pared from Va or V and one equivalent of sodium hydroxide. It was recrystallized by dissolving it in water and adding several volumes of alcohol.

Anal. Calcd. for $C_4H_5N_2O_6SNa$: C, 20.69; H, 2.17; N, 12.07; S, 13.81; neut. equiv., 232. Found (salt from V): C, 20.46; H, 2.13; N, 11.86; S, 13.80. Found (salt from Va): neut. equiv., 232.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

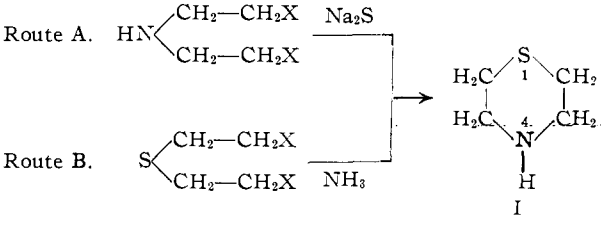
1,4-Thiazans. I. C-Alkyl Thiomorpholines

BY BERNARD IDSON[1] AND PAUL E. SPOERRI

RECEIVED NOVEMBER 12, 1953

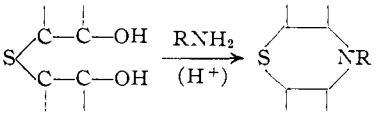
The nine possible C-monomethyl substituted thiomorpholines were prepared to study the properties of the 1,4-thiazan system. Cyclizations of either substituted bis-haloethyl sulfides or amines were the methods of choice.

Carbon substituted derivatives of the 1,4-tetrahydrothiazine ring system (1) (thiomorpholine) have rarely been studied. N-Substituted derivatives have been prepared,[2] but the only carbon-substituted compound which has been reported is 2,6-dimethylthiomorpholine.[3] This paper is concerned with the synthesis of all nine possible C-methyl-1,4-thiazans, prepared *via* the reaction of bis-2-haloethylamines with sodium sulfide (A) or bis-2-haloethyl sulfides with ammonia (B).

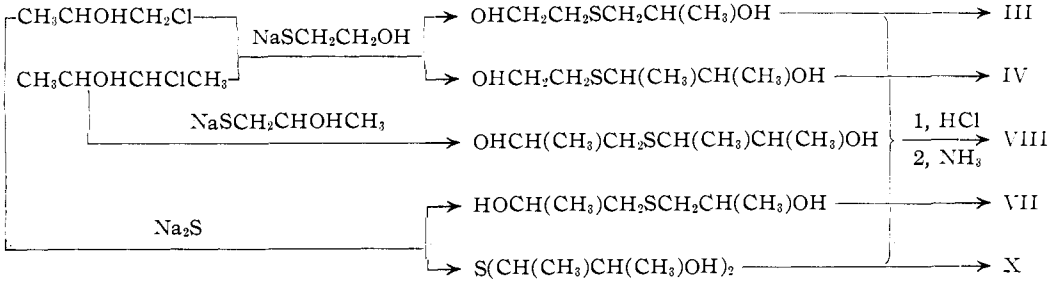


The relatively unstable nature of the nitrogen mustards usually rendered route B more desirable, unless rearrangements necessitated other methods. Rearrangements of both β-haloiospropyl sulfides[4] and 1,2-aminochloroalkanes[5] to the normal structures have been demonstrated *via* cyclic sulfonium and imonium intermediates.

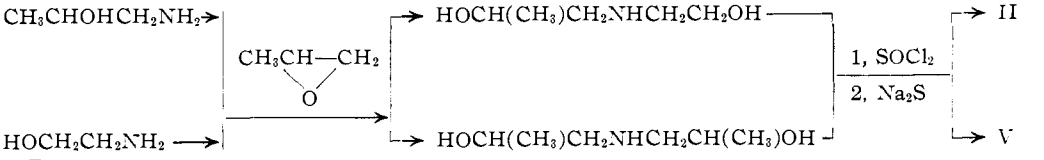
The vesicant nature of the haloethyl sulfides (mustard gases) prompted an attempt to bypass them *via* the reaction of the precursor hydroxy sulfide with amines. Small yields were obtained. Syntheses with aliphatic amines were less successful than with the less basic aromatic amines.



Reaction of C-methyl-substituted bis-(2-haloethyl) sulfides with ammonia (route B) was utilized to prepare the 3-methyl-(III), 2,3-dimethyl-(IV), 3,5-dimethyl-(VII), 2,3,5-trimethyl-(VIII) and 2,3,5,6-tetramethylthiomorpholines (X). Condensation of *vic*-chlorohydrins with 1,2-hydroxymercaptans served as the starting point for III, IV and VIII, while reaction of the chlorohydrins with sodium sulfide yielded the bis-(2-hydroxyethyl) sulfides necessary to reach VII and X.



The 2-methyl (II) and 2,6-dimethyl (V) isomers resulted from route A. The required amino diols were prepared from the addition of 1,2-aminoalcohols to propylene oxide.



(1) An abstract of a portion of a thesis submitted by Bernard Idson to the Polytechnic Institute of Brooklyn, 1952, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

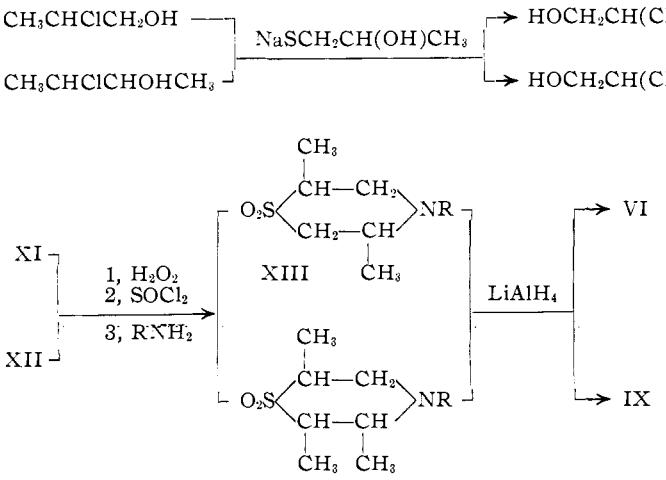
(2) H. T. Clark, *J. Chem. Soc.*, **101**, 1583 (1912); O. B. Helfrich and E. E. Reid, THIS JOURNAL, **42**, 1208 (1920); R. Robinson and F. W. Kay, British Patent 133,108 (June 26, 1918); W. E. Lawson and E. E. Reid, THIS JOURNAL, **47**, 2821 (1925); E. Fromm and B. Ungar, *Ber.*, **56B**, 2286 (1923); V. V. Korshak and Yu A. Strepikheev, *J. Gen. Chem.* (*U.S.S.R.*), **14**, 312 (1944); *C. A.*, **39**, 3790 (1945); A. H. Ford-Moore, A. G. Lidstone and W. A. Waters, *J. Chem. Soc.*, 819 (1946); W. F. Hart and J. B. Niederl, THIS JOURNAL, **66**, 1610 (1944); **68**, 714 (1946); *J. Org. Chem.*, **14**, 579 (1949).

(3) D. Harman and W. E. Vaughan, THIS JOURNAL, **72**, 631 (1950).

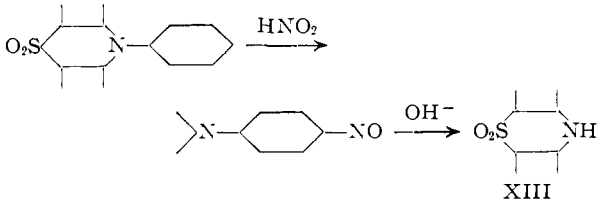
(4) R. C. Fuson, C. C. Price and D. M. Burness, *J. Org. Chem.*, **11**, 475 (1946).

(5) J. F. Kerwin, G. E. Ullyot, R. C. Fuson and C. L. Zirkle, THIS JOURNAL, **69**, 2961 (1947).

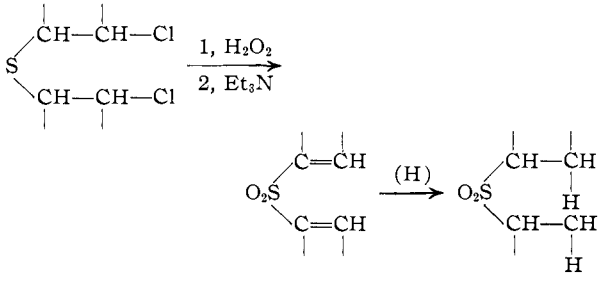
Synthesis of 2,5-dimethyl-(VI) and 2,3,6-trimethylthiomorpholine (IX) could not be accomplished *via* the usual sulfide or amine route due to rearrangements. However, conversion of the sulfide to the sulfone makes unavailable the electron pair necessary for rearrangement, preventing isomerization and hence rearrangement. The unsymmetrical 2,5-dimethylthiomorpholine was prepared by oxidation of 2-hydroxy-*n*-propyl 2′-hydroxyisopropyl sulfide (XI) to the sulfone, and final reduction of 2,5-dimethyl-1,4-thiazan-1,1-dioxide (XIII) with lithium aluminum hydride to the parent thiomorpholine. The 2,3,6-trimethyl compound resulted from similar treatment of 2-hydroxy-*n*-propyl 2′-hydroxy-*s*-butyl sulfide (XII).



An alternate approach to the parent cyclic sulfones (XIII) rested in nitrosation of the phenyl derivative and alkaline hydrolysis.



The structures of doubtful chloroethyl sulfides were proved by conversion to the sulfone, dehydrochlorination and catalytic hydrogenation to known alkyl sulfones.[4]



Experimental

N-2-Chloroethyl-1-amino-2-chloropropane.—N-2-Hydroxyethyl-1-amino-2-propanol[6] (30 g., 0.25 mole) was dissolved in 30 ml. of benzene and added dropwise with mechanical stirring to 64 g. of thionyl chloride dissolved in 65 ml. of benzene. After the addition of 25 g. of the diol, the mixture gelled. The remainder of the diol was added with vigorous stirring. The mixture was refluxed gently for two hours. Water was added (100 ml.) and the whole was mechanically shaken for one hour. The mixture was made strongly alkaline with sodium hydroxide (40%), saturated with sodium chloride and extracted with benzene. The combined benzene extracts were washed with water and dried over sodium sulfate. The solvent was evaporated *in vacuo* and the residue vacuum distilled. A colorless mobile liquid was obtained, b.p. 78–81° (8 mm.), yield 25 g. (64%).

Anal. Calcd. for $C_5H_{11}Cl_2N$: Cl, 45.51. Found: Cl, 45.32.

After standing at room temperature for seven days fine white needles precipitated. Analysis showed these to be quaternary ammonium salts with the same empirical formula as the parent amine.

2-Methyl-1,4-thiazan (II).—N-2-Chloroethyl-1-amino-2-chloropropane (15.6 g., 0.1 mole) was treated with 12.2 g. (0.052 mole) of sodium sulfide nonahydrate dissolved in 100 ml. of 95% ethanol. After one hour reflux the salt was filtered and the filtrate evaporated. The light yellow solution darkened perceptibly at this point. Vacuum distillation of the residue yielded a dark oil, together with some decomposition. Fractional redistillation resulted in 2.2 g. of a colorless material, b.p. 161° (760 mm.), yield 20%.

Anal. Calcd. for $C_5H_{11}NS$: N, 13.19. Found: N, 13.24.

The *p*-toluenesulfonamide derivative melted at 106–109°.

Anal. Calcd. for $C_{12}H_{17}NO_2S_2$: N, 5.16. Found: N, 5.19.

2-Hydroxyethyl-2-hydroxyisopropyl Sulfone.—2-Hydroxyethyl 2-hydroxyisopropyl sulfide[7] (27.2 g., 0.2 mole), dissolved in 60 ml. of glacial acetic acid was cautiously treated with 25 ml. of hydrogen peroxide (30%). The vigorous initial reaction was completed by one hour reflux. Volatile materials were removed on a steam-bath under reduced pressure. Water (50 ml.) was added to the residue which was then distilled under reduced pressure. The distillation process was repeated with 50 ml. of ethanol. After 3 weeks in a vacuum desiccator the residual sirup solidified. The solid was freely soluble in water, ethanol and acetone and insoluble in chloroform and ethyl acetate. It was crystallized by boiling with ethyl acetate and the addition of acetone to the hot suspension until the solid just dissolved. Crystallization of a hygroscopic sulfone occurred on storing this solution in a refrigerator for five days, m.p. 59–63°, yield 19 g. (57%).

Anal. Calcd. for $C_5H_{12}O_4S$: C, 35.7; H, 7.1. Found: C, 35.4; H, 7.2.

2-Chloroethyl 2-Chloroisopropyl Sulfone.—2-Hydroxyethyl 2-hydroxyisopropyl sulfone (4 g., 0.03 mole) was treated with concentrated hydrochloric acid (40 g.). The heavy oil which settled to the bottom was separated, dissolved in chloroform and washed with water. The chloroform was dried over sodium sulfate and was distilled under reduced pressure. After four weeks in a vacuum desiccator no crystallization occurred. The oil was redistilled, b.p. 137–142° (4 mm.), yield 4.7 g. (77%).

Anal. Calcd. for $C_5H_{10}Cl_2O_2S$: Cl, 34.6. Found: Cl, 34.4.

N-Phenyl-2-methyltetrahydrothiazine 1,1-Dioxide Hydrochloride.—2-Chloroethyl 2-chloroisopropyl sulfone (5.0 g., 0.025 mole) was added to redistilled aniline (2.1 g., 0.022 mole) which was dissolved in 25 ml. of ethanol containing sodium carbonate (2 g., 0.02 mole). The mixture was heated on a steam-bath for three hours, cooled, diluted with water and rendered strongly alkaline with sodium hydroxide. The excess aniline was removed by steam distilla-

(6) D. L. Cottle, A. E. Jeltsch, T. H. Stoudt and D. R. Walters, *J. Org. Chem.*, **11**, 286 (1946).

(7) A. Hamilton, R. C. G. Moggridge and F. N. Woodward, *J. Chem. Soc.*, 47 (1948).

tion. The organic residue was heated to boiling with dilute (6 *N*) hydrochloric acid. Cooling in an ice–salt-bath caused separation of light tan crystals, m.p. 129–132° (from methanol), yield 4.5 g. (76%).

Anal. Calcd. for $C_{11}H_{15}NO_2S$: N, 6.2. Found: N, 6.4.

2-Methyltetrahydrothiazine 1,1-Dioxide.—4-Phenyl-2-methyltetrahydrothiazine 1,1-dioxide (22.5 g., 0.1 mole) and concentrated hydrochloric acid (125 ml.) were treated with crushed ice until the temperature fell to 0°. A solution of sodium nitrite (6.9 g., 0.1 mole) in water (25 ml.) was added with hand stirring, and the temperature kept below 5°. After 30 minutes, the brown nitroso-hydrochloride was filtered off. The moist product was added to 85 ml. of 2 *N* ammonium hydroxide, the mixture warmed to 35°, and the free base was filtered off. The nitroso compound was mixed with water (100 ml.); 10% aqueous sodium hydroxide (50 ml.) was added, and the mixture was heated under reflux for two hours. After cooling, the mixture was acidified to congo red with dilute hydrochloric acid (6 *N*). The quinone oxime was filtered off and the filtrate was extracted once with ether. The ether extract was discarded. The aqueous portion was decolorized with activated charcoal, made alkaline with sodium carbonate and was evaporated to dryness. The residue was bleached several times with ethanol and the latter was evaporated. The residue was fractionated *in vacuo*. The portion boiling at 167° (10 mm.) was collected for analysis. No crystallization occurred after four weeks storage in the refrigerator.

Anal. Calcd. for $C_5H_{11}NO_2S$: N, 9.4. Found: N, 9.1.

The hydrochloride was prepared by adding dry hydrogen chloride to a benzene solution of the base, m.p. 301° dec.

Anal. Calcd. for $C_5H_{12}ClNO_2S$: Cl, 19.1. Found: Cl, 19.0.

2-Methyl-1,4-thiazane (II).—2-Methyl-1,4-tetrahydrothiazine 1,1-dioxide (3 g., 0.02 mole), dissolved in 20 ml. of absolute di-*n*-butyl ether was added slowly, with constant stirring, to 30 g. of lithium aluminum hydride, dissolved in 100 ml. of absolute di-*n*-butyl ether. After the addition was complete, the mixture was gently refluxed for six hours. The excess lithium aluminum hydride was decomposed by the addition of ice-water, and the solution was acidified (litmus paper) by the addition of dilute sulfuric acid. The ether layer was separated and the aqueous phase was extracted twice with 25-ml. portions of diethyl ether. The combined ether extracts were washed with 25 ml. of 1 *N* sodium carbonate, dried over magnesium sulfate and distilled to afford 0.94 g. (41%) of 2-methylthiomorpholine boiling at 163° (760 mm.). The *p*-toluenesulfonamide melted at 107°. Mixed melting point with the 2-methyl-1,4-thiazane obtained from N-2-chloroethyl-1-amino-2-chloropropane showed no depression.

2-Hydroxyethyl 2-Hydroxy-*n*-propyl Sulfide.—To 1 mole of sodium ethoxide, prepared from 300 ml. of absolute ethanol and 23 g. of sodium, was added 78 g. (1 mole) of mercaptoethanol. 1-Chloro-2-hydroxypropane (93 g., 0.98 mole) was added dropwise. Too rapid addition results in boiling of the ethanol. After completion of the addition the reaction mixture was refluxed for one-half hour. After cooling, the sodium chloride was filtered off, the filtrate was concentrated *in vacuo* and finally vacuum distilled, b.p. 147–151° (6 mm.).

Anal. Calcd. for $C_5H_{12}O_2S$: S, 23.54. Found: S, 23.42.

The bis-*p*-nitrobenzoate derivative melted at 82–86°.

Anal. Calcd. for $C_{19}H_{18}N_2O_8S$: C, 52.8; H, 3.7. Found: C, 52.4; H, 3.4.

2-Chloroethyl 2-Chloro-*n*-propyl Sulfide.—2-Hydroxy ethyl 2-hydroxy-*n*-propyl sulfide (27.2 g., 0.2 mole), contained in a three-neck flask equipped with a mechanical stirrer, separatory funnel and a water-cooled condenser, was placed in a water-bath kept between 80 and 90°. Concentrated hydrochloric acid (250 ml.) was added dropwise with constant stirring. After the addition of the acid, stirring was continued for another hour and a light colored oil separated. The reaction mixture was cooled and transferred to a separatory funnel. Chloroform was added and the upper layer was discarded. The chloroform solution was washed twice with one-half volumes of water, dried over sodium sulfate, and vacuum distilled, b.p. 110–118° (10 mm.).

Anal. Calcd. for $C_5H_{10}Cl_2S$: Cl, 41.04. Found: Cl, 41.17.

3-Methyl-1,4-thiazan (III).—2-Chloroethyl 2-chloro-*n*-propyl sulfide (17.3 g., 0.1 mole) and 60 ml. of a 9% ethanol solution of ammonia (5.4 g., 0.4 mole) were placed in a Carius bomb tube and heated at 60° for eight hours. The tube was cooled and carefully opened. The reaction mixture was transferred to a beaker with the aid of water which dissolved the ammonium chloride precipitate. The excess ammonia was expelled on a steam-bath. The brown residual solution was acidified with hydrochloric acid and steam distilled to remove the alcohol and any unreacted sulfide. After cooling, the contents of the flask were rendered strongly alkaline and extracted ten times with ethyl ether. The ethereal solution was washed, dried, evaporated and the residual red oil was distilled to yield 9 g. of colorless mobile liquid, b.p. 154–159° (760 mm.), yield 67%.

Anal. Calcd. for $C_5H_{11}NS$: N, 11.97. Found: N, 11.84.

The *p*-toluenesulfonamide derivative melted at 109–111°.

Anal. Calcd. for $C_{12}H_{17}O_2S_2N$: C, 53.1; H, 6.3. Found: C, 52.8; H, 6.5.

N-Phenyl-3-methyl-1,4-thiazan.—2-Chloroethyl 2-chloro-*n*-propyl sulfide (17.3 g., 0.1 mole) was added to 11 g. (0.12 mole) of redistilled aniline which was dissolved in 100 ml. of ethanol containing sodium carbonate (11 g., 0.1 mole). The mixture was refluxed for four hours and then filtered to remove the sodium salts. The bulk of the ethanol was removed *in vacuo*. Dilute hydrochloric acid was added (Congo red) and the amine hydrochloride solution extracted with ether to remove any unchanged sulfide. Sodium hydroxide (10%) was added to render the aqueous residue strongly alkaline. The solution was extracted with ether. The combined extracts were washed with water, dried and distilled to afford a viscous orange oil boiling between 115–175° (1 mm.). Fractionation *in vacuo* afforded 8.3 g. (45%) of a light yellow oil distilling between 114–118° (1 mm.), m.p. 36–39°.

Anal. Calcd. for $C_{11}H_{15}NS$: N, 7.25. Found: N, 7.34.

***p*-Methoxyphenyl-3-methylthiomorpholine.**—Prepared as for the N-phenyl derivative with anisidine replacing aniline, m.p. 81–84°.

Anal. Calcd. for $C_{12}H_{17}NOS$: N, 6.3. Found: N, 6.5.

N-*n*-Butyl-3-methylthiomorpholine.—The product is a colorless mobile liquid, b.p. 105–110° (16 mm.).

Anal. Calcd. for $C_9H_{19}NS$: N, 8.1. Found: N, 8.1.

N-*n*-Hexyl-3-methylthiomorpholine: b.p. 126° (9 mm.).

Anal. Calcd. for $C_{11}H_{23}NS$: N, 7.0. Found: N, 7.07.

Bis-(2-hydroxy-*n*-propyl) Sulfide.—1-Chloro-2-hydroxypropane (47 g., 0.5 mole) was added to 132 g. of sodium sulfide nonahydrate (0.55 mole) in 500 ml. of boiling ethanol. The mixture was refluxed for 15 minutes, cooled, filtered and vacuum distilled, b.p. 118° (3 mm.), yield 51 g. (69%).

Anal. Calcd. for $C_6H_{14}O_2S$: S, 21.3. Found: S, 21.0.

Bis-(2-chloro-*n*-propyl) Sulfide.—Thionyl chloride (98 g., 0.8 mole) was added dropwise with stirring to bis-(2-hydroxy-*n*-propyl) sulfide (50 g., 0.33 mole). When all the thionyl chloride had been added the reaction was heated on a steam-bath for one hour. The chloroform was evaporated at the water pump and the residue was vacuum distilled to yield a colorless liquid (56 g., 91%), b.p. 105° (11 mm.).

Anal. Calcd. for $C_6H_{12}Cl_2S$: S, 17.13. Found: S, 17.04.

3,5-Dimethyl-1,4-thiazan (VII).—Bis-(2-chloro-*n*-propyl) sulfide (37.4 g., 0.2 mole) and 120 ml. of 9% ethanolic ammonia (10.8 g., 0.8 mole) were heated at 60° for eight hours in a Carius bomb tube. The tube was chilled and carefully opened. The excess ammonia was expelled on a steam-bath. The brown solution was acidified with sodium hydroxide (10%). The alkaline solution was extracted with ten equal volumes of ether. The ethereal solution was washed, dried, evaporated and distilled, b.p. 183–187° (760 mm.), yield 20 g. (76%).

Anal. Calcd. for $C_6H_{13}NS$: N, 10.67. Found: N, 10.69.

The *p*-toluenesulfonamide derivative melted at 130–133°.

Anal. Calcd. for $C_{13}H_{19}NO_2S_2$: N, 4.91. Found: N, 5.02.

N-Phenyl-3,5-dimethyl-1,4-thiazan.—The procedure was as outlined for the 3-methyl analog, b.p. 142° (7 mm.).

Anal. Calcd. for $C_{12}H_{17}NS$: N, 6.75. Found: N, 6.54

N-*n*-Butyl-3,5-dimethyl-1,4-thiazan: b.p. 119–123° (7 mm.).

Anal. Calcd. for $C_{10}H_{21}NS$: N, 7.5. Found: N, 7.3.

N-*n*-Hexyl-3,5-dimethyl-1,4-thiazan: b.p. 133° (9 mm.).

Anal. Calcd. for $C_{12}H_{25}NS$: N, 6.5. Found: N, 6.4.

N-2-Chloroethyl-3-amino-2-chlorobutane.—N-2-Hydroxyethyl-3-amino-2-butanol[8] was treated with thionyl chloride as previously described for N-2-chloroethyl-1-amino-2-chloropropane. Carbonization and polymerization accompanied the final distillation, b.p. 107–109° (11 mm.), yield 17%.

Anal. Calcd. for $C_6H_{13}Cl_2N$: N, 8.2. Found: N, 8.4.

2,3-Dimethyl-1,4-thiazan (IV).—The reaction of N-2-chloroethyl-3-amino-2-chlorobutane (8.5 g., 0.05 mole) with sodium sulfide according to the previously noted procedure afforded a colorless liquid, b.p. 86–89° (25 mm.), yield 1.1 g. (17%).

Anal. Calcd. for $C_6H_{13}NS$: N, 10.7. Found: N, 10.6.

The *p*-toluenesulfonamide derivative melted at 119°.

Anal. Calcd. for $C_{13}H_{19}NO_2S_2$: N, 4.9. Found: N, 4.7.

2-Hydroxyethyl 2′-Hydroxy-*s*-butyl Sulfide.—Sodiomercaptoethanol (50 g., 0.5 mole) and 54 g. of 2,3-butylene chlorohydrin[9] (0.5 mole) reacted as previously noted for 2-hydroxyethyl 2-hydroxy-*n*-propyl sulfide. A colorless viscous oil was distilled at 118–123° (1.5 mole), yield 65 g. (87%).

Anal. Calcd. for $C_6H_{14}SO_2$: C, 48.0; H, 9.3. Found: C, 47.8; H, 9.0.

The same diol was prepared by refluxing methylvinylcarbinol[10] (36 g., 0.5 mole), mercaptoethanol (39 g., 0.5 mole) and sulfur (0.5 g.) for eight hours.

2-Chloroethyl 2′-Chloro-*s*-butyl Sulfide.—2-Hydroxyethyl 2′-hydroxy-*s*-butyl sulfide (50 g., 0.33 mole) and concentrated hydrochloric acid (500 ml.) reacted as noted for the preparation of 2-chloroethyl 2-chloro-*n*-propyl sulfide, b.p. 118° (17 mm.), yield 19 g. (32%).

Anal. Calcd. for $C_6H_{12}Cl_2S$: Cl, 19.0. Found: Cl, 18.8.

2-Chloroethyl 2′-Chloro-*s*-butyl Sulfone.—Hydrogen peroxide (3.4 g., 0.1 mole) was added slowly to 2-chloroethyl 2′-chloro-*s*-butyl sulfide (18.7 g., 0.1 mole), dissolved in 100 ml. of glacial acetic acid. An additional 6.8 g. (0.2 mole) of hydrogen peroxide was added rapidly and the reaction mixture was stirred at 60° for 24 hours. Removal of the solvents *in vacuo* and distillation afforded a colorless oil at 142–146° (2 mm.).

Anal. Calcd. for $C_6H_{12}Cl_2SO_2$: Cl, 32.4. Found: Cl, 32.1.

Butyl Ethyl Sulfone.—2-Chloroethyl 2′-chloro-*s*-butyl sulfone (11 g., 0.05 mole) was dissolved in 100 ml. of dry benzene and was treated with 11 g. (0.11 mole) of dry triethylamine. The mixture was stirred for 12 hours at room temperature and filtered. The amine hydrochloride salt was discarded. The benzene solution was washed with water, dried over potassium carbonate and the solvent removed. The residual butyl vinyl sulfone was dissolved in 75 ml. of absolute ethanol and hydrogenated in the presence of Raney nickel at 50 lb. pressure. The required amount of hydrogen was absorbed in five hours. Filtration and evaporation of the solvent yielded 4 g. of a straw colored oil which crystallized from a cold mixture of ether and petroleum ether as white needles, m.p. 47–49°.

Anal. Calcd. for $C_6H_{14}SO_2$: C, 48.0; H, 9.3. Found: C, 47.7; H, 9.2.

The melting point of butyl ethyl sulfone is given as 50–51°,[11] but the particular isomer is not noted.

2-Hydroxy-*n*-propyl 2′-Hydroxyisopropyl Sulfide.—2-Chloro-1-propanol[12] (20 g., 0.21 mole) was added to the sodium salt of 1-mercapto-2-propanol[13] (22.8 g., 0.2 mole), according to the procedure described for 2-hydroxyethyl 2-hydroxy-*n*-propyl sulfide. The final sulfide (25 g., 83%) distilled at 145–149° (10 mm.).

Anal. Calcd. for $C_6H_{14}SO_2$: C, 48.0; H, 9.3. Found: C, 47.9; H, 9.0.

The bis-*p*-nitrobenzoate derivative melted at 129°.

Anal. Calcd. for $C_{20}H_{20}N_2O_8S$: C, 53.7; H, 4.5. Found: C, 53.3; H, 4.8.

2-Hydroxy-*n*-propyl 2′-Hydroxyisopropyl Sulfone.—Oxidation with hydrogen peroxide was carried out as noted for 2-hydroxyethyl 2-hydroxyisopropyl sulfone to yield the product melting at 67–69°.

Anal. Calcd. for $C_6H_{14}SO_4$: S, 17.6. Found: S, 17.5.

2-Chloro-*n*-propyl 2′-Chloroisopropyl Sulfone.—The procedure was as noted for 2-chloroethyl 2-chloroisopropyl sulfone, b.p. 154–159° (3.5 mm.).

Anal. Calcd. for $C_6H_{12}Cl_2SO_2$: S, 14.6. Found: S, 14.3.

N-Phenyl-2,5-dimethyltetrahydrothiazine 1,1-Dioxide.—The procedure was as noted for N-phenyl-2-methyltetrahydrothiazine 1,1-dioxide, m.p. 139–142°.

Anal. Calcd. for $C_{12}H_{17}NO_2S$: N, 5.86. Found: N, 5.7.

2,5-Dimethyltetrahydrothiazine 1,1-Dioxide.—The procedure was as noted for 2-methyltetrahydrothiazine 1,1-dioxide, b.p. 177–180° (9 mm.).

Anal. Calcd. for $C_6H_{13}NO_2S$: N, 8.6. Found: N, 8.8.

2,5-Dimethyl-1,4-thiazine (V).—The reduction with lithium aluminum hydride was performed as noted for 2-methyl-1,4-thiazine, b.p. 77–82° (25 mm.).

Anal. Calcd. for $C_6H_{13}NS$: N, 10.7. Found: N, 10.4.

The *p*-toluenesulfonamide derivative melted at 107–109°.

Anal. Calcd. for $C_{13}H_{19}NO_2S_2$: N, 4.9. Found: N, 4.9.

2-Hydroxyisopropyl 2′-Hydroxy-*s*-butyl Sulfide.—Methylvinylcarbinol (36 g., 0.5 mole), 1-mercapto-2-propanol[13] (46 g., 0.5 mole) and 0.5 g. of sulfur were refluxed for eight hours. The dark yellow resultant solution was distilled to yield a colorless viscous oil, b.p. 117–119° (2 mm.); yield 19.2%.

The bis-*p*-nitrobenzoate derivative melted at 143–144°.

Anal. Calcd. for $C_{21}H_{22}N_2O_8S$: C, 52.2; H, 4.8. Found: C, 52.5; H, 4.9.

2-Hydroxyisopropyl 2′-hydroxy-*s*-butyl sulfone: m.p. 81–84°.

Anal. Calcd. for $C_7H_{16}O_4S$: S, 16.3. Found: S, 16.0.

2-Chloroisopropyl 2′-chloro-*s*-butyl sulfone: b.p. 167–169° (2 mm.).

Anal. Calcd. for $C_7H_{14}Cl_2O_2S$: S, 13.7. Found: S, 13.8.

N-Phenyl-2,3,6-trimethyltetrahydrothiazine 1,1-dioxide: m.p. 153–157°

Anal. Calcd. for $C_{13}H_{19}NO_2S$: S, 12.6. Found: S, 12.3.

2,3,6-Trimethyltetrahydrothiazine 1,1-dioxide: b.p. 169–174°.

Anal. Calcd. for $C_7H_{15}NO_2S$: N, 7.9. Found: N, 7.7.

2,3,6-Trimethyl-1,4-thiazane (IX): b.p. 83–87° (10 mm.).

Anal. Calcd. for $C_7H_{15}NS$: N, 9.7. Found: N, 9.9.

The *p*-toluenesulfonamide derivative melted at 131–134°.

Anal. Calcd. for $C_{14}H_{21}NO_2S_2$: C, 48.1; H, 7.1. Found: C, 48.0; H, 7.4.

2-Hydroxy-*n*-propyl 2′-Hydroxy-*s*-butyl Sulfide.—The sodium salt of 2-hydroxypropylmercaptan[13] (38 g., 0.33 mole) was treated with 38 g. of 2,3-butylene chlorohydrin (0.35 mole). The procedure was as previously noted for 2-hydroxy-*n*-propyl 2′-hydroxyisopropyl sulfide. The product was 36 g. (72%) of a colorless viscous oil distilling at 117–119° (2 mm.).

Anal. Calcd. for $C_5H_{14}SO_2$: C, 48.0; H, 9.3. Found: C, 47.4; H, 9.1.

2-Chloro-*n*-propyl 2′-Chloro-*s*-butyl Sulfide.—The procedure which was noted previously for bis-(2-chloro-*n*-propyl) sulfide was utilized for the chlorination of the above diol. The final colorless product distilled at 117–121° (10 mm.).

Anal. Calcd. for $C_6H_{12}Cl_2S$: S, 17.1. Found: S, 17.0.

2,3,5-Trimethyl-1,4-thiazan.—2-Chloro-*n*-propyl 2′-chloro-*s*-butyl sulfide was treated with ammonia as noted in

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the preparation of 3,5-dimethyl-1,4-thiazan, b.p. 88–92° (10 mm.).

Anal. Calcd. for $C_7H_{15}NS$: N, 9.7. Found: N, 9.7.

The *p*-toluenesulfonamide derivative melted at 139–141°.

Anal. Calcd. for $C_{14}H_{21}NO_2S_2$: C, 48.1; H, 7.1. Found: C, 47.7; H, 7.3.

Bis-(2-hydroxy-*s*-butyl) Sulfide.—2,3-Butylene chlorohydrin (43.4 g., 0.4 mole) was added to 50 g. of sodium sulfide nonahydrate (0.21 mole) contained in 500 ml. of boiling ethanol. Carbonization occurred during the concentration of the product which resulted in considerable loss, b.p. 113–117° (0.5 mm.), yield 19 g. (72%).

Anal. Calcd. for $C_8H_{18}O_2S$: C, 50.4; H, 10.1. Found: C, 50.3; H, 10.5.

Bis-(2-chloro-*s*-butyl) Sulfide.—The procedure described for bis-(2-chloro-*n*-propyl) sulfide was the method of choice. The colorless chlorosulfide distilled at 123–127° (17 mm.).

Anal. Calcd. for $C_8H_{16}Cl_2S$: S, 14.9. Found: S, 14.6.

2,3,5,6-Tetramethyl-1,4-thiazan (X).—The procedure which was previously described for 3,5-dimethyl-1,4-thiazan was used to cyclize the above chloro sulfide. The mobile colorless product distilled at 94–98° (10 mm.).

Anal. Calcd. for $C_8H_{17}NS$: N, 8.8. Found: N, 8.6.

The *p*-toluenesulfonamide derivative melted at 138°.

Anal. Calcd. for $C_{15}H_{24}N_2O_2S_2$: C, 54.8; H, 7.3. Found: C, 54.5; H, 7.7.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Some 1-Substituted Dibenzothiophene Derivatives

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RECEIVED JANUARY 16, 1954

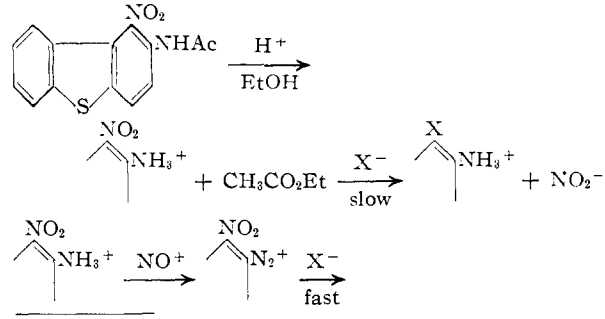
2-Acetamidodibenzothiophene reacts with nitric acid affording 1-nitro-2-acetamidodibenzothiophene which reacts with ethanolic hydrobromic or ethanolic hydrochloric acid yielding 1-bromo- and 1-chlorodibenzothiophene, respectively; however, ethanolic hydriodic acid affords only the nitroamine. 1-Nitro-2-acetamidodibenzothiophene may be diazotized in ethanol using sulfuric acid without the displacement of the nitro group, thus yielding 1-nitrodibenzothiophene.

Confirmed substitutions in the 1-position of dibenzothiophene have previously been made by electrophilic attack on a 4-substituted dibenzothiophene nucleus containing an activating group.[1] A nitro-2-acetamidodibenzothiophene has been obtained by the action of fuming nitric acid on 2-acetamidodibenzothiophene. This compound, upon treatment with ethanolic hydrochloric acid in an attempt to obtain the corresponding nitroamine, gave a compound which contained no nitrogen, and during the course of the reaction an odor resembling acetaldehyde was noticeable.[1]

1-Bromodibenzothiophene has been prepared by the action of 30% hydrobromic acid in ethanol on the above-mentioned nitro-2-acetamidodibenzothiophene and its structure has been established by the method of mixed melting points with an authentic specimen of 1-bromodibenzothiophene prepared in this Laboratory by a different method.[1] The very similar nature of the infrared spectra given by the product obtained by the ethanolic hydrochloric acid treatment of nitro-2-acetamidodibenzothiophene and that of 1-bromodibenzothiophene indicates that the compound is 1-chlorodibenzothiophene. Treatment of nitro-2-acetamidodibenzothiophene with either ethanolic hydriodic acid or ethanolic sodium hydroxide yields only the corresponding nitro-2-aminodibenzothiophene, which also gives rise to 1-bromo and 1-chloro derivatives when treated with ethanolic HBr or HCl, respectively.

Displacements of nitro groups during diazotization are to be found in the literature.[2-9] Recently[10-12] it has been shown that a chain reaction occurs with certain nitroamines initiated by displacement of a nitro group by halide ion from the conjugate acid of the nitroamine, the nitrite ion displaced then diazotizes more nitroamine which in turn gives rise to a more rapid displacement of nitrite ion by halide ion. It has been found[13] that in compounds of a similar nature the addition of a small amount of nitrite greatly accelerates the rate at which the diazonium salt is formed, thus indicating that one of the slow steps in the reaction is the displacement of nitrite from the conjugate acid of the nitroamine.

From the above observations and the fact that acetaldehyde was evolved during the reactions of the ethanolic HBr and HCl on nitro-2-acetamidodibenzothiophene and that when naphthol-2 was added to the reaction mixture coupling took place, it apears quite evident that nitration of 2-acetamidodibenzothiophene gave as a product 1-nitro-2-acetamidodibenzothiophene and the sequence of reactions for the formation of 1-chloro and 1-bromodibenzothiophene may be illustrated as



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