were derived from the reaction of styrene oxide with monochloroborane. Several of these compounds displayed retention times which were identical with the solvent interaction compounds formed in the reaction of styrene oxide with borane.[5] Other fractions appeared to contain chlorine; however, the product mixture was far too complex to separate and characterize adequately the products.

The reaction of styrene oxide with dichloroborane produced a 10% yield of 2-chloro-2-phenylethanol and 5–10% yields of phenylethanol in addition to many other higher boiling compounds which were not identified. Neither the chlorohydrin nor the simple alcohol could be isolated in sufficient quantities and purity to allow determination the stereochemistry of chloride introduction with optically active styrene oxide or the deuterium distribution on reaction with dichlorodeuterioborane.

The reactions of phenylthioborane,[4] borane,[5] and the chloroboranes differ substantially in many respects: extent of reduction, ease of nucleophilic attack by the heterofunctional group, extent of rearrangement, and the extent of high molecular weight product formation. Unfortunately all of these effects are intermingled and only qualitative statements can be made. As the Lewis acidity of the borane increases, borane $\lesssim$ phenylthioborane $<$ monochloroborane $<$ dichloroborane,[1] the relative rates of the reactions increase (borane $<$ phenylthioborane $<$ chloroboranes) and higher yields of higher molecular weight materials are obtained. As the nucleophilicity of the attacking nucleophilic portion of the borane increases, hydride $<$ chloride $<$ phenylthio, the yields of simple epoxide-opening products increase as do the rates of reaction. The final factor to be considered is the stability of boronium ion leaving group. The leaving group is the same, $BH_2\cdot(THF)_2^+$, with borane, phenylthioborane, and monochloroborane; however, with dichloroborane, $BHCl\cdot(THF)_n^+$ is the leaving group which would appear to be a better leaving group than $BH_2\cdot(THF)_2^+$ as evidenced by the higher yields of chlorohydrin.

Experimental Section

General.—The determination of yields by glpc was accomplished by the addition of a weighed amount of an internal standard to the sample and using relative response ratios in the calculations. Nuclear magnetic resonance (nmr) spectra were recorded on a Varian Associates HR-60 spectrometer.

The procedures described previously[1] were used to prepare monochloroborane and dichloroborane in tetrahydrofuran solution.

Reaction of Monochloro- and Dichloroborane with *cis*- and *trans*-2-Butene Oxides.—To a solution of 1.0 g (0.014 mole) of the epoxide[8] in 10 ml of tetrahydrofuran maintained at 0–5° was added slowly 0.014 mole of the chloroborane in tetrahydrofuran The reactions mixtures were allowed to stand at room temperature for 3 hr and were hydrolyzed by the addition of 50 ml of water. The hydrolyzed mixture was extracted three times with 150-ml portions of ether. The combined extracts were washed with water and dried over magnesium sulfate. After the careful removal of the solvent the residues were analyzed by glpc on a 5-ft 20% Carbowax 20 M on Chromosorb W column initially at 75° and finally at 200° (to elute the higher boiling fractions). The results of the analyses are given in Table I.

Preparation of *threo*- and *erythro*-3-Chloro-2-butanol.—To 10 ml of concentrated hydrochloric acid maintained at 0° was added slowly 2 g of the *cis*- or *trans*-2-butene oxide[8] keeping the temperature near 0°. The reaction mixtures were then stirred for 1 hr and then carefully neutralized by the slow addition of solid sodium carbonate. The resulting system was extracted repeatedly with ether and the combined extracts were dried over potassium carbonate and finally sodium sulfate. The solvent was removed by distillation at atmospheric pressure. The *threo*-3-chloro-2-butanol was distilled at 41° (21 mm), whereas the *erythro*-3-chloro-2-butanol was distilled at 47° (22 mm).

threo-3-Chloro-2-butanol had a retention time of 7.22 min on a 5-ft Carbowax 20 M on Chromosorb W column at 75°. Under identical conditions the *erythro* isomer had a retention time of 9.00 min. Glpc indicated a purity level of >98% approximating the purity of the starting epoxides.

Reaction of Styrene Oxide with Monochloro- and Dichloroborane.—To a solution of 4.0 g (0.033 mole) of styrene oxide in 32 ml of tetrahydrofuran maintained at 0–5° was added 0.033 mole of the monochloro- or dichloroborane. The reaction mixtures were allowed to stand at room temperature for 3 hr and were hydrolyzed by the addition of 75 ml of water. The hydrolyzed mixtures were extracted with three 150-ml portions of ether. The combined extracts were washed with water and dried over magnesium sulfate after which the solvent was removed under reduced pressure. The residue was carefully distilled giving fraction A, bp 62–69° (0.4 mm), and fraction B, bp 136–138° (1.0 mm), and a small amount of residue.

Analysis of fractions A and B by infrared spectroscopy and nmr indicated the absence of unreacted starting material and phenylacetaldehyde and the presence of 2-chloro-2-phenylethanol (styrene oxide, 2-chloro-2-phenylethanol, and phenylacetaldehyde all gave identical retention times by glpc, the former two undergoing rearrangement to the latter on the column as indicated by infrared analysis of the effluent peak) and 2-phenylethanol. The yields calculated from the nmr spectra are contained in Table I.

The 2-phenylethanol, isolated by preparative glpc, formed in a similar treatment of styrene oxide with monochlorodeuterioborane was shown to consist of 88% 1-deuterio-2-phenylethanol and 12% 2-deuterio-2-phenylethanol by integration of the nmr spectrum.

Preparation of 2-Chloro-2-phenylethanol.—2-Chloro-2-phenylethanol was prepared by treating styrene oxide with concentrated hydrochloric acid in dioxane solution according to the procedure of Ryan,[9] bp 83–84° (0.8 mm) [lit.[9] bp 76° (0.7 mm)].

(8) D. J. Pasto and C. C. Cumbo, *J. Org. Chem.*, **30**, 1271 (1965).

(9) J. D. Ryan, Ph.D. Dissertation, University of Notre Dame, 1960.

Organic Disulfides and Related Substances. XX. A Novel Preparation of Symmetrical Trisulfides Using Thiolsulfonates[1a–c]

JOHN D. BUCKMAN[1d] AND L. FIELD[1e]

Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37203

Received August 1, 1966

Other interests required synthesis of certain trisulfides, RSSSR. When conventional methods gave poor results, the possibility of thioalkylating metallic sulfides with thiolsulfonates was an attractive alternative; this approach was suggested by the smooth and useful preparation of unsymmetrical disulfides which results from thioalkylating thiols with thiolsulfo-

(1) (a) This investigation was supported by the U. S. Army Medical Research and Development Command, Department of the Army, under Research Contract No. DA-49-193-MD-2030. Taken from portions of the Ph.D. Dissertation of J. D. B., Vanderbilt University, June 1966. (b) Reported in part at the Southeast–Southwest Regional Meeting of the American Chemical Society, Memphis, Tenn., Dec 2–4, 1965. (c) Paper XIX: L. Field and W. B. Lacefield, *J. Org. Chem.*, **31**, 3555 (1966). (d) Du Pont Postgraduate Teaching Assistant, 1964–1965. (e) To whom correspondence should be addressed.

nates.[2] This paper reports application of the envisioned thioalkylation to synthesis of a symmetrical primary alkyl, a tertiary alkyl, and an aryl trisulfide in yields of 82–95% with good purity. The reaction thus seems both general and useful, and probably should be the method of choice for many trisulfides (syntheses of various types of requisite thiolsulfonates are described in earlier papers of this series). The equation and products are shown in Chart I.

CHART I

$$\underset{\mathbf{1,3,5,7}}{RSO_2SR'} + M_2{}^+S^{2-} \longrightarrow \underset{-RSO_2{}^-M^+}{} R'SS^-M^+ \xrightarrow{\quad} \underset{\mathbf{9}}{} \xrightarrow{\quad} \underset{RSO_2SR'}{}$$

$$R'SSSR' + RSO_2{}^-M^+$$
$$\mathbf{2,4,6,8}$$

$M^+ = K^+$ or Na^+

1, R = R′ = *p*-C_7H_7 — **2**, R′ = *p*-C_7H_7
3, R = R′ = $AcNHCH_2CH_2$ — **4**, R′ = $AcNHCH_2CH_2$
5, R = R′ = $Cl^-{}^+H_3NCH_2CH_2$ — **6**, R′ = $Cl^-{}^+H_3NCH_2CH_2$
7, R = *p*-C_7H_7; R′ = $(CH_3)_3C$ — **8**, R′ = $(CH_3)_3C$

Thioalkylation of sulfide ion by thiolsulfonates has received virtually no attention.[3] A metal sulfide reportedly reacts with a thiolsulfonate in a 1:1 molar ratio to give thiosulfonate and thiolate ions (eq 1),[4] and excess hydrogen sulfide reacts to give a tetrasulfide (eq 2).[5] Nevertheless, two molar proportions of *p*-tolyl

$$RSO_2SR + K_2S \longrightarrow RSO_2SK + RSK \quad (1)$$

$$RSO_2SR + H_2S \longrightarrow RSSSSR + RSSR + \text{other products} \quad (2)$$

p-toluenethiolsulfonate (**1**) reacted with potassium sulfide in methanol during 30 min at room temperature to give *p*-tolyl trisulfide (**2**) in 90% yield (Chart I). Reaction of the primary alkyl thiolsulfonate **3** gave trisulfide **4** in 82% yield; however, a similar reaction of the acidic thiolsulfonate **5** gave only ill-defined product which seemed not to be the trisulfide **6** (no formation of sulfur or hydrogen sulfide upon heating of an aqueous solution; the melting point of 170–185° with decomposition could not be improved).

t-Butyl *p*-toluenethiolsulfonate (**7**) reacted with sodium sulfide to provide *t*-butyl trisulfide (**8**, 95% yield, 98% purity). A heterogeneous (ether–water) system was best for this reaction. The homogeneous reaction in methanol was unpromising because contamination of trisulfide **8** with tetrasulfide became significant, possibly owing to air oxidation of the *t*-butyl hydrodisulfide ion, $(CH_3)_3CSS^-Na^+$ (**9**), which was not protected from air by the ether layer.

Reaction of a metal hydrosulfide was less satisfactory than of metal sulfides. Potassium hydrosulfide reacted with thiolsulfonates **1** and **3** to give *p*-tolyl trisulfide (**2**) and bis(2-acetamidoethyl) trisulfide (**4**), but in lower yields.

(2) (a) L. Field, T. F. Parsons, and D. E. Pearson, *J. Org. Chem.*, **31**, 3550 (1966); (b) L. Field and H. K. Kim, *J. Med. Chem.*, **9**, 397 (1966); (c) L. Field and W. B. Lacefield, *J. Org. Chem.*, **31**, 599 (1966); (d) T. F. Parsons, J. D. Buckman, D. E. Pearson, and L. Field, *ibid.*, **30**, 1923 (1965); (e) R. R. Crenshaw and L. Field, *ibid.*, **30**, 175 (1965); (f) L. Field, A. Ferretti, and T. C. Owen, *ibid.*, **29**, 2378 (1964); (g) L. Field, H. Härle, T. C. Owen, and A. Ferretti, *ibid.*, **29**, 1632 (1964); (h) L. Field, T. C. Owen, R. R. Crenshaw, and A. W. Bryan, *J. Am. Chem. Soc.*, **83**, 4414 (1961).

(3) *Cf.* (a) A. Schöberl and A. Wagner in "Methoden der Organischen Chemie" (Houben-Weyl), Vol. 9, E. Müller, Ed., 4th ed., Georg Thieme Verlag, Stuttgart, 1955, p 690; (b) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. I, Chemical Publishing Co., Inc., New York, N. Y., 1958, p 333.

(4) R. Otto and A. Rössing, *Ber.*, **19**, 3129 (1886).

(5) R. Otto and A. Rössing, *ibid.*, **20**, 2090 (1887).

Conventional syntheses for trisulfides involving reaction of sulfur dichloride and thiols, of Bunte salts with metal hydrosulfides, or of sulfenyl chlorides with metal sulfides (*cf.* the Experimental Section) gave much less satisfactory results than those with the thiolsulfonates.

Thus reaction of sulfur dichloride with *p*-toluenethiol gave only 12% of pure *p*-tolyl trisulfide (**2**) after repeated recrystallizations (eq 3). Synthesis of tri-

$$2RSH + SCl_2 \longrightarrow RSSSR + 2HCl \quad (3)$$

sulfide **4** by reaction of 2-acetamidoethanethiol with sulfur dichloride (eq 3) also was unsatisfactory; the product was insoluble in solvents in which trisulfide **4** is very soluble.

Bunte salts, like **10**, react with metal sulfides in the presence of excess formaldehyde at pH 8 to form trisulfides selectively if the trisulfide generated has a low water solubility (eq 4).[6] However, when the Bunte

$$\underset{\mathbf{10}}{2AcNH(CH_2)_2SSO_3{}^-} + S^{2-} \xrightarrow[\text{pH 8}]{H_2CO} \mathbf{4} + 2SO_3{}^{2-} \text{ (as } H_2CO \text{ adduct)} \quad (4)$$

salt **10** reacted with sodium hydrosulfide, pure bis(2-acetamidoethyl)trisulfide (**4**) could not be isolated, although it was shown to be a major reaction product by thin layer chromatography.

Reaction of 2-methyl-2-propanesulfenyl chloride with sodium or potassium sulfide (eq 5) gave *t*-butyl trisulfide (**8**); however, as with the reaction of 2-propanesulfenyl chloride with hydrogen sulfide,[7] a mixture resulted of di-, tri-, and higher sulfides.

$$2(CH_3)_3CSCl + S^{2-} \longrightarrow \mathbf{8} + 2Cl^- \quad (5)$$

Identity of trisulfides **2**, **4**, and **8** was established by elemental analysis and confirmed for the previously described trisulfides **2** and **8** by agreement of physical properties with reported values. Homogeneity of the bis(2-acetamidoethyl)trisulfide **4** was demonstrated by thin layer chromatography.

Significant differences can be noted in the infrared spectra of trisulfides **2**, **4**, and **8** and those of the corresponding disulfides in the region of 700–250 cm^{-1}. In the region of about 4000–700 cm^{-1} the infrared spectra of the trisulfides and corresponding disulfides are essentially identical.

Methods for preparing unsymmetrical trisulfides include reaction of an alkyl disulfide chloride with a thiol (eq 6),[8] of a sulfenyl chloride or thiocyanate with a hydrodisulfide (eq 7),[9] and of an N-arylamidothiosulfite with a thiol (eq 8).[10] Since these approaches are inconvenient owing to the relative unavailability

$$RSSCl + R'SH \longrightarrow RSSSR' + HCl \quad (6)$$

$$RSX + R'SSH \longrightarrow RSSSR' + HX \quad (7)$$

$$RNHS(O)SR' + 3R''SH \longrightarrow RNH_2 + R''SSSR' + R''SSR'' + H_2O \quad (8)$$

and instability of disulfide chlorides and hydrodisulfides, and the multiplicity of products obtained in

(6) B. Milligan, B. Saville, and J. M. Swan, *J. Chem. Soc.*, 3608 (1963).

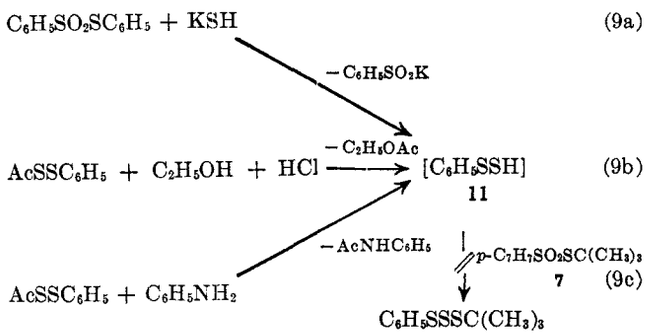
(7) H. Brintzinger and M. Langheck, *Chem. Ber.*, **87**, 325 (1954).

(8) (a) H. Böhme and E. v. Ham, *Ann.*, **617**, 62 (1958); (b) C. M. Himel and L. O. Edmonds, U. S. Patent 2,572,845 (1951); *Chem. Abstr.*, **46**, 9589 (1952).

(9) T. Nakabayashi and J. Tsurugi, *J. Org. Chem.*, **26**, 2482 (1961).

(10) G. Kresze and H-P. Patzschke, *Chem. Ber.*, **93**, 380 (1960).

eq 8, preparation of a model unsymmetrical trisulfide, *t*-butyl phenyl trisulfide, was attempted through various routes involving thioalkylation reactions of thiolsulfonates (eq 9a-c).



Reaction 9a was attempted using a mixture of the two thiolsulfonates because phenyl and *t*-butyl thiolsulfonates differ markedly in the rate of reaction with thiols.[2d] Acid-catalyzed ethanolysis of certain acetyl disulfides (9b) has been demonstrated to give hydrodisulfides,[11] and cleavage by an amine (9c) would be expected to occur as shown.[12] The hydrodisulfide **11** produced in these reactions (eq 9a–c) then was to be thioalkylated as shown. In all cases, however, complex mixtures resulted of *t*-butyl di-, tri-, and tetrasulfides, together with *t*-butyl phenyl disulfide (55–70% of the volatile reaction products, by gas chromatography). These products were not cleanly separable by distillation and thus these routes are unattractive for synthesis of unsymmetrical trisulfides.

Experimental Section[14]

Starting Materials. A.—Preparations were as reported for *p*-tolyl *p*-toluenethiolsulfonate (**1**),[15] *t*-butyl *p*-toluenethiolsulfonate (**7**),[2d] and 2-aminoethyl 2-aminoethanethiolsulfonate dihydrochloride (**5**).[2h] Potassium hydrosulfide was prepared by saturating a methanolic solution of potassium hydroxide with hydrogen sulfide; the sulfide was prepared by then adding a second equivalent of alkali (sodium sulfide, similarly); sulfide solutions were used immediately. *t*-Butyl disulfide was a commercial product; *t*-butyl trisulfide (**8**) was kindly supplied by W. B. Lacefield.[16]

B. Sodium S-(2-acetamidoethyl) thiosulfate (10)[17] was prepared by adding 75 ml[20] of a solution of 46.5 g (0.187 mole) of cupric sulfate pentahydrate in 100 ml of water (45 min) to a stirred mixture of 23.6 g (0.10 mole) of N,N′-diacetylcystamine,[2h] 23.6 g (0.187 mole) of anhydrous sodium sulfite, 100 ml of water, and 100 ml of concentrated ammonium hydroxide. Solvent was removed and the residue was extracted with two 100-ml portions of 95% ethanol. Evaporation of the extracts gave 25 g of light blue solid, which was recrystallized from methanol–2-propanol to give 15.0 g of **10** hemihydrate, mp 86–88°. Recrystallization from 1:2 methanol–1-propanol gave **10** hemihydrate with a constant melting point, 88–89°; infrared absorption bands (KBr) were at 3500–3300 (s, br), 1640 (s), 1560 (s), 1445, 1370, 1300, 1240–1200 (s, br), 1100 (w), 1040 (s), 750 (br), 640 (s), 540 (w), and 480 (w) cm^{-1}.

Anal. Calcd for $C_4H_8NO_4S_2Na \cdot 0.5H_2O$: C, 20.77; H, 3.92. Found: C, 20.74; H, 4.25.

To confirm the structure of the Bunte salt **10**, a solution of 0.234 g (1.0 mmole) of **10** and 0.156 g (1.3 mmoles) of 2-acetamidoethanethiol in 5 ml of methanol was made basic with 0.35 ml of 3 *N* sodium hydroxide. The mixture was diluted with 20 ml of chloroform and insoluble material was removed by filtration. Evaporation of the filtrate left an oil, which was triturated with dry ether (25 ml) to give crystalline N,N′-diacetylcystamine, which was removed by filtration to give 0.2161 g (92%) of the symmetrical disulfide, identified by infrared spectrum, melting point (88–90°), and mixture melting point.

C.—We have found that preparation of **2-acetamidoethyl 2-acetamidoethanethiolsulfonate (3)** by the previous method[2h] sometimes results in vigorous decomposition when the reaction mixture is evaporated (presumably because of residual hydrogen peroxide); low yields of dark products then result. Since it is more reliable (although the yield may be lower), we recommend the following modification to assure destruction of all hydrogen peroxide. Hydrogen peroxide (420 ml, 30%, 8.7 *M*) was added (2.5 hr) to a stirred solution of 290 g (2.43 moles) of 2-acetamidoethanethiol[21] and a crystal of potassium iodide in 1 l. of distilled water with ice cooling to maintain the temperature below 50°. The solution was allowed to stand at room temperature for 30 hr. It was then heated on a steam bath for 45 min (until a negative potassium iodide–starch test for peroxides resulted) and, only then, was evaporated to an oil, which was crystallized from 1-butanol to give 182 g (57%) of **3**, mp and mmp 95–96° (lit.[2h] mp 95–96°).

***p*-Tolyl Trisulfide (2). A. Preparation from *p*-Tolyl *p*-Toluenethiolsulfonate (1).**—Potassium sulfide (25 mmoles) in 58 ml of methanol was added (15 min) to a stirred slurry of 13.9 g (50 mmoles) of thiolsulfonate **1** in 100 ml of methanol. The mixture was stirred for 15 min more, and chilled (0°) for 30 min. Insoluble material, removed by filtration, amounted to 6.25 g (90%) of *p*-tolyl trisulfide (**2**): mp 81–82° (lit.[22] mp 81–82°), unchanged by recrystallizations from 2-propanol or methanol; λ_{max}^{hexane} 236 mμ (log ε 4.36), secondary band at 318 mμ (log ε 3.70) [lit.[23] 241 mμ (log ε 4.30), 313 mμ (log ε 3.64)]. Infrared spectrum below 2000 cm^{-1} (KBr) showed 1590 (w), 1485, 1390 (w), 1300, 1210 (w), 1170, 1100, 1010, 840 (w), 800 (s), 700 (w), 495 (s), and 455 (s); *p*-tolyl disulfide differs in having a band at 470 (s) and lacking them at 700, 495, and 455 cm^{-1}.

Anal. Calcd for $C_{14}H_{14}S_3$: S, 34.55. Found: S, 34.61.

Potassium hydrosulfide in the above procedure gave trisulfide **2** in 96% yield, mp 79.5–81°. Recrystallization gave 76%, mp and mmp 81–82°.

B. Preparation from Sulfur Dichloride.[24]—Freshly distilled sulfur dichloride (0.10 mole) in carbon tetrachloride was added to a stirred solution of *p*-toluenethiol (0.20 mole) in carbon tetrachloride (2 hr). The solution was stirred (30 min), heated at reflux (30 min), washed with water and aqueous sodium bicarbonate, dried, and evaporated to a semisolid. Recrystallization from methanol and 2-propanol gave 7.0 g (24%) of *p*-tolyl trisulfide (**2**), mp 76–77°. Seven more recrystallizations gave 3.2 g (12%) of **2**: mp and mmp 81–82°; λ_{max}^{hexane} 236 mμ (log ε 4.32), 314 mμ (log ε 3.61); infrared spectrum identical with that of **2** produced in A.

Bis(2-acetamidoethyl) Trisulfide (4). A. Preparation from 2-Acetamidoethyl 2-Acetamidoethanethiolsulfonate (3).—A solution of 25 mmoles of potassium sulfide in 50 ml of methanol was added (5 min) to a stirred solution of 13.4 g (50 mmoles) of thiolsulfonate **3** in 100 ml of methanol at 0–5°. The solution was stirred for 5 min and solvent then was removed. The residue was

(11) H. Böhme and G. Zinner, *Ann.*, **585**, 142 (1954).

(12) Acetanilide was isolated in the cleavage of acetyl phenyl disulfide with aniline.[13]

(13) J. D. Buckman, unpublished results.

(14) Melting points are corrected. Elemental analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Moist extracts were dried using anhydrous magnesium sulfate, and solvents were removed at *ca.* 25 mm using a rotating-flask evaporator. Infrared spectra were obtained using Perkin-Elmer Model 137B or Beckman IR-10 spectrophotometers with liquids neat and with solids in Nujol mulls or KBr pellets. Infrared absorptions are given in cm^{-1}; s signifies strong; absorptions not specified are medium; w signifies weak; br signifies broad. Ultraviolet spectra were obtained using a Beckman Model DB spectrophotometer.

(15) L. Field and T. F. Parsons, *J. Org. Chem.*, **30**, 657 (1965).

(16) Compound **8** was analytically pure material obtained by pyrolysis of *t*-butyl dithiosulfite.[10] Both **8** and the disulfide showed only one gas chromatographic peak.

(17) This preparation was based on an analytical procedure for determining disulfides developed by Kolthoff and Stricks,[18] and has been used for preparing Bunte salts from disulfides.[19]

(18) I. M. Kolthoff and W. Stricks, *Anal. Chem.*, **23**, 763 (1951).

(19) J. M. Swan, *Nature*, **180**, 643 (1957).

(20) A blue color which persisted for 2 min then indicated completion of the reaction.[18]

(21) R. Kuhn and G. Quadbeck, *Chem. Ber.*, **84**, 844 (1951).

(22) B. Holmberg, *Ber.*, **43**, 226 (1910).

(23) (a) Y. Minoura, *J. Chem. Soc. Japan*, **73**, 244 (1952), as reported in ref 23b; (b) C. C. Price and S. Oae, "Sulfur Bonding," Ronald Press Co., New York, N. Y., 1962, p 40.

(24) Based on the synthesis of *n*-hexadecyl trisulfide by J. O. Clayton and D. H. Etzler, *J. Am. Chem. Soc.*, **69**, 974 (1947).

extracted with three 50-ml portions of methylene chloride. The combined extracts, dried and evaporated, gave 5.50 g (82%) of trisulfide **4**, mp 92–94°. Recrystallization from acetone and chloroform–carbon tetrachloride gave bis(2-acetamidoethyl) trisulfide (**4**) with a constant melting point of 95.0–95.5°, $\lambda_{max}^{abs\ EtOH}$ 250 mμ (log ε 3.21); N,N′-diacetylcystamine[2h] has $\lambda_{max}^{abs\ EtOH}$ 245 mμ (log ε 2.55). Infrared spectrum (KBr) showed 3260 (s, br) 3060, 2930, 1630 (s, br), 1530 (s, br), 1420 (s), 1400, 1360 (s), 1300 (s), 1230 (s), 1180, 880 (w), 740, 690, 620, 590, 490 (w), 460 (w), 410 (w), and 320–270 (br) cm^{-1}; N,N′-diacetylcystamine differs from **4** in having bands at 805, 710 (br), 600 (s), 470, and 420, and lacking them at 880, 740, 620, 590, and 490 cm^{-1}.

Anal. Calcd for $C_8H_{16}N_2O_2S_3$: C, 35.80; H, 6.09; N, 10.43; S, 35.84. Found: C, 35.89; H, 5.92; N, 10.30; S, 35.69.

Substitution of potassium hydrosulfide in the foregoing procedure resulted in 26% of **4**, mp 95–95.5°, but only after repeated recrystallization.

Thin layer chromatography of trisulfide **4**, prepared by either of the above methods, on a 250-μ-thick Woelm silica gel G layer developed with acetone gave only one spot (located by exposure to iodine vapor; R_f 0.38).

B. Preparation from Sodium S-(2-Acetamidoethyl) Thiosulfate (10).[25]—An aqueous solution of 11.0 mmoles of sodium hydrosulfide was added to a stirred mixture of 24.3 mmoles of **10**, 65 ml of 0.2 *M* phosphate buffer (pH 8.0), 9 ml of 37% w/v formaldehyde solution, and 200 ml of chloroform. The chloroform layer gave an oil from which crystallization separated only 0.4 g (14%, calculated as **4**) of solid, mp 75–83°. This solid was mainly **4** (thin layer chromatographic R_f 0.38), but repeated recrystallization did not give pure **4**.

C. Attempted Preparation from Sulfur Dichloride.—Sulfur dichloride (50 mmoles) in absolute ether was added (45 min) to 100 mmoles of 2-acetamidoethanethiol[21] in chloroform. Filtration separated 14.5 g of hygroscopic material, which was completely insoluble in acetone and chloroform.

***t*-Butyl Trisulfide (8). A. Gas–Liquid Partition Chromatographic (Glpc) Separations.**—Products in these experiments were separated using an F & M Model 720 instrument (oven, 150°; detection and injection, 250°; flow rate of helium, 60 ml/min; bridge current, 150 ma) with a 30-cm column of 5% silicone gum rubber on Chromosorb P. *t*-Butyl disulfide and *t*-butyl trisulfide (**8**) were readily separated (retention times, 50 and 106 (±4) sec, respectively); their identities were established by peak enhancement using known samples. A third peak found with several preparations (retention time 290 sec) is assumed to be *t*-butyl tetrasulfide because a plot of log (retention volume) *vs.* molecular weight for the three components (assuming the least volatile to be *t*-butyl tetrasulfide) gave a straight line.[26] The composition was calculated by comparing the area of one peak (height × width at one-half height) to the total area of all three peaks (the method was confirmed at ±2% with known mixtures of *t*-butyl di- and trisulfide; pure *t*-butyl trisulfide gave a single peak and hence was stable).

B. Preparation from *t*-Butyl *p*-Toluenethiolsulfonate (7).—A solution of 24.4 g (0.10 mole) of thiolsulfonate **7** in 200 ml of ether and a solution of 0.05 mole of sodium sulfide in 100 ml of water were stirred together for 24 hr. The aqueous phase was separated and washed with ether. The ether extracts were washed with water, dried, and evaporated to give 10 g (95%) of oil comprised of at least 98% of trisulfide **8** (with a trace of *t*-butyl tetrasulfide). Distillation through a 2 × 10 cm Vigreux column gave 6.05 g (58%) of **8**: bp 108–110° (20 mm); $n^{24}D$ 1.5225 [lit.[27] bp 86° (4 mm); $n^{20}D$ 1.5225]; λ_{max}^{hexane} 257 mμ (log ε 3.28); infrared bands (neat) at 2960–2860 (s), 1460 (s), 1390, 1360 (s), 1220, 1160 (s), 1040, 1020 (w), 930 (w), 565 (w), 490, and 280 (s, br); *t*-butyl disulfide has a band at 560 (w) and lacks them at 565 and 490 cm^{-1}. This sample of trisulfide gave only one glpc peak (retention time, 110 sec).

Anal. Calcd for $C_8H_{18}S_3$: S, 45.72. Found: S, 45.81.

Increase in the reaction time to 72 hr resulted in 88% yield of crude trisulfide, shown by glpc to consist of 6% of *t*-butyl disulfide, 94% of *t*-butyl trisulfide (**8**), and a trace of *t*-butyl tetrasulfide. When the thiolsulfonate **7** and potassium sulfide (2:1 molar ratio) in methanol (homogeneous mixture) were allowed to react for 3 hr, 88% of the crude trisulfide **8** resulted, consisting of 83% of trisulfide **8** and 17% of the tetrasulfide.

C. Preparation from 2-Methyl-2-propanesulfenyl Chloride.[28]—2-Methyl-2-propanesulfenyl chloride[29] (0.20 mole) in pentane was stirred with an aqueous solution of sodium sulfide (0.10 mole) for 3 hr. The pentane layer, washed with water, dried, and evaporated gave 18.5 g (88%) of an oil, shown by glpc to consist of 8% of *t*-butyl disulfide, 58% of trisulfide **8**, and 34% of *t*-butyl tetrasulfide. Distillation gave 6.5 g of material with bp 54–75° (0.4 mm); redistillation (21-cm spinning-band column) did not give pure trisulfide **8**.

An identical experiment but with methanol as solvent and potassium sulfide gave 14.0 g (67%) of oil, shown by glpc to consist of 16% *t*-butyl disulfide, 55% trisulfide **8**, and 27% *t*-butyl tetrasulfide.

(25) Procedure based on that described in ref 6.

(26) *Cf.* ref 6.

(27) S. F. Birch, T. V. Cullum, and R. A. Dean, *J. Inst. Petrol.*, **39**, 206 (1953).

(28) Procedure somewhat similar to that of ref 7.

(29) W. A. Schulze, G. H. Short, and W. W. Crouch, *Ind. Eng. Chem.*, **42**, 916 (1950).

Thiomethoxymethylation of Phenols by Dimethyl Sulfoxide and Acetic Anhydride

YOSHIYUKI HAYASHI AND RYOHEI ODA

Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Kyoto, Japan

Received September 7, 1966

Burdon, *et al.*,[1a] and Pfitzner, *et al.*,[1b] have found recently that phenols can be thiomethoxymethylated by dimethyl sulfoxide (DMSO) in the presence of dicyclohexylcarbodiimide (DCC) and a proton source.

The authors have found that the same reaction occurred using acetic anhydride instead of DCC at room temperature. Thus, phenol was thiomethoxymethylated to give 2-thiomethoxymethylphenol (I) and 2,6-di(thiomethoxymethyl)phenol (II). Phenyl acetate and a small amount of acetate of I were also obtained (Table I).

TABLE I
THIOMETHOXYMETHYLATION OF PHENOL

Reacn time, hr	Yields of products, % I[a]	II[b]	Phenyl acetate
22	19	Trace	10
46	26	0.8	13
84	37	7.2	14
240	31	20	16

[a] Bp 100–101° (1.2 mm); lit.[1b] bp 73–74° (0.3 mm). [b] Bp 160–162° (4 mm); lit.[1b] bp 119–120 (0.3 mm). Disulfone mp 194–195° (from water). *Anal.* Calcd for $C_{10}H_{14}O_5S_2$: C, 43.17; H, 5.07; S, 23.05. Found: C, 43.43; H, 5.22; S, 22.89.

o-, *m*-, and *p*-cresol and 2,4-dimethylphenol gave the corresponding *ortho*-thiomethoxymethylated products (Table II).

Weakly acidic phenols such as those in Table II gave only 2–16% of phenol acetates, but more acidic phenols like *p*-nitrophenol gave the acetate quantitatively. α-Naphthol gave 71% of α-naphthyl acetate and 12% of β-thiomethoxymethyl-α-naphthyl acetate (VIII).

(1) (a) M. G. Burdon and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 4656 (1965); (b) K. E. Pfitzner, J. P. Marino, and R. A. Olofson, *ibid.*, **87**, 4658 (1965).