and *n*-butyl nitrite upon treatment with 1,4-butanedisulfinic acid under the conditions of the synthesis of bisthiolsulfonate **1**, but without additional *n*-butyl nitrite, likewise gave none of the thiolsulfonate **1**. Thus we conclude that neither reaction of the thiol or thionitrite (**3**) with the disulfonylhydroxylamine (**6**) nor of the sulfinic acid with the thionitrite (**3**) can be significant steps in the formation of the thiolsulfonate **1**. The most attractive explanation for the reaction of eq. 3 is that the thionitrite (**3**) and the nitrososulfone (**5**) are the reactive species directly involved in formation of the thiolsulfonate, as shown by eq. 8.

$$RSO_2NO + R'SNO \longrightarrow RSO_2SR' + 2NO \qquad (8)$$

This method should be useful in the synthesis of other bisthiolsulfonates using 1,4-butanedisulfinic acid with both aliphatic and aromatic thiols and hopefully also in the preparation of thiolsulfonates using aromatic sulfinic acids and alkylene dithiols. A limitation of the method may be that 1,4-butanedisulfinic acid is perhaps the only alkylene disulfinic acid which is quite stable as the free acid.[7] However, many disulfinic acids may be prepared as salts,[7] suggesting that acidification of these salts in the presence of an alkyl nitrite and a thionitrite might permit their use *in situ*. The presence of alkyl nitrites in the medium would not, of course, be compatible with certain functional groups such as amines or amine salts.

Since the model bisthiolsulfonate **1** was inactive as an antiradiation drug[1c] and also in antitumor activity,[1c] work with this class was discontinued.

Experimental Section[10]

Bis(2-acetamidoethyl) 1,4-Butanebisthiolsulfonate (1). A. From the Bissulfinate Salt.—A solution of 2-acetamidoethyl 2-acetamidoethanethiolsulfonate (28.85 g.)[6] in 100 ml. of water was added to a stirred mixture of 1.0 *N* aqueous sodium hydroxide (108 ml.) and 1,4-butanedisulfinic acid (10.00 g.) in 100 ml. of water. A voluminous white precipitate of the bisthiosulfonate 1 resulted immediately upon mixing. The solution was stirred at room temperature for 15 min., and the product was collected by filtration and recrystallized from 500 ml. of water to give 18.0 g. (80%) of 1 as off-white leaflets, m.p. 135–137°. Recrystallizations from water gave 13.3 g. (59%) of 1 having a constant melting point of 137–138°; the infrared spectrum contained strong bands (KBr pellet) at 3300, 1635, 1545, 1310, 1290, 1275, 1120, 640, and 505 cm.$^{-1}$. The dihydrobromide salt corresponding to 1 has been reported.[3d]

Anal. Calcd. for $C_{12}H_{24}N_2O_6S_4$: C, 34.27; H, 5.75; N, 6.66; S, 30.49. Found: C, 34.29; H, 5.83; N, 6.66; S, 30.34.

To confirm the structure of 1, a solution of 0.59 g. of *p*-toluenethiol in absolute ethanol (10 ml.) was added, in one portion, to a solution of 1.00 g. of 1 in absolute ethanol (10 ml.). The mixture was warmed to 35–38° and stirred for 48 hr. Solvent was removed below 40° to minimize disproportionation of the expected unsymmetrical disulfide. The residue was triturated under dry ether and the suspended solid (0.45 g., m.p. 105–115°) was collected by filtration. This solid was triturated with cold chloroform, collected by filtration, and dried. The yield of colorless 1,4-butanedisulfinic acid was 0.35 g. (79%), m.p. 114–118°, identical (mixture melting point, infrared spectrum) with an authentic sample.[7] The ether was removed from the filtrate and the residue was recrystallized from 1:1 benzene–pentane to yield 0.65 g. (57%) of 2-(*p*-tolyldithio)-1-acetamidoethane, m.p. and m.m.p. 62–64°, identical in infrared spectrum with authentic[6] material.

B. By the Method of Kresze and Kort.[9]—A solution of 2-acetamidoethanethiol (2.38 g.)[11] and *n*-butyl nitrite (3.15 g., Eastman White Label, used as received) in 50 ml. of absolute ethanol was heated at reflux for 15 min. During this time the red color due to the intermediate thionitrite (**3**) reached a maximum. *n*-Butyl nitrite (3.15 g.) was added in one portion, followed by dropwise addition of a solution of 1,4-butanedisulfinic acid (1.86 g.)[7] in 50 ml. of absolute ethanol during 15 min. Reflux was continued until the red color disappeared and the evolution of nitric oxide had ceased (2.5 hr.). The reaction mixture was cooled and the ethanol was removed. The residue was suspended in 25 ml. of ether, and the crude product was separated by filtration, washed with three 10-ml. portions of water, and dried: yield of bisthiolsulfonate 1, 2.70 g. (64%), m.p. 135–137°. The material was identical (mixture melting point, infrared spectrum) with the 1 described under A.

C. Exploratory Experiments with the Kresze–Kort Synthesis.—Lower yields resulted from addition of the sulfinic acid in one portion (50%), addition of the sulfinic acid to the thionitrite without additional nitrite (0%), use of excess sulfinic acid with excess nitrite (26%), use of excess thiol with excess nitrite (45%), and elimination of the reflux period necessary for the formation of thionitrite (33%).

When a solution of *n*-butyl nitrite (2.12 g.) in anhydrous ether (10 ml.) was added to a stirred solution at 0° of N,N-di(*p*-tolylsulfonyl)hydroxylamine (2.30 g.)[9] and *p*-chlorothiophenol (1.95 g.) in 40 ml. of anhydrous ether, color developed as before but did not disappear after 3.5 hr. at 0°. The mixture was warmed to 25° and stirred for 1 hr., during which time the color disappeared with evolution of nitric oxide. Addition of pentane and filtration separated 1.80 g. (78%) of the unchanged disulfonylhydroxylamine, m.p. and m.m.p. 121–126° (infrared spectrum identical with that of starting material). The filtrate contained 1.70 g. (88%) of *p*-chlorophenyl disulfide (identical by infrared spectrum), m.p. and m.m.p. 70–72°. The same reaction without added nitrite resulted in the recovery of unchanged disulfonylhydroxylamine (93%) and *p*-chlorothiophenol (94%).

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[10] Melting points are corrected. Elemental analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Infrared spectra were obtained using a Perkin-Elmer Model 137B or a Beckman IR-10 spectrophotometer with the sample in Nujol mulls or potassium bromide pellets. Evaporation of solvents usually was done under reduced pressure using a rotary evaporator.

[11] R. Kuhn and G. Quadbeck, *Chem. Ber.*, **84**, 844 (1951).

Mercaptan–Sulfur Reaction. Alkyl Trisulfides

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Trisulfides (I) can be obtained in good yields from the amine-catalyzed reaction of most mercaptans with sulfur at room temperature. Although the oxidation

$$2RSH + 2S \longrightarrow \underset{\text{I}}{RS_3R} + H_2S$$

of mercaptans with sulfur is well known, the reaction has been of little preparative value, since a mixture of polysulfides is usually formed.[1]

The course of the reaction is strongly influenced by the steric requirements of the mercaptan. From the sterically hindered *t*-butyl mercaptan, very little trisulfide is formed. Instead, the tetrasulfide is obtained in 85–90% yield. All the other mercaptans investigated (isopropyl, *sec*-butyl, isobutyl, and *n*-butyl) formed trisulfides as the predominant product in 70–95% yields.

If the sulfur is not used in excess of the stoichiometric amount for trisulfide formation, the charge

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[1] For a review of polysulfide chemistry, see E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. III, Chemical Publishing Co., New York, N. Y., 1960, p 387.

ratio is important only with the primary mercaptan. The trisulfide is the major product (75%) obtained from the stoichiometric charge of *n*-butyl mercaptan and sulfur (1:1 mole–atom ratio). If the *n*-butyl mercaptan:sulfur mole–atom ratio is 2, *n*-butyl disulfide is formed in 71% yield. Previous reports indicate that disulfides are formed in respectable yields from the base-catalyzed reaction of sulfur with primary mercaptans.[2,3] The results from variation in charge ratios are summarized in Table I.

TABLE I

REACTION OF MERCAPTANS WITH SULFUR. ALKYL POLYSULFIDES[a]

RS_xR

R	Charge, moles of RSH/g-atom of S	Product[b,c] % S_2	% S_3	% S_4
n-C_4H_9	1	[15.4]	[>75]	[<5]
n-C_4H_9	2	[71]	[29]	. . .
sec-C_4H_9	1	<3	>95	Trace
sec-C_4H_9	2	<3	>95	Trace
i-C_4H_9	1	[5]	[87]	[5]
t-C_4H_9	1	. . .	12.5	87.5
t-C_4H_9	2	. . .	10.6	89.4
i-C_3H_7	1	. . .	[>90]	[<10]

[a] The physical constants for all these polysulfides, except *sec*-butyl are given in ref 1. *sec*-$C_4H_9S_3C_4H_9$: bp 79–80° (0.4 mm), $n^{25}D$ 1.5290. [b] Yields in brackets were obtained by fractional distillation; all other yields were calculated from the nmr curves and confirmed by fractionation. [c] Total yields of product represent 90 to 100% of the sulfur charge.

The reaction is carried out by adding the mercaptan slowly to a slurry of sulfur and amine in an inert solvent at room temperature. Hydrogen sulfide evolution begins immediately and the reaction is complete in 2 to 4 hr. The mixture of products was separated by careful fractionation. In addition, the crude reaction products were examined by proton nmr spectroscopy. Recent work has shown that, as x increases in the formula, RS_xR, the chemical shifts for the protons nearest the sulfur are shifted downfield.[4,5] This was confirmed by preparing synthetic blends of di-, tri-, and tetrasulfides. The chemical shifts for the polysulfides investigated are reported in Table II.

TABLE II

H^1 CHEMICAL SHIFTS[a] OF POLYSULFIDES[b]

Compd	Values of x: 2	3	4
$CH_3CH_2CH(CH_3)S_xCH(CH_3)CH_2CH_3$	2.65	2.83	2.92
$CH_3CH_2CH_2CH_2S_xCH_2CH_2CH_2CH_3$	2.64	2.87	2.95
$CH_3CH(CH_3)CH_2S_xCH_2CH(CH_3)CH_3$	2.57	2.77	2.80
$CH_3CH(CH_3)S_xCH(CH_3)CH_3$	. . .	3.22	. . .
$(CH_3)_3CS_xC(CH_3)_3$[c]	1.28	1.35	1.38

[a] In ppm. [b] Hydrogens on carbon atom adjacent to sulfur. [c] Since there are no hydrogens on the carbon adjacent to the sulfur, these shifts are obviously those of the methyl groups.

The yields, as determined from nmr spectra, were in good agreement with the yields obtained by distillation. Polysulfides higher than tetra- were present in very small amounts.

Preliminary experiments indicate that the reaction is also applicable to the preparation of aromatic trisulfides.

Experimental Section

General Procedure for the Reaction of Mercaptans with Sulfur.—The mercaptan (1 or 2 moles) was added slowly over about 1 hr to a slurry of 1 g-atom of sulfur and *n*-propylamine (1–3 mole % of mercaptan charged) in methylene chloride at room temperature. Evolution of hydrogen sulfide began immediately and continued for 2 to 4 hr after the mercaptan addition. There was no detectable temperature change during the reaction. When hydrogen sulfide evolution ceased, the slightly hazy mixture was filtered, and the solvent was removed by vacuum distillation. A sample was removed for nmr analysis and the remainder was separated into its components by careful fractionation. Care was taken to keep the pot temperature below 140°, since disproportionation is known to occur above this temperature.[6]

Analytical Procedure.—A Varian A-60 high-resolution spectrometer was used to analyze the crude reaction mixtures after removal of methylene chloride. Semiquantitative yields were obtained from the chemical shifts for the protons nearest the sulfur. The yields were calculated from the peak heights with necessary allowance being made for the difference in molecular weights. Chemical shifts in Table II are reported with respect to tetramethylsilane with positive shifts being downfield.

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[2] F. H. McMillan and J. A. King, *J. Am. Chem. Soc.*, **70**, 4143 (1948).

[3] J. F. Olin, U. S. Patent 2,237,625 (April 8, 1941).

[4] D. Grant and J. R. VanWazer, *J. Am. Chem. Soc.*, **86**, 3012 (1964).

[5] I. B. Doughlas, presented at the Symposium on Fossil Fuels: Critical Discussion of Origin, Composition and Related Chemistry, sponsored by the American Petroleum Institute (Research Projects 48 and 52), University of Wyoming Science Camp, Laramie, Wyo., July 28–Aug 1, 1964.

[6] G. F. Bloomfield, *J. Chem. Soc.*, 1547 (1947).

The Reaction of *o*-Chlorobenzoic Acid with Certain Active Hydrogen Compounds and Sodamide in Liquid Ammonia[1]

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As an extension of the general benzyne–carbanion phenylation reaction,[3–4] the reaction of *o*-chlorobenzoic acid with certain nitriles and mercaptans and sodamide has been investigated. This paper represents the first time halobenzoic acids have been subjected to such treatment and the first time that benzynecarboxylate has been detected under these conditions. Thus, it has been found that this reaction yields exclusively the corresponding *m*-carboxyphenylated active hydrogen compound I (49–71%) and a mixture of *o*- and *m*-aminobenzoic acids (10–20%). Mercaptans also gave the *meta*-substituted benzoic acids, II. In

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[2] Robert A. Welch Predoctoral Fellow.

[3] For reviews, see J. F. Bunnett, *J. Chem. Educ.*, **38**, 278 (1961); H. Heanly, *Chem. Rev.*, **62**, 81 (1962).

[4] (a) F. W. Bergstrom and R. J. Agostinho, *J. Am. Chem. Soc.*, **67**, 2152 (1945); (b) P. H. Dirstini and F. W. Bergstrom, *J. Org. Chem.*, **11**, 55 (1946); (c) R. A. Seibert and F. W. Bergstrom, *ibid.*, **10**, 544 (1945); (d) W. W. Leake and R. Levine, *Chem. Ind.* (London), 1160 (1955); *J. Am. Chem. Soc.*, **81**, 1627, 1169 (1959).