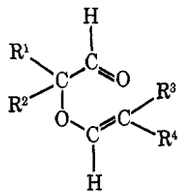
panied by the racemization of optically active **2b** or **2c**, and by the interconversions **2b** ⇄ **2c**, **2f** ⇄ **2e**, and **2f** ⇄ **2d**.



**2a**, $R^1 = R^2 = R^3 = R^4 = CH_3$
**b**, $R^1 = R^3 = CH_3$; $R^2 = R^4 = C_2H_5$
**c**, $R^1 = R^4 = CH_3$; $R^2 = R^3 = C_2H_5$
**d**, $R^1 = R^2 = R^3 = CH_3$; $R^4 = C_2H_5$
**e**, $R^1 = R^2 = R^4 = CH_3$; $R^3 = C_2H_5$
**f**, $R^1 = R^3 = R^4 = CH_3$; $R^2 = C_2H_5$

We find that the manganese dioxide oxidation of optically active α-methylbutyraldehyde (from the oxidation of *sec*-butylcarbinol from fusel oil) gave in agreement with the previous report a mixture of **2b** and **2c**, as shown by the nmr,[5] with no detectable rotation (<0.01° neat in a 1-dm tube). The oxidation of a mixture of isobutyraldehyde and α-methylbutyraldehyde gave a complex mixture. After steam distillation, the volatile fraction showed upon gas chromatographic analysis peaks of retention time corresponding to **2a**, the mixture of **2d**, **2e**, and **2f**, and the mixture of **2b** and **2c**. It was possible by preparative gas chromatography to further isolate and characterize **2f** and the mixture of olefinic stereoisomers **2d** and **2e**. All of these results are consistent with the proposed free-radical mechanism.

It did prove possible to separate partially the cis and trans isomers, **2b** and **2c**, by gas chromatography. From the roughly 1:1 mixture given by oxidation, a fraction containing a 3.8:1 ratio was obtained. This fraction on heating to 200° in a capillary tube for 95 min was converted to a mixture of 1.8:1 ratio, together with a good deal of polymer. If we assume an equilibrium constant of unity and equal rates of polymerization, this gives a rate constant for **2b** → **2c** (or the reverse) of roughly $6 \times 10^{-5}$ $sec^{-1}$. Assuming an $A$ factor of $10^{11}$ $sec^{-1}$, we calculate an activation energy of roughly 33 kcal/mol. Furthermore, we have observed that **2f** → **2d** and **2e** at 200° at about the same rate as the cis–trans isomerization.

A simple estimate of $\Delta H$ for the **3** → **1** process using average bond energies shows it to be exothermic by more than 100 kcal/mol. The activation energy for this reaction would be probably no more than half that for the symmetric **2** → **2** process. This low an activation energy would make the reaction **3** → **1** very fast and account for the failure to observe **3** even if formed, and the slower rate of the **2** → **2** process accounts for the temperature-independent nmr spectrum of **2a**.

**Registry No.**—**2d**, 33066-03-4; **2e**, 33066-04-5; **2f**, 33061-15-3; isobutyraldehyde, 78-84-2; α-methylbutyraldehyde, 96-17-3.

**Acknowledgment.**—We acknowledge gratefully the support of this research by a grant from the National Science Foundation. We also thank Dr. J. C. Leffingwell for telling us of an improved technique for the oxidation.

(5) J. C. Leffingwell, French Patent 1,544,604 (1968).



## Reduction of Sulfoxides with Sodium Hydrogen Sulfite[1]

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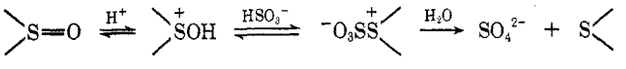
Sulfoxides can be reduced to sulfides under a variety of conditions.[2] The sulfoxide group is capable of oxidizing a carbon atom, but more typical are reactions in which heteroatoms are oxidized. Thiols are oxidized to disulfides,[3] phosphines to phosphine oxides,[4] phosphorus thioacids to phosphorus oxyacids,[5] halide ions to halogens,[6] and silanes to silicon–oxygen derivatives[7] with the concomitant reduction of a sulfoxide to the corresponding sulfide.

The sulfoxides of *dl*-methionine and α-ethyl thioglucoside were reported in 1939 to be reduced by aqueous sulfite.[8] More recently, aqueous solutions of sodium "metabisulfite" have been employed in the selective reduction of the sulfoxide group in α-methylsulfinylacetophenone and derived compounds.[9] Our interest in this method of reduction of sulfoxides was fostered by a fortuitous observation that brief treatment of a mixture of *cis*- and *trans*-2-methylthiolane 1-oxide[10] with aqueous sodium hydrogen sulfite results in the preferential destruction of the cis isomer. This experiment provided an easy method for the preparation of pure *trans*-2-methylthiolane 1-oxide. The more rapid consumption of the cis isomer immediately suggests to us that this reduction reaction involves a nucleophilic attack at sulfur. The "back-side" of the sulfoxide group is less sterically encumbered in the cis diastereomer. Similarly, we find that the *cis*-4-*tert*-butylthiane 1-oxide[11] is reduced somewhat faster than *trans*-4-*tert*-butylthiane 1-oxide. As a working hypothesis we propose the following mechanistic scheme



Analysis of reaction of thiolane 1-oxide and sodium hydrogen sulfite revealed that sulfate was formed in amounts equimolar with the consumption of the sulfoxide. As predicted from the scheme, aqueous sodium sulfite is not an effective reducing reagent for sulfoxides; the pH of the solution is not low enough to result in a significant concentration of protonated sulfoxide. On the other hand, aqueous solutions of

(1) Part XXXVII in the series "Chemistry of Sulfoxides and Related Compounds." We gratefully acknowledge support by the National Science Foundation (GP 8648).

(2) For recent leading references see D. W. Chasar, *J. Org. Chem.*, **36**, 613 (1971).

(3) T. J. Wallace and H. A. Weiss, *Chem. Ind. (London)*, 1558 (1966).

(4) H. H. Szmant and O. Cox, *J. Org. Chem.*, **31**, 1595 (1966); I. Granoth, A. Kalic, and Z. Pelak, *J. Chem. Soc. C*, 2424 (1969).

(5) M. Mikolajczyk and M. Para, *Chem. Commun.*, 1192 (1969).

(6) D. Landini, F. Montanari, H. Hogevein, and G. Maccagnani, *Tetrahedron Lett.*, 2691 (1964).

(7) T. H. Chan, A. Milnyk, and D. N. Harpp, *ibid.*, 201 (1969).

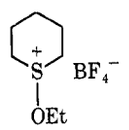
(8) F. Michael and H. Schmitz, *Chem. Ber.*, **72**, 992 (1939).

(9) G. A. Russell and E. T. Sabourin, *J. Org. Chem.*, **34**, 2336 (1969).

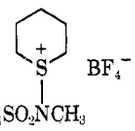
(10) J. J. Rigau, C. C. Bacon, and C. R. Johnson, *ibid.*, **35**, 3655 (1970).

(11) C. R. Johnson and D. McCants, Jr., *J. Amer. Chem. Soc.*, **87**, 1109 (1965).

sulfur dioxide (which is acidic) readily reduced sulfoxides to sulfides.[12] Compared to the free sulfoxide, the protonated sulfoxide has a more electrophilic sulfur and a better leaving group on sulfur ($^-OH$ *vs.* $O^{2-}$). Similar advantages should also be available in O-alkylated sulfoxides. It was found that alkoxysulfonium salts were rapidly and quantitatively reduced to sulfides by saturated aqueous solutions of either sodium hydrogen sulfite or sodium sulfite. The reactions of alkoxysulfonium salts are much faster than the direct reductions of sulfoxides by hydrogen sulfite; *e.g.*, the reduction of **1** is complete



**1**



**2**

in a few minutes at room temperature, whereas reduction of thiane 1-oxide is only 27% complete after 135 min. Other leaving groups on sulfur also facilitate the reaction. The aminosulfonium salt **2**[13] was quickly and cleanly converted to thiane by sulfite solutions.

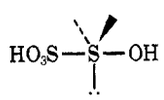
The relative rates of reduction of a series of sulfoxides under standardized conditions were examined in a semiquantitative fashion; partial data which reflect the trends found are summarized in Table I. These

TABLE I
REDUCTION BY SATURATED AQUEOUS SODIUM HYDROGEN SULFITE

| Sulfoxide | % Reduction after 60 min |
|---|---|
| Diethyl sulfoxide | 45 |
| Isopropyl methyl sulfoxide | 8 |
| Thietane 1-oxide | 18 |
| Thiolane 1-oxide | 100[a] |
| Thiane 1-oxide | 16 |
| Thiepane 1-oxide | 52 |

[a] Reduction complete at 10 min.

data appear to indicate that the reduction proceeds *via* a pathway involving substitution at the sulfoxide sulfur, which occurs in, or prior to, the rate-determining step. Branching at the carbon $\alpha$ to the sulfoxide has a retarding effect on the reaction. In the cyclic sulfoxides, the rate reaches a maximum in the case of the five-membered ring. In reactions which involve rehybridization from $sp^3$ to $sp^2$ of a carbon reaction center, five-membered rings react faster than four- or six-membered ones, and branching is known to retard rates.[14] Whether **3** represents a transition state



**3**

or an energetically contiguous intermediate, the response to substitution pattern and ring size should follow along the same general trends as observed for SN2 reactions at carbon. It appears to be typical of the thiolane ring system to display increased reactivity. In the case of thermally induced pyramidal inversion of cyclic sulfonium salts, the five-membered rings were found to invert slightly faster than a six-membered one.[15] In the hydrogen chloride catalyzed stereomutation of sulfoxides, the thiolane 1-oxides react some 300 times faster than thiane 1-oxides.[15] In periodate oxidations of sulfides to sulfoxides, thiolane reacts faster than either thietane or thiane.[16]

For preparative purposes, especially when stereoselectivity is not a consideration, the bisulfite reductions are conveniently run on a steam bath. A cosolvent such as dioxane or methanol may be added in the case of poorly soluble sulfoxides.

(12) Sulfurdioxide in ethanol or chloroform failed to reduce sulfoxides.
(13) For method of preparation see C. R. Johnson, J. J. Rigau, M. Haake, D. McCants, Jr., J. E. Keiser, and A. Gertsema, *Tetrahedron Lett.*, 3719 (1968).
(14) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 268.

### Experimental Section

**Reduction of *n*-Butyl Sulfoxide.**—*n*-Butyl sulfoxide (4 g) was added to a solution of 16 g of sodium hydrogen sulfite in 40 ml of water. The mixture was heated on a steam bath with stirring for 40 hr. The mixture was cooled and extracted several times with chloroform. Vpc analysis showed the extract to contain no sulfoxide. Distillation provided 2.5 g (70 %) of pure *n*-butyl sulfide.

***trans*-2-Methylthiolane 1-Oxide.**—Mixtures[10] enriched in the trans sulfoxide were treated briefly (10 to 20 min) with aqueous sodium hydrogen sulfite at room temperature. The reactions were followed by vpc analysis. The 2-methylthiolane was extracted with pentane. Pure *trans*-2-methylthiolane 1-oxide was obtained by extraction with chloroform.

Reaction of *trans*-2-methylthiolane 1-oxide with trimethyloxonium fluoroborate in methylene chloride gave *trans*-2-methyl-1-methoxythioniacyclopentane fluoroborate, mp 82–83°.

*Anal.* Calcd for $C_6H_{13}BF_4OS$: C, 32.75; H, 5.95. Found: C, 33.01; H, 6.24.

***cis*-2-Methylthiolane 1-Oxide.**—Hydrolysis of the above salt with aqueous sodium hydroxide gave pure cis sulfoxide, which was converted to *cis*-2-methyl-1-methoxythioiacyclopentane fluoroborate, mp 53–54°.

*Anal.* Calcd for $C_6H_{13}BF_4OS$: C, 32.25; H, 5.95. Found: C, 32.63; H, 5.96.

Basic hydrolysis of this salt gave 100% of the trans sulfoxide.

**1-Ethoxythioniacyclohexane fluoroborate (2)** was prepared by reaction of thiane 1-oxide with triethyloxonium fluoroborate in methylene chloride. The very hygroscopic salt had mp 35–37°.

*Anal.* Calcd for $C_7H_{15}BF_4OS$: C, 35.92; H, 6.46. Found: C, 36.20; H, 6.59.

**Registry No.**—**2**, 33143-36-1; sodium hydrogen sulfite, 7631-90-5; *n*-butyl sulfoxide, 2168-93-6; *trans*-2-methylthiolane 1-oxide, 25859-45-4; *trans*-2-methyl-1-methoxythioniacyclopentane fluoroborate, 33213-38-6; *cis*-2-methylthiolane 1-oxide, 25859-44-3; *cis*-2-methyl-1-methoxythioniacyclopentane fluoroborate, 33143-40-7.

(15) A. Garbesi, N. Corsi, and A. Fava, *Helv. Chim. Acta*, 1499 (1970).
(16) C. R. Johnson and P. E. Rogers, unpublished results.

## Cyclization of Dimethyl-1,6-octadienes

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In this paper, we describe the cyclization of 5,7-dimethyl-1,6-octadiene (**1**) and 3,7-dimethyl-1,6-octa-