# The Stereochemistry of Chlorination of Thiane 1-Oxides

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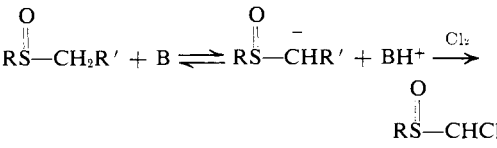
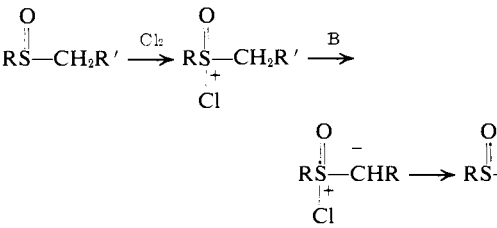
**Abstract:** The chlorination of thiane 1-oxides containing large substituents gave $\alpha$-chloro sulfoxides with the chlorine atom in the axial and the oxygen atom in the equatorial position, independent of the configuration at the sulfur of the starting material. Thiane 1-oxides containing small substituents do not undergo a sulfur but, rather, a ring inversion to place the oxygen in the equatorial position before being halogenated axially at the $\alpha$ positions. Stereochemically different products are obtained from different stereoisomers containing small substituents. The halogenation mechanism is assumed to proceed by way of a tetrahedral chlorosulfoxonium ion containing the oxygen in an equatorial position. Subsequent concerted trans-diaxial elimination of hydrogen chloride to give an "inverted ylide" followed by axial chloride ion attack leads to the observed products.

Sulfoxides were recently found to be very easily chlorinated at the $\alpha$ position by a number of halogenating agents such as nitrosyl chloride,[1] phenyliodonium dichloride,[2] *tert*-butyl hypochlorite,[3] *p*-toluenesulfonyl chloride,[4] chlorine,[5] sulfuryl chloride,[6,7] and 1-chlorobenzotriazole.[8] This great activity was aroused by the interest in the mechanism of exchange of hydrogens $\alpha$ to sulfinyl groups proceeding by a carbanion mechanism and, in general, the mechanism of substitution $\alpha$ to a sulfoxide group, which may be considered an analog of the carbonyl group. The stereochemical course of the hydrogen exchange is influenced by the kinetic acidity of the different hydrogens and the rate of interconversion and the stability of the isomeric anion.[9-22] Chlorination was assumed to proceed[5,23] by a first step proton abstraction followed by the reaction of the sulfinylcarbanion with chlorine (reaction 1). This mechanism does not seem probable since halogenation is very fast even at low temperatures and in the presence



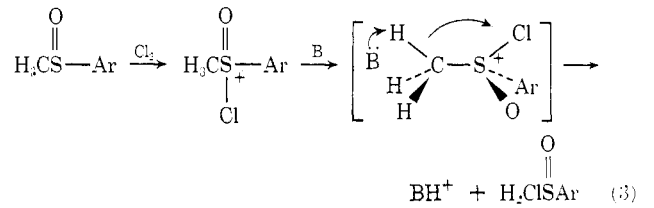
(1)

of weak bases. Product analysis indicated that oxidation and chlorination of sulfoxides had a common intermediate, a halosulfoxonium ion, the product of halogen attack on sulfur.[24] Moreover, the steric course of proton abstraction and halogenation was shown to be different.[2,13] Mechanism 2 was therefore proposed,



(2)

where proton abstraction occurred from the chlorosulfoxonium ion to give an ylide that then undergoes a Pummerer rearrangement. Since the mechanism of this last rearrangement is not entirely clear,[25] mechanism 2 cannot be considered to be complete. A more detailed mechanism 3 was recently proposed[26,27] involving simultaneous proton abstraction and chlorine migration. This was based on kinetic results which showed first order dependence on pyridine concentration, the primary isotope effect $k_H/k_D = 5.5$, and the absence of H/D exchange in the sulfoxide during chlorination.



(3)

We thought that much could be learned about the mechanism of halogenation of sulfoxides by studying

(1) R. N. Loeppky and D. C. K. Chang, *Tetrahedron Lett.*, 5415 (1968).
(2) M. Cinquini, S. Colonna, and F. Montanari, *Chem. Commun.*, 607 (1969).
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(14) J. E. Baldwin, R. E. Hackler, and R. M. Scott, *Chem. Commun.*, 1415 (1969).
(15) A. Rauk, S. Wolfe, and I. G. Csizmadia, *Can. J. Chem.*, **47**, 113 (1969).
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(20) T. Durst, R. R. Fraser, M. R., McClory, R. B. Swingle, R. Viau, and Y. Y. Wigfield, *Can. J. Chem.*, **48**, 2148 (1970).
(21) T. Durst, R. Viau, and M. R. McClory, *J. Amer. Chem. Soc.*, **93**, 3077 (1971).
(22) R. Lett, S. Bory, B. Moreau, and A. Marquet, *Tetrahedron Lett.*, 3255 (1971).
(23) S. Iriuchijima and G. Tsuchihashi, *Synthesis*, 588 (1970).
(24) T. Durst and K. C. Tin, *Can. J. Chem.*, **49**, 2374 (1971).
(25) G. A. Russel and G. J. Mikol, "Mechanisms of Molecular Migrations," Vol. 1, B. S. Thyagarajan, Ed., Wiley, New York, N. Y., 1968, pp 162–174.
(26) M. Cinquini, S. Colonna, and D. Landini, *J. Chem. Soc., Perkin Trans. 2*, 296 (1972).
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the stereochemistry of this reaction with substituted thiane 1-oxides.

## Results

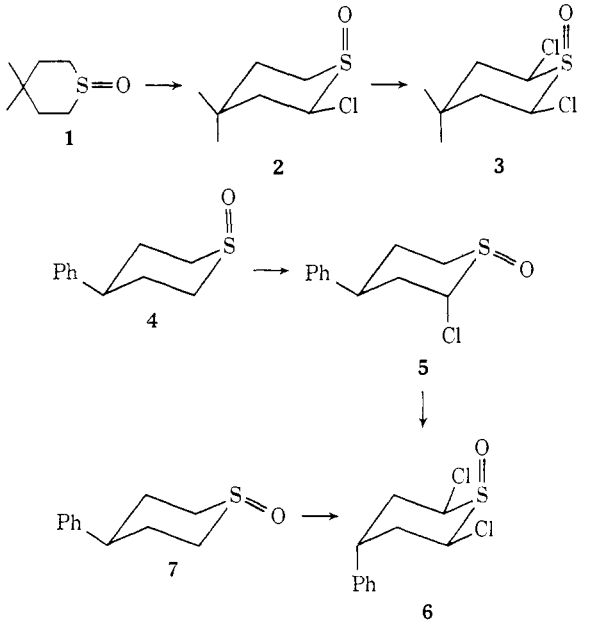
Halogenations were performed in dichloromethane by three reagents: (A) *tert*-butyl hypochlorite and pyridine;[3] (B) chlorine and pyridine;[5] and (C) sulfuryl chloride in the presence of calcium oxide.[6] All three methods gave similar results, internally consistent (Table I).

Chlorination of 4,4-dimethylthiane 1-oxide (**1**)[28] gave

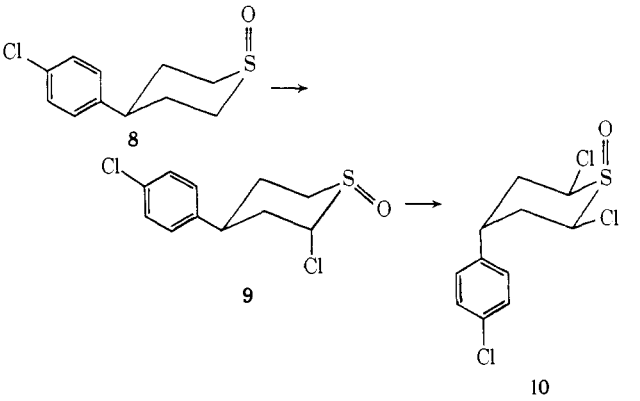
**Table I.** Chlorination of 4-Substituted Thiane 1-Oxides in Dichloromethane

| Starting material | Chlorinating agent[a] | Product (yield, %)[b] |
|---|---|---|
| **1** | A | **2** (83) |
| **1** | B | **3** (83) |
| **1** | C | **2** (45) |
| **2** | B | **3** (85)[c] |
| **4** | A | **5**[d] |
| **4** | B | **6** (64) |
| **4** | C | **5** (88)[c] |
| **7** | B | **6** (42) |
| **8** | A | **9** (71) |
| **8** | B | **10** (100)[c] |
| **11** | B | **13** (75) |
| **12** | B | **13** (61) |
| **22** | B | **24** (87)[c] |
| **23** | B | **25** (85)[c] |
| **1** | $(CH_3)_3COCl$ + anhydrous KOAc | **2** (90)[e] |
| **1** | $(CH_3)_3COCl$ (no additive) | **2** (15) + **3** (73)[e] |
| **4** | A + $AgNO_3$ | **5**[d] |
| **4** | $SO_2Cl_2$ + pyridine | **5** (34) |

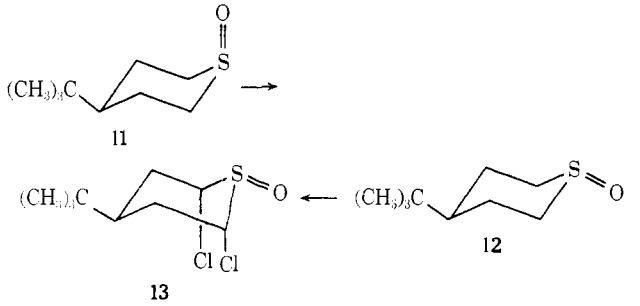
[a] For the reagents A, B, and C, see text. [b] By isolation after purication by recrystallization unless otherwise indicated. [c] Before recrystallization. Nmr indicated pure material. [d] Yield not established. Nmr indicated exclusive compound. [e] From glc analysis.



the monochloro (**2**) and dichloro derivative (**3**). *cis*-4-Phenylthiane 1-oxide (**4**)[12] also gave on chlorination a monochloro (**5**) and dichloro derivative (**6**). The same dichloro derivative, **6**, was obtained on chlorination of the trans isomer **7**.[12] Similar products, **9** and **10**, were obtained from *cis*-4-*p*-chlorophenylthiane 1-oxide (**8**).[29]

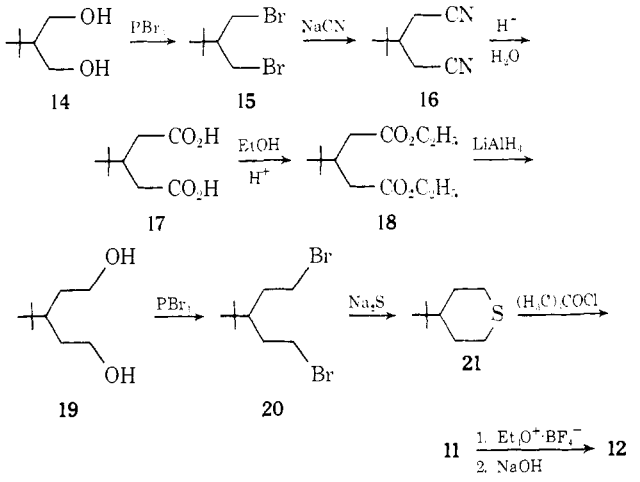


Chlorination of both *cis*- (**11**) and *trans*-4-*tert*-butyl-



thiane 1-oxide (**12**), which were obtained by a series of steps (Scheme I), yielded the same dichloro compound **13**.

**Scheme I**

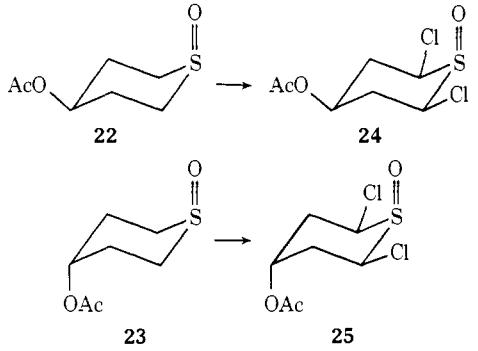


*cis*- (**22**) and *trans*-4-acetoxythiane 1-oxide (**23**) were prepared by acetylation of the corresponding alcohols.[30] The structures of these compounds follow from the correlation with the hydroxy compounds and from their physical properties, particularly the nmr of the $C_4$ protons. The half-widths of these protons are 17 and 11 Hz for **22** and **23**, respectively, thus supporting the axial conformation of the acetoxy group in the latter. The oxygen has the axial conformation in both compounds as found generally.[30] In contrast to the isomeric pairs **4**, **7** and **11**, **12**, in which the same dichloride was

(28) J. B. Lambert, D. S. Bailey, and C. E. Mixan, *J. Org. Chem.*, 37, 377 (1972).

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

(30) J. C. Martin and J. J. Uebel, *ibid.*, 86, 2936 (1964).




obtained from each member of the pair, chlorination of the isomeric acetoxythiane 1-oxides **22** and **23** gave different dichloro products, **24** and **25**, respectively.

The assignments of the structures of the chlorinated compounds were based on their physical properties. The configuration of the substituents on the carbons of the thiane ring was determined from the position and coupling constants of the protons geminal to them. The main problem was the assignment of the configuration of the sulfoxide group. This could be done in some cases by nmr correlations but final determination for important products was carried out by their dipole moments (Table II).

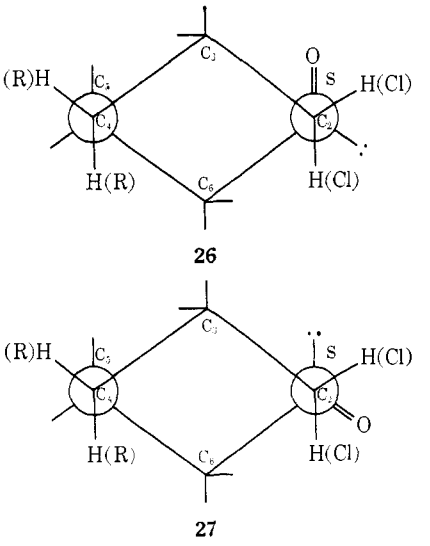
**Table II.** Experimental and Calculated Electric Dipole Moments, $\mu$, for Some of the Chlorination Products of 4-Substituted Thiane 1-Oxides

| Compd | $\mu$, D Exptl | $\mu$, D Calcd | $\Delta\mu$, D | $\Delta\mu/n$[a] | $\mu$ calcd for isomer with other S=O config |
|---|---|---|---|---|---|
| **3** | 5.0 | 6.4 | 1.4 | 0.7 | 6.4 |
| **5** | 4.4 | 5.0 | 0.6 | 0.6 | 2.3 |
| **9** | 3.0 | 3.1 | 0.1 | 0.1 | 2.6 |
| **10** | 3.4 | 5.0 | 1.6 | 0.8 | 6.5 |
| **13** | 5.2 | 6.6 | 1.4 | 0.7 | 1.7 |

[a] Number of chlorine atoms $\alpha$ to the sulfoxide group.

The dipole moments were measured in benzene solution at 30° using the method of Halverstadt and Kumler.[31] In calculating the theoretical moments, idealized models, **26** and **27**, were used in which all atoms are perfect tetrahedra and all gauche interactions are 60°. It was assumed[30,32] that the S=O dipole moment is directed at an angle of 38° out of the C–S–C plane toward the oxygen atom. The dipole moments of thiane 1-oxide, 4.19 D, cyclohexyl chloride, 2.24 D, and *p*-chlorotoluene, 1.95 D, were used to represent the moments of the sulfoxide, aliphatic halogen, and aromatic halogen groups, respectively. This is essentially the method used previously[29,30] for 4-substituted thiane 1-oxides.

As this appears to be the first report of dipole moment measurements of $\alpha$-chloro sulfoxides, the inductive effect of a chlorine atom on the dipole moment of an $\alpha$-sulfoxide group (or the converse inductive effect of sulfoxide on $\alpha$ chlorine) is not known. From Table II it is seen that, with the exception of **9**, the experimental




dipole moments are smaller than the calculated values by a factor ranging from 0.6 to 0.8 D/$\alpha$-chlorine atom. This difference must reflect both the inductive effect of the chlorine atoms as well as inaccuracies in the stereochemical models on which the calculated moments are based. Although the structures of the molecules differ greatly from one another in the series examined, yet in all cases the relation between the $\alpha$-chlorine atoms and the sulfoxide group is cis. The fact that the value of $\Delta\mu/n$, where $n$ is the number of chlorine atoms $\alpha$ to the sulfoxide group, remains fairly constant for the series indicates that the local geometry in the vicinity of the sulfoxide group does not differ greatly from molecule to molecule. Even though we cannot conclude with certainty which portion of the $\Delta\mu/n$ is due to inductive effects and which due to inaccuracies in the models, the constant value of this factor is useful and may be applied as a correction factor in calculating dipole moments of $\alpha$-chloro sulfoxides in which a cis relation exists between the sulfoxide and $\alpha$-chlorine groups.

The value of $\Delta\mu/n$ for **9** indicates that the geometry in the vicinity of $C_4$ is distorted from that assumed in the models. This distortion is not reflected in the dipole moment of **5** since there is no polar group at $C_4$ as is the case in **9**. It is also possible that the introduction of an additional dipole at $C_4$ changes the dipole–dipole interaction between the $\alpha$ chlorine and the sulfoxide dipoles.

In the nmr spectrum of **3** there are two quartets of two protons each at 1.77 and 4.83 ppm, each having coupling constants of 13 and 3.5 Hz. The quartet at 4.83 ppm is compatible with the axial CHCl protons. The higher field quartet at 1.77 ppm corresponds to the $\beta$-equatorial protons while the $\beta$-axial protons appear as a triplet at 2.41 ppm with a coupling constant of 13 Hz. Since the $\beta$-axial protons are at lower field than the $\beta$-equatorial ones, the sulfoxide group is assumed to be axial.[12,33]

The nmr spectrum of **2** has the remarkable feature that the absorptions of all seven of the ring protons are clearly distinguishable. Thus, the spectrum consists of: (1) a quartet at 4.74 ppm with coupling constants of 13 and 4 Hz, which is compatible with an axial CHCl proton; (2) a doublet ($J$ = 15 Hz) of triplets ($J$ = 4

(31) I. F. Halverstadt and W. D. Kumler, *J. Amer. Chem. Soc.*, **64**, 2988 (1942).

(32) C. W. N. Cumper and S. Walker, *Trans. Faraday Soc.*, **52**, 193 (1956).

(33) A. B. Foster, T. D. Inch, M. H. Qadir, and J. M. Webber, *Chem. Commun.*, 1086 (1968).

Hz) at 3.04 ppm attributed to the equatorial proton of the $-S(O)-CH_2$ group; (3) a doublet of doublets with coupling constants of 14 and 3 Hz at 2.68 ppm assigned to the axial $-S(O)-CH_2$ proton; (4) a triplet at 2.39 ppm with a coupling constant of 14 Hz corresponding to the $\beta$-axial proton adjacent to the CHCl group; (5) a triplet ($J$ = 13 Hz) of doublets ($J$ = 4 Hz) at 2.14 ppm attributed to the $\beta$-axial proton adjacent to the $-S-(O)-CH_2$ carbon; and (6) two doublets, at 1.68 and 1.30 ppm, each with a coupling constant of 15 Hz and each further split into closely spaced multiplets which represent the $\beta$-equatorial protons. Thus the $\beta$-axial protons are at a lower field than the $\beta$-equatorial ones indicating an axial configuration of the sulfoxide group.

Both nmr spectra of **5** and **9** show a narrow (half-width of 9 Hz) multiplet at 5.32 ppm integrating for one proton which corresponds to the equatorial CHCl proton. In addition, both spectra show aromatic protons at about 7.2 ppm as well as complex multiplets at 3.2 ppm (three protons), 2.4 ppm (two protons), and 2.1 ppm (two protons). For **5**, the experimental dipole moment value of 4.4 D indicates equatorial sulfoxide. Since the starting materials **4** and **8** differ only slightly and since the nmr spectra of the chlorination products are extremely similar, it is reasonable to conclude that the sulfoxide configuration in both **5** and **9** is the same, *i.e.*, equatorial.

The $\alpha$-chloro sulfoxide **9** has previously been reported,[13] but the authors were unable to draw conclusions about the sulfoxide configuration.

Both nmr spectra of **6** and **10** show a doublet of doublets at 4.7 ppm with coupling constants of 14 and 4 Hz and integrating for two protons. This is compatible with axial CHCl protons and therefore equatorial chlorine atoms. The $C_4$ protons appear as a quintet at 3.46 ppm with a coupling constant of 4 Hz and half-height width of 10 Hz which is compatible with an equatorial proton and axial aromatic group. The $\beta$-axial protons appear as a triplet ($J$ = 14 Hz) of doublets ($J$ = 4 Hz) at 2.81 ppm. The $\beta$-equatorial protons show a doublet ($J$ = 14 Hz) of triplets ($J$ = 4 Hz) at 2.48 ppm. Since the $\beta$-axial protons are at lower field than the $\beta$-equatorial ones, the sulfoxide group is assumed to be axial. This assignment was confirmed by the measurement of the dipole moment of **10**. The experimental value of 3.4 D is much closer to the calculated value for **10** than to the calculated value for the equatorial sulfoxide isomer.

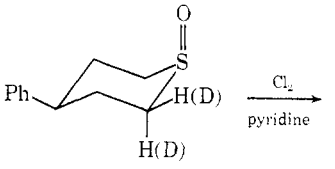
The nmr spectrum of **13** consists of a closely spaced multiplet at 5.25 ppm (two protons) which is assigned to the equatorial CHCl protons because of a narrow (9 Hz) peak width at half-height. The spectrum also exhibits a multiplet at about 2.3 ppm as well as a singlet at 1.1 ppm corresponding to the *tert*-butyl group. The experimental dipole moment value of 5.2 D clearly indicates that the sulfoxide group is equatorial.

In the nmr spectrum of **24** a quartet (two protons) appears at 4.64 ppm with coupling constants of 12 and 4 Hz, which is compatible with the axial CHCl protons. A broad (half-height width; 18 Hz) multiplet (one proton) at 4.84 ppm is attributed to the axial $C_4$ proton. This assignment is confirmed by the $\beta$-axial absorption at 2.55 ppm which consists of a quartet with a coupling constant of 12 Hz. The $\beta$-equatorial protons appear as a doublet ($J$ = 12 Hz) of triplets ($J$ = 4 Hz) at 2.33 ppm. The sulfoxide group is assumed to be axial because the $\beta$-axial protons are at lower field than the $\beta$-equatorial ones.

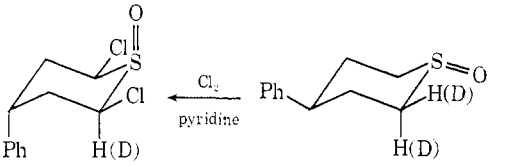
The nmr spectrum of **25** shows a two-proton quartet at 4.87 ppm with coupling constants of 12 and 4 Hz, which is compatible with the axial CHCl protons. A narrow (half-height width; 9 Hz) quintet (one proton) at 5.21 ppm is attributed to the equatorial $C_4$ proton. This assignment is confirmed by the $\beta$-axial absorption at 2.64 ppm which consists of a triplet ($J$ = 12 Hz) of doublets ($J$ = 3 Hz). The $\beta$-equatorial protons appear as a doublet ($J$ = 12 Hz) of triplets ($J$ = 4 Hz) at 2.26 ppm. Once again, the sulfoxide group is assumed to be axial because the $\beta$-equatorial protons are at a lower field than the $\beta$-equatorial ones.

The stereochemistry of the proton abstracted at the $\alpha$ position during the chlorination was explored by the preparation of the sulfoxides **4** and **7** predominantly axially or equatorially $\alpha$ deuterated. The result of the reaction of these compounds (Table III) shows clearly

**Table III.** Distribution of the Deuterium Label in Reactants and Products in the Reactions




**4a**




**7a**

| Run | Reactant | —Number of protons[a] $\alpha$ to S=O— —Starting material— Axial | Equatorial | Product |
|---|---|---|---|---|
| 1 | **4a** | 2.0 | 0.87 | 0.89 |
| 2 | **4a** | 0.04 | 0.32 | 0.32 |
| 3 | **4a** | 0.01 | 0.66 | 0.67 |
| 4 | **7a** | 0.01[b] | 0.66[b] | 0.65 |
| 5 | **7a** | 0.63 | 0.75 | 0.68 |

[a] From the 60 Mc nmr integrals. The $\beta$-equatorial peaks at 1.8 ppm in **4a**, the phenyl peak in **7a**, and the $C_4$-proton peak at 3.5 ppm in the dichloro product were used as integration references.[12] [b] The starting material of this run was obtained from the compound of run 3 by way of the triethyloxonium fluoroborate salt, a process which does not involve the $\alpha$ protons: C. R. Johnson, *J. Amer. Chem. Soc.*, **85**, 1020 (1963).

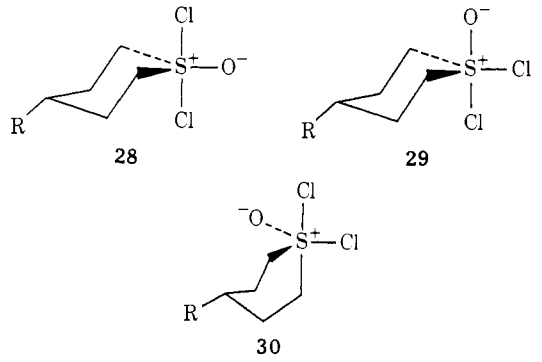
that in the *cis*- as well as *trans*-4-phenylthiane 1-oxide the axial proton is abstracted almost exclusively and that this stereochemical effect takes preference over the kinetic isotope effect as seen in the case of axially deuterated sulfoxides.

## Discussion

The mechanism of the chlorination has to account for several seemingly discordant effects: (a) the identical products obtained from the isomers **4**, **7** and **11**, **12**; (b) the different products obtained from the isomers **22** and **23**; (c) the axial chlorination of **4**, **8**, **11**, and **12** and the equatorial arrangement of the S=O bond in

these chlorination products; (d) the equatorial halogenation of **1**, **22**, and **23** and the axial arrangement of the S=O bond in these halogenation products; (e) the preferential axial proton abstraction in both isomeric sulfoxides, **4** and **7**; and (f) the absence of gem dihalogenation.

The formation of identical products in the chlorination of the isomeric axial and equatorial sulfoxides was at first interpreted as the consequence of the formation of an intermediate pentacoordinate (hexavalent) dichloro adduct, **28**, which would be the same for both



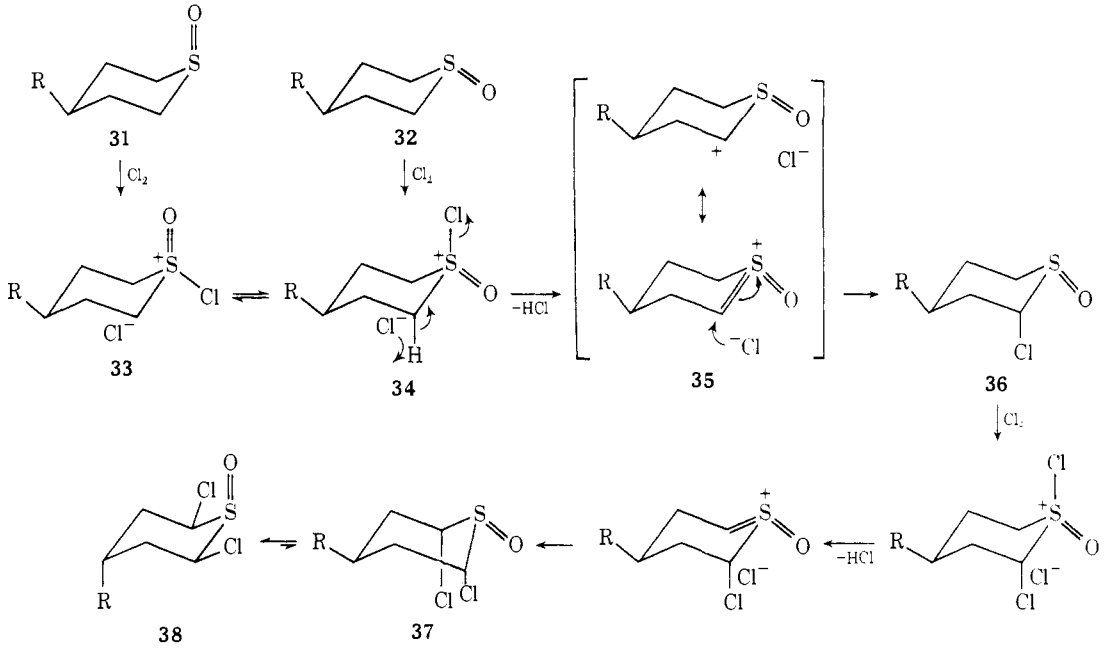
**28** **29** **30**

bipyramid structures are expected to be apical[37] and because they do not explain the stereochemical course of the reaction.

It is established[26] that the first step in the $\alpha$ chlorination of noncyclic sulfoxides is the attack of chlorine on sulfur to form a chlorosulfoxonium ion. In the case of thiane 1-oxides, the abstraction of a proton from the $\alpha$ carbon as the first step in the halogenation reaction can be eliminated not only on the evidence from parallel open-chain reactions and the high reaction rate in the presence of weak bases but also from the stereochemistry of proton abstraction in thiane 1-oxides, which is known[12] to be predominantly axial in sulfoxides with an axial S=O bond and predominantly equatorial in equatorial sulfoxides. In the chlorination reactions reported in this paper, exclusive axial proton abstraction is observed in both isomers.

We propose the following mechanism (Scheme II) for the $\alpha$ chlorination of thiane 1-oxides. Chlorination of the cis (**31**) and trans (**32**) sulfoxides, conformationally biased by a large substituent, R, results in the same pair of chlorosulfoxonium ions, **33** and **34**, which are in equilibrium with one another through a process of in-

**Scheme II**



**31** **32** **33** **34** **35** **36** **37** **38**

isomers. Such a structure was assumed from extrapolation of the physical properties of thiane–dihalogen adducts reported by Lambert, *et al.*[34] The bonding in such compounds has been studied theoretically by Musher.[35] Recently, Perozzi and Martin[36] have reported the isolation of a pentacoordinate dialkoxy sulfoxide. However, the different chlorination products obtained from the isomeric 4-acetoxythiane 1-oxides, **22** and **23**, eliminate **28** as a possible intermediate. Although the unsymmetrical pentacoordinate derivatives **29** and **30** cannot be excluded as intermediates, they are improbable since the chlorine atoms in such trigonal

version at sulfur by nucleophilic SN2 displacement of the chlorine in the chlorosulfoxonium ions by the chloride counterions. The steric course of all reactions here reported can be rationalized on the basis of two requirements: (1) a trans-diaxial elimination of hydrogen chloride, which can proceed only through **34**, to give the intermediate **35**, followed by (2) an axial addition of chloride ion (or hydrogen chloride) to the $\alpha$ carbon of **35**. This process results in the sulfoxide **36** in which the S=O bond is equatorial and the C—Cl bond is axial. This is analogous with compounds **5** and **9**. Repetition of this sequence with **36** leads to the dichloro sulfoxide **37** which is analogous with **13**. The steric requirements for the elimination and addition steps are large, since on dichlorination the two chlorine atoms

(34) J. B. Lambert, D. G. Johnson, R. G. Keske, and C. E. Mixan, *J. Amer. Chem. Soc.*, **94**, 8172 (1972).

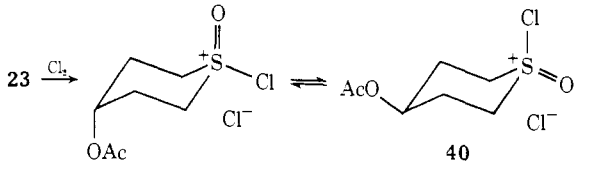
(35) V. B. Koutecky and J. I. Musher, in press; J. I. Musher, *Angew. Chem., Int. Ed. Engl.*, **8**, 54 (1969); *J. Amer. Chem. Soc.*, **90**, 7371 (1968); *Advan. Chem. Ser.*, **No. 110**, 44 (1972).

(36) E. F. Perozzi and J. C. Martin, *J. Amer. Chem. Soc.*, **94**, 5519 (1972).

(37) E. L. Muetterties and R. A. Schunn, *Quart. Rev., Chem. Soc.*, 245 (1966).

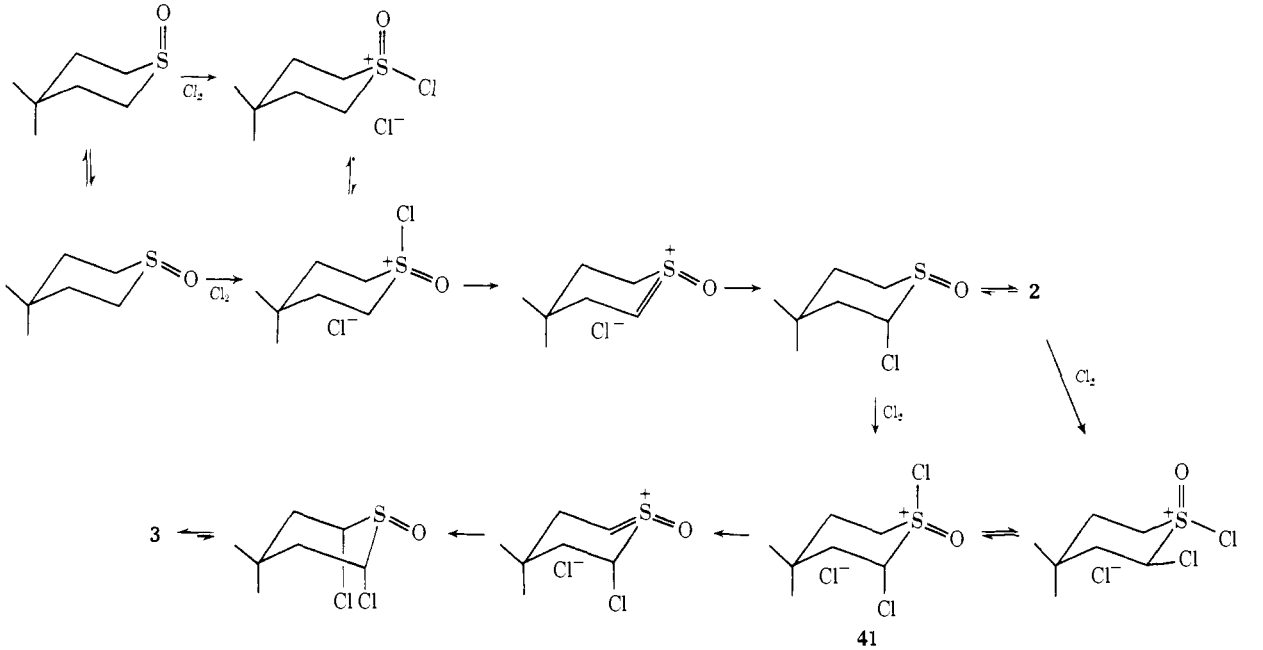
are in a 1,3-diaxial arrangement which should be of a rather high energy. Depending on the conformational energy of R, the energy of the 1,3-diaxial halogen system may be sufficient to cause the ring to flip to the conformation with R in an axial position, **38**. This is the case when R is phenyl and *p*-chlorophenyl (compounds **6** and **10**). The conformational energy of 1,3-diaxial dichlorocyclohexanes was found[38] to be 3.65 kcal/mol. The intermediate **35** has its charge distributed between the sulfur and $\alpha$-carbon atoms and thus resembles an ylide with a positive instead of a negative charge, a kind of an "inverted ylide." Since $\alpha$-chloro sulfoxides are obtained in which the sulfoxide groups are equatorial only, this suggests that the "inverted ylide" has a nonplanar structure around sulfur.

When the ring substituent, R, is a small group that can stabilize one conformation only slightly relative to the other, the initially formed chlorosulfoxonium ion may equilibrate with the other conformation of the ion by ring inversion. Thus chlorination of **23** gives the chlorosulfoxonium ion **39** which, after ring inversion,




39 40

**Scheme III**

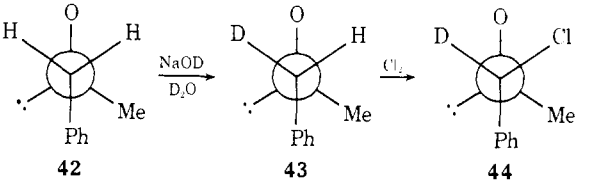



results in the isomeric ion **40**. Now **40** is analogous with **34** of Scheme II and the reaction proceeds according to the scheme leading to the dichloride **38,** which is analogous with compound **25**. Similar considerations with **22** account for the formation of the isomeric dichloride, **24**. Since the halogenation of the isomeric 4-acetoxy sulfoxides gave only one dichloro derivative in each case, the ring inversion and elimination steps are both faster than inversion at sulfur.

The results of chlorination of **1** support this mechanism. Although **1** exists in solution with approximately equal amounts[28] of the axial and equatorial S=O conformers, only one monochloro and one dichloro product are obtained. It is remarkable that no gem dichlorination occurs in spite of the fact that the CHCl proton of the monochloride is certainly more acidic than those on the other $\alpha$ carbon. The reason is clearly seen by examining Scheme III. In the only intermediate which is suitably disposed for a trans-diaxial elimination of HCl, **41**, the CHCl proton is equatorial and therefore cannot be eliminated; hence no gem dichlorination can occur. Similarly, the abstraction of the axial deuterium in preference to the equatorial hydrogen is also understood when the stringent requirement for trans-diaxial elimination is taken into account.

Addition of silver nitrate[8,39] or potassium acetate[3] did not change the steric course of the reaction since it could not change the conformation of the chlorosulfoxonium ions as it probably did in open-chain compounds.

It is of interest that in the conformationally biased[10] open-chain sulfoxide **42**, base-catalyzed H/D exchange led to the $\alpha$-deuterio sulfoxide **43**,[10,21] while chlorination was found to be stereospecific and involved the abstraction of the proton diastereotopic to that preferentially exchanged in $NaOD/D_2O$.[8] Thus chlorination of **43** gave **44**. The stereochemistry of the chlorination of conformationally biased open-chain sulfoxides can



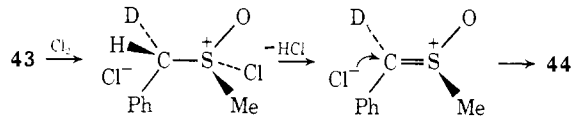

42 43 44

again be explained by trans elimination of hydrogen chloride in the favored conformation followed by a stereospecific chloride addition to the intermediate formed (Scheme IV). The stereospecificity of the chlo-

(38) J. Cantacuzene, R. Jantzen, and D. Ricard, *Tetrahedron*, **28**, 717 (1972).

(39) M. Cinquini, S. Colonna, and F. Montanari, *Chem. Commun.*, 1441 (1970).

**Scheme IV**



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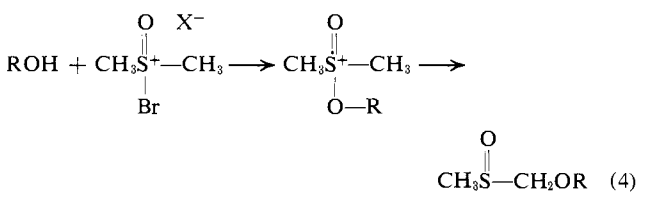
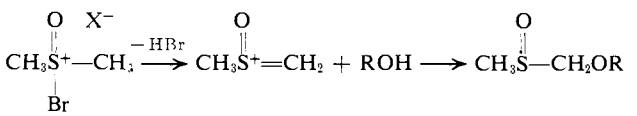
rination shows that rotation about the C=S bond in the intermediate **45** is slow relative to attack by the chloride anion and that the direction of attack at the $\alpha$ carbon is stereospecific, a result either of nonplanarity (and slow inversion) of the $\alpha$ carbon or of the directive influence of the bent $=S^{+}(O)Me$ group.

The reaction of dimethyl sulfoxide with *N*-halosuccinimides and alcohols has recently[40] been postulated to lead to $\alpha$ alkoxy sulfoxides which are assumed to result from a Pummerer-type rearrangement of an alkoxysulfoxonium ion formed by an SN2 displacement on a bromosulfoxonium ion (reaction 4). Formation of



(4)

$\alpha$-alkoxy sulfoxides in this reaction may be explained by the addition of the alcohol to the "inverted ylide" intermediate **46** which results from hydrogen bromide elimination in the bromosulfoxonium ion.



46

## Experimental Section

Melting points were observed in a Thomas-Hoover apparatus and are uncorrected as are boiling points. Infrared spectra were recorded as Nujol mulls, unless otherwise indicated, on Perkin-Elmer 337 and 457 spectrometers. Nuclear magnetic resonance spectra were recorded on Varian T-60 and HA-100 spectrometers in deuterochloroform with tetramethylsilane as internal standard. Gas liquid chromatography (glc) was performed on an Aerograph A-700 instrument with a 4-m Carbowax column, 5% on Chromosorb W, at a column temperature of 205°. Microanalyses were performed by Mrs. M. Goldstein of the microanalytical laboratory of the Hebrew University. Satisfactory elemental analyses were obtained for all new compounds herein reported.

**4,4-Dimethylthiane 1-Oxide (1).** This compound was prepared in 81% yield by the sodium metaperiodate oxidation of 4,4-dimethylthiane[41] according to the procedure of Leonard and Johnson.[42] After recrystallization from ether–hexane, the compound had mp 92–93°, ir 1035 $cm^{-1}$ (S=O).

**1,3-Dibromo-2-*tert*-butylpropane (15).** A portion of 65.5 g (0.24 mol) of phosphorous tribromide was slowly dropped onto 28.8 g (0.22 mol) of 2-*tert*-butylpropane-1,3-diol (**14**)[43] and cooled in an ice bath until a viscous slurry formed. The bath was removed and on gradual warming a clear mobile solution was formed with the evolution of white fumes. The bath was replaced and the remainder of the phosphorous tribromide was added with stirring. After warming to room temperature, the solution was heated at 160° for 3 hr, cooled in an ice bath, and water carefully added. An orange solid was filtered out and the filtrate was extracted with dichloromethane. The combined organic solutions were dried ($MgSO_4$) and the solvent was evaporated under vacuum giving 52.2 g of oily residue. Distillation gave 42.5 g (75%): bp 61–65° (1 mm); $n^{23}D$ 1.5089 [lit.[44] bp 94° (10 mm)].

**β-*tert*-Butylglutaronitrile (16).** To a warm solution of 11.8 g (0.24 mol) of sodium cyanide in 25 ml of water was added a solution of 25.8 g (0.1 mol) of 1,3-dibromo-2-*tert*-butylpropane (**15**) in 80 ml of ethanol, and the solution was refluxed for 42 hr. After evaporation of the solvent under vacuum the residue was dissolved in water, the aqueous solution was extracted with ethyl acetate, the combined organic solutions were dried ($Na_2SO_4$), and the solvent was removed under vacuum. Distillation of the residue gave 10.3 g (69%) of product: bp 115–120° (2.2 mm); $n^{25}D$ 1.4619; ir (liquid film) 2245 $cm^{-1}$ (C≡N).

**β-*tert*-Butylglutaric Acid (17).** A mixture of 35 g of sulfuric acid, 35 ml of water, and 9.8 g (0.065 mol) of β-*tert*-butylglutaronitrile (**16**) was refluxed for 14 hr. The solution was cooled, saturated with ammonium sulfate, and extracted with ether. The combined organic solutions were washed with water, dried ($Na_2SO_4$), and the solvent evaporated under vacuum. The crystalline residue, 9.5 g, was recrystallized from ether–hexane to give 6.4 (52%): mp 145–147° with decomposition; ir 1725 $cm^{-1}$ (C=O).

Concentration of the mother liquor gave an additional 1.9 g (16%), mp 142–146°.

**Diethyl β-*tert*-Butylglutarate (18).** A solution of 8 g (0.043 mol) of β-*tert*-butylglutaric acid (**17**) in 20 mol of dry benzene containing 8.8 g (0.19 mol) of absolute ethanol and 2.2 g of sulfuric acid was refluxed for 10 hr and then poured into 20 ml of water. The benzene layer was separated and the aqueous layer was extracted with ether. The combined organic solutions were washed with saturated aqueous sodium bicarbonate, then with water, dried ($Na_2SO_4$), and the solvent removed under vacuum. The residue, 8.2 g, was distilled to give 7.2 g (69%) of product: bp 78–80° (0.3 mm); $n^{25}D$ 1.4399; ir (liquid film) 1740 $cm^{-1}$ (ester).

**3-*tert*-Butylpentane-1,5-diol (19).** To a slurry of 2.5 g (0.066 mol) of lithium aluminum hydride in 50 ml of dry ether was added dropwise with stirring a solution of 7.2 g (0.03 mol) of diethyl β-*tert*-butylglutarate (**18**) in 50 ml of ether at such a rate that a gentle reflux was maintained. When addition was complete, the mixture was refluxed for an additional 2 hr and then treated successively with 2.5 ml of water, 2.5 ml of 15% aqueous sodium hydroxide, and 7 ml of water with stirring while cooling in an ice bath. After stirring for an additional 0.5 hr, a white granular precipitate formed which was filtered and washed several times with ether. The combined ethereal solutions were dried ($Na_2SO_4$) and the solvent was evaporated under vacuum. Distillation of the residue gave 3.5 g (73%) of product: bp 115–120° (0.5 mm); mp 29–32°; ir (liquid film) 3500–3100 $cm^{-1}$ (OH).

**1,5-Dibromo-3-*tert*-butylpentane (20).** This compound was prepared in 82% yield by the same procedure used to prepare 1,3-dibromo-2-*tert*-butylpropane (**15**): bp 94–102° (1 mm) [lit.[29] bp 87–88° (0.7 mm)].

Subsequent reactions in Scheme I were performed according to reported[29,45] procedures.

***trans*-4-Phenylthiane 1-Oxide (7).** This compound is reported[12] with mp 137–138.5°. We prepared and purified this compound according to the reported[12] procedures and obtained mp 119–120° and a correct elemental analysis.

The nmr spectrum of the product indicated that there was no contamination by the cis isomer.

***cis*-4-Acetoxythiane 1-Oxide (22).** A mixture of 509 mg (3.8 mmol) of *cis*-4-hydroxythiane 1-oxide[30] in 9 ml of dry pyridine and 3 ml of acetic anhydride was stirred overnight at room temperature. The clear solution was poured onto a mixture of crushed ice and sulfuric acid and the resulting mixture was extracted with dichloromethane. The combined organic solutions were washed with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and the solvent evaporated under vacuum giving a colorless oil which crystallized. Recrystallization from dichloromethane–ether–hexane gave 441 mg (66%) of product, mp 86–93°. Several more recrystallizations gave the analytical sample: mp 94–95°; ir 1730 (ester), 1020 $cm^{-1}$ (S=O).

***trans*-4-Acetoxythiane 1-Oxide (23).** This compound was similarly prepared in 57% yield from *trans*-4-hydroxythiane 1-oxide:[30] mp 94–96°; ir 1730 (ester), 1028 $cm^{-1}$ (S=O).

**Chlorination of 4,4-Dimethylthiane 1-Oxide (1). (a) Method A (*tert*-Butyl Hypochlorite–Pyridine).** Under a nitrogen atmosphere,

(40) S. Hanessian, G. Yang-Chung, P. Lavallee, and A. G. Pernet, *J. Amer. Chem. Soc.*, **94**, 8929 (1972).
(41) L. Schmerling and J. P. West, *ibid.*, **74**, 2885 (1952).
(42) N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).
(43) E. L. Eliel and Sr. M. C. Knoeber, *J. Amer. Chem. Soc.*, **90**, 3444 (1968).
(44) G. M. Lampman, K. E. Apt, E. J. Martin, and L. E. Wangen, *J. Org. Chem.*, **32**, 3950 (1967).
(45) C. R. Johnson, *J. Amer. Chem. Soc.*, **85**, 1020 (1963).

in a flask with a side neck containing a rubber diaphragm, a solution of 438 mg (3 mmol) of 4,4-dimethylthiane 1-oxide (**1**) in 20 ml of dichloromethane and 1.2 ml (15 mmol) of pyridine was cooled in an ice bath. By means of a hypodermic syringe inserted in the diaphragm, a solution of 325.5 mg (3 mmol) of *tert*-butyl hypochlorite[46] in a small volume of dichloromethane was added dropwise to the flask, with stirring. After 1 hr at 0°, 20 ml of water was added, the mixture was acidified with sulfuric acid, and the organic layer was separated. The aqueous layer was extracted with dichloromethane and the combined organic solutions were washed with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and the solvent was evaporated under vacuum to give 448 mg (83%) of *cis*-2-chloro-4,4-dimethylthiane 1-oxide (**2**), mp 101–103°. Recrystallization from ether gave the analytical sample: mp 106–107°; ir 1048 $cm^{-1}$ (S=O).

**(b) Method B (Chlorine–Pyridine).** The same procedure and one-third the quantities were used as described in A except that instead of adding *tert*-butyl hypochlorite, a slow stream of chlorine gas was introduced into the solution with stirring by means of a syringe needle inserted through the diaphragm. After a slight excess of chlorine had been added, as shown by the persistence of a yellow-green color in the solution, the solution was stirred at 0° for 1 hr and then treated as in method A. The residue obtained was recrystallized from dichloromethane–hexane to give 122 mg (57%) of *cis,cis*-2,6-dichloro-4,4-dimethylthiane 1-oxide (**3**), mp 175–176°. Concentration of the mother liquor gave a second crop, 13 mg (6%), mp 168–172°. Several recrystallizations from chloroform gave the analytical sample: mp 175–176°; ir 1063 $cm^{-1}$ (S=O).

**(c) Method C (Sulfuryl Chloride–Calcium Oxide).** Under a nitrogen atomsphere, a slurry of 146 mg (1 mmol) of 4,4-dimethylthiane 1-oxide (**1**) 168 mg (3 mmol) of calcium oxide, and 10 ml of dichloromethane, in a flask with a side neck containing a rubber diaphragm, was cooled in an acetone–Dry Ice bath. By means of a hypodermic syringe, 0.1 ml (167 mg, 1.24 mmol) of freshly distilled sulfuryl chloride was added to the flask, dropwise with stirring. When addition was complete, stirring at −78° was continued for 15 min and 5 ml of water was added. After warming to room temperature, the mixture was filtered, the organic layer was separated, and the aqueous layer was extracted with dichloromethane. The combined organic solutions were washed with saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and the solvent was evaporated under vacuum to give a white crystalline solid. Recrystallization from ether–hexane gave 82 mg (45%) of **2**, mp 103–105°, whose nmr spectrum was identical with that of the product obtained by method A.

**(d) With *tert*-Butyl Hypochlorite–Potassium Acetate.** Method A was repeated using one-third the quantities and 196 mg (2 mmol) of anhydrous potassium acetate instead of pyridine. The work-up was modified as follows. After stirring for 1 hr at 0°, the solution was filtered and the solvent was evaporated under vacuum to give 188 mg of a partly crystalline residue. Glc analysis showed the presence of two peaks only, corresponding to **2** and to an unidentified compound in the ratio of 9:1.

**(e) With *tert*-Butyl Hypochlorite (No Additives).** Method A was repeated using one-third the quantities and with the following modifications. No pyridine was added and after stirring for 1 hr at 0° the solvent was evaporated under vacuum to give 204 mg of partly crystalline residue. Glc analysis showed the presence of three peaks only, corresponding to **3**, **2**, and to an unidentified compound in the ratio of 73:15:12.

The following compounds were obtained as indicated in Table I.

***cis*-2-Chloro-*trans*-4-phenylthiane 1-oxide (5):** mp 154–157° ($CH_2Cl_2$–hexane); ir 1068 $cm^{-1}$ (S=O).

***cis,cis*-2,6-Dichloro-*trans*-4-phenylthiane 1-oxide (6):** mp 121–123° ($CCl_4$); ir 1085 $cm^{-1}$ (S=O). The products obtained from both **4** and **7** had identical ir and nmr spectra and an undepressed mixture melting point.

***cis*-2-Chloro-*trans*-4-*p*-chlorophenylthiane 1-oxide (9):** mp 123–124° ($CH_2Cl_2$–ether) [lit.[13] mp 126–127°]; ir 1065 $cm^{-1}$ (S=O).

***cis,cis*-2,6-Dichloro-*trans*-4-*p*-chlorophenylthiane 1-oxide (10):** mp 158–159° ($CCl_4$); ir 1064 $cm^{-1}$ (S=O).

***trans*-4-*tert*-Butyl-*cis,cis*-2,6-dichlorothiane 1-oxide (13):** mp 191–192° ($CCl_4$); ir 1078 $cm^{-1}$ (S=O). The products obtained from **11** and **12** had identical ir and nmr spectra and an undepressed mixture melting point.

***cis*-4-Acetoxy-*cis,cis*-2,6-dichlorothiane 1-oxide (24):** mp 167–168° ($CH_2Cl_2$–ether); ir 1748 (ester), 1068 $cm^{-1}$ (S=O).

***trans*-4-Acetoxy-*cis,cis*-2,6-dichlorothiane 1-oxide (25):** mp 190.5–191.5° ($CHCl_3$); ir 1730 (ester), 1020 $cm^{-1}$ (S=O).

**Chlorination of *cis*-4-Phenylthiane 1-Oxide (4). (a) Method A, in Presence of Silver Nitrate.** Chlorination of **4** was carried out, according to method A, on a 1-mmol scale with the modification that 264 mg (2.28 mmol) of silver nitrate was dissolved in the reaction solution before the addition of the *tert*-butyl hypochlorite. The reaction mixture was filtered before acidification. An nmr spectrum of the residue obtained was identical with that of the monochloride, **5**.

**(b) With Sulfuryl Chloride–Pyridine.** Method C was used with the modification that 1 ml of pyridine was added instead of the calcium oxide. The crude product was twice recrystallized from dichloromethane–hexane to give 77 mg (34%), mp 147–151°, whose nmr spectrum was identical with that of the monochloride, **5**.

**Preparation of α-Deuterated *cis*-4-Phenylthiane 1-Oxide (4a).** (a) To a solution of methylsulfinyl carbanion,[47] prepared from 360 mg of a 50% suspension of sodium hydride in mineral oil and 2 ml of hexadeuteriodimethyl sulfoxide, was added 582 mg (3 mmol) of *cis*-4-phenylthiane 1-oxide (**4**) and 3 ml of dry benzene. The resulting clear solution was stirred at room temperature for 1 hr, then cooled in an ice bath, and 3 ml of $D_2O$ was added followed by 12 ml of water. The organic layer was separated and the aqueous layer was extracted with chloroform. The combined organic solutions were washed with water several times and dried ($MgSO_4$), and the solvent evaporated under vacuum to give 586 mg of a white crystalline residue. Recrystallization from heptane gave 452 mg, mp 138–146°. A portion of this material was recrystallized from a large volume of heptane to give material of mp 148–151° whose nmr spectrum indicated starting material with almost complete exchange of the α protons by deuterium.

The material with mp 138–146° (300 mg, 1.55 mmol) was back exchanged in 47 ml of 0.54 *N* sodium hydroxide for 48 hr at 90 ± 5° according to the procedure of Hutchinson, Andersen, and Katritzky.[12] Recrystallization of the crude product from a large volume of heptane gave 181 mg, mp 147–148°. This material constituted the reactant of run 1, Table III.

(b) *cis*-4-Phenylthiane 1-oxide (**4**) (300 mg, 1.55 mmol) was exchanged in 31 ml of 0.75 *N* NaOD/$D_2O$ for 49 hr at 90 ± 5° as in a above. Recrystallization of the crude product from heptane gave 275 mg, mp 147–149°, which constituted the reactant of run 2.

(c) A 24-hr exchange using the same quantities as in b resulted in 279 mg of product, mp 148–150°, which constituted the reactant of run 3.

**Preparation of α-Deuterated *trans*-4-Phenylthiane 1-Oxide (7a).** (a) A portion of the material of run 3 (146 mg, 0.75 m mol) was converted to the trans isomer according to the procedure of Johnson.[45] Recrystallization of the crude product from heptane gave 65 mg (44%) of material, mp 117–120°, which constituted the reactant of run 4.

(b) To a slurry of 194 mg (1 mmol) of *trans*-4-phenylthiane 1-oxide (**7**) in 10 ml of dry ether, under a nitrogen atmosphere and cooled in an acetone–Dry Ice bath, was added with stirring 2.5 ml (4 mmol) of a 1.6 *N* solution of *n*-butyllithium in hexane. After about 10 min, a clear solution was obtained and stirring at −78° was continued for 1 hr. $D_2O$ (5 ml) was then added and, after warming to room temperature, the ether layer was separated and the aqueous layer was extracted with dichloromethane. The combined organic solutions were dried ($MgSO_4$) and the solvent was evaporated under vacuum to give a white crystalline residue which after recrystallization from heptane gave 160 mg of material, mp 119–121°. This constituted the reactant of run 5.

**Chlorination of α-Deuterated 4-Phenylthiane 1-Oxides.** The α-deuterated materials described above were chlorinated using method B. The crude products were recrystallized from carbon tetrachloride and the deuterium content of the pure products was determined by nmr. The results are given in Table III.

**Acknowledgment.** We are grateful to Dr. H. Weiler-Feilchenfeld for valuable assistance in determining the dipole moments.

(46) H. M. Teeter and E. W. Bell, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 125.

(47) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).