The Orientational Effects in Ring-Opening Reactions of Some Unsymmetrically Substituted Episulfides

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Received January 29, 1968

The reactions of propylene sulfide, isobutylene sulfide, and chloropropylene sulfide with hydrogen chloride, acetyl chloride, and anhydrous chlorine have been found, contrary to earlier reports, to yield mixtures of isomeric products resulting from ring opening at both C–S bonds. Propylene sulfide was treated with a number of other electrophilic reagents such as hydrogen bromide, acetyl bromide, bromine, acetic anhydride, and benzoyl chloride. In each case, mixtures of both possible isomeric products were found. The nucleophilic reagents, lithium aluminum hydride and sodium ethanethiolate, however, were found to give ring opening exclusively at the primary C–S bond of propylene sulfide. Some of the mechanistic implications of these results are discussed.

With one exception, all the ring opening reactions of unsymmetrically substituted episulfides that have been described in the literature reportedly yield products opened exclusively at either the least substituted C–S bond or the most substituted C–S bond to give only one of the two possible isomers.[1] The reaction of isobutylene episulfide with mercaptans and alcohols in the presence of either boron trifluoride or sodium ethoxide has been reported to give mixtures of both primary and tertiary thiol products.[2] Since some of the reactions of propylene oxide lead to mixtures of isomeric products, for example, the reactions with hydrochloric and hydrobromic acids,[3] it seems surprising that the same reagents should not give similar results with propylene sulfide.[4] The assignment of structure to the products reported in these earlier studies[4-6] rested entirely on chemical grounds, and it seemed worthwhile, therefore, to reexamine some of these reactions using the more sensitive techniques of gas–liquid partition chromatography (glpc) and nmr spectroscopy for the detection of isomers that might have been overlooked by the earlier workers.

By comparing the reactions of propylene sulfide, isobutylene sulfide and chloropropylene sulfide with certain electrophilic reagents, it was hoped to determine what influence the substituents on the episulfide had in determining the direction of ring opening.

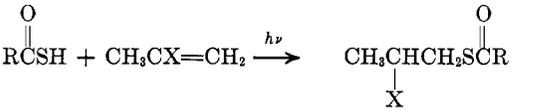
After this work was started, a number of reports appeared on the addition of alkane-, arene-, and acetylthiosulfenyl chlorides to unsymmetrically substituted olefins which have been found to yield mixtures of isomeric adducts.[7-9] The sulfenyl chloride additions to olefins and the additions of electrophilic reagents to episulfides have both been postulated to involve episulfonium ion intermediates, and if this is the case, certain similarities should be found in the isomer ratios of the adducts from both types of reaction.

Results

Schemes I, II, and III show the reaction products of various reagents with propylene sulfide, isobutylene sulfide, and chloropropylene sulfide, respectively. The relative amounts of the a and b isomers obtained from each of these reactions are shown in parentheses. In all cases, the a isomer is the result of ring opening at the primary C–S bond and has the sulfur on the secondary or tertiary carbon and the b isomer is the result from cleavage of the secondary or tertiary C–S bond and has the sulfur on the primary carbon. Except where otherwise noted, the isomer ratios were determined by glpc and confirmed by nmr spectra. The nmr spectra of these products are described in the Experimental Section.

The disulfides that are obtained from the reactions of episulfides with anhydrous halogen (**1a, b**; **2a, b**; **14a, b**; **18a, b**) are shown as having a symmetrical structure for convenience in writing, but are more likely to be mixtures of both symmetrical and unsymmetrical disulfides.

Propylene Sulfide.—The nmr spectra of the products from the various reactions of propylene sulfide shown in Scheme I all had two doublets in the region 1.3–1.6 ppm but the methyl group of either the a or b isomer from any of these reactions should be one doublet. The doublets occurring at higher field were in these cases assigned to the more shielded methyl protons of the a isomers.[9] The thiol esters **6b**, **7b**, and **8b** (X = H) were prepared by the light-catalyzed addition of thiol acetic or thiolbenzoic acid to the appropriate 2-halopropene[10] and confirmed our nmr assignments for these cases.

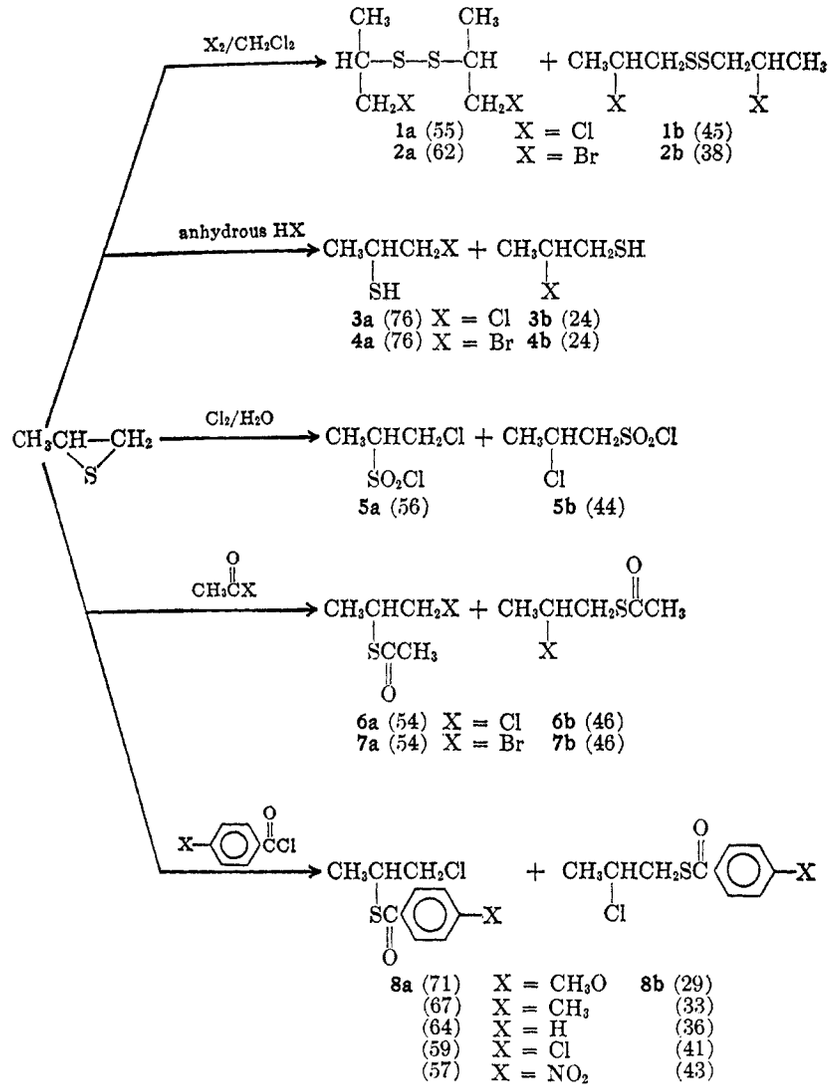


6b, X = Cl; R = CH_3
7b, X = Br; R = CH_3
8b, X = Cl; R = C_6H_5

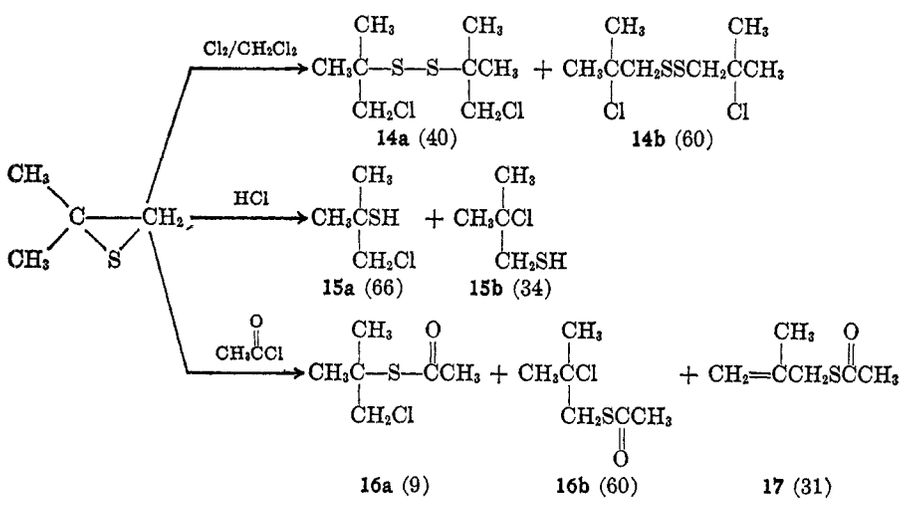
The pyridine-catalyzed reaction of propylene sulfide with acetic anhydride that was reported by Davies and Savige[4] was also reexamined. The relative amount of each isomer is shown in parentheses in Scheme IV. The earlier workers assigned the structure 1-acetoxypropane-2-thiol acetate (**9a**) to the reaction product on the basis of its hydrolysis to 2-mercaptopropanol (**10a**). Gas chromatographic analysis and the nmr spectrum of the propylene sulfide–acetic anhydride reaction product and of the mercaptopropanol derived from it show the presence of two isomers. The nmr spectra of these products have two doublets in the region 1.05–1.2 ppm due to the propylene methyl groups. The larger downfield doublets were assigned to the more deshielded

(1) For a recent review, see M. Sander, *Chem. Rev.*, **66**, 297 (1966).
(2) H. R. Snyder, J. M. Stewart, and J. B. Ziegler, *J. Amer. Chem. Soc.*, **69**, 2675 (1947).
(3) C. A. Stewart and C. A. VanderWerf, *ibid.*, **76**, 1259 (1954).
(4) W. Davies and W. E. Savige, *J. Chem. Soc.*, 317 (1950).
(5) W. Davies and W. E. Savige, *ibid.*, 774 (1951).
(6) J. M. Stewart and H. P. Cordts, *J. Amer. Chem. Soc.*, **74**, 5880 (1952).
(7) W. H. Mueller and P. E. Butler, *ibid.*, **88**, 2866 (1966).
(8) W. H. Mueller and P. E. Butler, *Chem. Commun.*, 646 (1966).
(9) W. H. Mueller and P. E. Butler, *J. Org. Chem.*, **32**, 2925 (1967).
(10) F. G. Bordwell and W. A. Hewett, *ibid.*, **23**, 636 (1958).

SCHEME I



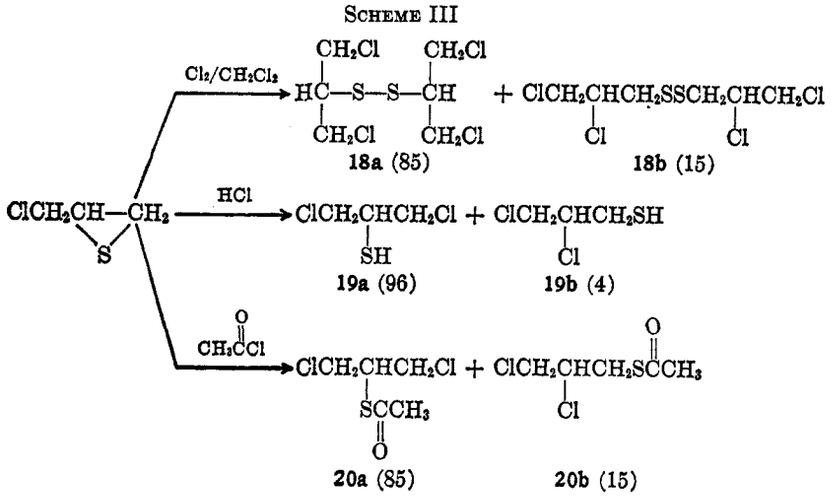
SCHEME II



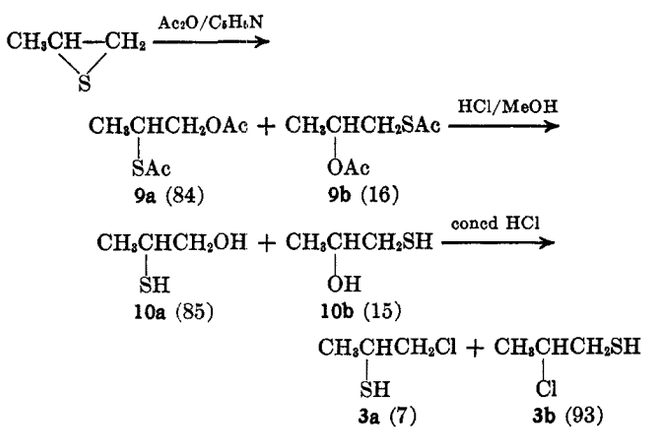
methyl protons of the a isomers in these two cases. Thus, propylene sulfide and acetic anhydride react to give a mixture of **9a** and **b** with the former predominating. Hydrolysis of this mixture yields mainly **10a**, but during the treatment of the latter with concentrated hydrochloric acid, a rearrangement takes place and the chloropropanethiol resulting is mainly the b isomer.

This facile rearrangement of 1-chloropropane-2-thiol was also observed during the reaction of propylene sulfide with aqueous hydrochloric acid. If the product is isolated after only short contact with the acid the thiol **3a** is the major isomer present, but the isomer ratio quickly changes to favor **3b**. The equilibrium ratio seems to be about 10:90 in favor of the b isomer, since

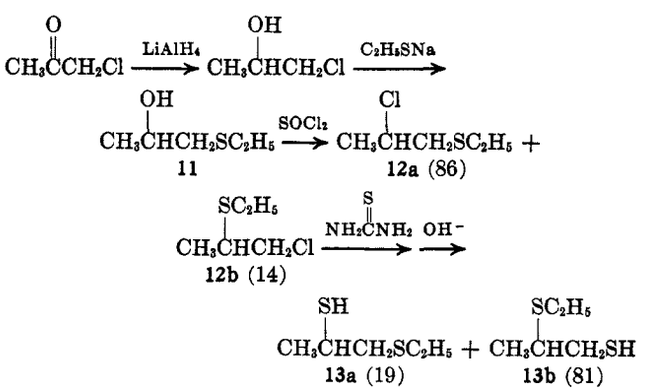
SCHEME III



SCHEME IV



SCHEME V

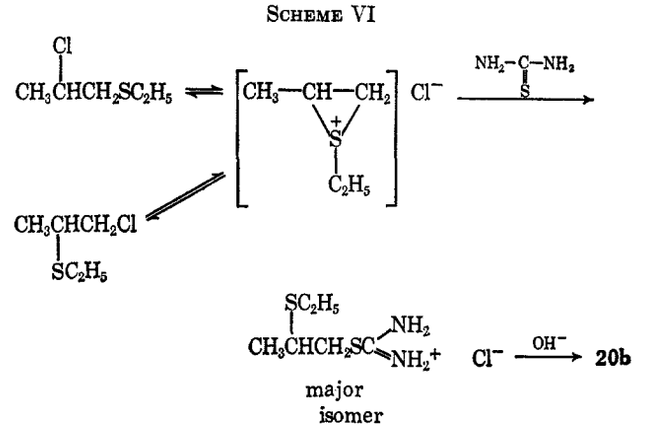


this ratio was also obtained when **3b** from hydrolysis of ester **6b** was stirred with concentrated hydrochloric acid for 18 hr. Water was also found to cause the rearrangement to take place. Thus, a mixture of **3a** and **b** in the ratio 71:29 stirred with water for several hours, contained **3a** and **b** in the ratio 10:90 along with about 60% propylene sulfide. A slower isomerization of the chloropropane thiols **3a** and **b** was observed to occur while standing for periods of several days at room temperature although little change occurred during distillation under reduced pressure, but the bromopropanethiol **4a** does isomerize during distillation at reduced pressure.

Although all the electrophilic reagents we examined gave appreciable ring opening of propylene sulfide at both the primary and secondary C–S bonds, two nucleophilic reagents that were examined opened propylene sulfide at the primary C–S bond with a high degree of selectivity. Thus, the monomeric product from the lithium aluminum hydride reduction of propylene sulfide was found to be 2-propanethiol as reported earlier[11] with only about 0.5% of 1-propanethiol detectable by glpc. In addition, the reaction of propylene sulfide with sodium ethanethiolate yielded 4-thiohexane-2-thiol (**13a**). None of the other isomer, 2-ethylthiopropane-1-thiol (**13b**), was detected by glpc. The identification of **13a** was based on nmr which shows a doublet at 1.90 ppm due to the secondary thiol proton. An attempt to synthesize the thiol **13a** *via* the chloride **12a** yielded instead a mixture of the isomeric thiols **13a** and **b** in the ratio 19:81 (Scheme V). The ratio of **13a** and **b** in the product was determined by glpc, while the nmr spectrum confirmed the presence of two isomeric thiols, with a doublet at 1.90 ppm for the secondary thiol proton of **13a** and a larger triplet at 1.62 ppm for the primary thiol proton of **13b**. The product from the reaction of the alcohol **11** with thionyl chloride was a mixture of the two isomeric chlorides **12a** and **b** in the ratio 86:14 as determined by nmr spectroscopy. A rearrangement during the reaction of the chlorides **12a** and **b** with thiourea must have occurred.

The latter rearrangement can be explained as occurring through an episulfonium ion intermediate (Scheme VI).

SCHEME VI

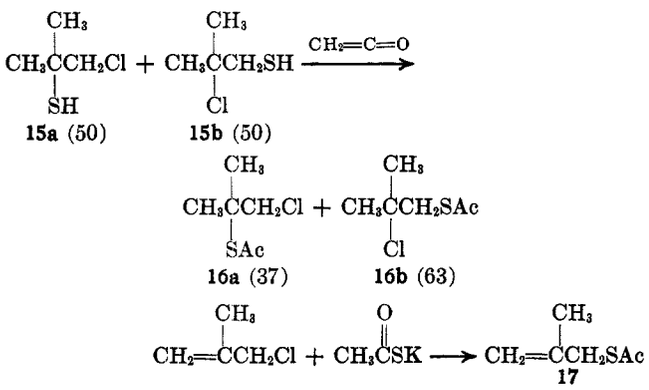


Isobutylene Sulfide.—The nmr spectrum of the reaction product of isobutylene sulfide and anhydrous

(11) F. G. Bordwell, H. M. Anderson, and B. M. Pitt, *J. Amer. Chem. Soc.*, **76**, 1082 (1954).

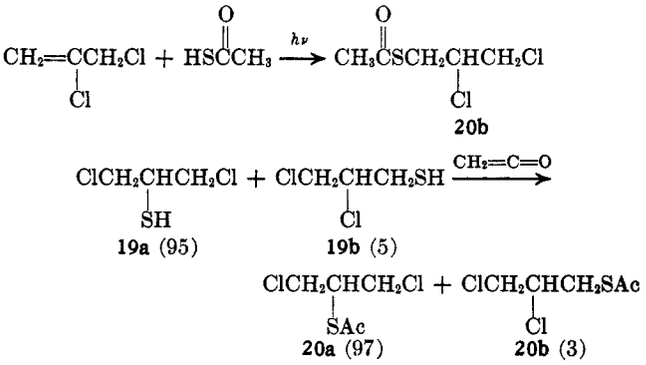
hydrogen chloride reveals the presence of the two isomers **15a** and **b**, which are readily separated by glpc. Similarly, the nmr spectrum of the product of the reaction of isobutylene sulfide with anhydrous chlorine shows the presence of the two species **14a** and **b** in the ratio 40:60. The nmr spectra of the products of these two reactions had a pair of singlets in the methyl region. The singlet occurring at lower field was assigned to the b isomer while the other was assigned to the a isomer. Like the chloropropanethiols **3a** and **b**, the chlorobutanethiols **15a** and **b** are fairly rapidly isomerized to an equilibrium mixture with a ratio of about 2:98 in favor of the b isomer. A mixture of **15a** and **b** was also found to isomerize, though more slowly, in the absence of water.

In contrast to the reactions of chlorine and hydrogen chloride with isobutylene sulfide, the addition of acetyl chloride (Scheme II) to this episulfide proceeds predominantly by ring opening at the tertiary C–S bond. The chlorobutylthiol ester **16b** (47%) and the unsaturated thiol ester **17** (24%) were the main products of the reaction. A small amount (7%) of the ester **16a** was also detected by glpc although the nmr spectrum of the crude reaction mixture did not reveal its presence. For purposes of comparison, a mixture of the esters **16a** and **b** (37:63) was prepared by adding ketene to the 1:1 mixture of chlorothiols **15a** and **b** from the reaction of isobutylene sulfide with anhydrous hydrogen chloride, while the unsaturated ester **17** was prepared from 1-chloro-2-methylpropene-2 and potassium thiolacetate.



Chloropropylene Sulfide.—The reaction of chloropropylene sulfide with hydrogen chloride yielded the two isomeric dichlorothiols **19a** and **b.** Because of extensive decomposition on the column, the ratio of these thiols could not be determined by glpc. The nmr spectra of these mixtures showed a doublet at 2.16 ppm due to the secondary thiol proton of **19a,** and two doublets at 1.72 ppm due to the primary thiol proton of **19b.** Evaluation of the ratios of **19a** and **b** was accomplished by integration of these peaks. It was found that the isomerization of **19a** to **b** in concentrated hydrochloric acid proceeds much more slowly than is the case for the isomerizations of the chlorothiols **3a** and **15a,** and reflects the lower reactivity of the chloropropylene sulfide with hydrogen chloride.[12]

The nmr spectrum of the acetyl chloride–chloropropylene sulfide adduct was not very revealing as to the structure of the adduct, but glpc showed the presence of two components. By the light-catalyzed addition of thiolacetic acid to 1,2-dichloropropene-2, the ester **20b** was obtained free from its isomer **20a.** Its identity with one of the components of the acetyl chloride–chloropropylene sulfide adduct was established by glpc. The addition of ketene to a mixture of the dichlorothiols **19a** and **b** (95:5) then yielded a mixture of the esters **20a** and **b** in the ratio 97:3. The unambiguous assignment of structures to the acetyl chloride–chloropropylene sulfide adducts followed from a comparison of the gas chromatograms. The addition of anhydrous chlo-



ride to chloropropylene sulfide produced predominantly the disulfide **18a.** The presence of about 15% of the disulfide **18b** was deduced from the nmr spectrum of the crude product.

Discussion

Oddon and Wylde, who recently reported on the kinetics of the reaction of anhydrous hydrogen chloride and hydrogen bromide with a number of substituted episulfides, found that the reactions with hydrogen chloride proceed with second-order kinetics.[12] On the basis of the observed kinetics as well as the work of Davies and Savige,[4,5] who reported that these reactions yield only primary thiols, Oddon and Wylde concluded that the reaction proceeds *via* attack by the halide ion on a carbonium ion intermediate, *i.e.*, an SN1Ac mechanism. Our work which shows that in anhydrous media hydrogen chloride yields mainly secondary thiol with both propylene sulfide and chloropropylene sulfide and yields more tertiary than primary thiol with isobutylene sulfide, is inconsistent with an SN1Ac mechanism. Attack by halide ion on an episulfonium ion intermediate would be consistent with our results since both steric as well as polar factors would have an effect on the site of attack by the nucleophile. The importance of steric factors in the direction of opening of some episulfonium ions has been demonstrated by Mueller and Butler.[7] However, the relatively larger amount of primary thiol obtained from isobutylene sulfide than is obtained from propylene sulfide on reaction with hydrogen chloride indicates that polar effects of the episulfide substituents are also important in this reaction.

The reaction products of the three episulfides studied with acetyl chloride indicate that polar effects become more important when the electron-withdrawing ability of the group attached to sulfur in the episulfonium ion is strong compared with hydrogen. In particular, the presence of the unsaturated ester **12** among the reaction products of the reaction of acetyl chloride with isobutylene sulfide strongly suggests that a tertiary carbonium ion is an intermediate in this reaction. A mixture of

(12) A. Oddon and J. Wylde, *Bull. Soc. Chim. Fr.*, 1607 (1967).

the two isomeric thiol esters **11a** and **b** prepared by the addition of a mixture of **10a** and **b** to ketene did not contain any of the ester **12**, hence **12** must arise by elimination of a proton from an intermediate of the ring-opening reaction (most likely a carbonium ion).

The reaction products of propylene sulfide with various 4-substituted benzoyl chlorides also indicate that as the electron-withdrawing ability of the electrophilic group is increased the proportion of b isomer also increases, although in this series, the effect is not very great.

Most of the work on the reactions of propylene sulfide with nucleophilic reagents leads to the conclusion that attack by the nucleophile occurs almost exclusively at the least hindered carbon of the episulfide. Thus, our results on the reaction of lithium aluminum hydride with propylene sulfide confirms the earlier work on this reaction.[11] A report[13] that propylene sulfide and dimethylamine yield the primary thiol rather than the secondary thiol has been shown to be incorrect,[14] while other work[15,16] has shown that attack of secondary amines on episulfides takes place at the least hindered carbon. In addition, we have found that the reaction of sodium ethanethiolate with propylene sulfide leads exclusively to primary thiol. All these results indicate that attack on propylene sulfide by nucleophilic reagents occurs at the least hindered carbon, and in the absence of strong polar effects these ring openings can be expected to be governed by steric factors.

Experimental Section

Nuclear magnetic resonance spectra were obtained on a Varian A-60. Chemical shifts are reported in parts per million from tetramethylsilane as internal standard. All glpc analyses were carried out on a Perkin-Elmer Model 800 gas chromatograph. All columns were 6 ft × 0.125 in. o.d. stainless steel. Column A contained 15 wt % diisodecylphthalate on 80/100 mesh Chromosorb W. Column C contained 15 wt % DC 200 silicone oil on 80/100 mesh Chromosorb W. Column K contained 15 wt % Carbowax 1500 on 80/100 mesh Chromosorb W. The microanalyses were carried out by A. B. Gygli, Toronto.

Reactions of Episulfides with Anhydrous Hydrogen Halides. General.—The anhydrous hydrogen halide was bubbled through a 20–25% w/v solution of the episulfide in anhydrous ether or methylene chloride guarded from the atmosphere by a calcium chloride drying tube, until the reaction was judged to be complete by the absence of an episulfide peak in the gas chromatogram. With the exception of the product of the reaction of propylene sulfide with hydrogen bromide, the ratio of a to b isomers was determined by glpc on the crude product. The ratios determined from the nmr spectra of the crude products were in good agreement with the glpc determinations with the exception noted above. The crude reaction product was then purified by distillation under reduced pressure. The nmr spectra were determined on the purified products, which were again analyzed by glpc.

Propylene Sulfide and Hydrogen Chloride.—The crude reaction mixture was analyzed on column A at 60° and showed, in addition to the ether peak, peaks at 15.4 and 16.9 min in the ratio 76:24 (**3a**:**b**). Distillation of the crude product yielded the mixture of 1-chloropropane-2-thiol (**3a**) and 2-chloropropane-1-thiol (**3b**) (bp 47–51° (49 mm); n^{20}D 1.4850) in a yield of 74%. Gas chromatography of this material showed the same two peaks to be present in the ratio of 71:29; nmr (CS_2) peaks were at δ 1.35 (d, J = 6 Hz, CH_3CS), 1.51 (d, J = 6 Hz, CH_3CCl), 1.73 (four lines, S H), 2.71 (m, CH_2S), 3.05 (m, CHS), 3.48 (m, CH_2Cl), 3.94 (m, CHCl).

Propylene Sulfide and Hydrogen Bromide.—The addition was carried out at −10° in CH_2Cl_2. Analysis of the crude product on column A at 75° showed the product to consist of two components with retention times of 15.7 and 17.0 min in the ratio 55:45, respectively. The solvent was removed under reduced pressure and the nmr spectrum (CS_2) was determined: δ 1.42 (d, J = 6.5 Hz, CH_3CSH), 1.73 (d, J = 6.5 Hz, CH_3CBr), 2.5–3.7 (m, CH_2 and CHSH), 4.04 (m, CHBr). From the ratio of the doublets at 1.42 and 1.73 it was determined that 1-bromopropene-2-thiol (**4a**) and 2-bromopropane-1-thiol (**4b**) were present in the ratio 76:24, respectively. Distillation of the crude product under reduced pressure afforded a mixture of **4a** and **4b** in 75% yield: bp 40–45° (12 mm); n^{20}D 1.5261. The nmr spectrum of this material showed the ratio of **4a** to **b** had changed to 33:67.

Isobutylene Sulfide and Hydrogen Chloride.—Analysis of the crude reaction product was carried out on column A at 75°. In addition to the ether peak, two other peaks were observed with retention times of 10.4 and 12.3 min in the ratio of 66:34, respectively (**15a**:**b**). Distillation of the crude material provided in 70% yield a mixture of 2-chloro-2-methylpropane-1-thiol (**15a**) and 1-chloro-2-methylpropane-2-thiol (**15b**), 56:44 by glpc: bp 37–39° (20 mm); n^{20}D 1.4762; nmr (CS_2), δ 1.42 (s, CH_3CS), 1.62 (s, CH_3CCl), 2.00 (s, MeCSH), 2.83 (d, J = 9 Hz, CH_2SH), 3.58 (s, CH_2Cl).

The isomer ratio of the above sample was found to change on standing at room temperature. Thus after 3 days it was found by glpc analysis that **15a** and **b** were present in the ratio of 28:72, and after 6 days in the ratio 11:89.

Chloropropylene Sulfide and Hydrogen Chloride.—Analysis of the crude reaction product by glpc could not be carried out due to extensive decomposition of the reaction products on the column. From the nmr spectrum of the crude product the ratio of **19a**:**19b** was determined as 97:3. Distillation of the product under reduced pressure yielded 25% of dichloropropane thiols: bp 62–64° (5.5 mm); n^{20}D 1.5213; nmr (CS_2), δ 1.72 (2d, J = 9 Hz, CH_2SH), 2.16 (d, J = 10 Hz, CHSH), 3.1–4.1 (complex envelope, CH_2 and CH). By integration of the thiol protons the ratio of **19a** to **b** was found to be 95:5. In addition to the mixture of **19a** and **b**, chloropropylene sulfide was recovered in 43% yield: bp 40–62° (5.5 mm); n^{20}D 1.5245. The ir spectrum of the latter showed some contamination by **19a** and **b**.

Reactions of Episulfides with Concentrated Hydrochloric Acid. General.—The episulfides were vigorously stirred with about ten volumes of 11.5 N hydrochloric acid for extended periods of time, the organic layer was then separated and the acid was extracted twice with methylene chloride. The combined organic phase and extracts, after drying over calcium chloride, were concentrated and distilled under reduced pressure. The isomer ratios were determined on the resulting products by glpc or nmr analysis.

For the shorter reaction times (1 to 10 min) a small amount of the episulfide was shaken with a larger volume of 11.5 N hydrochloric acid, the organic layer was quickly separated, washed with water, and then dried over calcium chloride. The chlorothiol isomer ratios were determined by glpc.

Propylene Sulfide.—The propylene sulfide was stirred with the acid for 18 hr. There was obtained a 52% yield of a mixture of of **3a** and **b** in the ratio 10:90 as determined by glpc (column A at 60°): bp 52–54° (52 mm); n^{20}D 1.4855.

When propylene sulfide was shaken with hydrochloric acid for about 1 min and worked up as described above, the ratio **3a**:**b** was found to be 56:44 by glpc. When the contact time with the acid was 10 min, the ratio **3a**:**b** was found to be 29:71.

Isobutylene Sulfide.—The isobutylene sulfide was stirred with the acid for 1 hr. There was obtained a 71% yield of a mixture of **15a** and **b** in the ratio 2:98 as determined by glpc (column A at 75°): bp 47–49° (30 mm); n^{20}D 1.4772; nmr (CS_2), δ 1.41 (s, CH_3CS), 1.62 (s, CH_3CCl), 1.63 (t, J = 9 Hz, CH_2SH), 2.82 (d, J = 4 Hz, CH_2SH). When isobutylene sulfide was shaken with hydrochloric acid for about 1 min the ratio **15a**:**b** was found to be 10:90 by glpc.

Chloropropylene Sulfide.—After 16 hr stirring with concentrated hydrochloric acid, the chloropropylene sulfide yielded 90% of dichloropropane thiols **19a** and **b** in the ratio 85 to 15: bp 61° (5 mm); n^{20}D 1.5257. Further stirring of this chlorothiol mixture with hydrochloric acid for another 84 hr yielded 60% of a mixture of **19a** and **b** in the ratio 30:70, whereas after stirring for a total of 14 days, the mixture was recovered in 51% yield

(13) B. Hansen, *Acta Chem. Scand.*, **13**, 151 (1959).
(14) S. D. Turk, R. P. Louthan, R. L. Cobb, and C. R. Bresson, *J. Org. Chem.*, **29**, 974 (1964).
(15) H. R. Snyder, J. M. Stewart, and J. B. Ziegler, *J. Amer. Chem. Soc.*, **69**, 2672 (1947).
(16) N. S. Isaacs, *Can. J. Chem.*, **44**, 395 (1966).

and had an isomer ratio of 23 to 77: bp 64° (5.5 mm); $n^{20}D$ 1.5240

All the isomer ratios were determined from the nmr spectra in CS_2 by integration of the peaks due to the thiol protons, which appeared as a doublet at δ 2.16 (J = 10 Hz) (**19a**) and a pair of overlapping doublets at δ 1.72 (J = 9 Hz) (**19b**).

Addition of Acetyl Halides to Episulfides. General.—The episulfide was added slowly with stirring to 1 equiv of the acetyl halide which was being cooled in an ice–water bath, except for the case of chloropropylene sulfide and acetyl chloride which were sealed together in an ampoule in a 1:1 molar ratio and heated to 45° for 18 hr. The reaction mixtures were stirred at 0° for 1 hr and then allowed to warm to room temperature. Gas chromatographic analysis was carried out on the crude reaction mixtures to determine the isomer ratios of the products.

Propylene Sulfide and Acetyl Chloride.—Analysis of the crude reaction product on column K at 80° showed components with retention times of 23.3 and 25.6 min in the ratio of 54:46, respectively. By admixture of this reaction product with 2-chloropropane-1-thiol acetate (**6b**) prepared from the addition of thiolacetic acid to 2-chloropropane (see below), the component with the longer retention time was identified as **6b**. Distillation of the crude product yielded 79% of the mixture of esters 1-chloropropane-2-thiol acetate (**6a**) and **6b**: bp 73° (12 mm); $n^{20}D$ 1.4900 (lit.[4] bp 70–71° (9 mm); $n^{15}D$ 1.491); nmr (CS_2), δ 1.32 (d, J = 6 Hz, CH_3 CS), 1.46 (d, J = 6 Hz, CH_3CCl), 2.21 (s, $CH_3C{=}O$), 2.23 (s, $CH_3C{=}O$), 3.2–4.2 (complex envelope, CH_2 and CH).

Propylene Sulfide and Acetyl Bromide.—Analysis of the crude mixture on column K at 100° showed only two large peaks with retention times of 14.8 and 16.2 min in addition to traces of low boiling impurity. The first component 1-bromopropane-2-thiol acetate (**7a**) made up 54% of the mixture, while the second, which had a retention time identical with that of 2-bromopropane-1-thiol acetate (**7b**), made up the remaining 46%. Distillation of the crude reaction mixture yielded 73% of the mixture of **7a** and **b** in the same ratio as before: bp 53–54° (0.6 mm); $n^{22}D$ 1.5179 (lit.[4] bp 45° (0.2 mm); $n^{13}D$ 1.521); nmr (CS_2), δ 1.29 (d, J = 6 Hz, CH_3 CS), 1.56 (d, J = 6 Hz, CH_3 CBr), 2.11 (s, $CH_3C{=}O$), 2.15 (s, $CH_3C{=}O$), 2.85–3.95 (complex envelope CH_2 and CH).

Isobutylene Sulfide and Acetyl Chloride.—The gas chromatogram of the crude product on column A or column K at 125° showed a fairly complex mixture. The two main fractions were identified as 2-chloro-2-methylpropane-1-thiol (**16b**), and 2-methylprop-2-ene-1-thiol acetate (**17**) (24%). A small peak was assigned to 1-chloro-2-methylpropane-2-thiol (**16a**) (7%) by comparison of retention times on both columns A and K with a mixture of **16a** and **b** prepared by the addition of a mixture of thiols **15a** and **b** to ketene. The nmr (C_6H_6) of the crude product in benzene had peaks at δ 1.46 (s, CH_3 CCl), 1.67 (three-line pattern, CH_3 C=C), 2.09 (s, $CH_3C{=}O$), 3.26 (s, Me_2CClCH_2S), 3.47 (d, J = 1 Hz, $SCH_2C{=}C$), 4.72 (m, $H_2C{=}C$), 4.88 (m, $H_2C{=}C$).

Chloropropylene Sulfide and Acetyl Chloride.—The crude reaction product was analyzed on column A at 150° and was found to contain, in addition to unreacted starting material, 1,3-dichloropropane-2-thiol acetate (**20a**) and 2,3-dichloropropane-1-thiol acetate (**20b**) in the ratio 83:17. The latter two were identified by comparison with chromatograms of independently synthesized **20b** and a mixture of **20a** and **b**. Distillation of the crude reaction mixture under reduced pressure yielded 28% of predominantly unreacted chloropropylene sulfide (bp 40° (20 mm); $n^{20}D$ 1.5268) and 43% of a mixture of **20a** and **b**: bp 80–85° (4 mm); $n^{20}D$ 1.5133 (lit.[5] bp 122° (25 mm), $n^{20}D$ 1.5155); nmr (CS_2), δ 2.35 (s, $CH_3C{=}O$), 3.83 (m, CH_2 and CH).

Preparation of 2-Chloropropane-1-thiol Acetate (6b).—The procedure of Bordwell and Hewett[10] for the light-catalyzed addition of thiolacetic acid to 2-chloropropene was followed to give 70% of 2-chloropropene-1-thiol acetate (**6b**): bp 74–76° (13 mm); $n^{20}D$ 1.4890 (lit.[10] bp 71° at 10 mm); nmr (CS_2), δ 1.42 (d, J = 6 Hz, CH_3CCl), 2.18 (s, $CH_3C{=}O$), 3.00 (three-line pattern, CH_2), 3.80 (m, CH).

Preparation of 2-Bromopropane-1-thiol Acetate (7b).—A solution of 12.0 g (0.1 mol) of 2-bromopropene and 7.6 g (0.1 mol) of thiolacetic acid was irradiated by a 60-W incandescent lamp for 12 hr. Distillation of the reaction mixture under reduced pressure yielded 4.9 g (25%) of 2-bromopropane-1-thiol acetate (**7b**): bp 46–47° (0.35 mm); $n^{20}D$ 1.5180; nmr (CS_2), δ 1.56 (d, J = 6 Hz, CH_3CBr), 2.17 (s, $CH_3C{=}O$), 3.08 (m, CH_2), 3.83 (m, CH). Gas chromatography of this sample on column K at 100° showed a single peak with retention time of 16.5 min.

Preparation of 2,3-Dichloropropane-1-thiol Acetate (20b).—A solution of 8.5 g (0.077 mol) of 2,3-dichloropropene and 5.8 g (0.077 mol) of thiolacetic acid were irradiated with a 100-W incandescent lamp for 12 hr and then distilled to yield 1.9 g (13%) of 2,3-dichloropropane-1-thiol acetate (**20b**): bp 64° (0.1 mm); $n^{20}D$ 1.5198. Gas chromatography of a mixture of this ester with the product of the addition of acetyl chloride to chloropropylene sulfide established the identity of the minor component of that reaction with **20b**.

Addition of 1,3-Dichloropropane-2-thiol (19a) and 2,3-Dichloropropane-1-thiol (19b) Mixture to Ketene.—Ketene, 1.4 g (33 mmol), was condensed into a glass tube cooled to −70° and containing 5.0 g (34.5 mmol) of a mixture of **19a** and **b** in the ratio 95:5 obtained from the reaction of chloropropylene sulfide with hydrogen chloride. The tube was sealed and after remaining at −70° for 18 hr, it was allowed to stand at room temperature for another 24 hr before being opened. Distillation of the contents under reduced pressure yielded 5.1 g (83%) of 1,3-dichloropropane-2-thiol acetate (**20a**): bp 53–55° (0.1 mm); $n^{20}D$ 1.5160. Gas chromatography of this material on column A at 150° showed the presence of 3% of the ester **20b**. The main component **20a** (97%) had the same retention time as the main component of the addition product of chloropropylene sulfide and acetyl chloride.

Additon of 2-Chloro-2-methylpropane-1-thiol (15a) and 1-Chloro-2-methylpropane-2-thiol (15b) Mixture to Ketene.—Ketene (2.2 g, 52 mmol) was condensed into a glass tube cooled to −70° and containing 6.6 g (53 mmol) of a mixture of **15a** and **b** in the ratio 53:47, respectively, and sealed. Gas chromatographic analysis of the solution after 4 days at −70° showed much of the thiols **15a** and **b** remained unreacted. Ketene was therefore bubbled through the solution at room temperature for 3 hr and the product was distilled at reduced pressure to yield 1.4 g (16%) of a mixture of the esters **16a** and **b** boiling at 30–32° (0.15 mm), $n^{20}D$ 1.4898. Gas chromatographic analysis of this material on column A or column K at 125° showed the two esters **16a** and **b** to be present in the ratio 33:67. The two components had the same retention times on both columns as the two components of the acetyl chloride–isobutylene sulfide reaction product which were assigned the structures **16a** and **b**.

Anal. Calcd for $C_6H_{11}ClOS$: C, 43.23; H, 6.65; Cl, 21.27; S, 19.23. Found: C, 43.47; H, 6.68; Cl, 20.89; S, 18.97.

The nmr spectrum of this material in benzene had singlets at 1.45, 2.07, and 3.24 ppm in the ratio 6:3:2 assigned to **16b** and a smaller set of singlets at 1.38, 1.96, and 3.81 ppm in the ratio 6:3:2 assigned to **16a**.

Preparation of 2-Methylpropene-3-thiol Acetate (17).—A solution of potassium thiol acetate was prepared by adding 16.8 g (0.22 mol) of freshly distilled thiolacetic acid to 14 g (0.25 mol) of potassium hydroxide in 100 ml of methanol under a nitrogen atmosphere. During the dropwise addition of 20 g (0.22 mol) of 3-chloro-2-methylpropene to the stirred alcohol solution, a white precipitate formed and the temperature of the reaction mixture rose to 40°. When the addition was completed, the mixture was heated to reflux for 1 hr, and was then cooled and mixed with excess water. The oil which separated was removed and the aqueous layer was extracted with three 25-ml portions of ether. The combined oil and extracts were dried ($CaCl_2$) and concentrated. Distillation of the residue under reduced pressure yielded 18.0 g (46%) of 2-methylpropene-3-thiol acetate (**17**): bp 48–50° (18 mm); $n^{20}D$ 1.4822; nmr (C_6H_6), δ 1.67 (three-line pattern, $CH_3C{=}C$), 2.06 (s, $CH_3C{=}O$), 3.51 (d, J = 1 Hz, CH_2S), 4.79 (m, $C{=}CH_2$), 4.95 (m, $C{=}CH_2$).

Anal. Calcd for $C_6H_{10}OS$: C, 55.37; H, 7.74; S, 24.63. Found: C, 55.82; H, 7.62; S, 24.37.

The gas chromatographic behavior of this material agreed with that of the unsaturated ester present in the acetyl chloride–isobutylene sulfide reaction product.

Addition of 4-Substituted Benzoyl Chlorides to Propylene Sulfide.—Equimolar solutions of freshly distilled propylene sulfide with each of benzoyl chloride, 4-chloro-, 4-methyl-, 4-methoxy-, and 4-nitrobenzoyl chloride, were sealed in glass ampoules and maintained at 50° for 10 days in a constant temperature bath. Each of the solutions was then pumped down for a short time to remove any volatiles and the a:b ratio of the esters were determined from the nmr spectra of the crude reaction product by measuring the areas of the overlapping doublets of the methyl protons. The results are given in Scheme I. In

the case of the mixture of 1-chloropropane-2-thiol benzoate (**8a**, X = H) and 2-chloropropane-1-thiol benzoate (**8b**, X = H) the downfield doublet was shown to be due to the b isomer by comparison with the nmr spectrum of an authentic sample of **8b** (X = H).

Preparation of 2-Chloropropane-1-thiol Benzoate.—Thiolbenzoic acid (bp 81–83° (8 mm), $n^{20}D$ 1.6022) was prepared according to Noble and Tarbell.[17] A solution of 13.8 g (0.1 mol) of thiolbenzoic acid and 7.8 g (0.1 mol) of 2-chloropropene was irradiated for 5 hr by a 150-W incandescent lamp. Distillation of the product yielded 15.9 g (74%) of 2-chloropropane-1-thiol benzoate (**8b**, X = H): bp 103–108° (1 mm); $n^{20}D$ 1.5754; nmr (C_6H_6), δ 1.35 (d, J = 6.5 Hz, CH_3), 3.29 (three-line pattern, CH_2), 3.99 (m, CH).

Anal. Calcd for $C_{10}H_{11}ClOS$: C, 55.94; H, 5.16; Cl, 16.51; S, 14.94. Found: C, 56.09; H, 4.96; Cl, 16.49; S, 15.29.

Reactions of Episulfides with Anhydrous Halogens. General.—The procedure of Stewart and Cordts[6] for the addition of chlorine or bromine to the episulfide was followed. Anhydrous methylene chloride was used as the solvent in each case. After removal of the solvent the reaction product was distilled under reduced pressure and the nmr spectrum of the distillate was used to determine the isomer ratios of the product formed.

Propylene Sulfide and Chlorine.—The mixture of bis(1-methyl-2-chloroethyl) disulfide (**1a**) and bis(2-chloropropyl)disulfide (**1b**) was obtained in 69% yield: bp 90–95° (0.25 mm); $n^{20}D$ 1.5405 (lit.[6] bp 98–101° (1 mm); $n^{20}D$ 1.5400); nmr (CS_2), δ 1.35 (d, J = 6 Hz, CH_3 CS), 1.56 (d, J = 6 Hz, CH_3 CCl), 2.8–4.2 (complex envelope, CH_2 and CH). The two methyl doublets had relative intensities of 55:45, respectively.

Propylene Sulfide and Bromine.—The mixture of bis(1-methyl-2-bromoethyl) disulfide (**2a**) and bis(2-bromopropyl) disulfide (**2b**) was obtained in 87% yield: bp 97–100° (0.4 mm); $n^{20}D$ 1.5839 (lit.[6] bp 114–117° (1 mm); $n^{20}D$ 1.5838); nmr (CS_2), δ 1.42 (d, J = 6.5 Hz, CH_3 C S), 1.80 (d, J = 7 Hz, CH_3 Br), 3.0–4.5 (complex envelope, CH_2 and CH). The two methyl doublets had relative intensities of 62:38, respectively.

Isobutylene Sulfide and Chlorine.—The mixture of bis(1,1-dimethyl-2-chloroethyl) disulfide (**14a**) and bis(2-chloro-2-methylpropyl) disulfide (**14b**) was obtained in 87% yield: bp 97–100° (0.75 mm); $n^{20}D$ 1.5262; nmr (CS_2), δ 1.36 (s, CH_3CS), 1.63 (s, CH_3CCl), 3.21 (d, J = 2.5 Hz, CH_2S), 3.55 (d, J = 3 Hz, CH_2Cl).

Anal. Calcd for $C_8H_{16}Cl_2S_2$: C, 38.87; H, 6.52; Cl, 28.69; S, 25.94. Found: C, 39.29; H, 6.57; Cl, 28.62; S, 26.06. From the nmr spectrum of this material it was determined that **14a** and **b** were present in the ratio 40:60, respectively.

Chloropropylene Sulfide and Chlorine.—After removal of the solvent from the reaction mixture a solid melting from 56 to 62° was obtained in 99% yield. The nmr spectrum of this material had a distorted doublet at δ 3.58 (J = 5.5 Hz), a multiplet centered at 3.06, and a very small multiplet at 4.07. From the areas of the two larger sets of peaks, it was concluded that the doublet represented the protons of the chloromethyl groups of **18a** and **b**, while the multiplet at 3.06 represented the methinyl proton of **18a** and the remaining methylene protons of **18b**, the two isomers being present in the approximate ratio 85:15, respectively. The small multiplet at 4.07 was assigned to the methinyl proton of **18b**. Recrystallization of this material from CS_2, then hexane, raised its melting point to 65.5–67.5°: nmr (CS_2), δ 3.02 (m, 1, CHS), 3.55 (d, 4, J = 5.5 Hz, CH_2Cl).

Anal. Calcd for $C_6H_{10}Cl_4S_2$: C, 25.01; H, 3.50; Cl, 49.21; S, 22.25. Found: C, 25.07; H, 3.44; Cl, 49.44; S, 22.45.

The mother liquor from the recrystallization of **18a** was chromatographed on a silica gel column. Elution with 20% benzene in hexane yielded an oil which proved to be a mixture of **18a** and **b** enriched in the latter. From the nmr in CS_2 [δ 2.98 (m), 3.55 (d, J = 5.5 Hz), 4.04 (m)], it was calculated that **18a** and **b** were present in the ratio 42:58, respectively.

Propylene Sulfide and Chlorine Water.—The procedure of Stewart and Cordts[6] for the addition of propylene sulfide to chlorine water was followed and gave a mixture of 1-chloro-2-propanesulfonyl chloride (**5a**) and 2-chloro-1-propanesulfonyl chloride (**5b**) in 54% yield: bp 57–60° (1 mm); $n^{20}D$ 1.4872 (lit.[6] bp 55–56° (1 mm); $n^{20}D$ 1.4859); nmr (C_6H_6), δ 1.36 (d, J = 6.5 Hz, CH_3CSO_2Cl), 1.38 (d, J = 6.5 Hz, CH_3CCl), 3.59 (m, CH_2, $CHSO_2Cl$), 4.22 (m, CHCl).

From the results of the oxidative chlorination of a 10:90 mixture of chlorothiols **3a** and **b**, the component with longer retention time was assigned structure **5a** while the other component was assigned structure **5b**.

Addition of 2-Chloropropane-1-thiol (3b) to Chlorine Water.—A mixture of **3b** containing about 10% of the isomer **3a** which was obtained from the reaction of propylene sulfide and hydrochloric acid was added to chlorine water as described by Stewart and Cordts.[6] There was obtained a 66% yield of pale yellow oil: bp 55–60° (1 mm); $n^{20}D$ 1.4940; nmr (C_6H_6), δ 1.38 (d, J = 6.5 Hz, CH_3CCl), 3.59 (m, CH_2SO_2Cl), 4.23 (m, CHCl). Gas chromatography of this material on column C at 125° showed two components with retention times of 8.5 and 9.1 min in the ratio of 87:13, respectively. The component with shorter retention time was assigned the structure **5b**, while the other was assigned the structure **5a**.

Reaction of Acetic Anhydride with Propylene Sulfide.—The pyridine-catalyzed reaction of acetic anhydride with propylene sulfide was carried out as reported by Davies and Savige.[4] The product which was obtained in 66% yield proved to be a mixture of 1-acetoxy-2-propanethiol acetate (**9a**) and 2-acetoxy-1-propanethiol acetate (**9b**): bp 54–56° (1 mm); $n^{20}D$ 1.4651 (lit.[4] bp 103–105° (11 mm); $n^{15}D$ 1.4702); nmr (CS_2), δ 1.08 (d, J = 6 Hz, CH_3COAc), 1.15 (d, J = 6 Hz, CH_3C SAc), 1.77 (s, CHC(=O)O), 2.04 (s, CH_3C(=O)S), 2.71 (m, CH_2SAc), 3.30 (m, CHSAc), 3.72 (m, CH_2OAc), 4.38 (m, CHOAc). Since the doublet at 1.15 was much larger than the doublet at 1.08, it was concluded that **9a** was the major isomer. Analysis by glpc on column C at 100° showed the presence of two components in the ratio 84:16.

Hydrolysis of the ester mixture in refluxing 1% hydrochloric acid in methanol for 1 hr gave in 75% yield, a mixture of 2-mercapto-1-propanol (**10a**) and 1-mercapto-2-propanol (**10b**): bp 58–59.5° (10 mm); $n^{20}D$ 1.4853 (lit.[4] bp 60–62° (12 mm); $n^{17}D$ 1.4818); nmr (CS_2), δ 1.08 (d, J = 6 Hz, CH_3COH), 1.15 (d, J = 6 Hz, CH_3CSH), 1.38 (t, J = 3.5 Hz, CH_2SH), 1.43 (d, J = 6 Hz, CH—SH), 2.15–3.45 (complex envelope, CH_2 and CH), 3.57 (s, OH). Since the doublet at 1.15 was much larger than the one at 1.08 it was concluded that **10a** was the major isomer. Gas chromatographic analysis of this material on column A at 125° showed the presence of two components in the ratio 85:15.

Addition of Sodium Ethanethiolate to Propylene Sulfide.—Sodium (0.1 g, 0.004 g-atom) was dissolved in a solution of 20 g (0.32 mol) of ethanethiol in 50 ml of dry tetrahydrofuran (THF), and then 7.5 g (0.1 mol) of propylene sulfide was added dropwise. The reaction mixture was then heated to reflux for 16 hr during which time a white precipitate formed. Some of the excess thiol and THF were removed by distillation. The addition of 10 ml of 3 N hydrochloric acid to the residue caused the disappearance of the precipitate, and after separation of the organic layer, the aqueous layer was extracted twice with 20-ml portions of ether. The ether extracts were combined with the organic layer, dried ($CaCl_2$), and distilled under reduced pressure, to yield 4.4 g (32%) of 4-thiahexane-2-thiol (**13a**): bp 60° (4.5 mm); $n^{20}D$ 1.5105. Gas chromatographic analysis of the liquid was carried out on column A at 125° and showed it to be a single compound with retention time of 10.5 min contaminated by trace amounts of low boiling impurities. The nmr spectrum indicated that the compound was a secondary thiol with the thiol proton appearing as a doublet at δ 1.90 (J = 5 Hz).

Anal. Calcd for $C_5H_{12}S_2$: C, 44.05; H, 8.87; S, 47.06. Found: C, 44.08; H, 8.65; S, 46.94.

Preparation of 2-Chloro-4-thiahexane.—1-Chloropropane-2-ol (bp 48–51° (25 mm), $n^{20}D$ 1.4381) was prepared by the lithium aluminum hydride reduction of 1-chloropropan-2-one.[3] 1-Chloropropan-2-ol (47 g, 0.5 mol) was added dropwise with stirring to a solution of 40 g (0.62 mol) of ethanethiol in 500 ml of ethanol containing 0.5 mol of sodium ethoxide. A white precipitate formed during the addition and the temperature of the mixture rose to 40°. Two hours after the addition was completed about 2 l. of water were added and the mixture was extracted with 600 ml of ether. The ether layer was dried over $CaCl_2$ and after removal of the ether, the residue was distilled under reduced pressure to yield 23 g (38%) of 4-thiahexan-2-ol (**11**): bp 70–74° (18 mm); $n^{20}D$ 1.4771.

Thionyl chloride (25 g, 0.21 mol) was added dropwise to a solution of 1 ml of pyridine in 22 g (0.18 mol) of the 4-thiahexan-2-ol, and the mixture was heated to reflux for 1 hr. The reaction mixture was then treated with 200 ml of dilute hydro-

(17) P. Noble, Jr., and D. S. Tarbell, *Org. Syn.*, **32**, 101 (1952).

chloric acid and extracted three times with methylene chloride. The extracts were dried over $CaCl_2$ and concentrated and the residue was distilled under reduced pressure to yield 17.2 g (68%) of liquid: bp 55–57° (14 mm); $n^{20}D$ 1.4809; nmr (CS_2), δ 1.25 (t, J = 7.5 Hz, CH_3CH_2), 1.31 (d, J = 7.5 Hz, CH_3CS), 1.57 (d, J = 6 Hz, CH_3CCl). The mixture was calculated to contain 86% 2-chloro-4-thiahexane (**12a**) and 14% 1-chloro-2-ethylthiopropane (**12b**).

Reaction of the Mixture of 12a and 12b with Thiourea.—A solution of 9.0 g (0.065 mol) of **12a** and **b** (86:14) obtained above with 5.5 g (0.072 mol) of thiourea in 100 ml of ethanol was heated to reflux for 16 hr and concentrated under reduced pressure. The solid residue was dissolved in water and was treated with 3.2 g (0.08 mol) of sodium hydroxide in 25 ml of water. An oil which separated was removed and the aqueous layer was extracted with ether. After combining the oil and the ether extract, drying ($CaCl_2$), and concentrating, the residue was distilled under reduced pressure to yield 5.1 g (58%) of liquid: bp 60–62° (2.5 mm); $n^{20}D$ 1.5127. Gas chromatography of this sample on column A at 125° showed, in addition to several minor impurities, a large peak at 11.2 min with a shoulder at 10.7 min. The shoulder was shown to correspond to the secondary thiol **13a**. The nmr spectrum (CS_2) confirmed the presence of the secondary thiol **13a** by the presence of a doublet at δ 1.90 (J = 5 Hz) due to the secondary thiol proton. A triplet at δ 1.62 (J = 8.5 Hz) was assigned to the primary thiol proton of **13b**. Integration of these two sets of peaks indicated that **13a** and **b** were present in the ratio 16:84. The ir spectra of **13a**, obtained from the base-catalyzed addition of ethanethiol to propylene sulfide, and of the mixture of **13a** and **b** obtained above, were very similar showing only some minor differences.

Lithium Aluminum Hydride Reduction of Propylene Sulfide.—Propylene sulfide (10 g, 0.135 mol) in an equal volume of dry ether was added with stirring to 5.0 g (0.13 mol) of lithium aluminum hydride in 40 ml of dry ether which was being cooled in an ice–water bath. When the addition was completed the mixture was heated to reflux for 1 hr. The mixture was then cooled and the excess hydride was destroyed by the careful addition of 220 ml of 3 N hydrochloric acid. After separation and drying over magnesium sulfate, the ether layer was analyzed by glpc (column A at 60°). The major monomeric product (99.5%) had a retention time identical with that of authentic 2-propanethiol while a trace component (0.5%) had a retention time identical with that of 1-propanethiol.

Registry No.—**1a**, 1561-70-2; **1b**, 16621-19-5; **2a**, 16621-20-8; **2b**, 16621-21-9; **3a**, 16621-22-0; **3b**, 814-64-2; **4a**, 16621-24-2; **4b**, 16621-25-3; **5a**, 16621-26-4; **5b**, 2386-59-6; **6a**, 16622-60-9; **6b**, 16621-28-6; **7a**, 16621-29-7; **7b**, 16621-30-0; **8a**, 16621-31-1; **8b**, 16621-32-2; **9a**, 16621-33-3; **9b**, 16621-34-4; **10a**, 3001-64-7; **10b**, 1068-47-9; **11**, 16621-37-7; **12a**, 692-30-8; **12b**, 16621-39-9; **13a**, 16621-40-2; **13b**, 16621-41-3; **14a**, 16621-42-4; **14b**, 16621-43-5; **15a**, 16621-44-6; **15b**, 16621-45-7; **16a**, 16621-46-8; **16b**, 16621-47-9; **17**, 16621-48-0; **18a**, 1561-69-9; **18b**, 16621-50-4; **19a**, 16621-51-5; **19b**, 7763-79-3; **20a**, 16621-53-7; **20b**, 16621-54-8.

Acknowledgment.—The author is grateful for the technical assistance of Messrs. K. C. Edwards, Z. Szentgyorgyi, and G. Takaki.

Acid-Catalyzed Brominations, Deuterations, Rearrangements, and Debrominations of Thiophenes under Mild Conditions

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Received February 28, 1968

Bromination and deuteration of some substituted thiophenes have been accomplished under remarkably mild conditions. Upon treatment with N-bromosuccinimide in acetic acid–chloroform solution at room or slightly elevated temperatures, 3-methyl, 3-phenyl, 3-phenylthio, and 3-bromothiophenes are rapidly brominated in the 2 position in nearly quantitative yields. Bromination of 2-methyl, 2-phenyl, 2-phenylthio, and 2-bromothiophenes under the same conditions yields the 5-bromo derivatives. In refluxing deuterioacetic acid 3-alkyl-, 3-phenyl-, and 3-phenylthio-substituted thiophenes undergo deuterium–hydrogen exchange at the 2 position while the corresponding 2-substituted derivatives are exchanged at the 5 position. In solutions of hydrogen bromide in acetic acid some 2-bromothiophenes undergo rearrangements. 2-Bromo-3-phenylthiophene, for example, forms 2-bromo-4-phenylthiophene, 3-phenylthiophene, and 2,5-dibromo-3-phenylthiophene. Preliminary investigations of the mechanism of this reaction have been made. Substitution of 3-phenylthiophene at the 2 position is the kinetically controlled reaction under all conditions investigated. When the bromine acceptor phenol is added to the hydrogen bromide–acetic acid mixture, bromothiophenes which are subject to rearrangement can be debrominated in good to high yields.

In the course of studies of the mechanisms of the photochemically induced rearrangements of thiophenes[1] we have needed a number of deuterium-labeled starting materials.[2,3] Our normal technique of introducing deuterium at a specific position in the thiophene ring involves conversion of a bromo into a deuterio substituent. The necessity of having isomer-free bromothiophene precursors led us to investigate conditions necessary to obtain selective, high-yield brominations. The possibilities of direct deuterium-hydrogen exchange were also explored. We find that with certain thiophene derivatives both bromination and direct hydrogen–deuterium exchanges occur under remarkably mild conditions to give selectively substituted products of kinetic control.[4] We have furthermore observed that some bromothiophenes readily undergo rearrangement in the presence of strong acid catalysts.

Bromination.—When treated with N-bromosuccinimide (NBS) in a 50:50 (v/v) mixture of chloroform and glacial acetic acid, 3-alkyl, 3-phenyl-,[5] and 3-phenylthiothiophenes are brominated nearly quantitatively at the 2 position (eq 1). Reaction is complete

(1) See, for example, H. Wynberg, R. M. Kellogg, H. van Driel, and G. E. Beekhuis, *J. Amer. Chem. Soc.*, **89**, 3501 (1967).

(2) R. M. Kellogg and H. Wynberg, *ibid.*, **89**, 3495 (1967).

(3) R. M. Kellogg, J. J. C. Vermeer, and H. Wynberg, unpublished work.

(4) See, for an excellent review of bromination as well as other aspects of thiophene chemistry, S. Gronowitz, *Advan. Heterocycl. Chem.*, **1**, 1 (1963).

(5) Selective bromination of 3-phenylthiophene with NBS in carbon tetrachloride has recently been reported: S. Gronowitz, N. Gjös, R. M. Kellogg, and H. Wynberg, *J. Org. Chem.*, **32**, 463 (1967).