in each case), and by their ir (Table I) and nmr spectra. The procedure for **2a** is given as a typical example.

N-Phenyl-N'-cyano-S-methylisothiourea (2a).—Dimethyl cyanodithioimidocarbonate[6] (10.0 g, 0.069 mol) was dissolved in 200 ml of ethanol. To the stirred solution was added 10 ml (0.11 mol) of aniline over a period of 30 min. The solution was kept at 80° for 5 hr and then reduced by evaporation to one-fourth the original volume. The white crystals which appeared while the solution was cooled at 0° for 2 hr were collected by filtration. Recrystallization from ethanol gave 11.0 g (83%) of white crystals: mp 194–196° (lit.[10] mp 195–196°); ir (KBr) 3210 (NH), 2160 and 2180 (shoulder) (C≡N), and 1520 cm^{-1} (C=N); nmr (DMSO-d_6) τ 0.05 (s, 1, NH), 2.4–2.9 (m, 5, C_6H_5), and 7.45 (s, 3, CH_3S).

Anal. Calcd for $C_9H_9N_3S$: C, 56.5; H, 4.70; N, 22.0; S, 16.7. Found: C, 56.5; H, 4.65; N, 21.9; S, 16.7.

1-Phenyl-2-cyanoguanidine from 2a. Method A.—A solution of 0.27 g (0.0016 mol) of silver nitrate in 20 ml of DMF was added to a solution of 0.30 g (0.0016 mol) of **2a** and 10 drops of triethylamine in 50 ml of DMF. A yellow precipitate of silver mercaptide formed immediately. After the mixture was stirred for 1 hr at room temperature and then cooled in a Dry Ice–acetone bath, the yellow precipitate was collected by filtration and washed with DMF. After drying it amounted to 0.235 g, a quantitative yield of silver mercaptide. Ammonia was bubbled through the filtrate for 1 hr at 0°. The mixture was then stirred at room temperature for several hours followed by removal of all but 10 ml of the DMF by vacuum distillation. Addition of 100 ml of ether and cooling in a Dry Ice–acetone bath led to the formation of 0.13 g (52%) of 1-phenyl-2-cyanoguanidine, mp 197–199° (lit.[11] mp 195–196°). The ir and nmr spectra were consistent with the proposed product, as was the microanalysis (below).

Anal. Calcd for $C_8H_8N_4$: C, 60.0; H, 5.00; N, 35.0. Found: C, 60.3; H, 5.11; N, 35.2.

Method B.—The thermal elimination of methyl mercaptan from **2a** was effected by heating a solution of 1.00 g(0.0053 mol) of **2a** in 100 ml of diphenyl ether for 2 hr at 150° while nitrogen gas swept the mercaptan into traps containing 5% aqueous silver nitrate solution. The silver mercaptide collected after 2 hr was 0.65 g or 79.5% of the theoretical amount. At this point 1.00 g (0.013 mol) of ammonium nitrate was added to the diphenyl ether solution and the temperature was held at 120° for 12 hr. The solvent was removed by vacuum distillation, leaving a red oil from which a white solid formed after a few hours. Purification of the solid by column chromatography (neutral alumina) afforded 0.27 g (32.2%) of white solid, mp 197–198°, ir and nmr spectra identical with those of the product from method A.

N-Phenyl-N'-cyano-O-methylisourea from 2a.—To a stirred solution of 1.00 g (0.0053 mol) of **2a** and 1 ml of triethylamine in 150 ml of absolute methanol at 50° was added 1.25 g (0.0062 mol) of mercuric chloride. A white precipitate formed immediately. After the reaction mixture was stirred at room temperature for 45 min, the precipitate of $HgClSCH_3$ was collected by filtration, yield 1.29 g (87%). Sodium methoxide (0.070 g, 0.0013 mol) was then added to the colorless filtrate as a catalyst and stirring was continued at 50° for 10 hr. Removal of solvent by distillation gave 0.425 g (46%) of long, white needles: mp 166–167°; nmr (DMSO-d_6) τ −0.3 (s, 1, NH), 2.4–2.7 (m, 5, C_6H_5), and 6.1 (s, 3, CH_3O).

Anal. Calcd for $C_9H_9N_3O$: C, 61.7; H, 5.14; N, 24.0. Found: C, 61.6; H, 5.03; N, 24.1.

1-Cyclohexyl-2-cyanoguanidine from 2b.—To a solution of 0.31 g (0.0016 mol) of **2b** and 1 ml of triethylamine in 50 ml of DMF was added a solution of 0.27 g (0.0016 mol) of silver nitrate in 20 ml of DMF. The yellow precipitate of silver mercaptide formed immediately and was removed by filtration after the solution had been stirred for 2 hr. The yield of silver salt was 0.226 g (97%). Dry ammonia was bubbled through the filtrate for 1 hr at 0° and then the mixture was stirred for 10 hr at room temperature. After the DMF solution was concentrated to 10 ml by vacuum distillation, it was diluted with ether and water and allowed to stand for 2 days. The crystals which formed during this time were collected and found to constitute a 54% yield: mp 157–158° (lit.[11] mp 158–160°); nmr (DMSO-d_6) τ 3.1–3.8 (m, 3, NH_2 and $C_6H_{11}NH$) and 8.0–9.0 (m, 11, C_6H_{11}).

Anal. Calcd for $C_8H_{14}N_4$: C, 57.8; H, 8.44; N, 33.8. Found: C, 58.1; H, 8.42; N, 33.8.

(11) B. C. Redmon and D. E. Nagy, U. S. Patent 2,455,807 (1948).

1-Ethyl-2-cyanoguanidine from 2c.—A solution of 0.255 g (0.0016 mol) of **2c** and 1 ml of triethylamine in 50 ml of DMF was combined with a solution of 0.27 g (0.0016 mol) of silver nitrate in 20 ml of DMF. After the resulting solution was stirred for 1 hr the precipitated silver mercaptide was collected, yield 0.200 g (86%). Dry ammonia was bubbled through the solution for 30 min and then stirring at 40° was maintained for 24 hr. Removal of the solvent by vacuum distillation left a red oil, which was further purified by column chromatography (neutral alumina). Collection of the band eluted with a 1:1 ethyl–cyclohexane mixture yielded a red oil, which could not be induced to crystallize despite repeated attempts. This oil amounted to 0.042 g (22%) and gave spectral and analytical results expected for the desired product: nmr (DMSO-d_6) τ 3.0–3.6 (m, 3, NH_2 and C_2H_5NH), 6.7–7.1 (q, 2, CH_3CH_2), and 8.8–9.1 (t, 3, CH_3CH_2).

Anal. Calcd for $C_4H_8N_4$: C, 42.8; H, 7.20; N, 50.0. Found: C, 42.7; H, 7.26; N, 50.0.

1-Cyclohexyl-2-cyanoguanidine from 2d.—To a stirred solution of 1.00 g (0.0087 mol) of **2d** and 2 ml of triethylamine in 100 ml of DMF was added 1.60 g (0.0094 mol) of silver nitrate in 50 ml of DMF. A light yellow solid precipitated and the solution was stirred for 45 min at 0°. An excess (2 ml) of cyclohexylamine was added to the filtrate after the removal of the silver mercaptide (1.37 g, 100%) and then the mixture was kept at reflux temperature for 6 hr. Vacuum distillation of solvent left a red oil, which was placed on a column of neutral alumina for further purification. The total yield of crystals from the 1:1 ether–chloroform fraction was 0.33 g (23%), mp 157–159° (lit.[11] mp 158–160°). A mixture melting point with the material previously described from **2b** and a consistent ir spectrum were taken as evidence for the product being 1-cyclohexyl-2-cyanoguanidine.

Dicyandiamide from 2d.—A solution of 1.00 g (0.0087 mol) of **2d** and 1 ml of triethylamine in 100 ml of DMF was stirred for 45 min with 1.60 g (0.0094 mol) of silver nitrate. The yellow silver mercaptide (1.3 g, 96%) was removed by filtration and then dry ammonia was passed through the filtrate for 1 hr at 0°. Concentration of the solution to 20 ml by vacuum distillation followed by cooling in a Dry Ice–acetone bath produced 0.46 g of white solid. Recrystallization from ethanol gave 0.40 g (50%) of white crystals, mp 208–209° (lit.[12] mp 209–211°). The ir spectrum matched the recorded spectra of dicyandiamide.[13]

Registry No.—**2a**, 21504-96-1; **2b**, 24010-75-1; **2c**, 5848-25-9; **2d**, 15760-26-6; methyl mercaptan, 74-93-1; N-phenyl-N'-cyano-O-methylisourea, 24010-78-4; 1-cyclohexyl-2-cyanoguanidine, 24010-79-5; 1-ethyl-2-cyanoguanidine, 24010-80-8.

(12) "Handbook of Chemistry and Physics," 46th ed, Chemical Rubber Co., Cleveland, Ohio, p C-954.

(13) "Sadtler Standard Spectra," Sadtler Research Laboratories, Inc., Spectra No. 497 and 13632.

Evidence for an Azomethine Ylide Intermediate in the Carbonyl-Assisted Decarboxylation of Sarcosine. A Novel Synthesis of *dl*-Phenylephrine Hydrochloride

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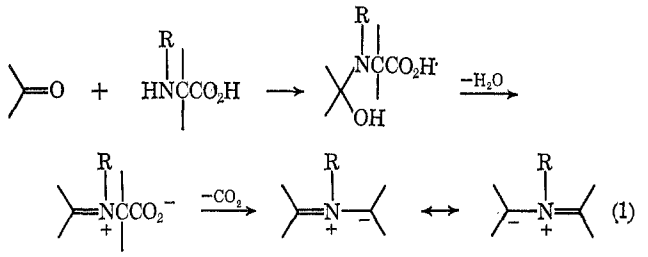
There is much evidence to indicate that the rate of thermal decarboxylation of α-amino acids is accelerated in the presence of certain aromatic carbonyl compounds.[1] For cases involving amino acids with primary amino groups, the effect has been interpreted mecha-

(1) A. F. Al-Sayyab and A. Lawson, *J. Chem. Soc., C*, 406 (1968), and references cited therein.

nistically.[2] Related N-alkyl α-amino acids also undergo carbonyl-assisted decarboxylation.[3] No attempt has been made, however, to explain their behavior mechanistically. The mechanisms which apply to ordinary unsubstituted amino acids cannot be applied to N-alkyl derivatives, since dehydration of initially formed carbinols (eq 1) must at least formally lead to



(1)

dipolar intermediates instead of the usual α-imino acids. The loss of carbon dioxide from betaines such as those shown offered the intriguing possibility of forming a resonance-stabilized azomethine ylide.[4] In this note we wish to report chemical evidence for this type of ylide intermediate in reactions of sarcosine (N-methylglycine) with benzophenone and benzaldehyde.

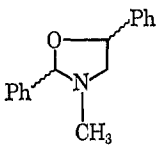
Results

When sarcosine was heated in a melt of benzophenone at 170° it dissolved slowly with concomitant loss of carbon dioxide and dimethylamine. Extraction of an ether solution of the cooled melt with dilute HCl yielded an oily, basic fraction from which 2,2,5,5-tetraphenyl-3-methyloxazolidine (**1**) and 1,1-diphenyl-2-methylaminoethanol (**2**) were isolated by fractional crystallization. The infrared spectrum of **1** showed typical N-methyl absorption at 3.55 μ. Its nmr spectrum indicated aromatic, methylene, and methyl protons in the predicted ratio of 20:2:3. The structure of **1** was confirmed by hydrolysis to form **2**. Compound **2** exhibited broad infrared absorption at 2.92 μ attributable to both OH and NH functionality. Nmr indicated the expected ratio of aromatic, methylene, and methyl protons (10:2:3). Acetylation of **2** with acetic anhydride in pyridine gave a crystalline N-acetyl derivative **3**, whose nmr spectrum indicated a new methyl signal at δ 2.00 with peak area equal to that under the N-methyl peak. The ir spectrum of **3** showed strong absorption at 6.15 μ characteristic of N,N-dialkylamides. When **3** was refluxed in toluene in the presence of *p*-toluenesulfonic acid, dehydration occurred to form N-acetyl-N-methyl-2,2-diphenylvinylamine (**4**) in high yield. The highly conjugated nature of **4** was clearly evidenced by strong ultraviolet absorption at 228 and 278 nm (ε 18,200 and 13,700, respectively).

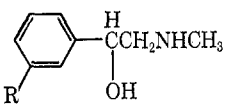
We concluded that **2** must have been formed by hydrolysis of **1** during work-up, since **2** did not react with benzophenone to form **1** under decarboxylation conditions and because no **2** was detected in crude sarcosine reaction mixtures by thin layer chromatography.

Acetylation of the crude sarcosine–benzophenone decarboxylation product followed by silica gel column chromatography led to the isolation of N-diphenylmethyl-N-methylacetamide (**6**). The amide had physical properties identical with those of an authentic specimen prepared by methylating N-acetylbenzhydrylamine. The isolation of **6** showed that N-methylbenzhydrylamine (**5**) must have been present in the original basic extract.

When sarcosine was heated in benzaldehyde, decarboxylation and formation of dimethylamine readily occurred at 150–170°. Fractional distillation of the reaction mixture gave a single, distillable product which was shown to be 2,5-diphenyl-3-methyloxazolidine (**7**) (27% yield). As in the case of **1**, compound **7** exhibited



7



8a, R = H
b, R = OCH_2Ph
c, R = OH (hydrochloride)

ir absorption at 3.55 μ characteristic of an N-methyl compound. The probable presence of *cis* and *trans* isomers made interpretation of the nmr spectrum difficult; however, the expected ratio of aromatic, methylene, and methyl protons was observed (10:2:3). Hydrolysis of **7** produced benzaldehyde and 2-methylamino-1-phenylethanol (**8a**) in 72 and 94% yields, respectively. When **8a** was heated in benzaldehyde under decarboxylation conditions, **7** was formed in 52% yield, suggesting that **8a** might actually have been a reaction intermediate. However, since no **8a** was detected in the crude decarboxylation product by thin layer chromatography prior to distillation, the hypothesis was not confirmed.

Comparable yields of **7** were formed when 2 equiv of benzaldehyde and 1 equiv of sarcosine were refluxed for several hours in benzene. This modification of the benzaldehyde reaction ultimately led to a novel synthesis of *dl*-phenylephrine hydrochloride (**8c**). Sarcosine and 3-benzyloxybenzaldehyde reacted in refluxing xylene to form (after hydrolysis) 1-(3-benzyloxyphenyl)-2-methylaminoethanol (**8b**) in 23% yield. Hydrogenolysis of **8b** in methanolic HCl then gave **8c** in nearly quantitative yield.

Discussion

The array of products observed when sarcosine was decarboxylated in benzophenone suggested the reaction sequence involving a resonance-stabilized azomethine ylide, shown in Scheme I.[5] Azomethine ylides have been reported previously;[6,7] however, none appears to have been observed in the course of amino acid decomposition. The formation of dimethylamine

(2) F. G. Baddar, *J. Chem. Soc.*, S163 (1949).

(3) G. Chatelus, *Bull. Soc., Chim. Fr.*, 2523 (1964). S. Akabori and K. Momotani, *J. Chem. Soc. Jap.*, **64**, 608 (1943); *Chem. Abstr.*, **41**, 3774 (1947). E. Takagi, *J. Pharm. Soc. Jap.*, **71**, 648 (1951); *Chem. Abstr.*, **46**, 8045 (1952); and subsequent papers by the latter author.

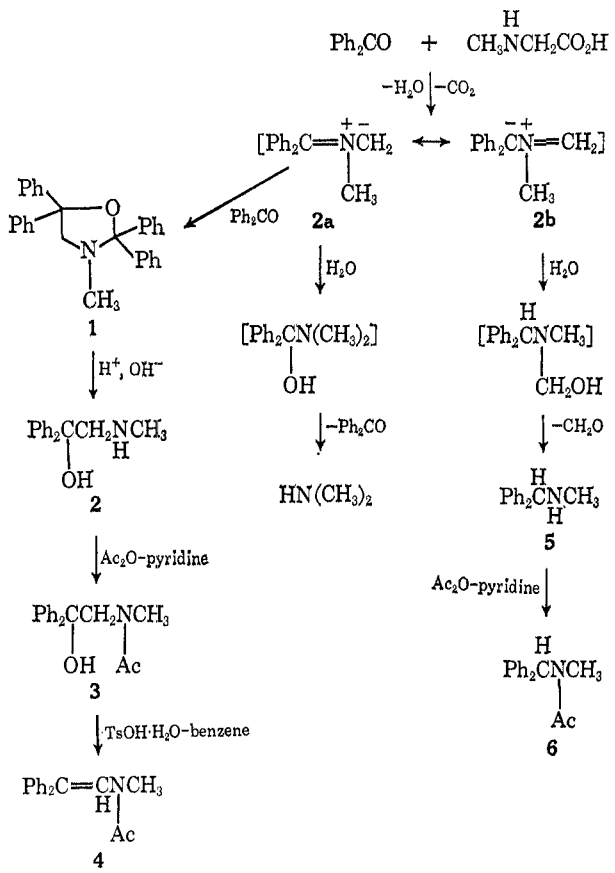
(4) Recently an ylide mechanism was proposed for the thermal decarboxylation of N-carboxymethylpyridinium bromide: W. G. Phillips and K. W. Ratts, *Tetrahedron Lett.*, **18**, 1383 (1969).

(5) Our results do not completely exclude the possibility that condensation of the intermediate betaine may have taken place prior to decarboxylation (*cf.* ref 4); however, we favor the mechanism shown in Scheme I because it also explains the facile formation of dimethylamine in all cases.

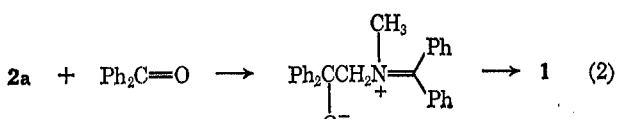
(6) R. Huisgen, *Angew. Chem. Int. Ed. Engl.*, **2**, 565 (1963).

(7) R. Huisgen, W. Scheer, and H. Huber, *J. Amer. Chem. Soc.*, **89**, 1753 (1967).

SCHEME I

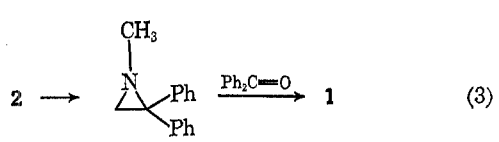


and **5** are explained in terms of hydrolysis of the ylide. Addition of water to the ylide probably leads to unstable amino alcohols, which readily collapse to form products. Compound **5** is of special interest, since it corresponds to the "transamination" products frequently encountered in carbonyl-assisted decarboxylations of α-amino acids. We envisage two possible routes for the formation of **1**. Like other dipolar species[6] **2a** may have undergone cycloaddition to excess ketone present (eq 2). The dipolar addition product

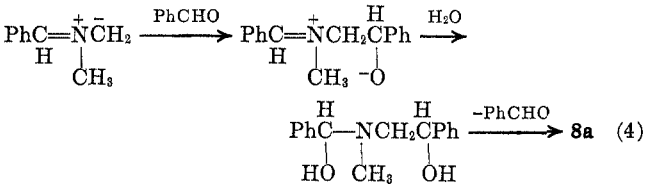


of **2b** and benzophenone (4,4,5,5-tetraphenyl-3-methyloxazolidine) was not isolated in the present work.

Alternatively, the ylide may have first collapsed to a valence-bond tautomeric aziridine[7] and subsequently reacted further[8] (eq 3). It seems likely that a similar



mechanism was operative in reactions of sarcosine and benzaldehyde. As mentioned earlier, since **8a** reacted with benzaldehyde to form **7**, the possibility remains that **8a** is actually a reaction intermediate. If this is the case it is possible to explain the formation of **8a** in terms of the well-known Hammick reaction[9] (eq 4).



Experimental Section[10]

Decarboxylation of Sarcosine in Benzophenone.—A mixture of sarcosine (1.79 g, 0.020 mol) and benzophenone (25 g) was heated to 150° for 2 hr and to 170° for another 2 hr. The heterogeneous melt rapidly evolved CO_2 and dimethylamine at 170°.[11] On cooling ether was added and the resulting solution was decanted from a small amount of gummy material. Extraction of the ether solution with 4 *N* HCl followed by neutralization with 6 *N* NaOH gave 0.89 g of yellow oil, which partially crystallized on treatment with ethanol at 0° to yield 0.10 g (1.3%) of **1**: mp 150.5–152°; 100-MHz nmr δ 2.04 (s, 3 H, $CH_3N<$), 3.73 (s, 2 H, CH_2), and 6.7–7.9 ppm (m, 2 H, aromatic protons); ir (KBr) 3.55 μ (NCH_3).

Anal. Calcd for $C_{28}H_{25}NO$: C, 85.90; H, 6.44; N, 3.58. Found: C, 85.5; H, 6.4; N, 3.4.

In a similar experiment prolonged cooling of the ethanolic solution yielded a second crystalline product (*ca.* 2 g) which was filtered, washed with ethanol, dried, and showed to be crude **2** by comparing ir and nmr data with those of authentic **2** described below. Part of **2** (1.537 g) was dissolved in dry pyridine (25 ml) and treated with acetic anhydride (2 ml). After 1.5 hr at 25° water was added and the mixture was extracted with ether. Concentration of the dried ($MgSO_4$) ether solution gave 1.65 g of white solid. Recrystallization from benzene–hexane yielded 0.503 g of **3**: mp 138.5–140°; 100-MHz nmr δ 2.00 (s, 3 H, CH_3CO), 2.42 (s, 3 H, CH_3N), 4.19 (s, 2 H, CH_2), 5.90 (s, 1 H, OH), and 7.08–7.60 ppm (m, 10 H, aromatic protons); ir (KBr) 3.05 (OH) and 6.15 μ (C=O, broad, partially split).

Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 76.2; H, 7.2; N, 5.1.

In a similar experiment starting with sarcosine (0.0506 mol) and benzophenone (25 g), 1.221 g of crude basic products were obtained. Acetylation gave 0.996 g of neutral products, which on trituration with ether afforded 0.409 g of **3**, mp 136–138.5°. The oil obtained after trituration (0.587 g) was chromatographed over 30 g of silica gel (28–200 mesh, B. Preiser and Co., grade 12). The column was eluted with mixtures of hexane, benzene, and ether. Elution with 50:50–20:80 hexane–benzene gave 0.106 g of **1**. Pure benzene gave *ca.* 0.2 g of benzophenone mixed with a trace of **1**. Further elution with increasing amounts of ether in benzene gave 0.248 g of an unseparated mixture of **3** and **6** (*ca.* 1:1 ratio). Fractions richest in **6** were pooled and rechromatographed over silica gel. Slow elution with 1–15% ether in benzene gave a pure sample of **6** whose solution, ir, and nmr spectra were identical with those of authentic **6**.

Hydrolysis of 3.—A mixture of **3** (1.23 g), mp 137–139°, reagent grade KOH (2.17 g), and redistilled 1-butanol (20 ml) was refluxed under N_2 for 3 hr. Butanol was distilled under

(8) Simple aziridines react with ketones to yield oxazolidines; *cf.* R. M. Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds," 2nd ed, Interscience Publishers, New York, N. Y., 1967, p 10.

(9) D. L. Hammick, *et al.*, *J. Chem. Soc.*, 3825 (1953).

(10) Melting points were determined on a Thomas–Hoover capillary apparatus and are not corrected. Ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer. Infrared spectra were recorded on a Perkin-Elmer Model 21 instrument unless otherwise noted. Nmr spectra were obtained with Varian Associates HA-60 or HA-100 spectrometers in $CDCl_3$ using tetramethylsilane (TMS) as internal reference. Chemical shifts are expressed in parts per million (δ) downfield from TMS. Multiplicity is indicated by letters, where s = singlet, t = triplet, and m = complex, unresolved multiplet. Microanalyses were performed by Mr. T. Atanovich and associates of this laboratory and by Spang Microanalytical Laboratory, Ann Arbor, Mich.

(11) The CO_2 was trapped as $BaCO_3$ (88% yield in the case of $Ph_2C=O$). Dimethylamine was trapped in aqueous HCl and identified as the hydrochloride by the method of J. Hrdlicka and G. Janicek [*Nature*, **201**, 1223 (1964)]; the bulk of the sarcosine nitrogen appeared to have been expelled in the form of dimethylamine. No attempt was made to identify formaldehyde among the gaseous reaction products.

reduced pressure, leaving an oil which was treated with dilute HCl and extracted with ether. Basification of the acid solution (NaOH) and reextraction with ether gave, after drying (Na_2SO_4) and concentration, 0.972 g of crude **2** as a viscous oil. The amino alcohol was purified *via* the hydrochloride. Dissolution of the crude product in dilute HCl followed by evaporation of excess water and HCl under reduced pressure gave 1.088 g (90%) of **2** HCl, mp 218–219° dec. Recrystallization from 2-propanol gave colorless microneedles, mp 217.5–219° dec.

Anal. Calcd for $C_{15}H_{18}NOCl$: C, 68.3; H, 6.8; Cl, 13.5; N, 5.3. Found: C, 68.3; H, 6.9; Cl, 13.6; N, 5.2.

A solution of the hydrochloride (0.396 g) in water (10 ml) was basified by dropwise addition of concentrated NH_4OH. An oil separated, which crystallized completely after several hours at 0°, yield 0.279 g (82%). Repeated recrystallizations from aqueous ethanol gave colorless needles of **2**: mp 80–115° (apparently polymorphic); 60-MHz nmr δ 2.47 (s, 3 H, NCH_3), 2.75 (s, 2 H, OH and NH), 3.34 (s, 2 H, NCH_2), and 6.98–7.64 ppm (m, 10 H, aromatic protons); ir (KBr) 2.92 (OH and NH), 3.57 (NCH_3, weak), 6.16 (CN), 6.28 (aromatic C=C), and 9.52 μ (CO).

Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.4; H, 7.4; N, 6.2.

Hydrolysis of 1.—A mixture of **1** (0.146 g), mp 149.5–151°, and 1 *N* HCl (10 ml) was refluxed under N_2 for 2.25 hr. The cooled reaction mixture was extracted with ether to remove benzophenone and the clear, aqueous phase was concentrated under reduced pressure to yield 0.097 g (99%) of **2** HCl, mp 207–209°. The identity of the product was confirmed by its ir spectrum.

Dehydration of 3.—A solution of the amido alcohol **3** (0.235 g), mp 138.5–140°, in toluene (10 ml) was treated with *p*-toluenesulfonic acid monohydrate (0.064 g) and refluxed for 1 hr under N_2. The toluene solution was diluted with ether, washed with $NaHCO_3$ solution, dried, and concentrated to yield 0.199 g of pale yellow oil which slowly crystallized at 25°. The crude product was chromatographed over 20 g of 40–200 mesh silica gel. Elution with benzene and 10% ether in benzene yielded a small amount of an unidentified, nonpolar by-product. Further elution with 20% ether in benzene gave 0.180 g (82%) of **4** as colorless crystals. Recrystallization from ether–hexane yielded prisms of pure **4**: mp 85–86.5°; 60-MHz nmr δ 2.15 (s, 3 H, CH_3CO), 2.78 (s, 3 H, $CH_3N<$), 6.74 (s, 1 H, HC=), and 7.08–7.58 ppm (m, 10 H, aromatic protons); ir (KBr) 5.91 (C=O), 6.12 (C=C), and 11.55 μ [-CH=C- (ν CH)]; uv max (ethanol) 228 (ϵ 18,200) and 278 nm (ϵ 13,800).

Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.6; H, 6.7; N, 5.4.

N-Diphenylmethyl-N-methylacetamide (6).—A solution of N-acetylbenzhydrylamine[12] (2.184 g, 0.00973 mol), mp 148–149°, in distilled diglyme (30 ml) was treated with 0.466 g (0.0109 mol) of 56% NaH (suspension in mineral oil, Metal Hydrides, Inc., Beverly, Mass.). The mixture was stirred at 65° under a nitrogen atmosphere for 25 min and cooled to 25°, and a solution of dimethyl sulfate (1 ml) in diglyme (4 ml) was added. After 16.5 hr at 65° water was added and the mixture was extracted with ether. Concentration of the dried ($MgSO_4$) ether solution gave an oil, which was shown by thin layer chromatography to contain a 1:1 mixture of starting material and a single new product. The oil was redissolved in diglyme (30 ml) and treated with NaH and dimethyl sulfate as previously described. After alkylation had been allowed to proceed for 48 hr at 65°, the mixture was worked up as before to yield a partially crystalline product. Pressing the crystals between layers of filter paper gave 1.64 g (71%) of **6**, mp 81–82°. Recrystallization from aqueous methanol gave 1.62 g of colorless prisms: mp 81–82° (corrected) (lit.[13] mp 80–83°); 100-MHz nmr δ 2.16 (s, 3 H, CH_3CO), 2.68 and 2.74 (two s, 3 H total area, rotamers of $CH_3N<$, peak at 2.68 disappeared at 55°), 6.15 (s, 1 H, CH), and 6.60–7.80 ppm (m, 10 H, aromatic protons); ir ($CHCl_3$)[14] 3.34, 6.06 (C=O), 6.90, 7.00, 7.14, 7.55, 7.65, 8.86, 9.28, 9.70, and 9.90 μ.

Decarboxylation of Sarcosine in Benzaldehyde.—A 100-ml, round-bottomed flask arranged for simple distillation was charged with sarcosine (10.0 g, 0.112 mol) and reagent grade benzaldehyde (50 ml). Upon heating with stirring at 170° the sarcosine dissolved rapidly with concomitant evolution of carbon dioxide and dimethylamine.[11] After 3 hr the clear yellow solution was cooled to 25°, diluted with ether (200 ml), and extracted with saturated, aqueous Na_2CO_3. Ether and benzaldehyde were removed on a rotary film evaporator to yield an oil, which was fractionated through a 3-in. Vigreux column. Following a negligible forerun 7.28 g (27%) of **7** was collected, bp 130–150° (0.1 mm). A viscous pot residue remained which could not be distilled at 280° (oil-bath temperature). A sample of the clear distillate, bp 132° (0.1 mm), showed the following properties: 100-MHz nmr δ 2.04 (s, 3 H, CH_3N), 3.73 (s, 2 H, CH_2), and 6.7–7.9 ppm (m, 10 H, aromatic protons); ir (liquid film) 3.55 μ (NCH_3).

Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.6; H, 6.9; N, 5.9.

A solution of the oxazolidine **7** (1.568 g) in 4 *N* HCl (10 ml) was stirred for 1.75 hr at 25° and extracted with ether, and the ether extract was concentrated. Treatment with an excess of 2,4-dinitrophenylhydrazine reagent (H_2SO_4) gave 1.354 g (72%) of benzaldehyde 2,4-dinitrophenylhydrazone, mp 233–234.5°. The aqueous phase from the ether extraction was concentrated to a syrup and neutralized with aqueous Na_2CO_3 solution. Extraction with ether followed by drying the extract (Na_2SO_4) and concentration under reduced pressure gave 0.935 g (94%) of crystalline **8a**. Recrystallization from ether yielded a pure specimen: mp 75.5–76.5° (lit.[15] mp 75.5–76°); 100-MHz nmr δ 2.38 (s, 3 H, CH_3N), 2.60–2.88 (unresolved group of peaks, 4 H, NH, OH, and CH_2), 4.66 (q, 1 H, >CHOH), and 7.25 ppm (s, 5 H, aromatic protons).

Reaction of 8a with Benzaldehyde.—A sample of the amino alcohol **8a** (0.148 g), mp 74–75°, was heated with benzaldehyde (1 ml) for 3 hr at 170° under a nitrogen atmosphere. On cooling, glpc analysis on a 10 ft × 0.25 in. column containing 5% DC-200 on 60–80 mesh siliconized Chromosorb W (120°) showed that **7** had been formed in 52% yield (0.076 g of hexadecane served as internal standard). The identity of **7** was confirmed by trapping a sample from the effluent He stream and comparing corresponding ir spectra.

dl-**Phenylephrine.**—A 100-ml, round-bottomed flask arranged with a Dean–Stark water trap was charged with sarcosine (0.897 g, 0.0101 mol), 3-benzyloxybenzaldehyde[16] (4.24 g, 0.020 mol), and xylene (50 ml). After refluxing 0.2 hr practically all the sarcosine had disappeared and water (*ca.* 0.2 ml) was collected. The pale yellow xylene solution was diluted with ether (100 ml), 4 *N* HCl (20 ml) was added, and the mixture was stirred vigorously at 25° for 20 hr. The xylene was separated and the aqueous HCl was concentrated under reduced pressure to yield a crystalline residue. The crystals were dissolved in water (10 ml), 3 *N* NaOH (10 ml) was added, and the final mixture was extracted with ether. The ether extract was washed with saturated brine, dried (Na_2SO_4), and concentrated under reduced pressure to yield 0.603 g (23%) of crude **8b**, mp 87–95°. Recrystallization from ethyl acetate gave colorless crystals, mp 102.5–103.5° (lit.[17] mp 103°).

A solution of **8b** (0.267 g), mp 101–102.5°, in methanol (3 ml) was added to 10% Pd on charcoal (0.075 g, prereduced with hydrogen) in a mixture of methanol (20 ml) and concentrated HCl (1 ml). Hydrogenolysis with H_2 at 1 atm was complete after 2.5 hr. Evaporation of the solvent and HCl gave crude **8c** in quantitative yield. Recrystallization from ethanol gave colorless prisms, mp 143–146.5° dec (lit.[18] mp 140–145° dec).

Registry No.—Sarcosine, 107-97-1; **1**, 24010-81-9; **2**, 24010-82-0; **2** hydrochloride, 24010-83-1; **3**, 21901-77-9; **4**, 24010-85-3; **6**, 24010-86-4; **7**, 24010-87-5; **8a**, 6589-55-5; **8c**, 20368-45-0.

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