from acetone–ether furnished the analytical specimen, m.p. 102–104°.

Anal. Calcd. for $C_{12}H_{16}N_2O_4$: C, 57.1; H, 6.4; N, 11.1. Found: C, 56.9; H, 6.4; N, 11.1.

B.—A solution of III (0.5 g.) in pyridine (3 ml.) and acetic anhydride (3 ml.) was heated on the steam bath for 90 min. and the reaction mixture was then evaporated to dryness under reduced pressure. Crystallization of the residual yellow gum from acetone–ether afforded the title compound, m.p. 103–104°. This did not depress the melting point of a specimen prepared by method A, m.m.p. 102–104°.

3-Amino-2-cyanobenzyl Acetate.—The diacetate II (1.0 g.) in a 25-ml. flask fitted with a distillation apparatus was immersed in an oil bath at 195°. A vacuum of 160 mm. was maintained in the apparatus by means of a water pump, nitrogen being aspirated through the system. The temperature of the oil bath was raised to 215° and, during 25 min., acetic acid (0.87 g., theoretical yield) distilled out. The pot residue, dark brown in color, crystallized on cooling. This was taken up in methylene chloride (25 ml.) and percolated through a column of silica gel. (25 g.). Elution of the column with methylene chloride containing 20% ethyl acetate afforded a pale yellow product which crystallized from ether–petroleum ether (b.p. 30–60°) as yellow plates, m.p. 63–64° (2.6 g., 83%). Two further crystallizations from the same solvent mixture led to the pure compound, m.p. 66°.

Anal. Calcd. for $C_{10}H_{10}N_2O_2$: C, 63.2; H, 5.3; N, 14.7. Found: C, 63.2; H, 5.2; N, 14.7.

7-Aminophthalide.—3-Amino-2-cyanobenzyl acetate (0.25 g.) was dissolved in 6 *N* hydrochloric acid (10 ml.) and the solution was heated on a steam bath for 24 hr. The liquid was then evaporated to dryness under reduced pressure and the resulting solid was triturated with sodium hydrogen carbonate solution. Removal of the solid by filtration gave an almost white product (0.256 g.) which when recrystallized from ether led to 7-aminophthalide as small, white, diamond-shaped crystals, m.p. 122°. One further recrystallization from ether gave the analytical sample, m.p. 122.5–123°.

Anal. Calcd. for $C_8H_7NO_2$: C, 64.4; H, 4.7; N, 9.4. Found: C, 64.3; H, 4.8; N, 9.3.

7-Hydroxyphthalide.—7-Aminophthalide (0.2 g.) was dissolved in a mixture of sulfuric acid (3.04 g.) and water (20 ml.) and diazotized at −5° with a solution of sodium nitrite (95 mg.) in water (5 ml.) during 8 min. The mixture was then stirred below 0° for 1 hr. and excess nitrous acid was decomposed thereafter by the addition of a small amount of urea. The liquid was then heated on a steam bath for 1.5 hr. and filtered while hot to remove a trace of a bright red precipitate. The filtrate on cooling deposited a crop of fine, needle-shaped crystals (0.153 g.) which were removed, dissolved in methylene chloride (5 ml.), and percolated through a column of alumina (3 g.). Elution with methylene chloride (40 ml.) gave white material which when recrystallized from ether–petroleum ether (b.p. 30–60°) afforded pure 7-hydroxyphthalide as colorless prisms, m.p. 135–136°. A mixture melting point of this material with an authentic sample prepared according to Blair, *et al.*,[15] showed no depression, m.m.p. 135–136°. The infrared spectra of the two specimens were also identical.

Acknowledgment.—The authors would like to thank Mr. J. P. Panella and Mr. A. A. Carlson who carried out much of the experimental work and Dr. C. K. Fitz who performed all elemental analyses.

Mechanism of the Desulfurization of Episulfides with Methyl Iodide[1]

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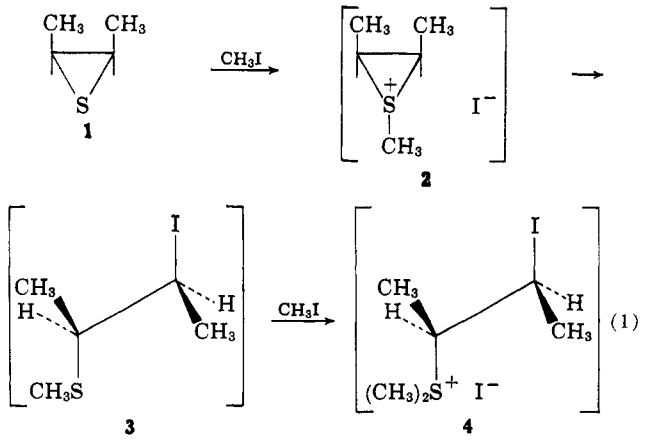
The principal route for the stereospecific desulfurization of 2-butene episulfides with methyl iodide involves the following sequence of intermediates: episulfonium salt, β-iodosulfide, β-iodosulfonium iodide. When methyl bromide was used as the alkylating agent, the sulfide and sulfonium bromide could be isolated. These were also converted to butene when treated with iodide ion or iodine under the original reaction conditions. All elimination reactions were highly stereospecific except that between iodide ion and the β-bromosulfonium bromides. The exceptional situation probably involves a bromide ion induced racemization *via* a vinylsulfonium intermediate or epimerization *via* nucleophilic displacement of the secondary bromide.

In an earlier report on the desulfurization of 2-butene episulfides, the mechanism was discussed in terms of the observed stereospecific formation of 2-butene corresponding to the starting episulfide.[3] The route proposed by Culvenor, Davies, and Heath[4] for olefin formation (eq. 1, 2, and 4) could be modified by substituting an alternate iodide-induced elimination (eq. 3).

Attempts to isolate any of the proposed intermediates **2**, **3**, and **4**, were unsuccessful, probably because of the high reactivity of iodide ion as a nucleophile and iodine-containing organic compounds as substrates. However, it seemed feasible to block the process and accumulate one or more of the intermediates by using methyl bromide in place of methyl iodide, for bromide ion should not be expected to be involved in an elimination



reaction of the type shown in the last step of either mechanistic route. It would seem most likely that intermediate **4** should accumulate.

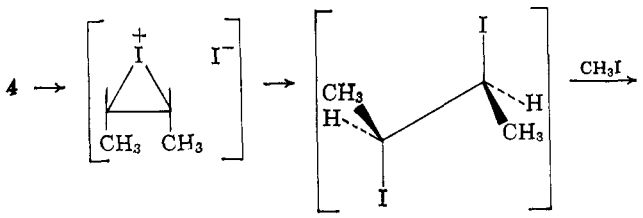
When *cis*-2-butene episulfide was allowed to react with methyl bromide in acetonitrile at room temperature (eq. 5), the threo-β-bromosulfonium bromide (**6**) slowly precipitated as large, white crystals. After a reaction time of 18 days the yield of solid was 47%. Evapora-

(1) This work was supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society and by Grant GM 8185 from the National Institutes of Health, U. S. Public Health Service. Grateful acknowledgment is hereby made to the granting institutions.

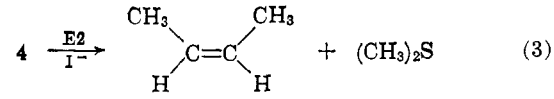
(2) Abstracted in part from the Ph.D. Thesis of D. J. Pettitt, March, 1964.

(3) G. K. Helmkamp and D. J. Pettitt, *J. Org. Chem.*, **25**, 1754 (1960).

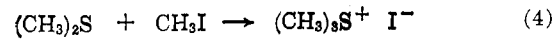
(4) C. J. Culvenor, W. Davies, and N. S. Heath, *J. Chem. Soc.*, 282 (1949).



(2)

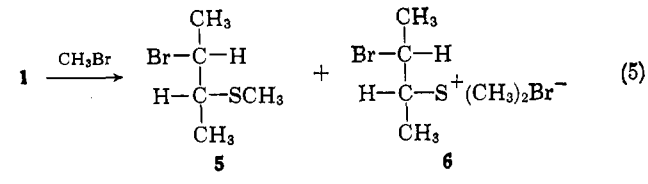


(3)

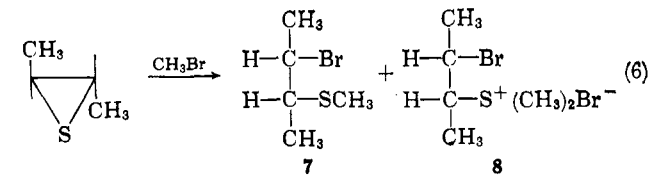


(4)

tion of the solvent left a colorless oil that was identified as *threo*-2-bromo-3-methylthiobutane (**5**). A similar reaction with *trans*-2-butene episulfide (eq. 6) gave the corresponding *erythro* isomers **7** and **8**. Optically active (*SS*)(−)-2-butene episulfide[5,6] yielded (*RS*)(−)-2-bromo-3-methylthiobutane and (*RS*)(−)-2-bromo-3-dimethylsulfoniobutane bromide.

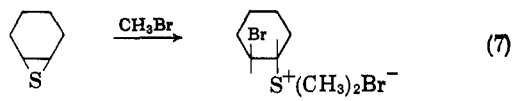


(5)



(6)

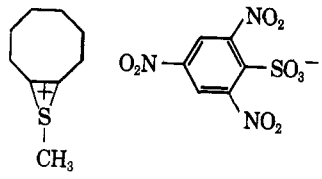
Cyclohexene sulfide and excess methyl bromide (eq. 7) in acetonitrile produced *trans*-1-bromo-2-dimethylsulfoniocyclohexane bromide (**9**) in 41% yield after 4 days. However, the sulfide precursor was not isolated.



(7)

Evidence for the structure of the products from the reaction between the episulfides and methyl bromide is provided by syntheses of the sulfides **5** and **7** from methanesulfenyl bromide and *cis*- and *trans*-2-butene, respectively. The stereochemistry of the products is assigned on the basis of kinetic and stereochemical data of Kharasch, *et al.*,[7,8] which indicates that the reaction of sulfenyl halides with olefins is a *trans*, ionic addition.

In an attempt to isolate an episulfonium salt related to **2**, it was found that the use of methyl nitrate, methyl sulfate, or methyl *m*-nitrobenzenesulfonate in the alkylation of episulfides led to none of the characteristic intermediates. In general, the major product was polymer. Apparently, when the nucleophilicity of the anion arising from the alkylating agent is reduced sufficiently, the episulfide itself serves as an effective nucleophile for opening the episulfonium ring. Although polymer was not detected in the products from 2-butene episulfides and methyl iodide in acetone or acetonitrile solvents, cyclooctene sulfide polymerized rapidly under identical conditions. A report on the isolation of complex mixtures from the reaction of ethylene and propylene sulfides with methyl iodide[4,9,10] suggests that these products resulted from polymerization of the substrate. Through the use of a very active alkylating agent with an anion of low nucleophilicity and a highly hindered substrate, an episulfonium salt could be isolated. When cyclooctene episulfide was treated with trimethyloxonium 2,4,6-trinitrobenzenesulfonate, the stable cyclooctene S-methylepisulfonium 2,4,6-trinitrobenzenesulfonate (**10**) was obtained.[11]



10

Elimination Reactions.—Each of the intermediates isolated from various alkylation reactions of episulfides was subjected to the reaction conditions for methyl iodide desulfurization. In addition, other conditions were investigated because it was shown that iodine (a product of the reaction) could be directly involved in the desulfurization of the episulfide,[12] and iodide ion could attack sulfur in episulfonium salts.[13]

Stereospecific desulfurization of **5** and **7** occurred upon treatment with iodine, sodium iodide, or methyl iodide in refluxing acetone or acetonitrile (Table I).

TABLE I

BUTENE COMPOSITION FROM REACTIONS OF 2-BROMO-3-METHYLTHIOBUTANES WITH IODINE, SODIUM IODIDE, AND METHYL IODIDE

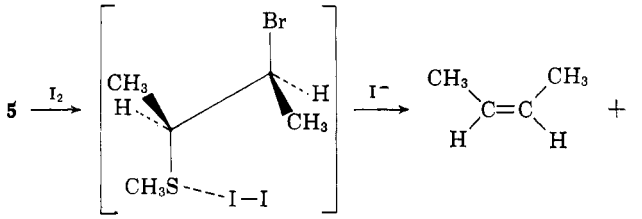
Isomer	Reagent	Solvent	—Butene composition— % *cis*	% *trans*
threo, **5**	I_2	Acetone	99.5	0.5
	I_2	Acetonitrile	97.7	2.3
	NaI	Acetone	98.6	1.4
	NaI	Acetonitrile	97.9	2.1
	CH_3I	Acetone	98.5	1.5
erythro, **7**	I_2	Acetone	1.1	98.9
	NaI	Acetone	2.2	97.8
	NaI	Acetonitrile	3.5	96.5

The starting sulfides were prepared from methanesulfenyl bromide and 2-butenes that contained 0.4–0.5% of the contaminating stereoisomer. Butene yields were estimated volumetrically. When the reactions appeared to be complete, indicated by a negligible rate of butene production, aqueous thiosulfate was added for determination of iodine. A pentane extract was analyzed by gas chromatography in order to determine the nature of the products containing sulfur.

In the reaction of **5** or **7** with iodine, a quantitative yield of butene was obtained. Although an iodine–sulfide ratio of 0.5 was sufficient to carry the reaction to

(5) G. K. Helmkamp and N. Schnautz, *Tetrahedron*, **2**, 304 (1958).
(6) C. C. Price and P. T. Kirk, *J. Am. Chem. Soc.*, **75**, 2396 (1953).
(7) N. R. Slobodkin and N. Kharasch, *ibid.*, **82**, 5837 (1960).
(8) K. D. Gundermann, *Angew. Chem., Intern. Ed. Eng.*, **2**, 674 (1963).
(9) M. Delepine, *Compt. rend.*, **171**, 36 (1920).
(10) M. Delepine and P. Jaffeux, *ibid.*, **172**, 158 (1921).
(11) D. J. Pettitt and G. K. Helmkamp, *J. Org. Chem.*, **28**, 2932 (1963).
(12) G. K. Helmkamp and D. J. Pettitt, *ibid.*, **27**, 2942 (1962).
(13) D. J. Pettitt and G. K. Helmkamp, *ibid.*, **29**, 2702 (1964).

completion, an equimolar amount of iodine was generally employed because of the observed shorter reaction periods. Considerable tar formation was noted in acetone as the solvent, but none was observed when the reaction was carried out in acetonitrile. The sulfur appeared in the product as methyl disulfide. The mechanism of the process probably involves the initial formation of a sulfur–iodine complex similar to **11**, followed by nucleophilic attack of iodide ion (or iodine) on bromine to yield butene, methanesulfenyl iodide, and iodine bromide (eq. 8). Disproportionation of the last two products would provide continuous regeneration of iodine and formation of methyl disulfide (eq. 9 and 10).



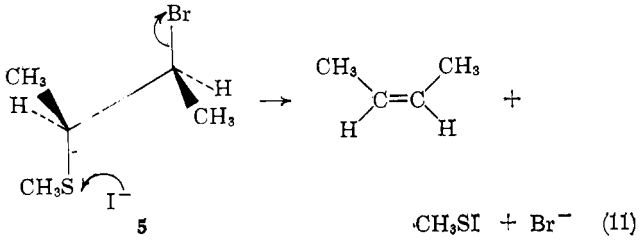
11

$$CH_3SI + IBr \quad (8)$$

$$2CH_3SI \longrightarrow CH_3SSCH_3 + I_2 \quad (9)$$

$$2IBr \rightleftharpoons I_2 + Br_2 \quad (10)$$

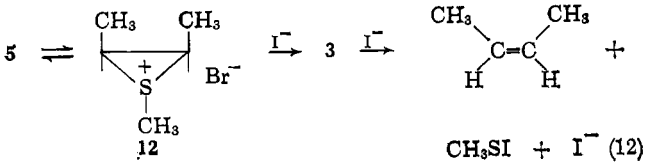
As noted in Table I, sodium iodide was also effective in quantitatively converting **5** and **7** to 2-butenes by an over-all *trans* elimination. Yields of iodine, determined by thiosulfate titration, were nearly quantitative, and methyl disulfide was the only sulfur-containing product detected. The stereochemistry of the olefin product is consistent with that expected for an iodide-induced elimination resulting from nucleophilic attack on sulfur (eq. 11) or bromine. However, it may also be possible that an episulfonium salt **12** is involved, for



5

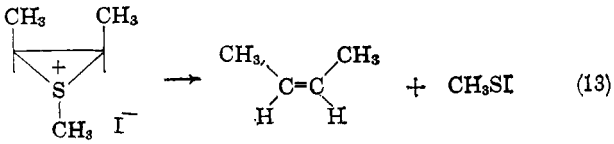
$$CH_3SI + Br^- \quad (11)$$

ring opening by iodide ion followed by elimination (eq. 12) or direct displacement of iodide ion on positively charged sulfur (eq. 13) is also consistent with the data. Nucleophilic attack at sulfur in the reaction of cyclooctene S-alkyl episulfonium 2,4,6-trinitrobenzenesulfonates with iodide ion and mercaptide ion has been proposed.[13]



12

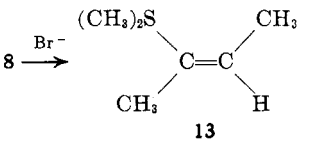
$$CH_3SI + I^- \quad (12)$$



$$+ CH_3SI \quad (13)$$

When the β-bromosulfide **5** was treated with methyl iodide, *cis*-2-butene was formed in moderate yield. Methyl bromide, methyl sulfide, and methyl disulfide were also detected. Initial alkylation of the sulfide with methyl iodide, followed by attack of iodide ion on bromine, would yield olefin, methyl sulfide, and iodine bromide Furthermore, iodine (from iodine bromide) may react directly with **5** as described in eq. 8. Methyl bromide could arise through the reaction of bromide ion with an S-methyl group of the sulfonium salt or from iodine bromide and methyl iodide.

When the sulfonium bromides **6** and **8** in acetone were heated under reflux with sodium iodide, high yields of butenes were isolated. However, iodine was formed in only 50–60% yield based on an attack of iodide on bromine with concomitant loss of methyl sulfide. However, only a trace of methyl sulfide was found, but a large quantity of methyl iodide was present. Nearly all of the sulfur was present as methyl disulfide. The data are rationalized in terms of a mechanism that involves conversion of the sulfonium bromides **6** and **8** to the corresponding sulfides prior to desulfurization. If such a process was slower than an elimination reaction illustrated by eq. 3, the major sulfur-containing material would be methyl sulfide. Unlike the desulfurization of sulfides, the reaction between iodide ion and the sulfonium salts was not highly stereospecific. The butene products invariably contained 10–20% of the contaminating stereoisomer. Under the reaction conditions, bromide ion may act as a moderately strong base[14] in bringing about dehydrohalogenation of the β-bromosulfonium compounds[15,16] (eq. 14). Michael addition



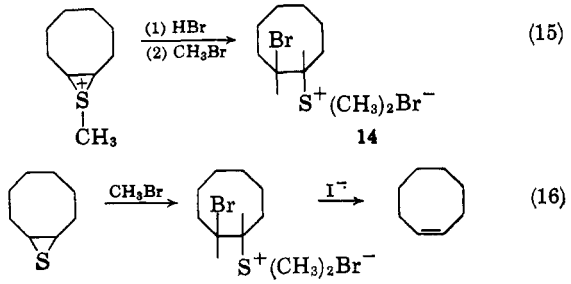
13 (14)

to the vinylsulfonium salt **13** would yield diastereomeric adducts which, in turn, would lead to isomeric butenes. Alternatively, bromide ion is also a sufficiently good nucleophile in acetone that it might cause epimerization by SN2 displacement at the β-carbon atom.

Mechanism.—A great variety of routes are available as potential mechanistic pathways for the desulfurization of episulfides with methyl iodide. On the basis of available data, a theoretical mechanistic sequence cannot be assigned with a great deal of confidence. However, certain reactions can be excluded on the basis of product analysis.

The reaction must be initiated by the formation of an episulfonium salt because no other reasonable alternative seems feasible. Such a salt could be isolated only in the special case of the cyclooctene derivative **10** but that salt did lead to a conventional β-bromosulfonium compound (eq. 15) identical with that obtained from the episulfide (eq. 16). The formation of cyclooctene from the reaction of **10** or **14** with sodium iodide in acetone excludes the possibility that **10** is a transannular product.[11]

(14) A. J. Parker, *Quart. Rev.* (London), **16**, 175 (1962).
(15) W. von E. Doering and K. C. Schreiber, *J. Am. Chem. Soc.*, **77**, 514 (1955).
(16) G. Cilento, *Chem. Rev.*, **60**, 147 (1960).



(15)

(16)

The sequence illustrated by eq. 2 is excluded because there is no accumulation of 2,3-dibromobutane in the analogous series with methyl bromide as the alkylating agent. Consequently, the steps given in eq. 1 are followed by those in eq. 3 and 4 until an appreciable amount of iodine is formed. Subsequently, iodine may bring about decomposition of the β-iodosulfide, **3**, or the β-iodosulfonium salt, **4**, with formation of methyl disulfide. The detection of the latter as a product of the methyl iodide desulfurization supports the proposal that at least one competing process is in operation.

Desulfurization of unchanged episulfide by iodine produced during the reaction appears to be negligible in the butene cases, since elemental sulfur was not detected as a reaction product.

As stated before, polymerization *via* interaction of starting material and intermediates is a competing process in certain instances. This competition, however, is not related directly to desulfurization.

Experimental[17]

Butene Episulfides.—The *meso*, *dl*, and optically active butene episulfides were prepared by the thiourea method of Bordwell and Andersen,[18] previously reported.[3,5] The active isomer had a specific rotation of $[\alpha]^{24}D$ −134.8° (neat) compared with $[\alpha]^{25}D$ −129.0°, the highest value previously reported.[5]

Cyclohexene Episulfide.—The same procedure as that reported[19] was used except that a reaction time of 56, rather than 36 hr., was found necessary.

Cyclooctene Episulfide.—The method of Youtz and Perkins[20] was used with modifications as described in a previous paper.[13]

***threo*-2-Bromo-3-dimethylsulfoniobutane Bromide.**—An ampoule containing 6.0 g. (0.068 mole) of *cis*-2-butene episulfide and 10 ml. of acetonitrile was cooled in a Dry Ice–acetone bath. To this was added 20 g. (0.21 mole) of methyl bromide. The ampoule was resealed and stored for 18 days at room temperature in the absence of light. The white solid that formed was isolated by filtration and washed successively with ether and petroleum ether (b.p. 60–80°): yield 8.8 g. Addition of ether to the acetonitrile solvent precipitated an additional 1.2 g. The crude salt was crystallized from 95% ethanol and air dried: yield 8.9 g. (47%). Upon heating, the solid volatilized without melting at 164–166°. Its analysis agreed with that expected for the β-bromosulfonium salt.

Anal. Calcd. for $C_6H_{14}Br_2S$: C, 25.91; H, 5.08; Br, 57.48; S, 11.53. Found: C, 26.20; H, 4.93; Br, 57.43; S, 11.39.

As an alternate method of preparation, a solution of 11.0 g. (0.060 mole) of *threo*-2-bromo-3-methylthiobutane and 20 g. (0.21 mole) of methyl bromide in 15 ml. of acetonitrile was sealed in an ampoule. After 1 week at room temperature, the white solid was collected by filtration and washed successively with two 25-ml. portions of ether and one portion of petroleum ether: yield 11.4 g. (68%). Crystallization from ethanol gave white crystals: yield 9.1 g. (54%), m.p. 164–166° (volatilization without melting).

***erythro*-2-Bromo-3-dimethylsulfoniobutane Bromide.**—The procedure described for the *threo* isomer was applied to *trans*-2-butene episulfide. The salt was crystallized from isopropyl alcohol: yield 11.4 g. (60%). The product melted, turned red, and immediately volatilized at 143–144°.

Anal. Calcd. for $C_6H_{14}Br_2S$: C, 25.91; H, 5.08; Br, 57.48; S, 11.53. Found: C, 26.04; H, 5.21; Br, 57.60; S, 11.38.

The same product was obtained from the reaction of methyl bromide with *erythro*-2-bromo-3-methylthiobutane. A solution of 11.0 g. (0.060 mole) of the *erythro* sulfide and 20 g. (0.21 mole) of methyl bromide in 15 ml. of acetonitrile was sealed in an ampoule. After 1 week at room temperature, the white solid was collected by filtration and washed successively with two 25-ml. portions of ether and one portion of petroleum ether: yield 14.6 g. (87%), m.p. 137–139° dec. The salt was crystallized from isopropyl alcohol, washed with pentane, and dried at reduced pressure: yield 12.0 g. (72%), m.p. 142–144° (melted, turned red, and volatilized).

(2*R*:3*R*)-2-Bromo-3-dimethylsulfoniobutane Bromide.—Freshly distilled episulfide (5.2 g., 0.059 mole) was mixed with 13.0 g. (0.14 mole) of methyl bromide and 10 ml. of acetonitrile in an ampoule. After 12 days the ampoule was opened and the white solid was collected by filtration, washed successively with ether and pentane, and air dried; crude yield, 8.4 g. (51%). After two recrystallizations from propyl alcohol–ether, the product melted at 134–136° with decomposition and had $[\alpha]^{23}D$ −58.3° (*c* 0.0222, absolute methanol).

***threo*-2-Bromo-3-methylthiobutane.**—A solution of 10.3 g. (0.110 mole) of methyl disulfide in 250 ml. of methylene chloride was placed in a dry, 500-ml., three-necked flask protected from moisture. The flask was kept in a cold bath at −20 to −25° and was protected from light during the subsequent reaction. A solution of bromine (16.0 g., 0.100 mole) in 75 ml. of methylene chloride was added dropwise over a 2-hr. period with moderate stirring. The mixture was allowed to warm to −15° during a 1-hr. period; then a slow stream of dry *cis*-2-butene was passed into the solution with stirring. After about 0.5 hr. the complete disappearance of the red color indicated completion of the reaction. Most of the solvent was carefully removed by distillation through a vacuum-jacketed Vigreux column without allowing the pot temperature to exceed 45°. The residual material was distilled under reduced pressure: yield of colorless product, 32.6 g. (89.0%); b.p. 43–44° (2 mm.); $n^{25}D$ 1.5140. The product showed no decomposition after several weeks in an ampoule kept at 5–10°.

Anal. Calcd. for $C_5H_{11}BrS$: C, 32.77; H, 6.06; Br, 43.66. Found: C, 32.34; H, 5.98; Br, 43.39.

***erythro*-2-Bromo-3-methylthiobutane.**—The procedure described for the previous synthesis was applied to *trans*-2-butene. Distillation gave 29.9 g. (81.5%) of product: b.p. 41–42° (0.5 mm.), $n^{25}D$ 1.5147. The structure of the product was verified as described earlier by conversion of the compound to *erythro*-2-bromo-3-dimethylsulfoniobutane bromide with methyl bromide.

***threo*-2-Bromo-3-methylthiobutane from *cis*-2-Butene Episulfide.**—After the sulfonium salt was removed from the products of the reaction of *cis*-2-butene episulfide with methyl bromide, the residue was distilled under reduced pressure. A colorless, viscous oil was isolated that had boiling point, refractive index and infrared spectrum similar to those of the *threo*-2-bromo-3-methylthiobutane prepared from *cis*-2-butene and methanesulfenyl bromide: yield 3.1 g. (25%), b.p. 48° (3 mm.), $n^{21}D$ 1.5142.

***erythro*-2-Bromo-3-methylthiobutane from *trans*-2-Butene Episulfide.**—After the sulfonium salt was removed from the products of the reaction of *trans*-2-butene episulfide with methyl bromide, the residue was distilled under reduced pressure: yield of clear, viscous oil, 1.8 g. (14%); b.p. 43–44° (3 mm.); $n^{23}D$ 1.5150. The boiling point, refractive index, and infrared spectrum were comparable with those of *erythro*-2-bromo-3-methylthiobutane prepared from *trans*-2-butene and methanesulfenyl bromide.

(2*R*:3*S*)-2-Bromo-3-methylthiobutane from (*SS*)-2-Butene Episulfide.—An optically active product was obtained from the residue of the reaction between the active episulfide and methyl bromide: b.p. 40–41° (2 mm.), $n^{21}D$ 1.5160, d^{25}_{20} 1.3571, $[\alpha]^{25}D$ −59.8° (neat).

***trans*-1-Bromo-2-dimethylsulfoniocyclohexane Bromide.**—A mixture of 3.0 g. (0.026 mole) of cyclohexene sulfide, 10 g. (0.10

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mole) of methyl bromide, and 10 ml. of acetonitrile was sealed in an ampoule. After 4 days, the solid product was collected by filtration, washed with ether and petroleum ether, and air-dried. The yield of white needles was 3.3 g., m.p. 140–143°. One crystallization from propyl alcohol–ether gave 2.9 g. (36.6%) of purified product. The salt volatilized without melting when it was heated in a capillary tube at 145–147°.

Anal. Calcd. for $C_8H_{16}Br_2S$: C, 31.60; H, 5.30; Br, 52.58. Found: C, 31.34; H, 5.31; Br, 52.41.

Trimethyloxonium Trinitrobenzenesulfonate and Precursors.—The oxonium salt was prepared by the diazomethane procedure previously described.[11]

Cyclooctene S-Methylepisulfonium 2,4,6-Trinitrobenzenesulfonate and Precursors.—The episulfonium salt was prepared from trimethyloxonium trinitrobenzenesulfonate and cyclooctene episulfide by a procedure previously described.[11]

Elimination Reactions Using Iodine.—The reaction of *threo*-2-bromo-3-methylthiobutane with iodine will serve as a model for the various substrates as listed in Table I.

A 100-ml., three-necked flask was fitted with a glass stopper, condenser, and nitrogen inlet tube reaching nearly to the bottom. A delivery tube from the top of the condenser led to a 10-ml. calibrated ampoule immersed in a Dry Ice–isopropyl alcohol bath. The condenser was cooled with water at 10–15°, and the reaction flask was heated with an oil bath at 3–5° above the boiling point of the solvent.

To 3.66 g. (0.0200 mole) of sulfide in 20 ml. of acetone or acetonitrile, 5.1 g. (0.020 mole) of iodine was added. The mixture was heated under reflux for 5 hr. while a slow stream of nitrogen was bubbled through the train. Although less iodine was effective in bringing about quantitative desulfurization, the reaction period was longer. The volatile fraction (about 5 ml.) was distilled into a second tube kept at −75°. The distillate contained mostly butenes (yields, 1.4–1.8 ml., 75–98%). The butenes were analyzed by gas chromatography on a 15-ft. column of 25% G. E. "SF-96" silicone oil on firebrick at room temperature.

The solvent residue remaining in the reaction flask was diluted with 100 ml. of 5% aqueous sodium thiosulfate and extracted with 10 ml. of pentane. The pentane extract was analyzed for the presence of methyl disulfide by chromatography on a 10-ft. column of silicone oil on Fluoropak at 100°.

Elimination Reactions Using Sodium Iodide.—The apparatus described for the iodine-induced eliminations was employed, and the same general procedure for analysis was applied.

To a warm solution of 9.0 g. (0.060 mole) of sodium iodide in 60 ml. of acetonitrile, 3.7 g. (0.020 mole) of the β-bromosulfide was added. A large quantity of sodium bromide precipitated immediately and the color of iodine appeared. Within 5 min. the reaction mixture was black. The mixture was heated under reflux with a slow stream of nitrogen flowing through the system. After 1 hr., a 1.0-ml. sample of the solution required 5.5 ml. of 0.10 *N* sodium thiosulfate (82% of theory) to titrate the iodine to a visual end point. After 4 hr., 5.7 ml. (84%) was required. Iodine yields varied from about 85–98% after 4 hr. Yields of butenes were 1.8–2.0 ml. (97–101%).

Methyl disulfide was detected by the extraction–chromatography procedure described before.

Elimination Reactions Using Methyl Iodide.—To 3.7 g. (0.020 mole) of the β-bromosulfide in 25 ml. of acetonitrile, 5.7 g. (0.040 mole) of methyl iodide was added, and the solution was brought to reflux temperature. The reaction mixture turned dark red within 10 min. After 3 hr., the yield of iodine, determined by thiosulfate titration, was 58%. Lower yields of iodine (30–40%) were found with acetone solvent. Yields of butenes were 0.5–1.0 ml. (28–55%).

A trace of methyl sulfide was detected in the volatile fraction. Since methyl bromide and *cis*-2-butene were not adequately separated by the chromatographic column used for butenes, the presence of methyl bromide in the butene fraction was verified by adding a small excess of bromine to volatile products and observing the disappearance of the *trans*-2-butene peak in the chromatogram. The adjacent peak (in the position corresponding to *cis*-2-butene and methyl bromide) remained strong.

Analysis by extraction–chromatography showed the presence of a small amount of methyl disulfide.

***trans*-1-Bromo-2-dimethylsulfoniocyclooctane Bromide.**—Anhydrous hydrogen bromide (1.0 g.) was passed into 10 ml. of acetonitrile containing 0.45 g. (0.0010 mole) of cyclooctane S-methylepisulfonium 2,4,6-trinitrobenzenesulfonate. After 5.5 hr. the solvent and excess hydrogen bromide were removed with a rotary evaporator and water aspirator. The residue was washed with two 10-ml. portions of pentane. Evaporation of the combined pentane washings at reduced pressure left a clear oil.

A solution of the oil in 5 ml. of acetonitrile and 2 g. of methyl bromide was placed in an ampoule and kept in the dark at room temperature. After 5 days the ampoule was opened and the white solid precipitate was isolated by filtration. After one crystallization from isopropyl alcohol, the product had a melting point of 147–148°; yield 0.11 g., 33%. A mixture melting point of the product with a sample of *trans*-1-bromo-2-dimethylsulfoniocyclooctane bromide from cyclooctene sulfide and methyl bromide[11] was undepressed.

The Mechanism of Dimethyl Sulfoxide Catalysis in Nucleophilic Displacement

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Kinetic data on nucleophilic aromatic substitution in several systems are reported which have bearing on the mechanism of catalysis by dimethyl sulfoxide and other dipolar aprotic solvents. Significant rate increases occur even at low dimethyl sulfoxide concentrations where desolvation of the nucleophile is not an important effect. The rate increase per mole of dimethyl sulfoxide is due to changes in ΔH^*; changes in ΔS^* are slight. Using substituted phenoxide molecules as nucleophiles, dimethyl sulfoxide concentration has little effect on ρ of a Hammett ρ–σ plot, although striking rate increases occur. Dimethyl sulfoxide catalysis is independent of the charge the nucleophile bears. The rate increase per mole of dimethyl sulfoxide is relatively independent of nucleophile or solvent system. The mechanism of dimethyl sulfoxide catalysis is thought to involve polarization of the substrate by a random dimethyl sulfoxide molecule and rapid nucleophilic attack upon this species. The change in solvent structure is thought to allow more rapid reaction rates where hydrogen-bond acceptors are present.

The dramatic increase in rates of nucleophilic or basic attack by certain anions in aprotic solvents has been the subject of considerable interest in recent years.[1–6] Cram and co-workers have shown that the rate of racemization of an optically active hydrocarbon using potassium *t*-butoxide is increased by a factor of 10^6 going from *t*-butyl alcohol to 80% dimethyl sulfoxide–20% *t*-butyl alcohol. A recent review article by Parker

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