Nucleophilic Displacement on Sulfur. The Inversion of Sulfoxide Configurations[1]

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The hydrolysis of alkoxysulfonium salts, obtained by the O-alkylation of sulfoxides, proceeds with inversion of configuration of the sulfur atom. The method has been employed to interconvert (R)- and (S)-benzyl p-tolyl sulfoxide and the cis and trans sulfoxides derived from a series of 4-substituted thianes. Several methods were employed successfully to separate the geometrical isomers of the 4-substituted thiane 1-oxides. The mechanism of displacement reactions on sulfur is discussed.

The scholarly studies of the Ingold school, beginning in the 1930's, provided the maxims for nucleophilic substitution at saturated carbon. In a natural course of events, the mechanism and stereochemistry of nucleophilic displacement at other atoms have only recently come under close scrutiny. The already classical studies by Sommer on substitution at the silicon atom provide a definitive example.[2] The stereochemistry of displacement reactions at the phosphorus atom has been the subject of a recent review.[3] This paper describes our results employing alkoxysulfonium salts which provide excellent examples of reactions proceeding by backside displacement on the sulfur atom.[4]

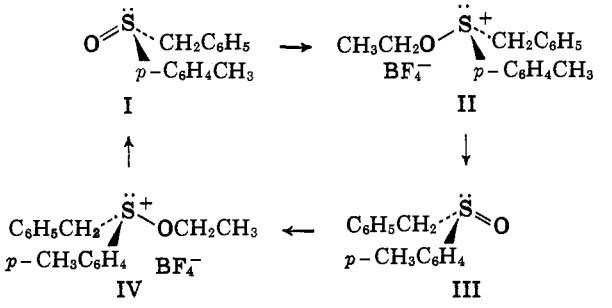
Phillips,[5] in a 1925 paper of great significance, in that it provided the first examples of optical isomerism involving a neutral pyramidal atom, demonstrated that sulfinates were capable of existing as optical isomers. The configurational stability of sulfoxides was confirmed in 1926 with the resolution of several sulfoxides by Harrison, Kenyon, and Phillips.[6] Soon thereafter, examples of geometrical isomerization attributable to the sulfoxide grouping were established.[7] Thus, although appropriate stereochemical isomers for a study of nucleophilic reactions at sulfur have been available for 4 decades few investigators have taken advantage of this opportunity. Work outlined by Phillips[5] was consistent with the hypothesis that the sulfur atom in sulfinates was inverted during *trans* esterification. A variety of other reactions at the sulfur atom apparently proceed by backside nucleophilic displacement. Certain of these have been established since our original communication on this subject. In the handy method developed by Anderson[8] for the synthesis of optically active sulfoxides by the addition of Grignard reagents to resolved sulfinates the sulfur atom is inverted. The hydrolysis of sulfinimines to sulfoxides[9] and the exchange reactions which occur when arylsulfonium salts are treated with organolithium reagents[10] also appear to fall into this category as does the reaction of phenyl radicals with disulfides.[11]

Smith and Winstein[12] demonstrated that alkoxysulfonium salts are readily solvolyzed, whereas the isomeric oxosulfonium salts are refractory even to boiling water. In order to test our hypothesis that such hydrolyses proceed by a nucleophilic displacement on sulfur rather than carbon, dimethylsulfonium perchlorate and other alkoxysulfonium salts were solvolyzed in isotopically enriched water, to yield the parent sulfoxide containing O^{18}.[13] These simple experiments provided the initial evidence that these salts were subject to nucleophilic attack on sulfur.

Results

In order to demonstrate that such hydrolyses of alkoxysulfonium salts do indeed occur with backside displacement an optically active sulfoxide and a series of geometrically isomeric sulfoxides were synthesized, alkylated on oxygen employing triethyloxonium fluoroborate, and hydrolyzed under basic conditions to regenerate sulfoxides of inverted configuration. Details are described in Chart I.

Chart I. Optical Isomers



Optically active (*R*)-(+)-benzyl *p*-tolyl sulfoxide was obtained by inverse addition of benzylmagnesium bromide to an ethereal solution of an equimolar amount of (−)-menthyl (−)-p-toluenesulfinate.[8] The (*R*)-benzyl *p*-tolyl sulfoxide (I), $[\alpha]D$ +94.6° (chloroform), was cleanly converted to the (*R*)-O-ethyl fluoroborate salt (II), $[\alpha]D$ +203°, with triethyloxonium fluoroborate. Hydrolysis of the salt by titration with 0.1 *N* sodium hy-

(1) (a) We gratefully acknowledge support by the National Science Foundation (Grant No. GP-1159); (b) part V in the series Chemistry of Sulfoxides; (c) part IV: C. R. Johnson and W. G. Phillips, *Tetrahedron Letters*, 2101 (1965).

(2) L. H. Sommer, *Angew. Chem. Intern. Ed. Engl.*, **1**, 143 (1962); "Stereochemistry, Mechanism and Silicon," McGraw-Hill Book Co., Inc., New York, N. Y., 1965.

(3) R. F. Hudson and M. Green, *Angew. Chem. Intern. Ed. Engl.*, 2, 11 (1963).

(4) Portions of this work have been reported in preliminary form: (a) C. R. Johnson, *J. Am. Chem. Soc.*, **85**, 1020 (1963); (b) C. R. Johnson and J. B. Sapp, Abstracts of Papers, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept. 1963, p. 23Q.

(5) H. Phillips, *J. Chem. Soc.*, 2552 (1925).

(6) P. W. B. Harrison, J. Kenyon, and H. Phillips, *ibid.*, 2079 (1926).

(7) E. V. Bell and G. M. Bennett, *ibid.*, 1798 (1927).

(8) K. K. Anderson, *Tetrahedron Letters*, 93 (1962).

(9) (a) G. Kresze and B. Wustrow, *Ber.*, **95**, 2652 (1962); (b) R. Appel and W. Büchner, *ibid.*, **95**, 849, 855 (1962); (c) J. Day and D. J. Cram, *J. Am. Chem. Soc.*, **87**, 4398 (1965).

(10) V. Franzen and C. Mertz, *Ann.*, **643**, 24 (1961).

(11) W. A. Pryor and H. Guard, *J. Am. Chem. Soc.*, **86**, 1150 (1964).

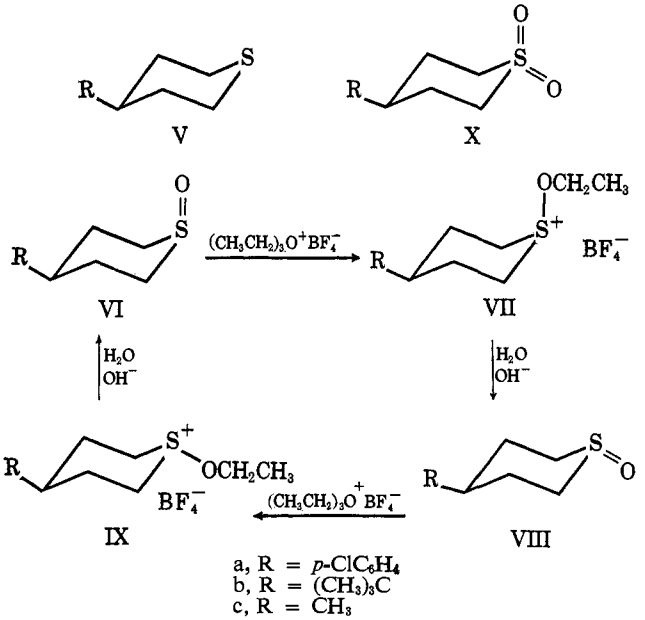
(12) S. G. Smith and S. Winstein, *Tetrahedron*, **3**, 317 (1958).

(13) N. J. Leonard and C. R. Johnson, *J. Am. Chem. Soc.*, **84**, 3701 (1962).

droxide to the phenophthalein end point provided levorotatory (*S*)-sulfoxide (III), $[\alpha]D$ −92.4. In like manner the (*S*)-sulfoxide was alkylated to provide levorotatory (*S*)-salt (IV), $[\alpha]D$ −202°, which in turn was hydrolyzed back to the dextrorotatory sulfoxide (I), $[\alpha]D$ +89.9°. In this example, each inversion sequence involving alkylation followed by hydrolysis results in slightly better than 98% inversion of configuration. The dextrorotatory sulfoxide obtained by the Walden cycle retained 95% of its original optical activity. The O.R.D. curves displayed in Figure 1 dramatically illustrate this inversion of configuration on hydrolysis and further serve to indicate that no extensive alteration of configuration occurs at the asymmetric center (sulfur) when the sulfoxide is converted to the O-alkyl salt. The authors wish to point out that the rotations reported here do not represent optically pure compounds (see the Experimental Section). The configurational assignments shown here correspond to those made previously[13,14] and can be considered absolute, based upon the assignment of the *S* configuration to the asymmetric sulfur in (−)-menthyl (−)-*p*-toluenesulfinate made by Fleischer, *et al.*,[15] and upon the evidence that the Grignard reaction proceeds with inversion of configuration about the sulfur atom.[16]

For comparative purposes, racemic benzyl *p*-tolyl sulfoxide was synthesized by oxidation of the corresponding sulfide with sodium metaperiodate.[17] The difference in the melting point of optically active (164–165°) and racemic (135–136°) material is noteworthy. The racemic melting point was reproduced with a sample obtained by admixture of equivalent amounts of dextrorotatory and levorotatory sulfoxide (see Chart II).

Chart II. Geometrical Isomers



Because of our interest in other aspects of their chemistry, examples from the thiane series were chosen for our studies on the interconversion of geometrical sulfoxide isomers. The first compounds examined in this series were the 4-*p*-chlorophenylthiane 1-oxides, which possess the obvious advantage that their configuration could be ascertained from dipole moments.

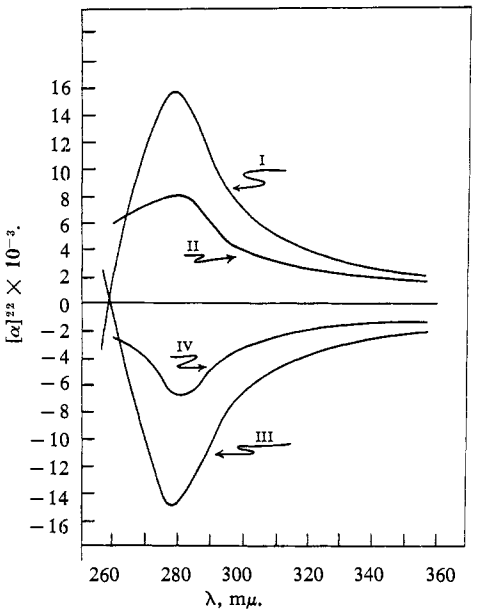


Figure 1. Optical rotatory dispersion curves of compounds I–IV determined in dioxane solution.

Cyclization of 3-(*p*-chlorophenyl)-1,5-dibromopentane was effected with sodium sulfide in absolute ethanol to provide 4-*p*-chlorophenylthiane (Va). Oxidation of the sulfide with aqueous sodium metaperiodate and recrystallization of the crude sulfoxide from ethyl acetate provided pure *cis*-4-*p*-chlorophenylthiane 1-oxide (VIa). The dipole moment of VIa in benzene solution was found to be 3.98 ± 0.02 D., in fair agreement with 4.30 D. calculated from models and model compounds for the chair conformation of a *cis*-sulfoxide.[18] Vapor pressure osmometry reveals that this sulfoxide is monomeric in benzene solution.

Alkylation of VIa with triethyloxonium fluoroborate in methylene chloride afforded in 94% yield the desired kinetically controlled alkylation product, *cis*-4-*p*-chlorophenyl-1-ethoxythioniacyclohexane fluoroborate (VIIa). When VIIa was dissolved in dilute aqueous sodium hydroxide, 1 equiv. of base was consumed and shiny platelets of a new sulfoxide, *trans*-4-*p*-chlorophenylthiane 1-oxide (VIIIa), precipitated in 93% yield. The dipole moment observed for this sulfoxide in benzene solution was 2.60 D. compared with 2.25 D. calculated for the chair conformation.[18] This *trans* sulfoxide could also be obtained by chromatography of the residue of the mother liquors from the recrystallization of the crude product from periodate oxidation. In agreement with this structural assignment, the *cis*-sulfoxide was eluted from alumina prior to the *trans*.

Reaction of *trans* sulfoxide VIIIa with triethyloxonium fluoroborate gave *trans*-4-*p*-chlorophenyl-1-ethoxythioniacyclohexane fluoroborate (IXa). Hydrolysis of IXa with dilute alkali provided a 92% yield of the *cis*-sulfoxide, identical in all respects with the

(14) K. Mislow, M. M. Green, and M. Raban, *J. Am. Chem. Soc.*, 87, 2761 (1965).
(15) E. B. Fleischer, M. Axelrod, M. Green, and K. Mislow, *ibid.*, 86, 3395 (1964).
(16) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *ibid.*, 87, 1958 (1965).
(17) N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, 27, 282 (1962).
(18) C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, 87, 1109 (1965).

material employed in the beginning of the cycle. Infrared spectra indicated that this crude sulfoxide obtained by solvolysis of the salts contained less than 5% of contaminating isomeric sulfoxide. Oxidation of the sulfide Va with potassium permanganate in glacial acetic acid gave the sulfone Xa which could also be obtained by oxidation of VIa and VIIIa with permanganate.

For the synthesis of sulfide Vb, 4-*t*-butylpyridine was catalytically reduced to the saturated 4-*t*-butylpiperidine which was converted to its N-benzoyl derivative. The N-benzoyl-4-*t*-butylpiperidine was subjected to treatment with bromine and phosphorus tribromide to provide 3-*t*-butyl-1,5-dibromopentane, in 40% yield based on starting pyridine. Cyclization of the dibromide with sodium sulfide afforded 4-*t*-butylthiane in 74% yield. The 4-methylthiane was likewise obtained by cyclization beginning with the dihalide. The assignments of configurations to the *cis*- and *trans*-4-*t*-butyl and 4-methyl sulfoxides were made by physical chemical comparisons with the 4-*p*-chlorophenyl compounds. The details of the syntheses and configurational assignments for the methyl and *t*-butyl compounds have been reported in a previous paper dealing with the stereochemistry of oxidation of 4-substituted thianes.[18]

Alkylation of pure *cis*-4-*t*-butylthiane 1-oxide (VIa) with triethyloxonium fluoroborate afforded the *cis* salt VIIb in 87% yield. Neutralization of this salt with aqueous alkali provided an apparent quantitative yield of sulfoxides consisting of 95% *trans* (VIIIb) and 5% *cis* (VIb). Likewise, alkylation of pure *trans*-sulfoxide (VIIIb) provides 90% of the *trans* salt IXb which was hydrolyzed to yield 97% *cis* (+3% *trans*) sulfoxide, thus completing the cycle.

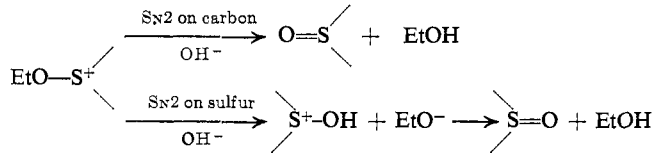
Application of the same methods to the 4-methylthiane oxides can be summarized as follows. O-Ethylation of pure *cis* sulfoxide VIc provided the corresponding salt VIIc in 75% yield, which in turn was hydrolyzed to provide 94% *trans* sulfoxide VIIIc and 6% *cis* sulfoxide VIc. This *trans* sulfoxide VIIIc was alkylated in 80% yield to the O-ethyl salt IXa which was hydrolyzed to yield 99% *cis* and 1% *trans* sulfoxide.

The isomeric sulfoxides were separated by several methods. As noted above, in some cases simple recrystallization or chromatography on alumina was used to effect separation. In another method, advantage was taken of the differential solubility of the mercuric chloride adducts of the sulfoxide. In those cases observed, the *trans* adduct precipitated from an aqueous alcohol solution of excess mercuric chloride while the more soluble *cis* isomer was recovered by concentration and cooling of the supernatant. The sulfoxides of unaltered stereochemistry were recovered by refluxing the adducts with an aqueous ethanolic potassium cyanide[18,19] or more simply by treatment of the adduct with excess sodium hydroxide in aqueous alcohol. Another procedure for effecting separation consisted of alkylation of the mixture with triethyloxonium fluoroborate. The *trans* adduct in each case was found to be less soluble in methylene chloride–ether mixtures and would crystallize out at room temperature. The *cis* salt was then recovered from the supernatant by cooling to 0°. The purified adducts were then dissolved in water and neutralized with dilute alkali; this procedure results in sulfoxide of inverted configuration.

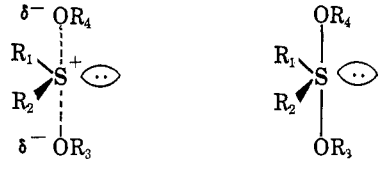
(19) H. B. Henbest and S. A. Khan, *Proc. Chem. Soc.*, 56 (1964).

Discussion

The experimental results outlined above have relevance both for practical and theoretical aspects of organic sulfur chemistry. O-Alkylation of sulfoxide is an efficient method for providing stable, crystalline derivatives characterized by relatively sharp melting points and neutralization equivalents. The hydrolysis of these salts is almost stereospecific, allowing one to easily and efficiently interconvert both optically active and geometrical isomers of sulfoxides. Although several methods[20] (hydrogen chloride, nitrogen tetroxide, and thermal) are known to equilibrate epimeric sulfoxides, our method provides the first case of a stereoselective method for the alteration of configuration at the sulfur atom in a compound and perhaps the most clear-cut cases yet reported of backside nucleophilic displacement on the sulfur atom in organic systems. Probably the stereoelectronic requirements for direct nucleophilic displacement on sulfur are as rigid as those for carbon displacements and the small amount of material found in each case with retained configuration is the result of competing reactions. Although several types of competing reactions can readily be envisioned, the most likely to occur in the systems under present study is simple alkylation of the nucleophile which would result in displacement of sulfoxide of retained configuration.[21]



Since our initial communication[4a] on this subject, others have observed inversion of configuration at the sulfur of sulfoxides by the intervention of intermediate alkoxysulfonium salts. Montanari, *et al.*, have observed neighboring group participation by sulfinyl oxygen in an iodolactonization reaction and have found evidence for participation by sulfinyl oxygen in the solvolysis of a series of aliphatic chlorosulfoxides.[22]



XIa, R_4 = H
b, R_4 = alkyl or aryl

XIIa, R_4 = H
b, R_4 = alkyl or aryl

Regrettably, neither our results nor those of others on the solvolytic behavior of alkoxysulfonium salts provide an answer to the question of intermediate *vs.* transition state. Both the oxygen exchange data and the observation that hydrolysis is accompanied by in-

(20) See ref. 18 and references cited therein.

(21) Competing reactions which result in sulfoxide of retained configuration should be highly dependent on the nature of the alkyl group attached to the oxygen. We are presently investigating this point.

(22) (a) S. Ghersetti, H. Hogeveen, G. Maccagnani, F. Montanari, and F. Taddei, *J. Chem. Soc.*, 3718 (1963); (b) H. Hogeveen, G. Maccagnani, and F. Montanari, *Boll. sci. fac. chim. ind. Bologna*, **21**, 257 (1963); (c) F. Montanari, D. Danieli, H. Hogeveen, and G. Maccagnani, *Tetrahedron Letters*, 2685 (1964).

version of configuration at the sulfur atom can be accounted for by transition state XIa or by the formation of intermediate XIIa. The trigonal bipyramid geometry shown for XI and XII is simply an attractive suggestive analogy[23] at this time. In XI and XII the entering and leaving groups are shown occupying axial (apical) positions. Inversion of configuration involving trigonal bipyramidal configuration can equally well be accounted for if both the entering and leaving groups occupy equatorial (radial) positions. It is interesting to consider that if such trigonal bipyramidal geometry is obligative for substitution at sulfur then one can conceive of constraints on the system such that retention might become the major pathway.

The state XIa is analogous to the transition state for bimolecular substitution on carbon (SN2)—a result that can be rationalized by use of a lone *p*-orbital to bind both the attacking and leaving groups. With elements such as silicon, phosphorus, and sulfur the situation is complicated by increased stability of the higher valency states. Substitution at silicon appears to proceed with comparative ease with inversion (SN2–Si) or retention (SNi–Si) of configuration.[2,24] The reactions at the silicon atom do not appear to involve an intermediate. In the SN2–Si mechanism Sommer and his co-workers have reached the conclusion that the transition state has trigonal bipyramidal geometry with the entering and leaving groups at axial positions; in the SNi–Si reactions one suggestion is that the transition state be pictured with the entering group occupying an equatorial position and the leaving group occupying an axial position (or *vice versa*) which results in retention of configuration at the central atom.

The formation of a trigonal bipyramidal intermediate in the reaction between phosphonium salts and hydroxide ions is consistent with the stereochemical and kinetic observations.[25] Stable pentaoxyphosphoranes are known; triisopropyl phosphite and phenanthrenequinone form a crystalline adduct in which the phosphorus is five-coordinated and is at the center of a trigonal bipyramid. In this complex one of the oxygens of the aromatic system occupies an axial position and the other an equatorial.[26]

We have observed that alkoxysulfonium salts rapidly interchange alkoxy groups when treated with alkoxide.[1c] When dimethylmethoxysulfonium fluoroborate labeled with carbon-14 in the O-methyl group was treated with sodium hydride correspondingly radioactive formaldehyde was obtained; however, when sodium methoxide in methanol was employed as base, the formaldehyde obtained exhibited less than 1% of the radioactivity of the starting salt, indicating that methoxy interchange with solvent occurs much more rapidly than elimination of the salt to carbonyl compound and dimethyl sulfide. Such data might seem to favor the direct displacement *via* transition state XIb rather than intervention of intermediates of type XIIb; one can only conclude that if such "sulfoxal"[13] (XIIb) intermediates do intervene in these reactions their formation is readily reversible.

(23) For example, numerous physical methods including electron diffraction in the gaseous state have led to the conclusion that sulfur tetrafluoride has a trigonal bipyramidal structure with two nonequivalent sets of F–S bonds and the nonbonded electron occupying an equatorial position. The SOF_4 structure has the same symmetry: K. Kimura and S. H. Bauer, *J. Phys. Chem.*, **39**, 3172 (1963).

(24) L. H. Sommer, C. L. Frye, and G. A. Parker, *J. Am. Chem. Soc.*, **86**, 3276 (1964); L. H. Sommer, G. A. Parker, and C. L. Frye, *ibid.*, **86**, 3280 (1964).

(25) M. Zanger, C. A. VanderWerf, and W. E. McEwen, *ibid.*, **81**, 3806 (1959); C. B. Parisek, C. A. VanderWerf, and W. E. McEwen, *ibid.*, **82**, 5503 (1960); M. Grayson and P. T. Keough, *ibid.*, **82**, 3919 (1960).

(26) W. C. Hamilton, S. J. La Placa, and F. Ramirez, *ibid.*, **87**, 127 (1965).

Experimental Section[27]

(−)-Menthyl (−)-p-Toluenesulfinate. The synthesis and resolution of (−)-menthyl (−)-*p*-toluenesulfinate from (−)-menthol and ethyl *p*-toluenesulfinate was accomplished by the method of Phillips[5] as modified by Herbrandson.[28] The resolved material had m.p. 105–106° (lit.[29] m.p. 105–106°) and $[\alpha]^{22}D$ −191° (*c* 4.14, acetone) (lit. $[\alpha]^{25}D$ −199°,[8] $[\alpha]^{21}D$ −201°[28]).

(R)-Benzyl p-Tolyl Sulfoxide (I). To 3.68 g. (0.8 mmole) of (−)-menthyl (−)-*p*-toluenesulfinate in 50 ml. of dry ethyl ether was added dropwise with stirring 1.5 equiv. of benzyl Grignard in 50 ml. of ether. The mixture was stirred for 30 min. and then was refluxed with stirring for 30 min. more and was poured into ice acidified with dilute sulfuric acid. The mixture was extracted with methylene chloride. The methylene chloride was evaporated and the residue was washed many times with pentane, in which the sulfinate and menthol are soluble but the sulfoxide is not. The crude sulfoxide thus obtained had m.p. 162–163°; recrystallization from ethanol–water provided 1.21 g. (66%) of sulfoxide, m.p. 164–165°, $[\alpha]^{22}D$ +94.6° (*c* 2, $CHCl_3$) (lit.[29] 169–170° for material $[\alpha]^{18}D$ 252° (*c* 1, acetone)).

Anal. Calcd. for $C_{14}H_{14}OS$: C, 72.98; H, 6.13. Found: C, 72.76; H, 6.35.

Based upon the highest reported rotations[28,29] for the compounds in question one would judge our menthyl *p*-toluene sulfinate to be approximately 95% optically pure whereas this benzyl *p*-tolyl sulfoxide is only 37.5% optically pure. This discrepancy is perhaps accounted for by racemization occurring during the lengthy interval between resolution of the sulfinate and production of the sulfoxide.

The (*R*)-sulfoxide, m.p. 164–165°, $[\alpha]D$ +89.9°, was also obtained by hydrolysis of (*S*)-benzyl-*p*-tolylethoxysulfonium fluoroborate.

(S)-Benzyl p-Tolyl Sulfoxide (III). To 30 ml. of distilled water was added 165 mg. (0.477 mmole) of (*R*)-benzyl-*p*-tolylethoxysulfonium fluoroborate with magnetic stirring. The sulfoxide began to precipitate out almost at once. A few drops of phenolphthalein were added and 0.02 *N* sodium hydroxide was added until the pink color persisted. The precipitated sulfoxide, 104 mg. (95%), was collected by suction filtration and had m.p. 164–165°, $[\alpha]D$ −92.4°. The infrared spectrum was identical with that obtained on enantiomeric and racemic material. On careful admixture with an equal quantity of enantiomeric sulfoxide the melting point (135–136°) of the racemic material was reproduced.

Benzyl-p-tolylethoxysulfonium Fluoroborate. The salts of the dextrorotatory, levorotatory, and racemic

(27) Microanalyses were performed by Midwest Microlab., Inc., Indianapolis, Ind.

(28) H. F. Herbrandson, R. T. Dickerson, Jr., and J. Weinstein, *J. Am. Chem. Soc.*, **78**, 2576 (1956); H. F. Herbrandson and R. T. Dickerson, Jr., *ibid.*, **81**, 4102 (1959).

(29) C. J. M. Stirling, *J. Chem. Soc.*, 5741 (1963).

Table I. 1-Ethoxythioniacyclohexane Fluoroborates

1-Ethoxythioniacyclohexane fluoroborate	Yield, %	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found
cis-4-*p*-Chlorophenyl (VIIa)	94	107–108	$C_{13}H_{18}BClF_4OS$	45.32	45.13	5.26	5.30	344.5	347
trans-4-*p*-Chlorophenyl (IXa)	83	166–167	$C_{13}H_{18}BClF_4OS$	45.32	45.33	5.26	5.06	344.5	343
cis-4-*t*-Butyl (VIIb)	87	106–106.5	$C_{11}H_{23}BF_4OS$	45.52	45.67	7.93	7.85	290	291
trans-4-*t*-Butyl (IXb)	90	150–151	$C_{11}H_{23}BF_4OS$	45.52	45.55	7.93	7.91	290	291
cis-4-Methyl (VIIc)	75	57–59[a]	$C_8H_{17}BF_4OS$	...	...	...	...	248	252
trans-4-Methyl (IXc)	80	83–85	$C_8H_{17}BF_4OS$	38.71	38.67	6.85	7.05	248	250

[a] Sealed tube.

Table II. Thiane 1-Oxide–Mercuric Chloride Complexes

Mercuric chloride adduct of thiane 1-oxide	Ratio of SO/$HgCl_2$	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Recrystn. solvent	Yield, %	M.p., °C.
cis-4-*p*-Chlorophenyl (VIa)	2/1	$C_{22}H_{26}Cl_4HgO_2S_2$	36.26	36.17	3.57	3.56	CH_2Cl_2	89	143–145
trans-4-*p*-Chlorophenyl (VIIIa)	1/1	$C_{11}H_{13}Cl_3HgOS$	26.46	26.49	2.61	2.88	CH_2Cl_2	98	160–161
cis-4-*t*-Butyl (VIb)	1/2	$C_9H_{18}Cl_4Hg_2OS$	15.04	15.25	2.51	2.66	EtOH	86	147–148
trans-4-*t*-Butyl (VIIIb)	1/2	$C_9H_{18}Cl_4Hg_2OS$	15.04	15.20	2.51	2.75	EtOH	90	122–123
cis-4-Methyl (VIc)	1/1	$C_8H_{12}Cl_2HgOS$	17.86	17.23	2.97	2.92	CH_2Cl_2	71	122–123
trans-4-Methyl (VIIIc)	1/2	$C_6H_{12}Cl_4Hg_2OS$	10.83	10.93	1.76	1.87	EtOH	69	111–113

sulfoxides were obtained in approximately 70% yield by the general method outlined below for the thiane 1-oxide salts. They were recrystallized from methylene chloride–ether mixtures.

Racemic benzyl-*p*-tolylethoxysulfonium fluoroborate had m.p. 130–131°.

Anal. Calcd. for $C_{16}H_{19}BF_4OS$: C, 55.57; H, 5.54; neut. equiv., 346. Found: C, 55.66; H, 5.57, 5.48; neut. equiv., 352.

The (*R*)-benzyl-*p*-tolylethoxysulfonium fluoroborate (II) had m.p. 115–117°, $[\alpha]^{22}D$ +203° (chloroform).

Anal. Calcd. for $C_{16}H_{19}BF_4OS$: C, 55.57; H, 5.54; neut. equiv., 346. Found: C, 55.42; H, 5.80; neut. equiv., 338.

The (*S*)-benzyl-*p*-tolylethoxysulfonium fluoroborate (IV) had m.p. 115–117° but $[\alpha]^{22}D$ −202°.

Preparation of the Ethoxysulfonium Salts (General). Triethyloxonium fluoroborate[30] (0.190 g., 1 mmole) was added to a solution of the sulfoxide (1 mmole) in 2–5 ml. of methylene chloride and stirred for 30 min. at room temperature. Addition of anhydrous ethyl ether at 0° effected precipitation of the white, crystalline solid. The product was purified by recrystallization from methylene chloride or methylene chloride–ether mixtures (see Table I).

Mercuric Chloride Adducts. A hot solution of mercuric chloride (4 mmoles) in 6 ml. of 60% aqueous ethanol was added to a solution of pure *cis*- or *trans*-sulfoxide (1 mmole) in 2 ml. of 95% ethanol. After heating on a steam bath for 5 min., the solution was cooled to 0° in an ice–water bath. Addition of water effected precipitation. The adduct was recrystallized from ethanol or methylene chloride (see Table II).

Isolation of Pure Isomers. A. Ethoxysulfonium Salts. To a mixture of the sulfoxides (1 mmole) of varying *cis*/*trans* ratio in 10 ml. of methylene chloride was added 1 equiv. of triethyloxonium fluoroborate. The solution was stirred at room temperature for 30 min. and anhydrous ethyl ether added until the solution became cloudy. After standing at room temperature for 1 hr., the white crystals (*trans* salt) were filtered and the filtrate was cooled to 0° with an ice–water bath with the subsequent precipitation of the *cis* salt. Both were recrystallized from methylene chloride.

Purified product was dissolved in distilled water and neutralized with 0.1 *N* sodium hydroxide. The aqueous solution was extracted three times with twice its volume of methylene chloride. The combined extracts were dried over anhydrous magnesium sulfate. Removal of the solvent followed by sublimation at 40° (0.1 mm.) or recrystallization provided pure sulfoxide.

B. Mercuric Chloride Complexes. Cooling an aqueous alcoholic solution of the isomeric sulfoxides and excess mercuric chloride provided the *trans* adduct. Concentration of the filtrate followed by cooling afforded the *cis* adduct. The adducts were recrystallized from ethanol or methylene chloride.

Purified complex (1 mmole) was dissolved in 60% aqueous ethanol and refluxed for 2 hr. with 100 ml. of a 1% potassium cyanide solution[19] in 50% aqueous ethanol. The solution was concentrated at reduced pressure. The resultant solution was extracted five times with 100-ml. portions of methylene chloride. The combined extracts were dried over anhydrous magnesium sulfate. Removal of the solvent followed by sublimation provided pure sulfoxide.

In an alternate procedure to a solution of the complex (1 mmole) in 10 ml. of 50% aqueous ethanol was added sodium hydroxide (0.12 g., 3 mmoles) in 10 ml. of water. The solution was stirred at room temperature for 15 min. The yellow solid was filtered and the filtrate was extracted three times with 25-ml. portions of methylene chloride. The combined extracts were dried and the sulfoxide was purified by sublimation.

4-(p-Chlorophenyl)thiane (Va). Cyclization of 3-(*p*-chlorophenyl)-1,5-dibromopentane[31] (31 g., 0.091 mole) was effected with anhydrous sodium sulfide (from 8 g. of sodium) in 200 ml. of absolute ethanol with 4 hr.

(30) H. Meerwein, E. Battenberg, H. Gold, E. Pfeil, and G. Willang, *J. prakt. Chem.*, **154**, 83 (1939).

(31) N. L. Allinger and S. Greenberg, *J. Am. Chem. Soc.*, **81**, 5733 (1959).

of reflux to yield 11.5 g. (59%) of 4-(*p*-chlorophenyl)-thiane, m.p. 70–71°, after recrystallization from ethanol.

Anal. Calcd. for $C_{11}H_{13}ClS$: C, 62.11; H, 6.16. Found: C, 62.10; H, 6.22.

cis-4-(p-Chlorophenyl)thiane 1-Oxide (VIa). Oxidation of 4-(*p*-chlorophenyl)thiane with aqueous sodium metaperiodate provided a quantitative yield of crude sulfoxides consisting of 70% *cis* and 30% *trans* sulfoxide. Recrystallization of the crude sulfoxide mixture from ethyl acetate provided pure *cis*-4-(*p*-chlorophenyl)thiane 1-oxide, m.p. 172.5–173°.

Anal. Calcd. for $C_{11}H_{13}ClOS$: C, 57.58; H, 5.76; S, 14.04. Found: C, 57.58; H, 5.76; S, 13.81.

Hydrolysis of IXa with dilute alkali provided in crude yield the *cis* sulfoxide VIa, identical (melting point, mixture melting point, and infrared spectrum) after a single recrystallization with that obtained above by the oxidation of the sulfide with periodate.

trans-4-(p-Chlorophenyl)thiane 1-Oxide (VIIIa). To 20 ml. of 0.1 *N* aqueous sodium hydroxide was added *cis*-4-(*p*-chlorophenyl)-1-ethoxythioniacyclohexane fluoroborate (VIIa) (650 mg., 1.88 mmoles). Shiny platelets began to precipitate almost immediately. The mixture was cooled in an ice bath and the precipitate was collected by suction filtration. The crude sulfoxide, m.p. 119–121°, was obtained in 93% yield. Recrystallization from ethyl acetate–hexane provided pure *trans*-4-(*p*-chlorophenyl)thiane 1-oxide, m.p. 120–120.5°.

Anal. Calcd. for $C_{11}H_{13}ClOS$: C, 57.76; H, 5.73. Found: C, 57.55; H, 5.76.

Material identical (melting point, mixture melting point, and infrared spectrum) with VIIIa was obtained by chromatography on neutral alumina of the residue from evaporation of the ethyl acetate mother liquors from the recrystallization of VIa.

4-(p-Chlorophenyl)thiane 1,1-Dioxide. Oxidation of the sulfide Va with potassium permanganate in glacial acetic acid gave 4-(*p*-chlorophenyl)thiane 1,1-dioxide (Xa), m.p. 208–209°, $\nu_{max}^{CH_2Cl_2}$ 1300, 1120 cm.$^{-1}$ (SO_2).

Anal. Calcd. for $C_{11}H_{13}ClO_2S$: C, 54.07; H, 5.35. Found: C, 53.90; H, 5.58.

The same sulfone was obtained by oxidation of VIa and VIIIa with permanganate.

Vapor Phase Analysis. Percentage compositions were ascertained by planimetric integration of curves obtained from an F and M. Model 720 chromatograph equipped with silicone gum nitrile (GE XE-60) columns. These columns were capable of excellent resolution of sulfide, sulfoxide, and sulfone. For the 4-*t*-butylthianes a 6-ft. column at 240° was employed; the same column at 175° was used for the 4-methylthianes; a 9-in. column at 225° was useful for the 4-*p*-chlorophenylthianes.

Optical Rotatory Dispersion Curves. The spectropolarimetric data were obtained on a Bendix-Ericsson instrument using freshly prepared samples in spectral grade dioxane. Ultraviolet absorption curves on the samples were obtained on a Cary Model 11 spectrophotometer; compounds I and III had λ_{max} 256 mμ (ε 7300) and compounds II and IV had λ_{max} 248 mμ (ε 12,500).

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The Effect of Dimethyl Sulfoxide on Neighboring Group Participation. I. Carboxyl Functions

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Solvolysis data on bromoacetic acid, 3-bromopropionic acid, and meso- and DL*-dibromosuccinic acids in water and dimethyl sulfoxide (DMSO) solutions are presented. Anchimeric assistance by carboxylate is thought to become increasingly important as the solvent mixture is enriched in DMSO, although solvolysis proceeds by diverse mechanisms in water. Activation parameters change strikingly in the solvent region in which the anion becomes poorly hydrogen bonded. Solvent isotope effects show a similar change. External ion return is shown to vary considerably with solvent and the charge the substrate bears. The meso-dibromosuccinic acid yields predominately olefinic products. The reaction is not subject to common ion rate depression and the rate is not accelerated by acetate. The* DL *isomer yields predominately substitution products. The reaction is subject to common ion rate depression and the rate is accelerated by acetate.*

Dipolar aprotic solvents have been found to strongly accelerate the rates of many reactions involving nucleophiles or bases.[1] In general, current thinking seems to favor a mechanism in which the anion is unsolvated in dipolar aprotic media and presumably much more reactive than its highly solvated counterpart in hydroxylic solvents.[2]

Recently, an attempt was made to focus attention upon one particular segment of the solvation phe-

(1) A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962), and references cited therein.

(2) W. Weaver and J. Hutchison, *J. Am. Chem. Soc.*, **86**, 261 (1964).