uct, m.p. 63–64°. Yield of crude product was 16.9 g., 41.9% of the theoretical yield.

Anal. Calcd. for $C_{16}H_{10}ON_2$: C, 68.94; H, 5.79; N, 16.08. Found: C, 69.11; H, 5.88; N, 16.24.

The reddish-orange salt of 5-ethoxyquinoxaline and methyl iodide was prepared by the procedure of Easley and Bahner,[7] m.p. 214–215° uncor. (with dec.).

Anal. Calcd. for $C_{11}H_{13}ION_2$: N, 8.85. Found: N, 8.60.

The scarlet salt with ethyl iodide was prepared in the same manner, m.p. 146–148° uncor. (with dec.).

Anal. Calcd. for $C_{12}H_{14}ION_2$: N, 8.50. Found: N, 8.22.

Acknowledgments.—The authors wish to thank Dr. E. Mosettig for use of his reduction apparatus and Miss Rita McCollum and Mr. T. S. Barker for microanalyses.

(7) W. K. Easley and C. T. Bahner, THIS JOURNAL, **72**, 3803 (1950).

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Ring Cleavage of 1-Benzenesulfonyl-2-benzylethylenimine with Hydrogen Bromide[1]

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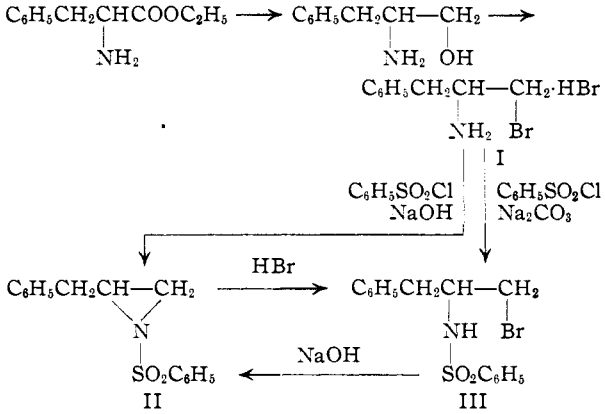
When 1-benzenesulfonyl-2-bromomethylethylenimine reacts with hydrobromic acid, ring cleavage occurs to form 1,3-dibromo-2-benzenesulfonamidopropane. In this process attack of the bromide ion occurs preferentially at the unsubstituted rather than at the substituted carbon of the three-membered ring.[2] We wish to record another example of this mode of cleavage in the production of 1-phenyl-2-benzenesulfonamido-3-bromopropane (III) from the action of hydrobromic acid on 1-benzenesulfonyl-2-benzylethylenimine (II). The



structure of the cleavage product was established by its identity with the product (III) obtained on treating 1-phenyl-2-amino-3-bromopropane hydrobromide (I) with benzenesulfonyl chloride and aqueous sodium carbonate. The ethylenimine compound (II) was prepared by treating the hydrobromide (I) with benzenesulfonyl chloride and aqueous alkali, or by treating 1-phenyl-2-benzenesulfonamido-3-propane (III) with alkali.

(1) Abstracted from a portion of the Thesis submitted by John C. Rockett to the Graduate School of Boston University in partial fulfillment of the requirements for the degree of Master of Arts.

(2) W. J. Gensler, THIS JOURNAL, **70**, 1843 (1948).

Experimental[3]

1-Phenyl-2-amino-3-bromopropane Hydrobromide (I).—*dl*-Phenylalanine ethyl ester was converted to *dl*-phenylalaninol, m.p. 67–68°, by reduction with lithium aluminum hydride.[4]

A sealed tube containing 1.0 g. (0.006 mole) of *dl*-phenylalaninol and 25 ml. of 48% hydrobromic acid was heated at 170–175° for five hours. The dark colored reaction mixture, in which some carbonized material was present, was diluted with 100 ml. of water and was decolorized with charcoal (Nuchar). The resulting water-white, strongly acid solution was taken to dryness under reduced pressure on the steam-bath. The dry residue after crystallization from absolute alcohol weighed 1.27 g. (65%) and melted at 173–176°. A second crystallization (from 3 ml. of absolute alcohol) afforded 0.97 g. (49%) of pure 1-phenyl-2-amino-3-bromopropane hydrobromide, m.p. 174–175°.

Anal. Calcd. for $C_9H_{13}NBr_2$: C, 36.8; H, 4.4. Found: C, 36.7; H, 4.4.

When the reaction was carried out at 100° instead of at 170°, the hydrobromide of *dl*-phenylalaninol was the only material isolated. This salt was prepared in a separate experiment by evaporating a mixture of 1.0 g. (0.0066 mole) of *dl*-phenylalaninol and 25 ml. of 48% hydrobromic acid under reduced pressure, and crystallizing the dry residual solids from ethyl alcohol. The hydrobromide obtained in this way (1.21 g. or 79%) melted at 148–149°, and showed no change in melting point after admixture with the material (m.p. 148–149°) obtained from the reaction at 100°.

Anal. Calcd. for $C_9H_{14}NOBr$: C, 46.5; H, 5.6. Found: C, 46.3; H, 5.3.

1-Benzenesulfonyl-2-benzylethylenimine (II) from 1-Phenyl-2-amino-3-bromopropane Hydrobromide (I).—To a vigorously stirred solution of 1.5 g. (0.0050 mole) of the hydrobromide (I) in 10 ml. of water was added 0.78 ml. (0.0060 mole) of benzenesulfonyl chloride followed immediately by a solution of 1.0 g. (0.0025 mole) of sodium hydroxide in 10 ml. of water. The mixture was stirred for 40 minutes at room temperature. The solids were collected by filtration, washed on the funnel with water and air-dried. The dry material (1.22 g. or 89%; m.p. 54–56°) was taken up in ether, the ether solution was washed with several portions of water, and was dried over sodium sulfate. On crystallizing the oil remaining after the ether solvent had been removed from ethyl alcohol, there was obtained 1.03 g. (75%) of 1-benzenesulfonyl-2-benzylethylenimine, m.p. 55–56°.

Anal. Calcd. for $C_{15}H_{15}NSO_2$: C, 65.9; H, 5.5. Found: C, 65.7; H, 5.6; ash, 0.3.

1-Benzenesulfonyl-2-benzylethylenimine (II) from 1-Phenyl-2-benzenesulfonamido-3-bromopropane (III).—A mixture of 0.5 g. (0.0014 mole) of compound III, 0.4 g. (0.010 mole) of sodium hydroxide and 10 ml. of water was shaken for 15 minutes. The crystalline solids (0.36 g. or 95%; m.p. 53–55°) were collected and crystallized from 5 ml. of ethyl alcohol. The product obtained weighed 0.31 g. (81%), and melted both before and after admixture with the 1-benzenesulfonyl-2-benzylethylenimine prepared as indicated above at 55–56°.

1-Phenyl-2-benzenesulfonamido-3-bromopropane (III) from 1-Benzenesulfonyl-2-benzylethylenimine (II).—A mixture of 10 ml. of 48% hydrobromic acid and 0.40 g. (0.00146 mole) of ethylenimine II was heated on the steam-bath for one hour. Twenty milliliters of water was added, and the cold mixture was thoroughly extracted with ether. The ether extract, after washing with water, was dried over anhydrous sodium sulfate. Removal of the solvent left a residual oil (0.44 g.) which, after crystallization from ethyl alcohol, furnished 0.34 g. (65%) of white crystalline 1-phenyl-2-benzenesulfonamido-3-bromopropane, m.p. 22–23°.

Anal. Calcd. for $C_{15}H_{16}NSO_2Br$: C, 50.8; H, 4.5. Found: C, 50.6; H, 4.6.

The mixed melting point with the same material prepared as described below was 22–23°.

(3) Melting points are uncorrected. The elementary analyses were carried out by Carol K. Fitz, 115 Lexington Avenue, Needham Heights 94, Mass.

(4) P. Karrer, P. Portmann and M. Suter, *Helv. Chim. Acta*, **31**, 1617 (1948); M. C. Rebstock, *et al.*, THIS JOURNAL, **73**, 3666 (1951).

1-Phenyl-2-benzenesulfonamido-3-bromopropane (III) from 1-Phenyl-2-amino-3-bromopropane Hydrobromide (I).—To a vigorously stirred solution of 1.5 g. (0.0051 mole) of compound I in 10 ml. of water was added 0.78 ml. (0.0060 mole) of benzenesulfonyl chloride followed immediately by a solution of 0.83 g. (0.010 mole) of sodium carbonate in 10 ml. of water. After the reaction mixture had been stirred for one hour at room temperature, the oily product was extracted with ether. The ether solution was washed thoroughly with water, and dried over magnesium sulfate. Crystallization of the oil obtained on removal of the ether solvent from ethyl alcohol afforded 1.03 g. (57%) of 1-benzene-2-benzenesulfonamido-3-bromopropane, m.p. 22–23°.

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Some Alkyl and Heterocyclic Sulfides and Sulfones

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In connection with some studies on the pharmacological activity of certain sulfur-containing compounds, a series of alkyl and heterocyclic sulfides and sulfones has been prepared. The germicidal properties of some sulfides[1] have been demonstrated. The antistreptococcal activity of 4,4′-diaminodiphenyl sulfone,[2] the antitubercular effect of this and similar compounds,[3–5] and the indicated antimalarial activity[6] of its derivatives suggested the preparation of some quinolyl or other heterocyclic sulfones.

Of interest was the effect of incorporating a fat-soluble group into the molecule with a view toward increased absorption of the drug by the animal body.[7] Also, introduction of the physiologically active dialkylaminoalkyl grouping[8] was considered worthy of investigation.

The unsymmetrical sulfides were prepared by treatment of the sodium mercaptide with the proper organic halide. The sodium mercaptide was best prepared by addition of the mercaptan to a sodium ethoxide–ethanol solution. The sulfones were prepared from the corresponding sulfides by treatment with 30% hydrogen peroxide, with glacial acetic acid as a solvent. Additional derivatives of certain of these compounds have been prepared. Physical constants and analytical data of these sulfides and their derivatives are given in Tables I and II.

Of interest is the observation that quinine is oxidized in animals to 2-hydroxyquinine, thus the 2-substituted quinoline nucleus might be rendered more stable in the animal body.[9]

Results of pharmacological tests of these compounds will be reported elsewhere.

(1) N. E. Foss, F. Dunning and G. L. Jenkins, THIS JOURNAL, **56**, 1978 (1934).

(2) G. A. H. Buttle, D. Stephenson, S. Smith, T. Dewing and G. E. Foster, *Lancet*, **1**, 1331 (1937).

(3) N. Rist, F. Block and V. Hamon, *Ann. Inst. Pasteur*, **64**, 203 (1940).

(4) G. W. Raiziss, *Science*, **98**, 350 (1943).

(5) L. L. Bambas, THIS JOURNAL, **67**, 671 (1945).

(6) H. Heymann and L. F. Fieser, *ibid.*, **67**, 1979 (1945).

(7) H. Gilman and S. P. Massie, *ibid.*, **71**, 744 (1949).

(8) (a) H. Gilman and R. M. Pickens, *ibid.*, **47**, 245 (1925); (b) H. Gilman, L. C. Heckert and R. McCracken, *ibid.*, **50**, 437 (1928); (c) H. Gilman and M. A. Plunkett, *ibid.*, **71**, 3667 (1949).

(9) (a) F. E. Kelsey, E. M. K. Geiling, F. K. Oldham and E. H. Dearborn, *J. Pharmacol.*, **80**, 391 (1944); (b) J. F. Mead and J. B. Koepfli, *J. Biol. Chem.*, **154**, 507 (1944).

Experimental

Preparation of the Sulfides.—The sodium mercaptide was prepared by reaction of the theoretical amount of sodium with an excess of absolute ethanol; to the resulting sodium ethoxide solution was added an equivalent amount of mercaptan. Subsequently, the resulting mercaptide was refluxed with an organic halide and the sulfide thus obtained was extracted with ether. Following drying of the ethereal solution over sodium sulfate and removal of the solvent, purification of the sulfide was effected by vacuum distillation, recrystallization from an appropriate solvent, or in some cases both. Recrystallization solvents for the solid sulfides are given in Table I. In the preparation of the heterocyclic alkyl sulfides, the heterocyclic chlorides were employed; and with the dodecyl sulfides, the dodecyl group was introduced *via* the mercaptan. The dialkylaminoalkyl chlorides were prepared in accordance with a previously reported procedure.[10] The preparation of two typical sulfides follows. All melting points in Tables I and II are uncorrected.

2-[*n*-Octadecylmercapto]-quinoline.—To 100 ml. of absolute ethanol was added 0.7 g. (0.03 g. atom) of sodium. After completion of the reaction, 8.6 g. (0.03 mole) of *n*-octadecylmercaptan was added dropwise. After 30 minutes, 5.0 g. (0.03 mole) of 2-chloroquinoline was added dropwise and the resulting solution refluxed for 10 hours. The solvent was then removed by distillation and the residue extracted with an ether–dilute sodium hydroxide mixture. Following separation of the ethereal solution and drying over sodium sulfate, the ether was distilled off. Vacuum distillation of the residue gave a yellow liquid, b.p. 234–240° (0.2 mm.) which solidified on standing. Recrystallization from petroleum ether (b.p. 60–70°) gave 10.7 g. (85%) of white crystals, melting at 53–54°.

Preparation of *n*-Dodecyl γ-Hydroxypropyl Sulfide.—Sodium metal, 34.5 g. (1.5 g. atoms), was cut into small pieces and added slowly to 600 ml. of absolute ethanol until all of the sodium had dissolved (1.5 hours). To this solution was added 303.6 g. (1.5 moles) of *n*-dodecyl mercaptan; then 146 g. (1.54 moles) of trimethylene chlorohydrin was added over a period of one hour to the refluxing sodium mercaptide solution. The reaction mixture was refluxed for 12 hours and then filtered to remove the white precipitate formed. The solvent was distilled from the filtrate to give 413 g. of a solid residue. This solid was then vacuum distilled; there was thus obtained 336.8 g. (86%) of distillate, b.p. 157–159° (0.5 mm.). The product solidified on standing yielding a white solid, m.p. 34–35°.

Preparation of the Sulfones.—The sulfide was dissolved in a minimum amount of glacial acetic acid. An excess of 30% hydrogen peroxide was slowly added and the resulting solution refluxed for 1–4 hours. The sulfone which separated on cooling was filtered and recrystallized from an appropriate solvent (see Table II).

Carbonation of γ-*n*-Dodecylmercaptopropyllithium.—γ-*n*-Dodecylmercaptopropyl chloride (22.4 g., 0.08 mole) was added dropwise, in a dry nitrogen atmosphere, to a vigorously stirred mixture of 1.2 g. (0.17 g. atom) of lithium in 100 ml. of anhydrous ether. This addition required 30 minutes, during which period the ether was gently refluxing. The milky-white mixture was then stirred for 4 hours at room temperature. The mixture was filtered, in a nitrogen atmosphere, through glass wool into a dropping funnel and then added to a Dry Ice–ether slurry,[11] with the tip of the dropping funnel immersed in the slurry. Following return to room temperature, the carbonation mixture was carefully neutralized with dilute hydrochloric acid. The ethereal solution was separated and extracted twice with 5% sodium hydroxide. Removal of the solvent by distillation gave 8.8 g. (43%) of impure di-γ-*n*-dodecylmercaptopropyl ketone, melting at 50–57°. Three recrystallizations from absolute ethanol raised the m.p. to 67–68°. The pure product weighed 6.5 g. (32%). The alkali extract was acidified and shaken with dry ether. From the ethereal solution was obtained 6.2 g. (27%) of γ-*n*-dodecylmercaptobutanoic acid, melting at 51–54°. Two recrystallizations from petroleum ether (b.p. 28–40°) raised the m.p. to 57.5–58.5°. The pure product weighed 4.7 g. (20%).

In another experiment the corresponding Grignard reagent was prepared according to the entrainment method[12]

(10) H. Gilman and D. A. Shirley, THIS JOURNAL, **66**, 888 (1944).

(11) H. Gilman and J. A. Beel, *ibid.*, **71**, 2328 (1949).

(12) M. V. Grignard, *Compt. rend.*, **198**, 625 (1934).