[CONTRIBUTION FROM THE KETTERING-MEYER LABORATORY,[1] SOUTHERN RESEARCH INSTITUTE]

Some *S*-Substituted Derivatives of 2-Aminoethanethiol[2]

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Several new *S*-substituted derivatives of 2-aminoethanethiol hydrobromide have been prepared for testing as antiradiation drugs; the preferred procedure involved the aminoethylation of an appropriate sulfur-containing anion in *N,N*-dimethylformamide. The oxidation of 2-aminoethanethiol hydrochloride through the action of trichloromethanesulfenyl chloride is described as a simple and convenient method applicable to the preparation of large amounts of 2,2'-dithiobisethylamine (cystamine) dihydrochloride.

2-Aminoethanethiol and its isothiuronium derivative, 2-(2-aminoethyl)-2-thiopseudourea dihydrobromide—effective chemical protective agents against radiation damage in experimental animals—may be too toxic for extensive human use.[3-5] The need for a nontoxic but effective transport form of 2-aminoethanethiol might be fulfilled through drug latentiation[6]; for example, an appropriate *S*-substituted derivative might liberate the parent drug *in vivo* at an efficacious rate.

The release of 2-aminoethanethiol from 2-(2-aminoethyl)-2-thiopseudourea dihydrobromide is probably superseded by intratransguanylation[7-9] at the physiological *p*H,[10,11] and the resulting (2-mercaptoethyl)guanidine is likely the active yet toxic form.[12,13] Another *S*-substituted derivative of 2-aminoethanethiol, *S*-(2-aminoethyl) thiosulfuric acid,[14] has recently been described as a less toxic antiradiation agent in mice than 2-aminoethanethiol,[15] but the effectiveness of this intra Bunté salt may be due to its direct and rapid reaction with protein sulfhydryl groups to give mixed disulfides rather than to a release of 2-aminoethanethiol.[15,16] *S*-(2-Guanidinoethyl) thiosulfuric acid, a structure that combines the guanidine and thiosulfuric functions of protective compounds in the same molecule, has recently been synthesized and reported to have good protective properties in preliminary experiments.[17] The protective behavior of the recently prepared monosodium salt of *S*-(2-aminoethyl) phosphorothioic acid[18] has not yet been reported.

The results reported thus far for *S*-substituted 2-aminoethanethiols encouraged us to prepare several other derivatives of this type for screening as antiradiation drugs:

$$RSCH_2CH_2NH_2 \cdot HBr$$

I. R = CH_3SO_2— IV. R = $(CH_3)_2NC(=S)$—
II. R = $C_6H_5C(=O)$— V. R = $(C_2H_5)_2NC(=S)$—
III. R = $C_6H_5C(=S)$— VI. R = $(CH_3)_2NNHC(=S)$—

Each compound was prepared by the aminoethylation of the appropriate sulfur-containing anion with 2-bromoethylamine hydrobromide in *N,N*-dimethylformamide, the hydrobromide being isolated in each case. The reactions were usually carried out at room temperature, but the optimum reaction conditions for each preparation were not determined. The aminoethylation of potassium methanethiosulfonate at 60° gave a better yield of I than at room temperature, but the aminoethylation of sodium dimethyldithiocarbamate at 65° afforded a much poorer yield of IV than at room temperature. Compound I was also prepared by evaporating an aqueous solution of the reactants to dryness, but the crude product obtained in this manner was more difficult to purify than the one prepared in *N,N*-dimethylformamide.

The sulfur-to-nitrogen migration of the acyl groups of *S*-acyl derivatives of 2-aminoethanethiol at various *p*H values has been investigated by Wieland and Bokelmann,[19] and their results would seem to indicate that *N*-(2-mercaptoethyl)benzamide might be slowly formed *in vivo* from II at the physiological *p*H. The rate of rearrangement of the *S*-acetyl derivative is greater than that of the S-benzoyl derivative, and the product, 2-(mercaptoethyl)acetamide, has exhibited a moderate protective effect in mice and rats.[20]

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2-Amino-2-thiazoline hydrobromide is the major product of the interaction of potassium thiocyanate and 2-bromoethylamine hydrobromide in *N,N*-dimethylformamide, just as it is in the previously described ring closure in an aqueous medium.[21,22] With 2-bromo-*N,N*-dimethylethylamine hydrobromide, thiazoline formation is precluded, and a good yield of 2-dimethylaminoethyl thiocyanate hydrobromide was obtained in *N,N*-dimethylformamide, and smaller yields in water and acetonitrile. This thiocyanate is of interest because of the moderate protective effect shown by 2-dimethylaminoethanethiol[20]; the corresponding isothiuronium chloride, however, shows no protective effect.[20]

The recently observed facile interchange between *p*-nitrophenyl disulfide and certain thiols[23] suggests that unsymmetrical disulfides derived from 2-aminoethanethiol and thiols containing electron-withdrawing groups might undergo such an interchange with sulfhydryl groups in a biological system, thereby affording radiation protection. Our attempts to prepare 2-aminoethyl trichloromethyl disulfide hydrochloride by the reaction of 2-aminoethanethiol hydrochloride and trichloromethanesulfenyl chloride in ethanolic solution, even in the cold and irrespective of the order of addition, produced 2,2′-dithiobisethylamine dihydrochloride in high yield. Because the interchange takes precedence over the reaction of 2-aminoethanethiol hydrochloride with the sulfenyl chloride, the desired unsymmetrical disulfide, unlike many unsymmetrical trichloromethyl disulfides prepared by this method,[24] has only transitory existence in the reaction mixture. In effect, the oxidation of 2-aminoethanethiol hydrochloride through the action of trichloromethanesulfenyl chloride constitutes a simple and convenient procedure applicable to the preparation of large amounts of pure 2,2′-dithiobisethylamine (cystamine) dihydrochloride.

EXPERIMENTAL

Potassium methanethiosulfonate. The interaction of potassium hydrosulfide and methanesulfonyl chloride according to the published method[25] gave an 83% yield of potassium methanethiosulfonate, m.p. 203°,[26] the isolation being modified as follows: (1) The reaction mixture was evaporated to dryness under reduced pressure and the residue extracted with warm *N,N*-dimethylformamide and (2) the *N,N*-dimethylformamide extract was evaporated to dryness under reduced pressure and the residue washed with isopropyl alcohol until colorless and dried *in vacuo* over phosphorus pentoxide at room temperature.

S-(2-Aminoethyl) methanethiosulfonate hydrobromide (I). A solution of 13.5 g. (90 mmoles) of potassium methanethiosulfonate in 35 ml. of *N,N*-dimethylformamide was added to a solution of 17.4 g. (85 mmoles) of 2-bromoethylamine hydrobromide[27] in 15 ml. of *N,N*-dimethylformamide, a precipitate being formed immediately. The mixture was stirred and heated at 60° for 3 hr., and the solids were removed by filtration. The filtrate was evaporated to dryness under reduced pressure at 60°, the residual yellow-orange viscous oil dissolved in 100 ml. of hot acetonitrile, and the solution filtered to remove a trace of insoluble solid. The filtrate was evaporated to dryness *in vacuo*, and the residual liquid was triturated with a mixture of 25 ml. of acetonitrile and 25 ml. of ethyl ether. The solid that formed was collected, washed with ethyl ether, and dried *in vacuo* over phosphorus pentoxide for 4 hr. at room temperature: crude yield 19.3 g. (96%), m.p. 105°.[26] Two recrystallizations from ethyl alcohol gave 10.5 g. (52%) of *S*-(2-aminoethyl) methanethiosulfonate hydrobromide as off-white needles, m.p. 114–115°.[26]

A 2-mmole run carried out in *N,N*-dimethylformamide at room temperature for 20 hr. gave a 37% yield of a crude product that crystallized in the acetonitrile extract. Recrystallization of the crude product from ethyl alcohol gave analytically pure needles, m.p. 115°.[26]

Anal. Calcd. for $C_3H_9NO_2S_2 \cdot HBr$: C, 15.25; H, 4.26; S, 27.15. Found: C, 15.55; H, 4.17; S, 27.00.

When an aqueous solution of the reactants was evaporated to dryness and the residue extracted, a 90% yield of crude product having an indefinite melting point was obtained; recrystallization decreased the yield to 36%; m.p. 115°.[26]

S-(2-Aminoethyl) thiobenzoate hydrobromide[28] *hemihydrate* (II). To 332 mg. (2.4 mmoles) of thiobenzoic acid[29] was added 1.35 ml. of 10% ethanolic potassium hydroxide, and the resulting solution was evaporated to dryness. The residue, light-yellow crystals of potassium thiobenzoate, was dissolved in 2.5 ml. of *N,N*-dimethylformamide and added to a solution of 410 mg. (2.0 mmoles) of 2-bromoethylamine hydrobromide[27] in 2.5 ml. of *N,N*-dimethylformamide, immediate precipitation occurring. The mixture was heated at 60–70° for 3 hr., then cooled and filtered. The filtrate was evaporated to dryness under reduced pressure, and the yellow residual solid was triturated with 5 ml. of acetonitrile, giving pink-white crystals that were collected and dried *in vacuo* over phosphorus pentoxide for 16 hr. at room temperature: yield 411 mg. (76.5%), m.p. 192–194°.[26] A 250-mg. sample of the crude product was dissolved in 10 ml. of boiling ethyl alcohol. Addition of 10 ml. of ethyl ether to the cooled filtered solution gave a white crystalline solid that was dried *in vacuo* over phosphorus pentoxide at room temperature for 20 hr.; weight 153 mg.; m.p. 196°,[26] 197° (capillary, from 160°).

Anal. Calcd. for $C_9H_{11}NOS \cdot HBr \cdot {}^1/_2H_2O$: C, 39.86. H, 4.83; S, 11.82. Found: C, 39.86; H, 4.47; S, 11.70.

Evaporating an aqueous solution of the reactants to dryness on a water bath and extracting the residue with boiling acetonitrile gave a 35% yield of a crude product, m.p. 195°.[26]

2-Aminoethyl dithiobenzoate hydrobromide (III). Crude dithiobenzoic acid, freshly prepared by the method of Houben[30] and obtained as a violet-red oil in 13% yield by evaporation of an ethereal extract, was redissolved in 300 ml. of ethyl ether, and the ethereal solution extracted with 59.1 ml. of 0.903*N* (53.4 mmoles) of sodium hydroxide solution. The orange-red aqueous layer, *p*H 8, was evaporated to dryness under reduced pressure, and the dark red semisolid residue, 12.5 g., was triturated with benzene. The resulting solid was collected, washed with benzene until the filtrate was colorless, and dried *in vacuo* over phosphorus pentoxide

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(26) Determined on a Kofler Heizbank.

(27) Eastman Kodak Co., Rochester, N. Y.

(28) The hydrochloride, prepared from benzoyl chloride and 2-aminoethanethiol hydrochloride, has been reported.[19]

(29) L. Light and Co., Ltd., Colnbrook, Bucks, England.

(30) J. Houben, *Ber.*, 39, 3219 (1906).

at room temperature for 4 hr.; yield of sodium dithiobenzoate 3.45 g. (30–35%).

A solution of 3.69 g. (18 mmoles) of 2-bromoethylamine hydrobromide[27] in 10 ml. of *N,N*-dimethylformamide was added to a solution of the sodium dithiobenzoate described above (19 mmoles) in 15 ml. of *N,N*-dimethylformamide. The resulting dark red solution was stirred at room temperature for 24 hr., and then evaporated to dryness under reduced pressure. The residual red solid was dried for 1 hr. at 60° *in vacuo* and then extracted with boiling acetonitrile until the filtrate was colorless. The pink solid that precipitated from the cooled combined extracts was dried *in vacuo* over phosphorus pentoxide for 16 hr. at room temperature: yield 1.92 g.; m.p. 212° dec.,[26] 156–157° dec. (capillary). An additional 0.36 g. of pink solid, m.p. 203° dec.[26] was obtained by evaporating the filtrate to dryness and triturating the residue with 25 ml. of cold acetonitrile; the total yield was 45%. Recrystallization of a 250-mg. sample of the second crop from 40 ml. of acetonitrile afforded 85 mg. of analytically pure 2-aminoethyl dithiobenzoate hydrobromide (dried in the same manner as that described above for the first crop), m.p. 160° dec. (capillary)

Anal. Calcd. for $C_9H_{11}NS_2 \cdot HBr$: C, 38.85; H, 4.35; S, 23.05. Found: C, 38.78; H, 4.48; S, 23.09.

2-Aminoethyl dimethyldithiocarbamate hydrobromide (IV). A solution of 365 mg. (2.4 mmoles) of sodium dimethyldithiocarbamate hemihydrate[31] in 2.5 ml. of *N,N*-dimethylformamide was added to a solution of 410 mg. (2.0 mmoles) of 2-bromoethylamine hydrobromide[27] in 2.5 ml. of *N,N*-dimethylformamide. The resulting solution was stirred at room temperature for 24 hr., then evaporated to dryness under reduced pressure. The residue, a cloudy oil, was extracted with 25 ml. of boiling acetonitrile. The white needles that formed as the extract cooled were collected and dried *in vacuo* over phosphorus pentoxide for 20 hr. at room temperature: weight 261 mg., m.p. 158°.[26] A second crop of 39 mg., m.p. 156–158°,[26] was obtained from the filtrate concentrated to 5 ml.; total yield 51%. Recrystallization of a 150-mg. sample of the crude product from 10 ml. of acetonitrile afforded 100 mg. of pure 2-aminoethyl dimethyldithiocarbamate hydrobromide, m.p. 158°,[26] 158° (capillary, from 125°), as white needles.

Anal. Calcd. for $C_5H_{12}N_2S_2 \cdot HBr$: C, 24.48; H, 4.93; N, 11.42; S, 26.15. Found: C, 24.66; H, 5.36; N, 11.15 S, 26.02.

When the reaction was carried out at 60–70° for 5 hr., the yield of pure product was less than 15%.

2-Aminoethyl diethyldithiocarbamate hydrobromide[32] (V). The aminoethylation of sodium diethyldithiocarbamate trihydrate[27] by essentially the same procedure as that used to prepare IV gave a 39% yield of the crude dithiocarbamate V, m.p. 148°.[26] For analysis, recrystallization of a 200-mg. sample from 4 ml. of acetonitrile gave 119 mg. of white platelets, m.p. 152°,[26] 153–154° dec. (capillary).

Anal. Calcd. for $C_7H_{16}N_2S_2 \cdot HBr$: C, 30.76; H, 6.27; S, 23.46; Found: C, 30.67; H, 6.14; S, 23.38.

When water and acetonitrile were the reaction media, the yields were roughly the same as that when *N,N*-dimethylformamide was used, but the crude products were less pure.

2-Dimethylaminoethyl thiocyanate hydrobromide. 1. *In water.* Aqueous solutions of 534 mg. (5.5 mmoles) of potassium thiocyanate and 1.16 g. (5.0 mmoles) of 2-bromo-*N,N* dimethylethylamine hydrobromide[33] were mixed (total volume 10 ml.) and evaporated to dryness under reduced pressure on a water bath. The residual reddish white solid (after being washed down with methyl alcohol and then acetonitrile, and the mixture evaporated to dryness after each treatment) was extracted with hot acetonitrile (5 × 5 ml.). The extract was evaporated to dryness under reduced pressure, and the residue, dried *in vacuo* at 60° for 30 min., was recrystallized from 7.5 ml. of acetonitrile. The shining white plates thus obtained were dried *in vacuo* over phosphorus pentoxide at room temperature for 4 hr.; yield 530 mg. (50%), m.p. 145°.[26] Recrystallization of a 250-mg. sample from 4 ml. of acetonitrile gave 156 mg. of analytically pure thiocyanate as white needles, m.p. 148°,[26] 142–143° dec. (capillary); ν_{max}^{KBr} (cm.$^{-1}$) 2160 (—SCN),[34] very sharp.

Anal. Calcd. for $C_5H_{10}N_2S \cdot HBr$: C, 28.44; H, 5.25; S, 15.19. Found: C, 28.34; H, 5.33; S, 15.11.

2. *In N,N-dimethylformamide.* A mixture of 11.65 g. (0.050 mole) of 2-bromo-*N,N*-dimethylethylamine hydrobromide and 5.34 g. (0.055 mole) of potassium thiocyanate in 75 ml. of *N,N*-dimethylformamide was stirred at room temperature for 24 hr., and then evaporated to dryness under reduced pressure. The residual tan solid, dried *in vacuo* at 60° for 1 hr., was extracted with boiling acetonitrile (3 × 50 ml.). The white solid that precipitated from the extract was collected and dried *in vacuo* over phosphorus pentoxide; yield 7.60 g. (72.5%), m.p. 147°,[26] 142–143° dec. (capillary).

3. *In acetonitrile.* By adding potassium thiocyanate to a warm solution of 2-bromo-*N,N*-dimethylethylamine hydrobromide in acetonitrile, and working up the reaction mixture in a manner similar to that described above, a 25% yield of the thiocyanate, m.p. 145°,[26] was obtained.

Derivatives of 3,3-dimethyldithiocarbazic acid. 1. *Sodium 3,3-dimethyldithiocarbazate.* A solution of 4.0 g. (0.1 mole) of sodium hydroxide in 20 ml. of water was added dropwise to a vigorously stirred mixture of 7.6 ml. (0.1 mole) of 1,1-dimethylhydrazine, 25 ml. of water, and 6.7 ml. (0.11 mole) of carbon disulfide, and the resulting mixture stirred at 30–40° for 7 hr. Two crops of colorless crystals were deposited when the resulting solution was successively concentrated: yield 12.4 g. (*ca.* 78%); m.p. 216 dec.,[26] 174° dec. (capillary) with darkening from 170°. Precipitated from an ethanolic solution (treated with Norit) with ethyl ether and dried *in vacuo* over phosphorus pentoxide at room temperature, a sample of the product had melting characteristics identical with those described above; analyses (C, H, S), though somewhat varying, indicate the material to be a hemihydrate of the desired sodium 3,3-dimethyldithiocarbazate.

2. *Methyl 3,3-dimethyldithiocarbazate.* To a stirred cold solution of 380 mg. (2.4 mmoles) of unrecrystallized sodium 3,3-dimethyldithiocarbazate in 5 ml. of *N,N*-dimethylformamide was added 0.12 ml. (2.0 moles) of iodomethane. Stirring was continued for 3 hr. while the mixture was allowed to warm to room temperature. The cloudy reaction mixture was then evaporated to dryness at 60° under reduced pressure. The fluid residue was triturated in 5 ml. of water, giving a white gummy solid. The aqueous mixture was heated to boiling, 1 ml. of ethyl alcohol was added, and the resulting solution, after being filtered and cooled, deposited long white needles, which were collected and dried *in vacuo* over phosphorus pentoxide at room temperature: yield 218 mg. (73%), m.p. 97°.[26]

Anal. Calcd. for $C_4H_{10}N_2S_2$: C, 31.96; H, 6.70. Found: C, 31.65; H, 6.88.

3. *2-Aminoethyl 3,3-dimethyldithiocarbazate hydrobromide* (VI). A solution of 410 mg. (2.0 mmoles) of 2-bromoethylamine hydrobromide[27] in 2.5 ml. of *N,N*-dimethylformamide was added to a solution of 370 mg. (2.2 mmoles) of sodium 3,3-dimethyldithiocarbazate hemihydrate in 2.5 ml. of *N,N*-dimethylformamide. The mixture was stirred at room temperature for 24 hr., the solvent removed under reduced pressure at 60°, and the residue dried *in vacuo* at 60°.

(31) M. Delépine, *Bull. soc. chim. France* [4], **3**, 650 (1908).

(32) The hydrochloride was recently reported by J. Postovskii, N. F. Karazinova, G. B. Afanasyeva, and N. I. Latosh, *Doklady Akad. Nauk S.S.S.R.*, **132**, 141 (1960).

(33) Columbia Organic Chemicals Co., Inc., Columbia, S. C.

(34) L. S. Luskin, G. E. Gantert, and W. E. Craig, *J. Am. Chem. Soc.*, **78**, 4965 (1956).

The semisolid residue was extracted with boiling acetonitrile (5 × 10 ml.), and the extract evaporated to dryness under reduced pressure. The resulting white crystalline residue was triturated with 1 ml. of cold acetonitrile, collected and dried *in vacuo* over phosphorus pentoxide at room temperature: yield 358 mg. (69%), m.p. 166° dec.[26] Recrystallization of a 150-mg. sample from 30 ml. of acetonitrile afforded 66 mg. of analytically pure 2-aminoethyl 3,3-dimethyldithiocarbazate hydrobromide as colorless cubic crystals, m.p. 166° dec.,[26] 148° dec. (capillary, from 125°).

Anal. Calcd. for $C_5H_{13}N_3S_2 \cdot HBr$: C, 23.07; H, 5.42; S, 24.64. Found: C, 23.38; H, 5.50; S, 24.40.

2,2'-Dithiobisethylamine dihydrochloride from the reaction of 2-aminoethanethiol hydrochloride and trichloromethanesulfenyl chloride. A solution of 172 g. (0.924 mole) of trichloromethanesulfenyl chloride[27] in 750 ml. of absolute ethyl alcohol was added dropwise to a cooled, vigorously stirred solution of 100 g. (0.882 mole) of 2-aminoethanethiol hydrochloride[35] in 750 ml. of absolute ethyl alcohol, the rate of addition being such that the temperature of the mixture did not exceed 50°. A precipitate formed, and the reaction mixture was stirred for 1 hr. after the addition was complete. Then 1 l. of anhydrous ethyl ether was added, and the mixture was chilled for 2 hr. The precipitated solid was collected, washed with 200 ml. of ethyl ether, and dried *in vacuo* over phosphorus pentoxide at 80° for 17 hr.; m.p. 200°.[26] The crude product was dissolved in 1 l. of boiling methyl alcohol, and the solution was treated with Norit, filtered, cooled, and then treated with 1 l. of ethyl ether. After 1 hr., the resulting precipitate was collected and dried as described above; yield 88.5 g. (89%) of 2,2'-dithiobisethylamine dihydrochloride as a white crystalline powder, m.p. 211°.[26,36]

Anal. Calcd. for $C_4H_{12}N_2S_2 \cdot 2HCl$: C, 21.07; H, 6.24; S, 28.60. Found: C, 20.97; H, 6.27; S, 28.48.

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(35) Evans Chemetics, Inc., 250 East 43rd St., New York, 17, N. Y.

(36) The disulfide that was isolated from a preliminary run in which equimolar quantities of reactants and a reversed order of addition were used had a m.p. of 216°[26]; reported melting points for the dihydrochloride range from 203° [W. Coblentz and S. Gabriel, *Ber.*, **24**, 1122 (1891)] to 217° [A. H. Nathan and M. T. Bogert, *J. Am. Chem. Soc.*, **63**, 2361 (1941)].

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

Preparation and Reactions of 1-Cyanoformimidic Acid Hydrazide

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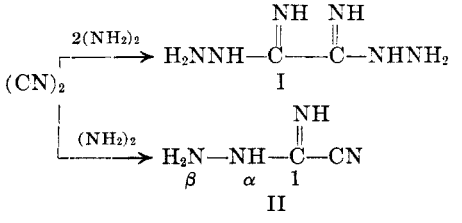
1-Cyanoformimidic acid hydrazide [$NH_2NHC(=NH)CN$] has been synthesized in good yield by the reaction of cyanogen and hydrazine. The chemistry of this new compound has been investigated and a number of derivatives have been prepared. These include the β-alkylidene, β-acyl, β-carbamoyl, and β-phenylcarbamoyl derivatives; substituted *as*-triazine-3-carbonitriles; substituted *s*-triazole-3-carbonitriles; substituted 1,3,4-oxadiazoles; and tetrazole-5-carbonitrile.

The reaction of cyanogen with two moles of hydrazine to form oxalimidic acid dihydrazide (I) has been known for over sixty years.[1-3] 1-Cyanoformimidic acid hydrazide (II), the product from equimolar amounts of cyanogen and hydrazine, however, has not been reported.



In the course of some studies on the reactions of cyanogen with hydrazine we isolated, in addition to a large quantity of oxalimidic acid dihydrazide, a small amount of a second solid material. From its elemental analysis, molecular weight, and infrared spectrum we determined that 1-cyanoformimidic acid hydrazide had been obtained. With this material in hand we were able to study its solubility characteristics and thereby devise a suitable synthesis. We believe that the major reason that this material had eluded discovery is that, under the conditions employed heretofore, the marked insolubility of oxalimidic acid dihydrazide in most solvents tended to favor its formation and isolation almost exclusively.[4] It was therefore necessary to find conditions under which 1-cyanoformimidic acid hydrazide would form readily and then precipitate immediately from solution to render it unavailable for further reaction.

(1) A. Angeli, *Gazz. chim. ital.*, **23**, II, 101–4 (1893).

(2) T. Curtius, *J. prakt. Chem.*, [2], **52**, 272 (1895).

(3) G. Dedichen, *Avhandl, Norske Videnskaps-Akad. Oslo, I, Mat.-Naturv., Kl.*, **1936**, No. 5, pp. 161–7.

(4) We have found that procedures which would normally be expected to favor our desired reaction are inadequate. Thus the slow addition of hydrazine to a stirred ethanolic solution of cyanogen (equimolar with the hydrazine or in threefold excess) produces little or no 1-cyanoformimidic acid hydrazide.