The *picric acid salt* melted at 81° with decomposition.

*Anal.* Calc'd for  $C_{10}H_{24}N_6 \cdot 2C_6H_3N_3O_7$ : C, 38.5; H, 4.4; N, 24.5; O, 32.6.

Found: C, 38.3; H, 4.5; N, 24.5; O, (by difference), 32.7.

*sym-Bis*-(2-n-propylaminoethyl)oxamidine. From N-n-propylethylenediamine in 63% yield; liquid, b.p. 135–137°/4 mm.

The *picric acid salt* melted at 148° with decomposition.

*Anal.* Calc'd for  $C_{12}H_{28}N_6 \cdot 2C_6H_3N_3O_7$ : C, 40.3; H, 4.8; N, 23.6; O, 31.3.

Found: C, 40.6; H, 4.7; N, 23.9; O (by difference), 30.8.

*sym-Bis*-(2-isopropylaminoethyl)oxamidine. From N-isopropylethylenediamine in 41% yield; liquid, b.p. 133–134°/4 mm.

The *picric acid salt* melted at 153–154°.

*Anal.* Calc'd for  $C_{12}H_{28}N_6 \cdot 2C_6H_3N_3O_7$ : C, 40.3; H, 4.8; N, 23.6; O, 31.3.

Found: C, 40.7; H, 4.8; N, 23.5; O (by difference), 31.0.

*sym-Bis*-(2-n-butylaminoethyl)oxamidine. From N-n-butylethylenediamine in 67% yield; liquid, b.p. 135°/4 mm.

The *picric acid salt* melted at 150°.



*Anal.* Calc'd for  $C_{14}H_{22}N_6 \cdot 2C_6H_5N_3O_7$ : C, 42.0; H, 5.1; N, 22.6; O, 30.3.  
Found: C, 41.8; H, 5.1; N, 22.7; O (by difference), 30.4.

## REACTIONS OF CYANOGEN WITH N,N'-DIALKYLETHYLENEDIAMINES

The conditions for these reactions were identical with those described above for N-alkylethylenediamines. Yields are based on diamine used up in the reaction.

*N,N'*-Dimethyl-*N,N'*-bis-(2-methylaminoethyl)oxamidine. From *N,N'*-dimethylethylenediamine in 55% yield; liquid, b.p. 84–85°/5 mm.

The picric acid salt melted at 181°.

*Anal.* Calc'd for  $C_{16}H_{24}N_8 \cdot 2C_6H_5N_3O_7$ : C, 38.5; H, 4.4; N, 24.5; O, 32.6.

Found: C, 38.5; H, 4.4; N, 24.6; O (by difference), 32.5.

*N,N'*-Diethyl-*N,N'*-bis-(2-ethylaminoethyl)oxamidine. From *N,N'*-diethylethylenediamine in 48% yield; liquid, b.p. 125–126°/4 mm.

The picric acid salt melted at 138–139°.

*Anal.* Calc'd for  $C_{14}H_{22}N_6 \cdot 2C_6H_5N_3O_7$ : C, 42.0; H, 5.1; N, 22.6; O, 30.3.

Found: C, 42.2; H, 5.1; N, 22.4; O (by difference), 30.3.

*N,N'*-Di-*n*-propyl-*N,N'*-bis-(2-*n*-propylaminoethyl)oxamidine. From *N,N'*-di-*n*-propylethylenediamine in 52% yield; liquid, b.p. 117°/5 mm.

The picric acid salt melted at 84–85°.

*Anal.* Calc'd for  $C_{18}H_{26}N_8 \cdot 2C_6H_5N_3O_7$ : C, 45.1; H, 5.8; N, 21.1; O, 28.0.

Found: C, 45.3; H, 5.6; N, 20.9; O (by difference), 28.2.

*N,N'*-Diisopropyl-*N,N'*-bis-(2-isopropylaminoethyl)oxamidine. From *N,N'*-diisopropylethylenediamine in 27% yield; liquid, b.p. 109–110°/4 mm.

The picric acid salt melted at 134°.

*Anal.* Calc'd for  $C_{18}H_{26}N_8 \cdot 2C_6H_5N_3O_7$ : C, 45.1; H, 5.8; N, 21.1; O, 28.0.

Found: C, 45.2; H, 5.6; N, 20.9; O (by difference), 28.3.

*N,N'*-Di-*n*-butyl-*N,N'*-bis-(2-*n*-butylaminoethyl)oxamidine. From *N,N'*-di-*n*-butylethylenediamine in 33% yield; liquid, b.p. 134–135°/4 mm.

The picric acid salt decomposed above 200°.

*Anal.* Calc'd for  $C_{22}H_{30}N_8 \cdot 2C_6H_5N_3O_7$ : C, 47.8; H, 6.3; N, 19.7; O, 26.2.

Found: C, 47.8; H, 6.1; N, 19.4; O (by difference), 26.7.

## REACTION OF CYANOGEN WITH N-DIALKYLETHYLENEDIAMINES

Treatment of buffered aqueous solutions of these compounds with cyanogen produced only tars from which no product could be isolated. Cyanogenation therefore was carried out in ether solution. The procedure is described in detail for *N*-dimethylethylenediamine.

A solution of 4.5 g. (0.051 mole) of *N*-dimethylethylenediamine in 200 ml. of ether was cyanogenated at 0° until the solution began to turn orange. A white solid began to form after cyanogen had passed through for about ten minutes. This was filtered immediately after the cyanogen was shut off and washed well with ether which had been previously cooled in a Dry Ice-chest. Recrystallization from ether gave 1.6 g. (22% yield) of a white powder melting at 116° (dec.) and giving the analysis consistent with *N*-(2-dimethylaminoethyl)cyanofornamidine.

*Anal.* Calc'd for  $C_8H_{12}N_4$ : C, 51.4; H, 8.6; N, 40.0; M. W., 140.

Found: C, 51.7; H, 8.2; N, 39.7; M. W. (cryoscopic), 134.

Hydrolysis by four hours' refluxing with 10% aqueous sodium hydroxide produced ammonia, sodium oxalate, and *N*-dimethylethylenediamine (identified as the picrate.)

*N*-Diethylethylenediamine with cyanogen produced a 45% yield of white solid melting at 105° dec. and believed to be *N*-(2-diethylaminoethyl)cyanofornamidine.

*Anal.* Calc'd for  $C_8H_{14}N_4$ : C, 57.1; H, 9.5; N, 33.3; M. W., 168.

Found: C, 57.0; H, 9.6; N, 33.0; M. W. (cryoscopic), 166.

Hydrolysis gave ammonia, sodium oxalate, and *N*-diethylethylenediamine.

Infrared curves were obtained with a Baird Associates split-beam recording spectrophotometer. The compounds (as 10% solutions in chloroform or carbon tetrachloride)

were run against the solvent. A sodium chloride prism and 0.1-mm. absorption cells with sodium chloride windows were used.<sup>5</sup>

*Molecular weights* were determined cryoscopically with acetic acid and ebullioscopically with ethyl alcohol in a modified Cotrell boiling point apparatus.

#### SUMMARY

The effect of *vicinal* amino or alkylamino groups on the reaction of aliphatic amines with cyanogen has been studied by the investigation of a series of ethylenediamines. The products of the reaction do not conform in most cases with those predicted from previous work with aliphatic amines.

1. Compounds which have two primary amino groups on adjacent carbon atoms form bis-( $\Delta^2$ -2-imidazoliny)ls.

2. Compounds which contain one primary and one secondary amino group on vicinal carbon atoms give products in which only the primary amino group has reacted to form oxamidine derivatives.

3. When there are two secondary amino groups on adjacent carbon atoms only one group reacts forming a substituted oxamidine.

4. Compounds which contain one primary and one tertiary amino group on adjacent carbon atoms react to form products which appear to be cyanoformamidines but do not give completely characteristic infrared absorption curves.

BUFFALO 14, NEW YORK

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<sup>5</sup> The assistance of the National Aniline Division of Allied Chemical and Dye Corporation in obtaining the infrared curves is gratefully acknowledged.