catalysis by 2-hydroxypyridine would indicate that reactions 5 and 6 are improbable under these conditions.

Experimental

Reagents.—1-Dodecanethiol (Columbia Organic Chemicals) and α-toluenethiol (Evans Chemetics) were obtained as reagent grade materials. Gas chromatographic analysis indicated that each thiol was at least 98% pure. Tetramethylene sulfoxide (K and K Laboratories) was purified by distillation over Linde-13X Molecular Sieves to remove any adsorbed water. The sieves were previously conditioned by calcination under nitrogen at 400° for 4 hr. The sulfoxide gave only one peak when analyzed by gas chromatography on a 3-ft., 20 wt. % Carbowax (20 MM) on Chromosorb-W column. 2,6-Lutidine, N,N-dimethylaniline, 1-dodecylamine, tri(*n*-butyl)amine, and pyrrole, which were used in catalysis studies, were purified by distillation through a 16-in. column equipped with a tantalum-wire spiral. The physical properties of each amine agreed with the known literature values.

General Procedure for Kinetic Studies.—A general procedure was employed in all kinetic studies. The sulfoxide, an equimolar amount of internal hydrocarbon standard, and catalyst were weighed into a vial in a nitrogen drybox with the aid of an analytical balance. The vial was capped (under nitrogen) with a self-sealing Neoprene stopper. The stopper extended down from the mouth of the vial and further sealing was accomplished by wrapping a piece of heavy copper wire around this portion of the stopper. Thus, the contents of the vial were doubly protected against moisture and oxygen. Upon sealing, the vial was placed in a Primoil-D constant-temperature bath (±0.1°). After the vial had reached thermal equilibrium, the desired quantity of prethermostated thiol was injected into the vial by a syringe, the vial was immediately shaken to obtain a homogeneous solution, and an initial sample was withdrawn by another syringe. When perfected, this operation can be performed in about 3 sec. Sampling was also accomplished with the aid of a syringe. At the desired time, an aliquot was withdrawn (5 to 10 μl.) and immediately injected into a sealed vial containing a small quantity (0.25-to 0.50 ml.) of cold acetone (0° or below). The last step stopped the reaction. A portion of the acetone solution was withdrawn by a syringe and subsequently analyzed by gas–liquid chromatography. Quantitative data was obtained from the areas of the internal standard and reactant in question using predetermined molar response factors.

Gas–Liquid Chromatographic Techniques.—The g.l.c. unit employed was an F and M Model 609 flame ionization gas chromatograph equipped with a Minneapolis Honeywell recorder and a disk integrator (Model 201). The injection port of the unit was maintained at 305° and the inlet pressure of helium was 36 p.s.i.g. The block of the detector was maintained at a constant temperature of 245°. The helium flow through the column was 100 cc./min. when measured by a flow meter. Quantitative data for each thiol was obtained on a 3-ft., 20% Carbowax (20 MM) on Chromosorb-W column (0.25-in. stainless steel tubing). This column gave excellent separation of all the thiol–hydrocarbon–sulfoxide mixtures investigated. No interference by sulfide or disulfide was encountered.[11]

Diphenylmethane and mesitylene were employed as the internal standards for measuring the rate of α-toluenethiol and 1-dodecanethiol disappearance. The column temperatures ranged from 200–225°. The response factor between α-toluenethiol and diphenylmethane was 1.87 and that between 1-dodecanethiol and mesitylene was 1.54[12] (see Table VII). Usually, the sulfoxide was eluted from the column before the thiol and its internal standard.

In the catalysis studies with 2-hydroxypyridine reactions were conducted in mesitylene since the catalyst was not completely soluble under the above conditions. Mesitylene (5 ml.) was used and the total volume of each solution was 9.63 ml. The kinetic analyses of these solutions were performed on a 2-ft. silicone rubber column at 185°. Cetane (6.25 mmoles) was employed as the internal standard and the predetermined molar response factor for 1-dodecanethiol was 1.61 at 185°.

Acknowledgment.—The authors are indebted to the Esso Research and Engineering Company, especially the Process Research Division, for the privilege of publishing this work and to Dr. S. Bank, Professor H. C. Brown, and Professor W. von E. Doering for helpful discussions.

(11) T. J. Wallace and J. J. Mahon, *Nature*, **201**, 817 (1964), contains a detailed description of these techniques.

(12) For a detailed discussion on the significance of molar response factors, see A. E. Messner, D. M. Rosie, and P. A. Argabright, *Anal. Chem.*, **31**, 230 (1959).

Azomethine Chemistry. IV. Chemistry of Fused Thiazolidines[1,2]

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Several fused thiazolidines have been prepared by standard methods. Bromination, reduction, oxidation, and hydrolysis of these compounds have been studied. The n.m.r. spectra are rationalized in terms of the molecular geometry.

In connection with another study concerned with nucleophilic additions to azomethines,[4] the reaction of several β-aminoethylmercaptans with various keto acids were of interest. Reactions of this type are well known and have been shown to provide saturated thiazolo[2,3-*a*]isoindoles,[5] thiazolo[3,2-*a*]pyridines,[6] and thiazolo[2,1-*b*]pyrroles.[7] The present report concerns the preparation of several hexahydropyrrolo[2,1-*b*]-thiazoles[8] and a study of their chemical reactions and n.m.r. spectra.

When β-benzoylpropionic acid (**1**) was refluxed with 2-mercaptoethylamine in methanol, the fused thiazolidine (**2a**) was obtained in 60–65% yield. Azeotropic distillation of a benzene solution of **1** and 2-mercapto-2-methylpropylamine provided **2b**[4] in 50% yield. A similar reaction involving γ-benzoylbutyric acid and the

(1) Supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society.

(2) Part III of this series: R. G. Hiskey and R. C. Northrop, *J. Am. Chem. Soc.*, **87**, 1753 (1965).

(3) Abstracted in part from the Ph.D. Dissertation of S. J. Dominianni, University of North Carolina, Aug. 1964.

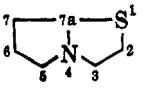
(4) R. G. Hiskey and J. M. Jung, *J. Am. Chem. Soc.*, **85**, 578 (1963).

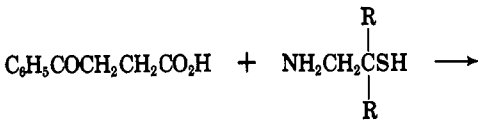
(5) G. L. Oliver, J. R. Dann, and J. W. Gates, *ibid.*, **80**, 702 (1958).

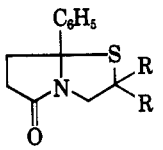
(6) D. Todd and S. Teick, *ibid.*, **75**, 1895 (1953).

(7) H. H. Wasserman, F. M. Precopio, and T. C. Liv, *ibid.*, **74**, 4093 (1952).

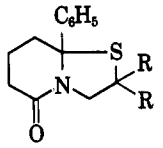
(8) The numbering system for hexahydropyrrolo[2,1-*b*]thiazoles follows.







2a, R=H
b, R=CH_3



3a, R=H
b, R=CH_3

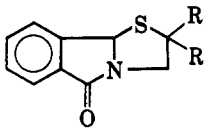
same mercaptoamines provided **3a** and **3b** in approximately the same yields.

Hydrolysis of **2a** with *p*-toluenesulfonic acid in refluxing methanol provided 2-mercaptoethylammonium *p*-toluenesulfonate; hydrolysis of **2a** with refluxing aqueous hydrochloric acid produced **1**. Desulfurization of **2a**, followed by lithium aluminum hydride reduction of the product, yielded 1-ethyl-2-phenylpyrrolidine, identical with an authentic sample.

Although **2a** and **b** and **3a** and **b** reacted readily with a solution of bromine in acetic acid, only in the case of **3a** could a crystalline monobromo derivative be isolated. Attempts to dehydrobrominate the substance with triethylamine, sodium acetate, or γ-collidine were unsuccessful and provided only recovered starting material.

Oxidation of **2a** was attempted using hydrogen peroxide in acetone and chromium trioxide in aqueous acetic acid but provided only unchanged thiazolidine. Treatment of **3a** with sodium metaperiodate provided the sulfoxide in 65% yield.

The n.m.r. spectra of the thiazolidines reflect the "bent" geometry of the fused ring system. For example the spectrum of **2a** consists of a multiplet, corresponding to the hydrogens of the 7a-phenyl group, at τ 2.7; a complex multiplet at 5.65 (one proton); and a series of overlapping multiplets from 6.8–8.0 (seven protons). The identities of the various proton groupings in **2a** could be established by comparison with the spectra of **2b** and the tetrahydrothiazolo[2,3-*a*]isoindoles, **4a** and **4b**. For example, replacement of the C-2 hydrogens of **2a** by methyl



4a, R=CH_3
b, R=H

groups (**2b**) caused the multiplet at τ 5.65 and part of the multiplet at τ 6.8 to collapse to an AB quartet centered at τ 5.8 and 7.2 (two protons, J_{AB} = 11 c.p.s.). The AB quartet may therefore be assigned to the methylene protons on C-3. The remaining portion of the multiplet (τ 7.35 to 7.60) results from the protons at C-6 and C-7. The chemical shifts of protons at C-6, C-7, and C-7a could be determined by inspection of the spectra of **4a** and **4b**.

The field separation (τ 0.27) of the methyl signals in the spectrum of **4a** is somewhat larger than expected. Normally[9] the difference in chemical shifts between geminal methyl groups is less than τ 0.15. If it is assumed that the normal chemical shift of the C-2 methyl groups is nearer τ 8.69 than 8.42, the observed field separation can be rationalized on the basis of the geometry of the molecule. Molecular models indicate one of the C-2 methyls is held directly over the portion of the aromatic ring current which is parallel to the main field; this methyl would be slightly deshielded and would undergo the observed paramagnetic shift.

Experimental[10]

2,2-Dimethyl-5-oxo-tetrahydrothiazolo[2,3-*a*]isoindole (4a).—A solution of 1.50 g. (0.010 mole) of phthalaldehydic acid and 1.41 g. (0.010 mole) of 2-mercapto-2-methylpropylamine hydrochloride[11] in 80 ml. of benzene and 10 ml. of methanol was treated with 1.40 ml. (0.010 mole) of triethylamine and boiled vigorously until solid began to appear. The mixture was allowed to cool by stirring under a blanket of dry nitrogen. After the addition of 0.62 ml. (0.010 mole) of thionyl chloride, the mixture was stirred under nitrogen at ambient temperature for 12 hr., diluted with 50 ml. of ether, and filtered. The filtrate was washed with water, dried (magnesium sulfate), and filtered through a short column of alumina. Removal of the solvent *in vacuo* afforded an oil which was extracted with several portions of boiling cyclohexane. Concentration of the cyclohexane extracts afforded an oily solid which was recrystallized several times from *n*-hexane to provide 0.73 g. (33%) of white needles: m.p. 82–83°; n.m.r. spectrum, τ 2.40 m (5), 3.92 s (1), 5.76, 6.76 q (2) (J = 12 c.p.s.), 8.42 s (3), and 8.69 s (3); ν_{CO}^{KBr} 1710 cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{13}NOS$: C, 65.72; H, 5.98; N, 6.39; S, 14.62. Found: C, 65.55; H, 6.16; N, 6.14; S, 14.38.

5-Oxotetrahydrothiazolo[2,3-*a*]isoindole (4b).—The method described above (chromatography not required) afforded a 63% yield of white needles from *n*-hexane: m.p. 98–100.5° (lit.[5] m.p. 97–100°); n.m.r. spectrum, τ 2.54 m (4), 4.22 s (1), 5.50 m (1), and 6.75 m (3); ν_{CO}^{KBr} 1700 cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74; N, 7.32; S, 16.77. Found: C, 62.79; H, 4.75; N, 7.44; S, 16.56.

7a-Phenyl-5-oxotetrahydropyrrolo[2.1-*b*]thiazole (2a).—A solution of 1.78 g. (0.010 mole) of β-benzoylpropionic acid, 1.10 g. (0.010 mole) of 2-mercaptoethylamine hydrochloride, and 1.40 ml. (0.010 mole) of triethylamine in 100 ml. of methanol was refluxed 12 hr., cooled, and evaporated *in vacuo*. The residue was extracted with several portions of boiling *n*-hexane. The combined hexane extracts were concentrated to the cloud point, decanted from a small amount of yellow oil, and chilled. Filtration and further concentration of the mother liquor afforded several crops of white solid which were combined and recrystallized from *n*-hexane to yield 1.37 g. (63%) of mica-like plates: m.p. 76–78°; n.m.r. spectrum, τ 2.65 m (5), 5.65 m (1), and 6.65–8.0 m (7); ν_{CO}^{KBr} 1710 cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{13}NOS$: C, 65.72; H, 5.98; N, 6.39; S, 14.62. Found: C, 66.09; H, 6.10; N, 6.41; S, 14.35.

8a-Phenyl-5-oxohexahydrothiazolo[3,2-*a*]pyridine (3a).—A solution of 1.92 g. (0.010 mole) of δ-benzoylbutyric acid, 1.10 g. (0.010 mole) of 2-mercaptoethylamine hydrochloride, and 1.40 ml. (0.010 mole) of triethylamine in 100 ml. of 2-propanol was refluxed 12 hr., cooled, and evaporated *in vacuo*. The residue was dissolved in ether and the ether solution was washed with water, 5% sodium bicarbonate, and water and dried (magnesium sulfate). Removal of the solvent and recrystallization of the

(9) Some pertinent examples are cited in (a) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Vol. II, Palo Alto, Calif., no. 421, 513, and 677; (b) O. L. Chapman, T. A. Rettig, A. A. Griswold, A. I. Dutton, and P. Fitton, *Tetrahedron Letters*, **No.**, **29**, 2049 (1963).

(10) Melting points and boiling points are uncorrected. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill. N.m.r. spectra were obtained on a Varian Associates A-60 using deuteriochloroform solutions containing tetramethylsilane. The following multiplicity notations are used: s, singlet; d, doublet; q, quartet; and m, multiplet; area ratios of peaks are given in parentheses.

(11) F. I. Carroll, J. D. White, and M. E. Wall, *J. Org. Chem.*, **28**, 1236 (1963).

residue from *n*-hexane afforded 2.10 g. (48.1%) of thick needles, m.p. 104–106°. An analytical sample (from *n*-hexane) had m.p. 109–110°; n.m.r. spectrum, τ 2.68 m (5), 5.65 m (1), 6.38 m (1), and 6.80–8.82 m (8); ν_{CO}^{KBr} 1640 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48; N, 6.00; S, 13.74. Found: C, 66.76; H, 6.60; N, 6.30; S, 14.34, 14.00.

2,2-Dimethyl-7a-phenyl-5-oxotetrahydropyrrolo[2,1-*b*]thiazole (2b).—A solution of 3.56 g. (0.020 mole) of β-benzoylpropionic acid, 2.82 g. (0.020 mole) of 2-mercapto-2-methylpropylamine hydrochloride, and 2.80 ml. (0.020 mole) of triethylamine in 220 ml. of benzene and 30 ml. of methanol was refluxed 2 hr. and then distilled until the distillate was homogeneous (100 ml. collected). The mixture was refluxed an additional 12 hr., cooled, and filtered. The filtrate was washed with water, 2% bicarbonate, and water and dried (magnesium sulfate). Removal of the solvent afforded an oil which was taken up in carbon tetrachloride and chromatographed over a 20 × 120 mm. column of Florisil. Rapid elution with 600 ml. of chloroform and evaporation of the eluate afforded 1.09 g. (20.3%) of thick oil, homogeneous on t.l.c. A sample was purified for analysis by sublimation at 90–95° (0.75 mm.) and appeared as a thick colorless oil which was dried *in vacuo* over phosphorus pentoxide: n.m.r. spectrum, τ 2.68 m (5), 5.80, 7.20 q (2) (J = 12 c.p.s.), 7.45 m (4), 8.61 s (3), and 8.63 s (3); ν_{CO}^{KBr} 1715 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66; S, 12.96. Found: C, 67.97; H, 6.87; N, 5.64; S, 12.50.

2,2-Dimethyl-8a-phenyl-5-oxohexahydrothiazolo[3,2-a]pyridine (3b).—The procedure used was as described above for **2b**. The initial product, 2.82 g. (78.4%) of pale yellow oil, was not chromatographed but directly sublimed at 90–95° (0.55 mm.) to afford the analytical sample as a thick colorless oil: n.m.r. spectrum, τ 2.75 m (5), 5.29, 6.96 q (2) (J = 12 c.p.s.), 7.59 m (6), 8.60 s (3), and 8.71 s (3); ν_{CO}^{KBr} 1650 cm.$^{-1}$.

Anal. Calcd. $C_{15}H_{19}NOS$: C, 68.93; H, 7.33; N, 5.36; S, 12.27. Found: C, 68.34, 68.58; H, 7.46, 7.47; N, 5.52; S, 12.00.

2-Mercaptoethylammonium *p*-Toluenesulfonate. A. From Cleavage of 2a.—A solution of 1.1 g. (5.0 mmoles) of **2a** and 0.95 g. (5.0 mmoles) of *p*-toluenesulfonic acid monohydrate in 50 ml. of methanol was refluxed 10 days, cooled, and evaporated. The brown residue was washed with benzene and ether to afford 1.05 g. (84%) of tan solid, m.p. 163–166°. Several recrystallizations from methanol–ether (charcoal) provided glittering white flakes, m.p. 165–167°.

Anal. Calcd. $C_9H_{15}NO_3S_2$: C, 43.35; H, 6.06; N, 5.62; S, 25.72. Found: C, 43.47; H, 6.18; N, 5.90; S, 26.02.

B. From 2-Mercaptoethylamine Hydrochloride.—A mixture of 0.11 g. (1.0 mmole) of 2-mercaptoethylammonium chloride, 0.14 ml. (1.0 mmole) of triethylamine, and 10 ml. of benzene was stirred at room temperature 10 min., diluted with 40 ml. of ether, and filtered into a solution of 0.19 g. (1.0 mmole) of *p*-toluenesulfonic acid monohydrate in methanol–benzene (5:15 v./v.). The solution was boiled to 10–15 ml., kept overnight, and filtered to yield a white solid. Recrystallization from methanol–ether afforded white needles, m.p. 165–166°, identical in all respects with the sample prepared in A.

Hydrolysis of 2a.—A solution of 0.22 g. of **2a** in 10 ml. of tetrahydrofuran, 10 ml. of water, and 1.0 ml. of concentrated hydrochloric acid was refluxed overnight, concentrated to 10–12 ml. by boiling, and cooled. The initially precipitated oil solidified on seeding with β-benzoylpropionic acid. Recrystallization from hot water afforded needles, m.p. 115–116°, identical in all respects with an authentic sample of the acid.

1-Ethyl-2-phenylpyrrolidine. A. From 2a.—A solution of 2.19 g. (0.010 mole) of **3a** in a 300 ml. of ethanol was treated with 18–20 g. of Raney nickel W-2[12] and the mixture was refluxed 12 hr. The cooled mixture was filtered through asbestos; removal of the solvent from the filtrate afforded 1.88 g. (99.4%) of a clear colorless oil. Sodium fusion demonstrated the absence of sulfur. A solution of 1.18 g. of this product in 60 ml. of anhydrous ether was added dropwise over 20 min. to a well-stirred suspension of 4.73 g. of lithium aluminum hydride in 100 ml. of dry ether. The mixture was refluxed 1 hr. after the addition was complete, cooled, and decomposed with water and 20% sodium hydroxide. The ether layer was removed, dried (potassium carbonate), and distilled to afford 1.00 g. (91.7%) of pale tan oil, whose infrared spectrum had no bands in the carbonyl region. For characterization, a portion of the amine was converted to a **picrate** which crystallized as pale yellow plates, m.p. 154–155°, from ethanol.

Anal. Calcd. for $C_{18}H_{18}N_4O_7$: C, 53.73; H, 4.51; N, 13.93. Found: C, 53.50; H, 4.93; N, 13.73.

B. By Synthesis.—A mixture of 3.56 g. (0.020 mole) of β-benzoylpropionic acid, 13.6 g. of 30% aqueous ethylamine, and 5.1 g. of 95% formic acid was boiled to remove water and then heated at 195–200° for 2 hr. The mixture was then refluxed with 60 ml. of 1:1 hydrochloric acid, cooled, and extracted with ether. The ether extracts were washed with water, 2% bicarbonate, and water and dried (magnesium sulfate). Removal of the solvent and distillation of the residue afforded 1.13 g. (29.9%) of pale yellow oil, b.p. 74–76° (0.35 mm.). Reduction of this material with lithium aluminum hydride by the procedure described above provided 1.01 g. (95.6%) of amine, identical in all respects with that prepared in A. The **picrates** of the two samples were also identical.

Oxidation of 2a.—A solution of 0.44 g. (2.0 M. mole) of **2a** and 0.46 g. of sodium metaperiodate in 10 ml. of ethanol and 15 ml. of water was kept at room temperature 24 hr. and then extracted with chloroform. Removal of the solvent from the dried (magnesium sulfate) extracts afforded a pale yellow solid. After washing with small amounts of ether to remove unchanged **2a**, the product (0.40 g., 85%) melted at 141–143° dec. An analytical sample crystallized from methylene chloride–*n*-hexane as needles, m.p. 144.5–145.5° dec., ν^{KBr} 1055 cm.$^{-1}$ (=S$^+$—O$^-$).

Anal. Calcd. for $C_{12}H_{13}NO_2S$: C, 61.25; H, 5.57; N, 5.95; S, 13.63. Found: C, 61.23; H, 5.69; N, 6.19; S, 13.73.

Bromination of 3a.—A solution of 1.16 g. (5.0 mmoles) of **3a** in 25 ml. of chloroform was treated dropwise with a concentrated solution of bromine in acetic acid until the orange color persisted. Evolution of hydrogen bromide began immediately and was allowed to proceed 1 hr. The solution was washed with sodium bisulfite, dried (magnesium sulfate), and refluxed 10 hr. after the addition of 2 ml. of triethylamine. Removal of the solvent *in vacuo* and trituration of the residue with water afforded a pale yellow solid which was recrystallized from acetone–*n*-hexane (charcoal) to provide 0.75 g. (65%) of white blocks, m.p. 159–160° dec.

Anal. Calcd. for $C_{13}H_{14}BrNOS$: C, 50.01; H, 4.52; N, 4.49; S, 10.27; Br, 25.59. Found: C, 50.23; H, 4.40; N, 4.56; S, 10.02; Br, 25.65.

(12) R. Mozingo, "Organic Syntheses," Coll. Vol. III, E. C. Horning Ed., John Wiley and Sons, Inc., New York, N. Y., 1955, p. 181.