

1-Methyl-2-(3-methoxypropylamino)ethanethiol (2).—An aqueous (260 ml) mixture of 50 g (0.29 mol) of AgNO_3 and 63.5 g (0.71 mol) of methoxypropylamine was made up as described above and 19 g (0.26 mol) of propylene sulfide was slowly added. An oily semisolid separated out. After stirring for 2 hr, 70% HClO_4 was slowly added until no further precipitation occurred. The supernatant was decanted off and the residue was washed with water until the washings were at pH 7. The free mercaptoethylamine was liberated from its silver complex as described above. Claisen distillation led to 1 g of forerun, 17 g (40% yield) of clear liquid distilling at 56° (0.95 mm), n_D^{20} 1.4705, and 9 g of residue. *Anal.* Calcd for $\text{C}_7\text{H}_{17}\text{NOS}$: C, 51.48; H, 10.49; N, 8.58; S, 19.64. Found: C, 51.65; H, 10.37; N, 8.58; S, 19.67.

1,1-Dimethyl-2-(3-di-*n*-butylaminopropylamino)ethanethiol (3).—An aqueous (160 ml) mixture of 34 g (0.20 mol) of AgNO_3 , 53 g (0.53 mol) of triethylamine, and 35.3 g (0.19 mol) of di-*n*-butylaminopropylamine was made up in the usual way, and 16.5 g (0.18 mol) of isobutylene sulfide was slowly added to it. During the episulfide addition the reaction mixture became more viscous. After stirring overnight, H_2S was bubbled through the reaction mixture and the Ag_2S precipitate was filtered off. Further work-up as described above led to an oil residue. Claisen distillation of the oil residue led to 4 g of forerun distilling at $114\text{--}123^\circ$ (0.45 mm), n_D^{20} 1.4644, 10 g distilling at $123\text{--}128^\circ$ (0.5 mm), n_D^{20} 1.4666, and 10.5 g distilling at 128° (0.45 mm), n_D^{20} 1.4666. The yield based on the last two cuts was 40%. *Anal.* Calcd for $\text{C}_{15}\text{H}_{34}\text{N}_2\text{S}$: C, 65.63; H, 12.48; N, 10.20; S, 11.68. Found: C, 65.64; H, 12.22; N, 10.34; S, 11.46.

1,1-Dimethyl-2-hexadecylammoniumethanethiol Perchlorate (4).—An aqueous (300 ml) mixture of 65 g (0.38 mol) of AgNO_3 , 105 g (1.04 mol) of triethylamine, and 77 g (0.32 mol) of hexadecylamine was made up and 31.5 g (0.36 mol) of isobutylene sulfide was slowly added. After stirring for 3.5 hr, 110 g (0.78 mol) of 70% HClO_4 was added. Within 10 min the mixture agglomerated. The supernatant was decanted off and 600 ml of 50% aqueous ethanol was added. The mercaptoethylamine was liberated from its silver complex with H_2S , and HClO_4 (about 30 g) was added until the mixture was below pH 2. After heating on the steam bath to help dissolve the product, the mixture was filtered. The Ag_2S precipitate was treated with ethanol, heated, and again filtered. Upon addition of water to the combined filtrates a white solid came out of solution which was dried over P_2O_5 . The yield of crude product was 84 g (61% yield). Recrystallization from hexane-methanol and twice from ethanol gave the disulfide salt,¹⁰ mp $224\text{--}228^\circ$ dec. *Anal.* Calcd for $\text{C}_{40}\text{H}_{86}\text{N}_2\text{S}_2\text{Cl}_2\text{O}_8$: C, 55.98; H, 10.10; N, 3.27; S, 7.47; Cl, 8.26. Found: C, 56.38; H, 10.26; N, 3.59; S, 7.61; Cl, 8.02.

1,1-Dimethyl-2-methylaminoethanethiol Hydrochloride (5).—An aqueous (120 ml) mixture of 88.5 g (0.52 mol) of AgNO_3 and 163 g (2.10 mol) of 40% methylamine was made up and 44.5 g (0.51 mol) of isobutylene sulfide was slowly added. Toward the end of the episulfide addition a yellow solid precipitated out which congealed after 45 min of stirring. The supernatant was decanted off and the residue was washed repeatedly with water to remove excess methylamine. Aqueous HCl was added and the mercaptoethylamine was liberated from its silver complex with H_2S . The Ag_2S was filtered off and the filtrate was evaporated to dryness *in vacuo*. The residue was triturated with hot CHCl_3 , leaving behind $\text{CH}_3\text{NH}_2\text{Cl}$. The dried solvent was removed under reduced pressure. The resulting residue was triturated with ether to yield 62 g (79% yield) of white solid which was crystallized from dioxane-methanol:¹⁰ mp $222\text{--}224^\circ$ dec; ir (KBr) 2950, 1457 (CH), 2645, 2490, 2400, 1585 (NH_3^+), 1415 (CH_2N^+), 1390, 1365, 1175, 1162 cm^{-1} [$(\text{CH}_3)_2\text{C}$]; nmr (D_2O) δ 1.43 [6, s, $\text{C}(\text{CH}_3)_2$], 2.77 (3, s, NCH_3), 3.16 (2, s, CH_2). *Anal.* Calcd for $\text{C}_5\text{H}_{14}\text{NSCl}$: C, 38.57; H, 9.06; N, 9.00; S, 20.60. Found: C, 38.73; H, 9.35; N, 8.84; S, 20.97.

2-(*p*-Dimethylaminophenyl)-3,5,5-trimethylthiazolidine Dihydrochloride.—A mixture of 2 g (0.013 mol) of **5**, 1.1 g (0.013 mol) of NaHCO_3 , and 2 g (0.013 mol) of *p*-dimethylaminobenzaldehyde in 100 ml of 95% ethanol was refluxed through a Soxhlet extractor containing CaC_2 for an overnight period. The NaCl was filtered off and the filtrate was evaporated to dryness. The resulting oil was dissolved in absolute ethanol and the solu-

tion was made acidic with gaseous HCl . Upon cooling a yellow solid came out of solution which was recrystallized from ethanol-ether to give 2.2 g (48% yield) of white product: mp $216\text{--}217^\circ$ dec; ir (KBr) 3000, 2940, 2900, 1460, 1137, 827 (CH), 2670–2300 (NH^+), 1610, 1510 cm^{-1} (aromatic); nmr (D_2O) δ 1.77, 1.80 [6, $\text{C}(\text{CH}_3)_2$], 2.93 (3, s, NCH_3), 3.40 [6, s, $\text{N}(\text{CH}_3)_2$], 3.67 (1, A of AB q, $J = 12$ Hz, CH_2), 4.03 (1, B of AB q, $J = 12$ Hz, CH_2), 5.96 (1, s, CH), and an AA'BB' pattern centered at 7.84 (4, m, C_6H_4). *Anal.* Calcd for $\text{C}_{14}\text{H}_{24}\text{N}_2\text{SCl}_2$: C, 52.00; H, 7.48; N, 8.66; S, 9.92. Found: C, 51.93; H, 7.51; N, 8.65; S, 9.78.

1,1-Dimethyl-2-methylaminoethanethiol Hydrochloride (5) by Reduction of Mercaptoisobutyraldehyde Schiff Base.—A solution of 2.5 g of $\text{NaSH}\cdot x\text{H}_2\text{O}$ in 10 ml of methanol was added to 4 g (0.026 mol) of bromoisobutyraldehyde¹¹ in 20 ml of methanol. After standing for 1.5 hr, 2.5 g (0.032 mol) of 40% methylamine and 20 ml of acetic acid were added and the mixture was stirred for 5 min. While cooling, 10 ml of acetic acid and 8.5 g (0.22 mol) of NaBH_4 were alternately added in small portions.¹² The mixture was stirred for 1.5 hr and water was added to destroy the excess NaBH_4 . Methanol and HCl were added and the mixture was distilled until the distillate no longer showed a green flame test for boron. The remainder of the solvent was removed under reduced pressure and the residue was extracted with CHCl_3 . The CHCl_3 was removed under vacuum and the residue was triturated with ether to give 1 g (25% yield) of crude product which was recrystallized from dioxane-methanol.

Registry No.—1, 5891-06-5; 2, 39981-44-7; 3, 39981-45-8; 4 disulfide perchlorate salt, 39981-46-9; 5 HCl , 39981-47-0; decylamine, 2016-57-1; ethylene sulfide, 420-12-2; 3-methoxypropylamine, 5332-73-0; propylene sulfide, 1072-43-1; di-*n*-butylaminopropylamine, 102-83-0; isobutylene sulfide, 3772-13-2; hexadecylamine, 143-27-1; methylamine, 74-89-5; 2-(*p*-dimethylaminophenyl)-3,5,5-trimethylthiazolidine dihydrochloride, 39981-49-2; *p*-dimethylaminobenzaldehyde, 100-10-7; bromoisobutyraldehyde, 13206-46-7.

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The Mechanism of the Robinson-Gabriel Synthesis of Oxazoles

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One of the most commonly used methods for the preparation of oxazoles is the Robinson-Gabriel synthesis, in which an α -acylamino ketone undergoes cyclization and dehydration on treatment with PCl_5 or a strong mineral acid.^{2,3} This synthesis is especially applicable to the formation of 2,5-diaryloxazoles, compounds of current interest in our studies on the reactions of heterocyclic systems with singlet oxygen.

As pointed out by Cornforth,⁴ there are two reason-

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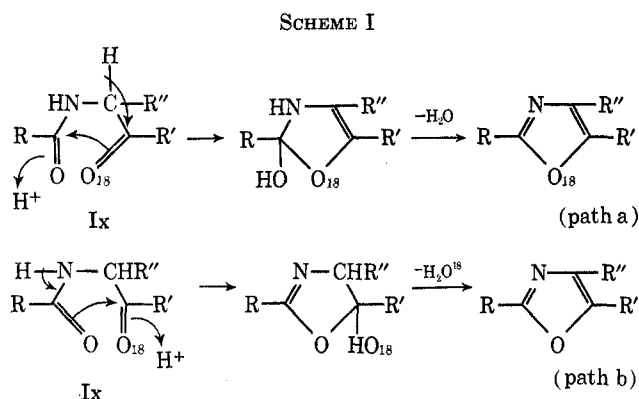
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(10) A % SH test using 2,2'-dithiodipyridine as described by D. R. Grasseti and J. F. Murray, Jr., *Arch. Biochem. Biophys.*, **119**, 41 (1967), showed that repeated recrystallization of the aminoethanethiol salt led to the disulfide salt, presumably via aerial oxidation.

able pathways which may be considered in viewing the mechanism of this reaction. These alternative routes, summarized in Scheme I, differ in the nature of the ox-



xygen atom incorporated into the oxazole, *i.e.*, ketone oxygen (path a) *vs.* amide oxygen (path b). We sought to differentiate between these two possibilities using oxygen-18 tracer methods in conjunction with high-resolution mass spectrometry.

For these studies, we prepared α -benzamidopropiophenone^{5,6} (Ix) with an oxygen-18 label in the keto portion of the molecule, and, in a second case (Iy),



with an oxygen-18 label in the amide carbonyl group.

To incorporate the labeled oxygen into Ix, the keto amide was allowed to equilibrate with 30% $H_2^{18}O$ in anhydrous THF with no catalyst present.⁷ It is well known that under these conditions the ketone oxygen undergoes rapid exchange with the labeled water while the amide oxygen undergoes no exchange.⁸ Mass spectrometric analysis indicated $26.7 \pm 0.5\%$ label in the keto oxygen. Cyclization with concentrated sulfuric acid afforded 2,5-diphenyl-4-methyloxazole,⁶ the mass spectrum of which showed $0.2 \pm 0.5\%$ label present, thereby indicating that the amide oxygen is incorporated, and the ketone oxygen expelled in the formation of the oxazole, in accord with path b.

In an independent proof of mechanism, α -amino-propio-phenone⁵ was allowed to react with O-18 enriched benzoyl chloride⁹ (from *ca.* 9.5% doubly labeled benzoic acid), yielding Iy with $9.6 \pm 0.5\%$ ^{18}O in the amide oxygen. Cyclization as above gave 2,5-diphenyl-4-methyloxazole containing $9.7 \pm 0.5\%$ oxygen-18 as shown by mass spectrometric analysis. These results clearly show that in this case the amide oxygen is retained in the product, again in accord with pathway b.¹⁰

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(10) This is the pathway favored by Paquette in picturing the mechanism of oxazole formation by the cyclization of α -acylamino ketones. See L. Paquette, "Principles of Modern Heterocyclic Chemistry," W. A. Benjamin, New York, N. Y., 1968, p 191.

Experimental Section

Ketone- ^{18}O -Labeled α -Benzamidopropiophenone (Ix).— α -Benzamidopropiophenone^{5,6} (1.00 g, 3.96 mmol), 30% $H_2^{18}O$ (0.10 ml), and 5 ml of tetrahydrofuran (distilled from lithium aluminum hydride) were refluxed for 1.5 hr. The solvent was removed *in vacuo* and the labeled keto amide was recrystallized from diethyl ether, mp 103–104° (lit. mp 104–105°). The high-resolution mass spectrum shows the parent peak (m/e 253) with a P + 2 peak indicating an ^{18}O enrichment of $26.7 \pm 0.5\%$.

Amide- ^{18}O -Labeled α -Benzamidopropiophenone (Iy).—Amino-propio-phenone stannic chloride⁵ (1.82 g, 2.89 mmol of amino ketone) was suspended in 18 ml of water with stirring and ice-bath cooling. Benzoyl- ^{18}O chloride⁹ (1.21 g, 8.65 mmol) of *ca.* 9.5% enrichment and aqueous potassium hydroxide (5.50 g in 8 ml) were added successively, and the mixture was stirred for 0.5 hr. Ether extraction followed by drying over anhydrous magnesium sulfate, filtration, and removal of solvent yielded 0.60 g (82%) of Iy, mp 104–105°, tlc behavior identical with Ix. The high-resolution mass spectrum shows the parent peak (m/e 253) with a P + 2 peak having $9.6 \pm 0.5\%$ enrichment in ^{18}O .

2,5-Diphenyl-4-methyloxazole. A.—A 0.3-g portion of ketone-labeled α -benzamidopropiophenone (Ix) was added to 3 ml of concentrated sulfuric acid with stirring. After 10 min, copious quantities of water were added to the reaction mixture until the milky white product was completely precipitated. The 2,5-diphenyl-4-methyloxazole was collected by filtration and recrystallized from petroleum ether (bp 30–60°) to yield 0.20 g (72%), mp 80–81° (lit. mp 82°). The high-resolution mass spectrum shows the parent peak (m/e 235) with a P + 2 peak having $0.2 \pm 0.5\%$ ^{18}O enrichment.

B.—A 0.5-g portion of amide-labeled α -benzamidopropiophenone (Iy) was cyclized as described previously for Ix. The oxazole obtained (81%, mp 81–82°) was analyzed by high-resolution mass spectroscopy. The parent peak (m/e 235) had a P + 2 peak showing an ^{18}O enrichment of $9.7 \pm 0.5\%$.

Registry No.—Ix, 39982-24-6; Iy, 39982-25-7; 2,5-diphenyl-4-methyloxazole, 2549-31-7.

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The Reaction of Trityloxyamine with Lead Tetraacetate

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Considerable interest continues to be expressed in the generation of *O*-nitrene intermediates, although rarely has their existence been substantiated by the weight of experimental evidence.¹ A notable exception may be cited in the work of Brois,² who successfully trapped methoxynitrene with tetramethylethylene during the lead tetraacetate (LTA) oxidation of methoxyamine. Recently the oxidation of several *O*-arylalkylhydroxylamines with LTA has been studied by Carey³ and Partch.⁴ The suggestion by the latter author that such oxidations may involve the intermediate unstable hyponitrite esters as well as the actual isolation

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