tion of concentrated aqueous potassium carbonate. The mixture was then extracted with chloroform. After removal of solvent, the residual oil was distilled in vacuum, b.p. 107–110° (0.5 mm.). The yield of colorless oil was 21.2 g. (62.5%). Infrared analyses indicated the presence of a mixture of isomers.

Anal. Calcd. for $C_7H_9NO_2$: C, 60.41; H, 6.52; N, 10.07. Found: C, 59.90; H, 6.30; N, 10.02.

The product was dissolved in ether and cooled to a low temperature; white crystals, m.p. 62°, separated which proved to be 2-methoxy-6-methylpyridine 1-oxide (VIIa) identical with a product prepared from 2-bromo-6-methylpyridine 1-oxide as described later. The remainder of the reaction mixture was 1-methoxy-6-methyl-2-pyridone (VIIIa), identical with the product obtained by methylation of 1-hydroxy-6-methyl-2-pyridone which is described later. Pure, fresh peracetic acid gave by a similar procedure just 2-methoxy-6-methylpyridine 1-oxide.

2-Methoxy-6-methylpyridine 1-Oxide (VIIa).—A solution of 28.6 g. of 2-bromo-6-methylpyridine 1-oxide in 50 ml. of absolute methanol was added slowly to a mechanically stirred solution of 10 g. of sodium in 100 ml. of methanol. A vigorous reaction took place. After the addition was completed, the mixture was stirred and heated under reflux for two hours. The precipitated sodium bromide was removed by filtration and was washed with methanol. The filtrate was then acidified with dilute hydrochloric acid and the methanol distilled off in vacuum. The remaining aqueous solution was made alkaline by adding potassium carbonate and was extracted with chloroform. The chloroform extract was dried, the chloroform evaporated and the residue was distilled in vacuum, b.p. 109–110° (0.5 mm.). The colorless distillate solidified and was recrystallized from methanol–ether, m.p. 62°. The yield was 14.0 g. (66.2%).

Anal. Calcd. for $C_7H_9NO_2$: C, 60.41; H, 6.52. Found: C, 60.32; H, 6.64.

1-Hydroxy-6-methyl-2-pyridone (X).—To 160 ml. of 5% aqueous sodium hydroxide was added 18.8 g. of 2-bromo-6-methylpyridine 1-oxide and the mixture was heated on the steam-bath for 30 minutes. After cooling to room temperature, the clear solution was acidified with concd. hydrochloric acid and was extracted with chloroform. After evaporation of the solvent the solid residue was recrystallized from ethyl acetate and was then sublimed in vacuum at 80° (0.5 mm.); colorless crystals, m.p. 144–145° (lit.[2] 141–142°). The yield was 9.6 g. (76.7%).

Anal. Calcd. for $C_6H_7NO_2$: C, 57.59; H, 5.64; N, 11.20. Found: C, 57.69; H, 5.48; N, 11.11.

1-Methoxy-6-methyl-2-pyridone (VIIIa).—To a solution of 0.4 g. of sodium in 25 ml. of absolute methanol was added 1.8 g. of 1-hydroxy-6-methyl-2-pyridone, followed by 3 g. of methyl iodide. The mixture was then boiled under reflux for 2 hours. The solvent was distilled off in vacuum and the residue was taken up in chloroform. After removal of the chloroform 1.8 g. (89.9%) of a yellowish oil remained. The oil was dissolved in a small amount of ether and the solution was cooled to −70°. The substance crystallized and was recrystallized from ether; large colorless crystals, m.p. 33–34°.

Anal. Calcd. for $C_7H_9NO_2$: C, 60.41; H, 6.52; N, 10.07. Found: C, 60.07; H, 6.78; N, 9.92.

Reaction of the Mixture of 2-Methoxy-6-methylpyridine 1-Oxide and 1-Methoxy-6-methyl-2-pyridone with Diethyl Oxalate: Ethyl 2-methoxy-6-pyridylpyruvate 1-Oxide (VIIb) and Ethyl 1-Methoxy-2-pyridone-6-pyruvate (VIIIb).—A potassium ethoxide solution was prepared by adding 20 ml. of ethanol to 4.0 g. of potassium covered with 25 ml. of ether. To this solution was added 7.5 g. of diethyl oxalate dissolved in 50 ml. of ether, followed by a solution of 7.0 g. of the mixture of 2-methoxy-6-methylpyridine 1-oxide and 1-methoxy-6-methyl-2-pyridone in 30 ml. of ethanol. The reaction mixture turned yellow, and the potassium salt of the pyruvate precipitated. After standing overnight, the yellow precipitate was collected by filtration and was added to a mixture of 100 g. of ice and 6 ml. of concd. sulfuric acid. After standing for one hour, 2.4 g. of fine crystals had separated. The compound was recrystallized from benzene–petroleum ether (b.p. 30–60°); yellow needles, m.p. 153°. This compound was ethyl 1-methoxy-2-pyridone-6-pyruvate (VIIIb) as shown by comparison with an authentic sample obtained by condensation of pure 1-methoxy-6-methyl-2-pyridone with diethyl oxalate.

Anal. Calcd. for $C_{11}H_{13}NO_5$: C, 55.22; H, 5.48. Found: C, 55.44; H, 5.53.

The acidic solution remaining after filtration of the compound VIIIb was extracted with chloroform, the chloroform extract was dried and the chloroform evaporated. The residue was recrystallized from benzene–petroleum ether (b.p. 30–60°); yellow plates, m.p. 132°. The yield was 5.0 g. The compound was 2-methoxy-6-pyridylpyruvate 1-oxide (VIIb) as shown by comparison with an authentic sample prepared from pure 2-methoxy-6-methylpyridine 1-oxide.

Anal. Calcd. for $C_{11}H_{13}NO_5$: C, 55.22; H, 5.48. Found: C, 55.34; H, 5.48.

URBANA, ILL.

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

The Preparation and Reactions of 1-Cyanoformamide

BY RICHARD P. WELCHER, MARY E. CASTELLION AND V. P. WYSTRACH

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Conditions have been found for the rapid hydration of cyanogen to 1-cyanoformamide by excess water in high yield. Several carboxylic acids and phosphorus acids can perform the dual role of catalyzing the reaction and stabilizing the product, but other mineral acids are unable to do both. Chemically, 1-cyanoformamide was found to be very reactive with water, alcohols, hydrogen sulfide and amines, with reaction occurring at the nitrile C–N bond or the C–C bond depending on the conditions. Physical and toxicological properties of 1-cyanoformamide are also presented.

Chemical studies of cyanogen, both in these laboratories and elsewhere, have shown it to be one of the most active nitriles. For example, at room temperature it is quickly hydrated to oxamide in high yield by concentrated hydrochloric acid,[1] sulfhydrated to dithioöxamide quantitatively with a trace of aqueous base as a catalyst,[2] and transformed to N,N′-disubstituted oxamidines by the addition of amines.[3] Most nitriles require more vigorous conditions for these reactions. In view of the rapid transformation of both nitrile groups of cyanogen, it is not surprising that products formed by the reaction of only one cyano group with these reagents—derivatives of 1-cyanoformic acid and 1-cyanoformimidic acid—have not been obtained easily.[4–6]

(1) J. E. Bucher (to Nitrogen Products Co.) U. S. Patent 1,194,354 (1916).

(2) D. W. Kaiser and R. P. Welcher (to American Cyanamid Co.) U. S. Patent 2,806,879 (1957).

(3) H. M. Woodburn, B. A. Morehead and W. H. Bonner, *J. Org. Chem.*, **14**, 555 (1949); also papers II-X, *ibid.*, 1950 to date.

(4) R. Anschütz, *Ann.*, **254**, 262 (1889).

(5) J. Nef, *ibid.*, **287**, 265 (1895).

(6) N. Beketoff, *Chem. Ber.*, **3**, 872 (1870).

Preparation.—During an investigation of the reactions of cyanogen we found that 1-cyanoformamide could be prepared in high yield from cyanogen and water in the presence of formic acid and other moderately strong acids.[7] 1-Cyanoformamide was first prepared by Beketoff, who obtained up to a 35% yield by prolonged treatment of cyanogen with glacial acetic acid containing a small amount of water.[6] However, his attempts to improve the yield by increasing the molar ratio of water to cyanogen led to the formation of oxamide. In this paper we present some qualitative aspects of the surprisingly effective catalyst system by which 1-cyanoformamide can be prepared, as well as report on the physical, chemical and toxicological properties of this substance.

1-Cyanoformamide was best obtained by the reaction of cyanogen and excess water in the presence of formic acid. The reactants, catalyst and solvent were heated in a closed vessel for 3-15 hr. at 55–75°. Yields of 1-cyanoformamide ranged up to 99%, and oxamide was never formed in greater than 1% yield. The molar ratio of water to cyanogen was changed from 4:1 to 16:1 without significant effect, but the yield decreased when the ratio was less than 4:1. Other useful acids were acetic and chloroacetic acids, phosphoric acid and benzenephosphonic acid.

The most remarkable aspect of the preparation of 1-cyanoformamide was the stabilizing effect of formic acid upon the product. Beketoff found that 1-cyanoformamide was quantitatively hydrolyzed by warm water alone to cyanide ion, carbon dioxide and ammonia.[6] In addition, results to be described below showed that the remaining nitrile group of 1-cyanoformamide is highly reactive under other conditions. Nevertheless, we found that with formic acid present 1-cyanoformamide, whether formed *in situ* from cyanogen or prepared and isolated in a preliminary reaction, was quite stable to warm water alone or water plus a small amount of sulfuric acid or *p*-toluenesulfonic acid. In the absence of formic acid the 1-cyanoformamide was quickly destroyed by the same concentration of mineral acid. Acetic acid, chloroacetic acid, phosphoric acid and benzenephosphonic acid also had a stabilizing effect, shown by the fact that 1-cyanoformamide, forming in their presence, was not attacked by the excess water present. This effect was particularly surprising with phosphoric acid and benzenephosphonic acid because much less than molar quantities of these acids were needed per mole of 1-cyanoformamide.

Apart from their stabilizing effect, these acids had a catalytic action without which no 1-cyanoformamide would have formed. This was clearly shown by the experiments using sulfuric acid, in which no 1-cyanoformamide or oxamide was found, and in which considerable quantities of cyanogen were recovered despite the presumably much higher concentration of hydrogen ion. With hydrochloric acid, on the other hand, also at a higher hydrogen ion concentration, cyanogen was hydrated to oxamide in very good yield, and no 1-cyanoformamide was found.

(7) R. P. Welcher (to American Cyanamid Co.) U. S. Patents 2,804,470; 2,804,471 (1957).

The molar ratio of catalyst to cyanogen was also of some importance. With formic acid the yield became very low when the molar ratio of catalyst to cyanogen was less than 1:1. When 75 mole % of the formic acid was replaced by its sodium salt reaction was very slow. Phosphoric and benzenephosphonic acids, on the other hand, gave fair yields of 1-cyanoformamide at a molar ratio of only 1:10.

In line with the results of the stability experiments, the presence of small amounts of sulfuric or *p*-toluenesulfonic acids during the preparation of 1-cyanoformamide using formic acid had a deleterious effect, but neither phosphoric acid, benzenephosphonic acid or a cation exchange resin was harmful.

The stabilizing activity of formic and acetic acids disappeared at temperatures much above 85°: at 89°, with excess water present, ammonium formate and formamide were found, perhaps formed by way of thermal decomposition of 1-cyanoformamide. At 100°, with excess acetic acid present but with a deficiency of water, an 84% yield of oxamide together with acetic anhydride was obtained. This latter reaction is analogous to that recently described for aliphatic nitriles.[8]

$$H_2NCCN + 2RCO_2H \rightleftharpoons H_2NC(=O)-C(=O)NH_2 + (RCO)_2O$$

The evidence at hand does not warrant writing a particular mechanism for the catalyzed formation or stabilization of 1-cyanoformamide. Although one or more intermediates can be envisioned, none was isolated in two experiments having that object. When the reaction was carried out under the preferred conditions but with water absent, substantially all the cyanogen was recovered, and nothing else found. In a second experiment, a similar result was obtained when water was added to the reaction vessel after the heating period.

The literature, moreover, sheds little light on the subject. It seems unlikely that a reaction between a nitrile and a carboxylic acid[8] would give an isomide-type intermediate stable in water and aqueous mineral acid, although perhaps such a hypothesis is no more unlikely than the observed fact of survival of 1-cyanoformamide. On the contrary, the presence of carboxylic acids has been reported to accelerate the hydration of hydrogen cyanide by 1–7 N sulfuric acid,[9] and to bring about the alkylation of nitriles in 85–96% sulfuric acid,[10] probably by increasing the activity of the mineral acid.

Properties.—Pure 1-cyanoformamide is a white odorless crystalline solid melting at 58–60°. When stored at room temperature in the absence of a stabilizer it developed a brown color within a month, and the odor of hydrogen cyanide became apparent. Light was not a factor. The evolution of hydrogen cyanide from pure 1-cyanoformamide in a humid atmosphere was observed after only

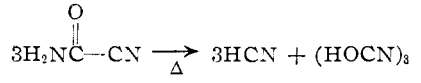
(8) D. Davidson and H. Skovronek, THIS JOURNAL, **80**, 376 (1958).

(9) V. K. Krieble, F. C. Duennebier and E. Colton, *ibid.*, **65**, 1479 (1943).

(10) E. E. Magat, B. F. Faris, J. E. Reith and L. F. Salisbury, *ibid.* **73**, 1028 (1951).

two days. Traces of water or caustic accelerated the appearance of color, which was presumed to be due to hydrolytic cleavage of 1-cyanoformamide by traces of moisture followed by polymerization of hydrogen cyanide.[11] Formic acid markedly retarded the appearance of color in 1-cyanoformamide, probably by preventing the base-catalyzed hydrolysis. Surprisingly, a trace of hydrochloric acid apparently had the same effect as sodium hydroxide.

Although 1-cyanoformamide is sensitive to heat, it could be distilled at reduced pressure if the still-pot residence time was short. Prolonged exposure to elevated temperature resulted in decomposition to hydrogen cyanide and cyanuric acid,[6] and also cyamelide.

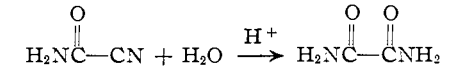


After an induction period, presumably caused by poor heat transfer within the sample, the rate of decomposition appeared to depend closely on the amount of undecomposed 1-cyanoformamide. At 97° approximately half the 1-cyanoformamide decomposed in 6.5 hr.

The chemical reactivity of 1-cyanoformamide was not surprising. Most of the reactions of the nitrile group, like those of the amide group, are of the carbonyl-addition type.[12] With basic catalysts the first step is probably nucleophilic attack at the positive carbon of the nitrile bond.[13] With acid catalysts the picture is less clear. In the hydrolysis of a variety of nitriles, the reaction with oxonium ion predominates at low acidities, but at high acidities the rate of reaction greatly depends on the anion of the acid.[14] For 1-cyanoformamide the strongly electronegative carbamoyl group would be expected to increase markedly the positive character of the nitrile carbon. This should lead to an accelerated reaction rate for both base-catalyzed reactions and those run under strongly acid conditions. For the same reason, the nitrile group should increase the positive character of the amide carbon atom.[15] The results to be described below showed 1-cyanoformamide indeed to be a very reactive compound. Under mild conditions reaction occurred at the C–N bond, leading to derivatives of oxamic acid. In these cases 1-cyanoformamide was as reactive as cyanogen. With more vigorous conditions the C–C bond was cleaved to give derivatives of hydrogen cyanide and cyanic acid.

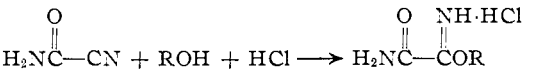
Reaction at the C–N Bond.—The high order of reactivity of the cyano group of 1-cyanoformamide was demonstrated by its vigorous reactions with water and primary alcohols in strong acid solution and with hydrogen sulfide in basic solution.

1-Cyanoformamide was quickly hydrated to oxamide at 30° with 12 *N* hydrochloric acid. After one hour the yield was 95%.

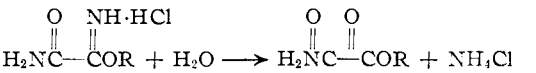


1-Cyanoformamide was hydrated by alkaline hydrogen peroxide also. Under the conditions described for cyanogen and other nitriles,[16] it reacted with basified 3% hydrogen peroxide to give oxamide in 61% yield.

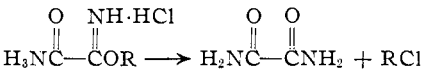
Although nitriles in general react with alcohols and anhydrous hydrogen chloride to give imidic ester hydrochlorides,[17] Pinner reported no success using acyl cyanides, possibly because the desired products were unstable. We found, however, that 1-cyanoformamide reacted readily to give oxamidic ester hydrochlorides in high yields.



The ethyl, cyclohexyl and dodecyl derivatives were prepared using the corresponding alcohols, but with phenol the ester was not obtained. With the primary alcohols vigorous reactions occurred, reminiscent of the reaction of hydrogen cyanide and cyanogen,[17a] but with the secondary alcohol the exothermic reaction was more moderate, and crystallization occurred more slowly. The products were hydrolyzed in good yield to the corresponding oxamic esters[17a]



All three oxamimidic ester salts decomposed on standing to oxamide and the alkyl halide[17]



The ethyl imidate salt was quite unstable, but the cyclohexyl and dodecyl homologs could be stored for some time. There are very little quantitative data in the literature on the decomposition of imidic ester salts at room temperature,[17b] but several investigations at elevated temperatures have been reported.[18] All three salts were more stable than methyl formimidate, data for which were available.[19]

1-Cyanoformamide reacted rapidly with hydrogen sulfide in dilute aqueous base at room temperature. Crystalline yellow monothioöxamide was formed in 70% yield. Its color was lighter than the bright orange of dithioöxamide which has two conjugated thiono groups. In its ease of sulfhydration under mild conditions 1-cyanoformamide was comparable to cyanogen, which was

(11) V. Migrdichian, "The Chemistry of Organic Cyanogen Compounds," Reinhold Publishing Corp., New York, N. Y., 1947, p. 349.

(12) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chap. XI.

(13) K. B. Wiberg, THIS JOURNAL, **75**, 3961 (1953).

(14) (a) V. K. Krieble and J. G. McNally, *ibid.*, **51**, 3368 (1929); (b) V. K. Krieble and A. Peiker, *ibid.*, **55**, 2326 (1933); (c) V. K. Krieble and C. I. Noll, *ibid.*, **61**, 560 (1939).

(15) For a review of the chemistry of acylcyanides see J. Thesing and D. Witzel, *Angew Chem* **68** 425 (1956).

(16) (a) Br. Radziszewski, *Chem. Ber.*, **18**, 355 (1885); (b) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 44.

(17) (a) A. Pinner, "Die Imidoather und Ihre Derivate," Robert Oppenheim, Berlin, 1892, pp. 1–7; (b) C. A. MacKenzie, G. A. Schmidt and L. R. Webb, THIS JOURNAL, **73**, 4990 (1951).

(18) (a) R. H. Hartigan and J. B. Cloke, *ibid.*, **67**, 709 (1945); (b) C. A. MacKenzie and L. R. Webb, *J. Org. Chem.*, **18**, 594 (1953).

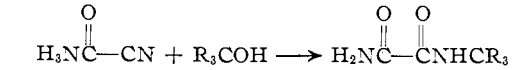
(19) J. G. Erickson, unpublished results.

recently found to be much more readily sulfhydrated than most other nitriles.[20-23]

Monothioöxamide reacted readily with methylamine, butylamine and dodecylamine to form the corresponding N-alkyl monothioöxamides.

Reactions of this general type have been previously described.[20b,24] The analogous N-phenyl analog has been prepared by another route.[25]

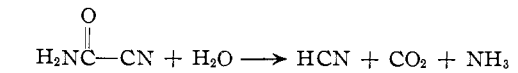
1-Cyanoformamide was readily alkylated under the conditions described by Ritter.[26] With *t*-



butyl alcohol the product was *t*-butyloxamide, with diisobutylene, the homologous *t*-octyloxamide. The structure of the latter was presumed to be 2,2,4,4-tetramethylbutyloxamide by analogy with Ritter's products.[26a]

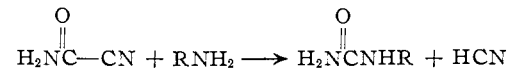
Reaction at the C–C Bond.—Cleavage of the C–C bond of 1-cyanoformamide was observed in two cases: very rapid reaction with dilute aqueous caustic, and reaction with primary amines.

Beketoff reported that 1-cyanoformamide reacted quantitatively with aqueous silver nitrate at 50° to form silver cyanide, carbon dioxide and ammonium ion.[6] We found that hydrolysis was quantitative in 3 min. with hot 0.5 *N* caustic,



giving similar products. During prolonged hydrolysis there was no decrease in the cyanide titer, showing that the liberated cyanide ion was relatively resistant to further hydrolysis under these conditions. This facile hydrolysis of 1-cyanoformamide, followed by determination of cyanide ion, provided a convenient method of assay having a precision of ±1%. The attack at the amide carbon rather than the nitrile carbon is in accord with the finding of Rabinovitch that amides are hydrolyzed ten times as fast as the corresponding nitriles over a wide range of base concentrations.[27]

Erickson prepared N-substituted formamides by reaction of hydrogen cyanide and amines, followed by hydrolysis of the unstable N-substituted formamidines.[28] DeBenneville prepared these compounds in one step in aqueous solution.[21b] With 1-cyanoformamide, attempts to prepare N-alkyl oxamides by similar procedures gave N-alkylureas.



Experimental Section[29]

Materials.—Cyanogen was prepared according to a published procedure,[30] purified by low-temperature distillation, and stored in stainless steel cylinders.[31] Its infrared spectrum showed less than 1% of impurities, chiefly cyanogen chloride. The ethanol used was 2B alcohol (anhydrous ethanol containing 0.5% benzene). All other materials were reagent grade, and were used without further purification.

1-Cyanoformamide. A. Preparation.—A mixture of 150 ml., of acetonitrile, 216 g. (4.13 moles) of 88% formic acid, 217 g. of water (12.1 moles including that in the formic acid) and 103 g. (1.98 moles) of cyanogen was heated in a rocking Inconel autoclave at 55° for 7 hr. The final pressure at 24° was 320 p.s.i.g. The autoclave was vented and freed of volatile material at 25 mm. pressure, then emptied and rinsed with acetonitrile. The solution was filtered, then concentrated at 25 mm. pressure until the liquid temperature reached 66°. The liquid crystallized on cooling to off-white crystals, which were dried at reduced pressure to give 138 g. of 1-cyanoformamide (99% yield). A portion, recrystallized from ethyl ether, gave snow-white crystals, m.p. 58–60°.

Anal. Calcd. for $C_2H_2N_2O$: C, 34.29; H, 2.88; N, 40.00. Found: C, 34.39; H, 3.13; N, 40.18.

1-Cyanoformamide could be distilled at reduced pressure, b.p. 90–100° (12 mm.), provided the still-pot residence time was short. Purification of 1-cyanoformamide by recrystallization was preferred because its high vapor pressure and relatively high melting point led to troublesome plugging during distillation. It is soluble in cold water, acetonitrile, dioxane, methanol, isopropyl alcohol, ethanol, hot ether (1 g./1.5 ml.), chloroform, methylene chloride and ethylene dichloride (1 g./11 ml.), slightly soluble in hot benzene, and insoluble in hot hexane and carbon tetrachloride. Its infrared spectrum shows absorption peaks at 3340(s) cm.$^{-1}$, 3170(s), 2250(w), 1700(s), 1630(m), 1350(m), 1115(w), 785(m). The LD_{50} toxicity to white albino mice by single intraperitoneal dose is 32 mg./kg., and by oral dose is 90 mg./kg.

B. Effect of Variables Upon the Preparation.—Pyrex bottles designed to be closed with a crown cap for work at moderate pressures were used. The bottles were heated in a thermostated diethylene glycol-bath, which was controlled to ±0.5°.

In the preparative experiments a bottle was charged with solvent, carboxylic acid, catalyst, water and mineral acid, chilled in a Dry Ice–acetone-bath while evacuated at 1 mm. pressure for 5 min., brought to atmospheric pressure with nitrogen and weighed. After re-evacuation it was charged with gaseous cyanogen in the desired amount, refilled with nitrogen and reweighed. The bottle was immediately capped and reweighed. The bottles were put in the diethylene glycol bath at 25° to avoid thermal shock, and heated to the desired reaction temperature. Acetonitrile and tetrahydrofuran were used successfully as solvents. Acetamide was not formed under these conditions. When formic acid was used the final pressure was considerably higher than the initial pressure, and carbon monoxide was now present. Details of the individual experiments are summarized in Table I.

At the end of the heating period the bottle was cooled slowly to −80° and weighed to learn whether any of the contents had escaped. The bottle was vented, connected to a vacuum pump by way of a caustic scrubber and cold trap, freed of cyanogen at room temperature and reduced pressure, and emptied into a flask connected to the same scrubber. After neutralization of strong acid with sodium formate, the mixture was concentrated at reduced pressure

(20) (a) K. Kindler, *Ann.*, **431**, 187 (1923); (b) P. Chabrier and S. H. Renard, *Bull. soc. chim. France*, D272 (1949).

(21) (a) A. E. S. Fairfull, J. L. Lowe and D. A. Peak, *J. Chem. Soc.*, 742 (1952); (b) P. L. deBenneville, J. S. Strong and V. T. Elkind, *J. Org. Chem.*, **21**, 772 (1956); P. L. deBenneville, C. L. Levesque, L. J. Exner and E. Hertz, *ibid.*, **21**, 1072 (1956).

(22) D. W. Kaiser and R. P. Welcher (to American Cyanamid Co.) U. S. Patent 2,806,879 (1957).

(23) G. B. DeLaMater (to Mallinckrodt Chemical Works) U. S. Patent 2,732,401 (1956).

(24) M. P. Doerner (to Dow Chemical Co.) U. S. Patent 2,772,309 (1956).

(25) A. Reissert, *Chem. Ber.*, **37**, 3708 (1904).

(26) (a) J. J. Ritter and P. P. Minieri, THIS JOURNAL, **70**, 4045 (1948); (b) F. R. Benson and J. J. Ritter, *ibid.*, **71**, 4128 (1949).

(27) B. S. Rabinovitch and C. A. Winkler, *Can. J. Res.*, **20B**, 185 (1942).

(28) J. G. Erickson, *J. Org. Chem.*, **20**, 1569 (1955).

(29) Melting points and boiling points are uncorrected.

(30) B. S. Lacy, H. A. Bond and W. S. Hinegardner (to E. I. du Pont de Nemours and Co.) U. S. Patent 2,399,361 (1946); *C. A.*, **40**, 4745 (1946).

(31) R. P. Welcher, D. J. Berets and L. E. Sentz, *Ind. Eng. Chem.*, **49**, 1755 (1957).

TABLE I

REACTION OF CYANOGEN WITH WATER. EFFECT OF VARIABLES UPON PREPARATION OF CYANOFORMAMIDE

$(CN)_2$, moles	H_2O/$(CN)_2$,[a] molar ratio	Catalyst/$(CN)_2$,[b] molar ratio	Time, hr.	Temp., °C.	Yield,[c] %	Recovery of $(CN)_2$, %
1.98[d]	6:1	HCO_2H, 2:1	7	55	99	..
		Effect of choice of acid				
0.30	4:1	HCO_2H, 2:1	7	74	79,69[e]	7
.32	4:1	HCO_2H, 2:1[f]	15	68	69	..[g]
.32	4:1	CH_3CO_2H, 2:1	15	74	54[h]	7
.29	4:1	$ClCH_2CO_2H$, 2:1	15	74	20	38
.35	4:1	H_3PO_4, 1:13	15	74	29	..
.31	4:1	$PhP(O)(OH)_2$, 1:10	15	74	47	15
.31	4:1	H_2SO_4, 1:20	7	74	0	69
.31	4:1	H_2SO_4, 1:1	3.5	74	0[i]	42
.18	1:1	HCl, 1:18[j]	15	60	0[k]	..
		Effect of combination of acids				
0.31	4:1	HCO_2H, 2:1 + p-TSA, 1:50[l]	15	73	45	..
.33	4:1	HCO_2H, 2:1 + H_2SO_4, 1:100	15	74	50	..
.32	4:1	HCO_2H, 2:1 + H_2SO_4, 1:20	7	74	15	32
.29	4:1	HCO_2H, 2:1 + H_3PO_4, 1:10	15	74	68	..
.29	4:1	HCO_2H, 2:1 + $PhP(O)(OH)_2$, 1:10	7	74	67	..
		Effect of relative proportions of reactants				
0.33	1:1	HCO_2H, 1:1[f]	15	65	5	..
.34	2:1	HCO_2H, 1:1[f]	15	65	23	..
.30	4:1	HCO_2H, 1:1[f]	15	68	57	..
.32	4:1	HCO_2H, 4:1[f]	15	68	71	..
.20	16:1	HCO_2H, 2:1	3.5	74	66,66	3
.30	4:1	HCO_2H, 1:2 + HCO_2Na, 1.5:1	3.5	74	1[h]	40–50
		Effect of other factors				
0.34	4:1	HCO_2H, 2:1[m]	3.6	74	67	6
.32	4:1	HCO_2H, 2:1	15	89	0[n]	..
.35	1:1	CH_3CO_2H, 8:1	15	100	0[o]	..
.36	0	HCO_2H, 2:1[f]	15	74	0	83[p]
.32	4:1[q]	HCO_2H, 2:1[f]	15	74	0	84

[a] Includes the water in the formic acid. [b] Solvent was 75 ml. of acetonitrile. [c] Yield of oxamide was zero. [d] This optimum procedure is described in the text. [e] Yields in repeated experiments. [f] Amberlite IR 120H cation exchange resin was present, 6.0 g. = 0.030 equiv. [g] No attempt to recover cyanogen. [h] Yield of oxamide, 1%. [i] Acetamide, 0.5 g., found. [j] Solvent was 150 ml. of acetic acid. [k] Yield of oxamide was 75%. [l] p-Toluenesulfonic acid. [m] Solvent was 75 ml. of tetrahydrofuran. [n] Product consisted of ammonium formate, formamide and oxamide (7% yield). [o] Yield of oxamide was 84%; acetic anhydride found upon removing acetic acid. [p] The small loss of cyanogen was within the precision of the work-up procedure. [q] Water absent during heating; vessel then chilled and water added; sealed vessel let stand 2.3 hours at 20°.

and a maximum temperature of 75°. The residual liquid crystallized on cooling. If sodium sulfate or other salt was present the dry solid was extracted with ether to recover 1-cyanoformamide. The scrubber solution was analyzed for cyanide by the Liebig–Denigès method.[32] In some cases total cyanide and cyanate was determined by Volhard titration. Comparison of the two values showed whether hydrocyanic acid had been present with cyanogen in the off-gases of these products.

Attempts to account for the cyanogen in these experiments were satisfactory only when the yield of 1-cyanoformamide was high or when very little reaction occurred. In several experiments reproduced yields inspired confidence in the work-up procedure for 1-cyanoformamide and cyanogen. There was evidence for conversion of 1-cyanoformamide to carbon dioxide and hydrogen cyanide in one case.

(32) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, N. Y., 1952, 3rd. ed., p. 458.

C. Stability to Hydrolysis.—In determining the stability of 1-cyanoformamide, no cyanogen was added to the bottle. Instead, a mixture of 1-cyanoformamide (0.21 mole), water (1.00 mole), acid and acetonitrile (75 ml.) was heated at 73–75°. These amounts of 1-cyanoformamide and water corresponded to a 70% conversion of cyanogen to 1-cyanoformamide. The bottle was charged as above, with the 1-cyanoformamide added last, degassed without chilling, brought to atmospheric pressure with nitrogen, and then treated as before. In these stability tests there was no unreacted cyanogen, but the product was worked-up to determine hydrocyanic acid. The experimental details are shown in Table II.

TABLE II

STABILITY OF 1-CYANOFORMAMIDE TO HYDROLYSIS

Acid, mole	Time, hr.	Recovery of 1-cyanoformamide, %	Yield of oxamide, %
0.60 HCO_2H	15	97	0
.60 HCO_2H[a]	15	93	0
0.60 HCO_2H + .0017 H_2SO_4	15	85	6
.60 HCO_2H + .015 H_2SO_4	15	83	8
.60 HCO_2H + .033 p-TSA[b]	15	73[c]	0
.015 H_2SO_4	3.5	0[d]	0
.30 H_2SO_4	3.5	0[d]	0

[a] Amberlite IR-120 H cation exchange resin was present, 6.0 g. = 0.030 equiv. [b] p-Toluenesulfonic acid. [c] Gas sample of the bottle contents contained carbon monoxide, carbon dioxide and hydrogen cyanide. [d] Only product was a brown resin.

D. Hydrolysis and Assay Method.—A 1.171-g. portion of analytically pure 1-cyanoformamide was rinsed into 100.0 ml. of 0.5004 *N* sodium hydroxide at 99–100° with 10.0 ml. of water. Periodically, 10.0-ml. aliquots of the solution were analyzed for cyanide. Over the time 3–33 min. the values averaged 99% of the theoretical cyanide with a precision of ±1%.

E. Storage Stability at 25°.—One-gram samples of pure 1-cyanoformamide in clean 1-oz. screw cap vials were stored at 25° under nitrogen in the presence of 5% of various materials. The vials were observed periodically for first appearance of color and the results are summarized in Table III. In a separate test a small open vial containing 0.11 g. of 1-cyanoformamide was suspended inside a stoppered test-tube containing 25 ml. of 0.1 *N* silver nitrate. After two days at 25° there was a film of silver cyanide at the surface of the solution.

TABLE III

CHEMICAL AND LIGHT STABILITY OF 1-CYANOFORMAMIDE AT 25°

Test	Additive[a]	Time until first appearance of color, days
1	None	25
2	None; vial kept in complete darkness	25
3	Deionized water	8
4	91% formic acid	>38[b]
5	0.1 *N* NaOH	1
6	0.5 *N* NaOH	< 1
7	0.1 *N* HCl	18

[a] Ratio of additive to 1-cyanoformamide, 5% by wt. [b] Color developed very gradually after this time.

F. Stability at 97°.—A 3.2-g. sample of 1-cyanoformamide was put into a 25 × 150 mm. test-tube fitted with a thermometer, gas inlet tube reaching to the bottom, and a gas outlet tube connected to a scrubber flask containing a known volume of 0.77 *N* sodium hydroxide to absorb hydrogen cyanide. The apparatus was swept with a slow stream of nitrogen while heated with an oil-bath to give a melt temperature of 97 ± 1°. A yellow color appeared after 0.5 hr., but heating was continued for 6.5 hr. during which time the

scrubber solution was periodically analyzed for cyanide ion. The extent of decomposition was taken as the ratio of total cyanide found in the scrubber to total cyanide in the starting material, with results as follows:

After an induction period 1-cyanoformamide decomposed at a rate corresponding to a first-order reaction with an average $k \times 10^5 = 3.0 \pm 0.1$ sec.$^{-1}$, and $t_{1/2} = 6.5$ hr. The yellow-white residue in the test-tube consisted of 1-cyanoformamide (isolated and identified), cyanuric acid and cyamelide (identified by their infrared spectra), and other unidentified substances.

Oxamide.—When a solution of 6.2 g. (0.087 mole) of 1-cyanoformamide in 15 ml. of water was added dropwise to 67 ml. (0.80 mole) of 12 *N* hydrochloric acid over a period of 35 min. at 26–30° there was a mild exotherm, and a precipitate formed within 7 min. After 1 hr., 7.3 g. (95% yield) of pure oxamide was recovered. Its infrared spectrum showed that 1-cyanoformamide was absent.

1-Cyanoformamide (0.05 mole) was added to a mixture of 3 drops of 6 *N* sodium hydroxide and 0.11 mole of 3% hydrogen peroxide. Gas was evolved and the temperature rose to 43° over a period of 30 min. After another 30 min. heating at 45° and cooling, the slurry was filtered to give 2.7 g. (61%) of pure oxamide.

Oxamimidic Esters.—To the dry apparatus was added 0.15 mole of 1-cyanoformamide, 0.18 mole of absolute ethanol and 40 ml. of dry ether, followed by 0.25 mole of dry hydrogen chloride at 0–5°. Crystalline **ethyl oxamimidate hydrochloride** began to appear after 15 min., and at 20 min. the slurry set to a solid cake and the temperature rose abruptly to 26° despite vigorous cooling. The mixture stood overnight at 5°, was warmed to 30° and quickly filtered using a rubber dam, and dried at reduced pressure. The 21.2 g. (93%) of ester salt was initially at least 94% pure. The absence of ammonium chloride[33] was shown by determination of chloride and by hydrolysis of a weighed sample to the oxamic ester. The imidic ester salts were characterized by their chloride content because their melting points are not reliably reproducible.

A solution of 10.1 g. of ethyl oxamimidate hydrochloride in 30 ml. of water was warmed on the steam-bath for 15 min., causing a mild exotherm. The product was **ethyl oxamate**, 5.2 g., 67% yield, m.p. 115–116°; Wallach reported[34] m.p. 114–115°. It was soluble in cold water, ethanol and acetonitrile, hot ethylene dichloride (1 g./6 ml.), benzene (1 g./35 ml.) and ether.

Anal. Calcd. for $C_4H_7NO_3$: N, 11.96. Found: N, 11.86.

A sample of the freshly prepared oxamimidate hydrochloride was stored in a desiccator over potassium hydroxide at 25° and periodically analyzed for chlorine by the Volhard method. The results are shown in Table IV. After three weeks the white residue was washed with warm water, dried, and identified as oxamide by its infrared spectrum.

Cyclohexyl and dodecyl oxamimidate hydrochlorides were prepared similarly using the corresponding alcohols. A 90% yield of 93% pure cyclohexyl oxamimidate hydrochloride was obtained. During the preparation of the dodecyl derivative a vigorous exotherm occurred; a 97% yield of 97% pure dodecyl oxamimidate hydrochloride resulted. The decomposition of these two salts is summarized in Table IV.

Hydrolysis of these salts gave the corresponding esters. **Cyclohexyl oxamate** (89% yield) was soluble in hot methanol, ethanol, acetonitrile (1 g./5 ml.), benzene, ethylene dichloride, dioxane and water (1 g./38 ml.), and insoluble in hot hexane; m.p. 136.5–137.5°.

Anal. Calcd. for $C_8H_{13}NO_3$: C, 56.13; H, 7.65; N, 8.18. Found: C, 56.21; H, 7.73; N, 8.48.

Dodecyl oxamate (99% yield) was soluble in hot methanol, ethanol (1 g./11 ml.), ethylene dichloride, acetonitrile (1 g./11 ml.), dioxane, benzene, and insoluble in hot water, ether, hexane; m.p. 108–109.5°.

Anal. Calcd. for $C_{14}H_{27}NO_3$: C, 65.33; H, 10.58; N, 5.44. Found: C, 65.05; H, 10.40; N, 5.71.

The preparation of **phenyl oxamimidate hydrochloride** was attempted using the same conditions but allowing the reaction mixture to stand 5 days at 0–2°. The solid which was obtained was a mixture of unreacted phenol and a small amount of oxamide.

TABLE IV

DECOMPOSITION OF ALKYL IMIDIC ESTER HYDROCHLORIDES[a]

Compound	Time,[b] hr.	Amount decomposed, %
Ethyl oxamimidate·HCl	2.5	6
	76	45
	174	79
Cyclohexyl oxamimidate·HCl	4	7
	31	8
	910	25
n-Dodecyl oxamimidate·HCl	3.5	3
	408	7
Methyl formimidate·HCl	24	24[c]
	66	62
	90	100

[a] Compounds stored individually at room temperature (25°) and 1 mm. pressure in a desiccator over potassium hydroxide. [b] The -time was measured from the filtration of the reaction mixture. [c] These values calculated from data based on loss of weight by the compound on standing in a desiccator at room temperature and pressure over potassium hydroxide.[19]

A mixture of 0.15 mole of 1-cyanoformamide, 1.0 mole of ethanol and 0.15 mole of 96% sulfuric acid was heated at 70–75° for 4 hr., concentrated, neutralized, and extracted with chloroform to give 1.9 g. of yellow liquid which appeared to be impure diethyl oxalate. When the heating time was reduced to 1 hr., unreacted 1-cyanoformamide was recovered, possibly containing ethyl oxamate as an impurity.

Monothioöxamide.—The reaction apparatus, containing 0.036 mole of 0.2 *N* ammonium hydroxide cooled to 12°, was connected to a scrubber flask containing 0.67 *N* sodium hydroxide. Hydrogen sulfide, approximately 0.8 mole, was passed in through a flowmeter over a period of 85 min., while a solution of 0.52 mole of 1-cyanoformamide in 70 ml. of water was added simultaneously. The yellow crystalline monothioöxamide began to precipitate after 9 minutes. An 85% yield was obtained.

It was soluble in cold 6 *N* sodium hydroxide, hot ethanol (1 g./11 ml.), acetonitrile (1 g./17 ml.) and water, and insoluble in cold 6 *N* hydrochloric acid and ether; m.p. 179–181°, decomposing at 195°.[35]

Anal. Calcd. for $C_2H_4N_2OS$: N, 26.91; S, 30.79. Found: N, 27.17; S, 30.56.

Analysis of the scrubber water showed sulfide equal to 10–15% of the hydrogen sulfide added, and cyanide corresponding to 1% of the starting 1-cyanoformamide.

N-Alkyl Monothioöxamides.—For the preparation of **N-methylthioöxamide** a solution of 0.15 mole of sodium hydroxide in 20 ml. of water was added to a mixture of 0.100 mole of thioöxamide, 0.100 mole of methylamine hydrochloride and 40 ml. of water. After a mild exotherm the solution was heated at 72–82° for 30 minutes, causing the evolution of ammoniacal fumes, then cooled, acidified with 0.15 mole of hydrochloric acid and extracted with ether to give 2.9 g. of N-methylthioöxamide as yellow crystals, a 25% yield. It was soluble in cold ethanol, acetonitrile, hot water (1 g./10 ml.), ethylene dichloride (1 g./7 ml.) and benzene; m.p. 121–122°.

Anal. Calcd. for $C_3H_6N_2OS$: N, 23.71; S, 27.13. Found: N, 23.97; S, 27.31.

N-Butylthioöxamide was prepared similarly and distilled. The product was obtained in 38% yield as a golden liquid; b.p. 150–152° (1 mm.), m.p. 21–24°, $n^{25}D$ 1.5567. It was soluble in cold ether, acetone, acetonitrile, ethanol and benzene, and slightly soluble in hot water.

Anal. Calcd. for $C_6H_{12}N_2OS$: N, 17.49; S, 20.01. Found: N, 17.19; S, 19.87.

N-Dodecylthioöxamide was prepared similarly, in 65% yield. The lemon-yellow crystals were soluble in cold benzene and ethylene dichloride, hot acetonitrile (1 g./6 ml.) and hexane (1 g./11 ml.), and insoluble in hot water; m.p. 69–70°.

(33) Ammonium chloride is a likely by-product arising from traces of moisture or orthoester formation.[15a]

(34) O. Wallach, *Ann.*, **184**, 1 (1877).

(35) A. Weddige, *J. prakt. Chem.*, [2] **9**, 137 (1874).

Anal. Calcd. for $C_{14}H_{28}N_2OS$: S, 11.77; N, 10.28. Found: S, 11.45, 11.23; N, 10.50, 10.52.

t-**Butyloxamide.**—To a mixture of 0.12 mole of *t*-butyl alcohol in 30 ml. of acetic acid was added 0.11 mole of 96% sulfuric acid at 5°, and 0.10 mole of 1-cyanoformamide in 20 ml. of acetic acid. After 4 hr. at 25°, the wine-red mixture was poured onto ice and extracted with ether to give 62% yield of *t*-butyloxamide. It was soluble in hot acetonitrile (1 g./3 ml.), ethanol and benzene, slightly soluble in hot ether, water and hexane; m.p. 141–142°, subliming at 80° at reduced pressure.

Anal. Calcd. for $C_6H_{12}N_2O_2$: C, 49.98; H, 8.39; N, 19.43. Found: C, 50.28; H, 8.50; N, 19.43.

t-**Octyloxamide** was prepared similarly from diisobutylene in 55% yield. It was soluble in cold acetonitrile, 2B alcohol, ethylene dichloride, benzene, ether, hot hexane (1 g./4 ml.), and slightly soluble in hot water; m.p. 85–86°.

Anal. Calcd. for $C_{10}H_{20}N_2O_2$: C, 59.96; H, 10.06; N, 13.99. Found: C, 60.23; H, 10.20; N, 13.96.

Aminolysis of 1-Cyanoformamide.—A mixture of 0.10 mole of 1-cyanoformamide and 0.11 mole of butylamine in 50 ml of dry ether was stirred at 5°. Silver platelets were observed, and then a color change to yellow and brown. After the addition of 10 ml. of water the two-phase mixture was stirred for 1.5 hours, at 5–25°. Concentration at reduced pressure gave a tarry residue. It was triturated with ether, decolorized with charcoal and recrystallized from ethylene dichloride and benzene to give white crystals of **butylurea** in 28% yield, identified by its m.p. 97.5–98°, infrared spectrum and analysis. Authentic butylurea melts at 96°[36]; the expected product, butyloxamide, melts at 197–198°.[37]

Anal. Calcd. for $C_5H_{12}N_2O$: C, 51.69; H, 10.42; N, 24.12. Found: C, 51.69; H, 10.22; N, 23.52.

A mixture of 0.050 mole of 1-cyanoformamide, 0.055 mole of dodecylamine hydrochloride, 0.055 mole of sodium hydroxide, 0.10 mole of water and 15 ml. of methanol was refluxed 7 hours, neutralized and filtered. Repeated recrystallization of the brown solid from ethanol and ethylene dichloride gave white crystals of **dodecylurea**, m.p. 100–102°.

Anal. Calcd. for $C_{13}H_{28}N_2O$: C, 68.37; H, 12.46; N, 12.27. Found: C, 67.46, 67.74; H, 12.15, 12.29; N, 12.12, 12.17.

Authentic dodecylurea[38] had m.p. 102–103.5°, mixed m.p. 101–103°. The infrared spectra were identical.

Acknowledgment.—We wish to thank C. B. Shaffer for toxicity data, N. Colthup for assistance in interpreting infrared spectra, and M. Sabia and D. J. Wilson for assistance with the pressure experiments.

(36) T. L. Davis and K. C. Blanchard, THIS JOURNAL, **51**, 1790 (1929).

(37) J. Reiger, *Monatsh. Chem.*, **9**, 603 (1888).

(38) J. G. Erickson, THIS JOURNAL, **76**, 3977 (1954).

STAMFORD, CONN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Aromatic Cyclodehydration. XXXIX.[1,2] The Morphanthridizinium Ion—A New Heterocyclic System

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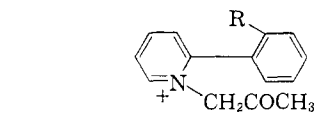
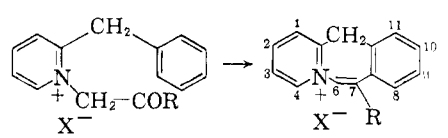
The synthesis and proof of structure of a derivative of a new heterocyclic system, the 7-methylmorphanthridizinium ion, have been described. Three other substituted morphanthridizinium salts have been prepared and characterized.

The success[1,4] met with in the cyclization of 1-acetonyl-2-arylpyridinium salts (I) to yield benzo[a]quinolizinium salts, raised the question whether 1-acetonyl-2-benzylpyridines (III) would undergo a similar cyclization to yield a new heterocyclic system (IV) with a seven-membered ring. Since the



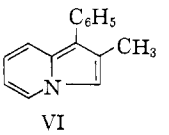
I, R = H; II, R = CH_3



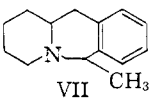
III, R = CH_3 IV, R = CH_3 V, R = C_6H_5

central ring of IV is not aromatic by Dewar's[5] definition, there was some doubt whether it would withstand the long hours of refluxing with mineral acid needed for cyclization.

Benzylpyridine reacted readily with iodoacetone, and the resulting quaternary iodide (III, X = I) was converted to the chloride, and refluxed for 5 days with 48% hydrobromic acid. The product, isolated as the perchlorate, had the composition expected for the new heterocyclic derivative (IV, X = ClO_4). All of our observations would have been accounted for if the product were really the hydroperchlorate of the known[6] 1-phenyl-2-methylpyrrocoline (VI), a base known to be formed when 1-acetonyl-2-benzylpyridinium salts are treated with



VI



VII

sodium bicarbonate. We prepared the pyrrocoline VI and found that its hydroperchlorate differs both in melting point and ultraviolet absorption from the product obtained in the acid cyclization.

Further evidence that the acid cyclization product had the structure IV was afforded by perman-

(1) For the preceding communication in this series, see THIS JOURNAL, **81**, 1941 (1959).

(2) This research was supported in part by a research grant (NSF-G2364) of the National Science Foundation.

(3) Monsanto Chemical Co. Research Fellow, 1957–1958.

(4) C. K. Bradsher and L. E. Beavers, THIS JOURNAL, **77**, 453 (1955).

(5) M. J. S. Dewar, "Electronic Theory of Organic Chemistry," Oxford University Press, Oxford, 1949, p. 160.

(6) A. E. Tschitschibabin, *Forts. Teerfarbenfabrikation*, **16B**, 2651 (1931).