

# The Stereochemistry of Oxidation at Sulfur. Oxidation of 4-Substituted Thianes to Sulfoxides<sup>1</sup>

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It has been shown that the proportions of *cis* and *trans* sulfoxides obtained by the oxidation of 4-substituted thianes vary over a wide range with change in the oxidizing agent. The mechanisms of certain of these oxidations are discussed with reference to steric approach control, product development control, and thermodynamic product control. It has been observed that dinitrogen tetroxide rapidly and cleanly equilibrates sulfoxides and that a six-membered ring sulfoxide is more stable with the oxide in the axial position.

Numerous methods of synthetic utility for the oxidation of sulfides to sulfoxides have been examined. In certain cases details of the mechanism of the oxidation have been elucidated.<sup>2</sup> However, the literature is almost devoid of systematic information concerning the stereochemistry of the oxidation at sulfur where geometric isomers were formed.<sup>3</sup> We have undertaken such a study with the thought that this information could not only be of value in planning syntheses but could also lead to an increased understanding of the mechanistic pathways involved in these oxidations. In this paper we report on the oxidation of several 4-substituted thianes by a variety of reagents.

We have previously indicated that the proportions of *cis* and *trans* sulfoxides shows considerable variance with change in oxidant for 4-*p*-chlorophenylthiane (I).<sup>4</sup> In order to eliminate the possibility that the polar *p*-chlorophenyl grouping was exerting significant directive effects on the stereochemistry of the oxidation, we chose to parallel this study with that of the oxidation of a 4-*t*-butyl- (II) and 4-methylthianes (III). These bulky 4-alkyl or -aryl substituents should have the effect of anchoring the thiane in the chair form with the substituent occupying an equatorial position.<sup>5</sup> With such geometry the two available directions for reagent approach are typologically different and variance from a 50:50 *cis-trans* mixture of sulfoxide will provide a measure of the directive effects of the reaction.

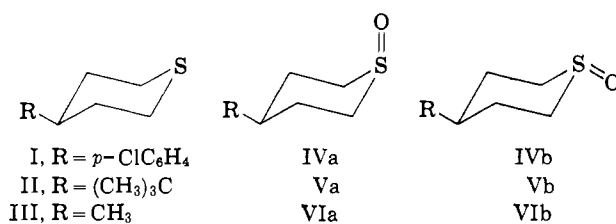
(1) (a) We gratefully acknowledge support by the National Science Foundation (Grant No. GP-1159); (b) part III in the series "Chemistry of Sulfoxides"; (c) part II: C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, **86**, 2935 (1964).

(2) For a review see D. Barnard, L. Bateman, and J. I. Cunneen, "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press Inc., New York, N. Y., 1961, p. 229.

(3) The distribution between racemic and *meso* disulfoxides resulting from the oxidation of the corresponding bisulfides has been studied by G. Farina, F. Montari and A. Negrini, *Gazz. chim. ital.*, **89**, 1548 (1959).

(4) C. R. Johnson, *J. Am. Chem. Soc.*, **85**, 1020 (1963).

(5) The utility of *t*-butyl as a holding group was first established by S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955). The *p*-chlorophenyl and methyl groups are somewhat less effective in this respect; for example, at room temperature only about 95% of methylcyclohexane molecules are in the equatorial form (see E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962).



For the synthesis of the sulfide II, 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 corresponding dichloride could be obtained by a similar method but in considerably reduced yield. Cyclization of the dichloride to II was effected in 89% yield. The 4-methyl- and 4-*p*-chlorophenylthianes<sup>4</sup> were likewise obtained by cyclization beginning with dihalides.

**Assignment of Configuration.** The assignments of configuration to the *cis*- and *trans*-4-*t*-butyl sulfoxides (Va and Vb) were made by physical and chemical comparisons with the 4-*p*-chlorophenyl compounds (IVa and IVb). The configuration of the latter had been previously determined in this laboratory by dipole moment studies.<sup>4</sup> In each case, the compound assigned the *cis* structure has the higher melting point; the *cis* compounds eluted during column and vapor phase chromatography prior to the *trans*; and there is a striking resemblance in the 1000–1100-cm.<sup>-1</sup> region of the infrared spectra of compounds of like assignment (Figure 1). The remarkable consistency in isomer distribution throughout the entire series of oxidizing reagents (Table II) provides strong additional evidence for the assignment indicated. For example, periodate oxidation of 4-substituted thianes has been found to result in a preponderance of the *cis* sulfoxide with both 4-*p*-chlorophenyl- and 4-chlorothianes.<sup>6</sup> If one assumes that the relatively remote from sulfur, although polar *p*-chlorophenyl and chloro groups do not alter completely the direction of the reaction, then one can assume the *cis* isomer to be the predominant 4-*t*-butylthiane 1-oxide obtained by periodate oxidation. The observation (see below) that in each case the compound assigned the *cis* configuration is found to be the more stable isomer corroborates these assignments. By similar arguments, the geometries of the 4-methylthiane 1-oxides have been assigned.

**Equilibration Studies.** To interpret the results of these oxidations it was first necessary to determine the equilibrium *cis-trans* composition of these sulf-

(6) J. C. Martin and J. J. Uebel, *J. Am. Chem. Soc.*, **86**, 2936 (1964).

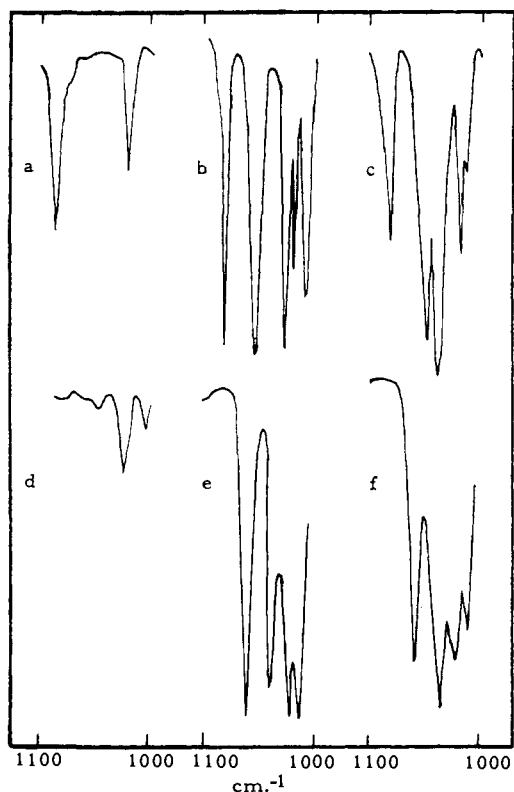


Figure 1. Infrared spectra from 1100 to 1000  $\text{cm}^{-1}$ ; 5% solutions in methylene chloride: a, 4-*p*-chlorophenylthiane (I); b, *cis* sulfoxide (IVa); c, *trans* sulfoxide (IVb); d, 4-*t*-butylthiane (II); e, *cis* sulfoxide (Va); and f, *trans* sulfoxide (Vb).

oxides within a six-membered ring. Equilibration of the sulfoxide groups in the 4-substituted thianes has been accomplished by three independent methods.<sup>1c</sup>

The thermal liability of the sulfoxide grouping has long been established.<sup>7</sup> Thermal equilibration of 4-*t*-butylthiane oxides in decalin at 190° results in a mixture containing 80 parts of the axial isomer and 20 parts of the equatorial isomer. This thermal equilibration was first reported by Henbest and Kahn who apparently achieved identical experimental results.<sup>8</sup> However, their configurational assignment was opposite to that reported here. Their assignments were apparently made on the *a priori* assumption that the equatorial isomer has the greater stability.

Treatment of our 4-substituted thiane 1-oxides either as pure isomers or as mixtures, according to the hydrogen chloride-dioxane method of Mislow,<sup>9</sup> in each case resulted in a predominance of the *cis* isomer (Table I). It has been suggested that the mechanism of this reaction involves the reversal formation of a sulfur dichloride ( $\text{R}_2\text{SCl}_2$ ) intermediate.<sup>9</sup>

Of particular interest is the observation that dinitrogen tetroxide, a reagent of choice for many sulfide-sulfoxide transformations,<sup>10</sup> is capable of equilibration

(7) We refer here to the stereochemical liability (see K. Mislow, P. Schneider, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **86** (1964), and references cited therein). Sulfoxides are known to readily undergo *cis*-pyrolytic elimination (C. A. Kingsbury and D. J. Cram, *ibid.*, **82**, 1810 (1960)); however, this should not be a problem in the cases reported here because of the inaccessibility of the  $\beta$ -hydrogens to the sulfoxide oxygen in the six-membered ring; cf. *N*-methylpiperidine oxide (A. C. Cope and N. A. LeBel, *ibid.*, **82**, 4656 (1960)).

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

(9) K. Mislow, T. Simmons, J. T. Mellilo, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **86**, 1452 (1964).

Table I. Equilibration of 4-Substituted Thiane 1-Oxides

Thiane 1-oxide	Method <sup>a</sup>	—Equilibrium— composition		$\Delta F$ , <sup>b</sup> kcal./ mole
		<i>cis</i>	<i>trans</i>	
4- <i>t</i> -Butyl	A	90	10	1.3
	B	80	20	1.3
	C	81	19	0.8
4-Methyl	A	80	20	0.8
	B	65	35	0.6
	C	76	24	0.6
4- <i>p</i> -Chlorophenyl	A	80	20	0.8
4-Chloro <sup>c</sup>	A	65	35	0.4

<sup>a</sup> A, hydrochloric acid in dioxane at 25°; B, decalin at 190°; C, dinitrogen tetroxide at 0° (for details see Experimental section).

<sup>b</sup> For the reaction  $cis \rightleftharpoons trans$ . <sup>c</sup> Generously provided by Professor Martin. With the relatively "small" chlorine group both the *cis* and *trans* sulfoxides appear to exist predominantly in the form with the axial oxygen.<sup>8</sup>

of sulfoxides.<sup>1c</sup> Pure *cis*, *trans*, or mixtures result in an equilibrium composition of sulfoxides at 81% axial and 19% equatorial in the case of the 4-*t*-butylthiane 1-oxides. The identical result is obtained beginning with the sulfide. In this connection, it is noteworthy that optically active (+)-benzyl-*p*-tolyl sulfoxide is rapidly racemized by this reagent.

Depending upon conditions and the identity of the 4-substituent, there is considerable variation of the equilibrium compositions of these cyclic sulfoxides; however, the isomer bearing the axial oxygen in each case is found to be more stable. The best value for the conformational free energy difference for the sulfoxide within the six-membered ring, is probably that ( $A$  value =  $-1.3$  kcal./mole) obtained with the very bulky and nonpolar 4-*t*-butyl grouping from both thermal and hydrogen chloride catalyzed equilibrations. Free sulfoxides are probably not involved in the equilibrations employing dinitrogen tetroxide.<sup>10</sup>

The evidence available to us at this time does not allow a conclusion to be made as to why an axial oxide on sulfur in these thianes is energetically favored over the equatorial. The simplest explanation is that this preference is merely a reflection of the relative steric requirements of oxygen vs. the free electron pair. If this were true, it would be unlikely that the electron pair of sulfoxide is located in a 3s orbital as has been proposed.<sup>11</sup> On the other hand, the lone pair could reasonably be expected to occupy a 3sp<sup>3</sup> orbital on sulfur.<sup>12</sup> From models it is estimated that the 1,3-oxygen-axial hydrogen internuclear distance is 2.6 Å., a value within the range of the sum of a van der Waals contact radii of hydrogen and oxygen. It is possible that London attractive terms outweigh van der Waals repulsions and create a favorable interaction between the oxygen and the ring. The observation that an axially disposed oxygen on sulfur within a six-membered ring is energetically favored over the equatorial configuration is not limited to those examples herein described. Martin and Uebel<sup>6</sup> have found that both *cis*- and *trans*-4-chlorothiane 1-oxide prefer the conformer bearing an axial oxide. These workers

(10) C. C. Addison and J. C. Sheldon, *J. Chem. Soc.*, 2705 (1956).

(11) C. C. Price and S. Oae, "Sulfur Bonding," Ronald Press, New York, N. Y., 1962.

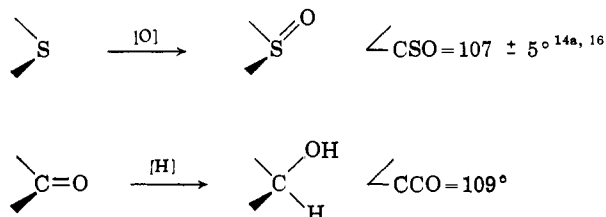
(12) G. Leandri, A. Mangini, and R. Passerini, *J. Chem. Soc.*, 1386 (1957); A. B. Burg, "Organic Sulfur Compounds," N. Kharasch, Ed., Pergamon Press Inc., New York, N. Y., 1961.

Table II. Oxidation of 4-Substituted Thianes to Sulfoxide

Oxidizing reagent	Reaction solvent (temp., °C.)	Thiane					
		4- <i>t</i> -Butyl		4-Methyl		4- <i>p</i> -Chlorophenyl	
		<i>cis</i>	<i>trans</i>	<i>cis</i>	<i>trans</i>	<i>cis</i>	<i>trans</i>
Ozone	CCl <sub>4</sub> or CH <sub>2</sub> Cl <sub>2</sub> (-40)	10	90	15	85	16	84
Chromic acid	C <sub>6</sub> H <sub>5</sub> N (25)	27	73	..	..	..	..
<i>t</i> -Butyl hydroperoxide	MeOH (50)	27	73	32	68	..	..
Hydrogen peroxide	AcOH (25)	35	65	..	..	..	..
<i>t</i> -Butyl hydroperoxide	C <sub>6</sub> H <sub>6</sub> (50)	36	64	35	65	35	65
<i>m</i> -Chloroperbenzoic acid	CH <sub>2</sub> Cl <sub>2</sub> (0)	36	64	30	70	33	67
Hydrogen peroxide	CH <sub>3</sub> COCH <sub>3</sub> (25)	37	63	40	60	30	70
Iodosobenzene	C <sub>6</sub> H <sub>6</sub> (80)	46	54	49	51	51	49
Nitric acid	Ac <sub>2</sub> O (0)	67	33	..	..	..	..
Sodium metaperiodate	H <sub>2</sub> O (0)	75	25	72	28	76	24
Dinitrogen tetroxide	... (0)	81	19	76	24	81	19
<i>t</i> -Butyl hypochlorite	MeOH (-70)	100	0	89	11	98	2

concluded that in these compounds there is an "axial preference of the sulfoxide oxygen in the absence of interactions with the C-Cl dipole" to the extent of 0.2 to 0.6 kcal./mole. In the dithiane series, 1,4-dithiane 1-oxide appears to prefer the conformer bearing the axial oxygen<sup>13</sup> and *trans*-1,4-dithiane 1,4-dioxide is reported to prefer the form with both oxygens in the axial position.<sup>14</sup> Trimethylene sulfite is reported to exist almost exclusively with an axial oxide.<sup>15</sup>

*Oxidation of 4-Substituted Thianes.* The spacial alteration at atom 1 in the thiane ring accompanying oxidation to sulfoxide is reminiscent of that occurring when the trigonal ketone carbon of, for example, 4-*t*-butylcyclohexanone, is reduced to the tetrahedral configuration of alcohol. As in these reductions of ketones it is necessary to consider three possible interpretations of the stereochemical results.<sup>17</sup> First,



the conditions employed may equilibrate any initially formed products so that the final isomer distribution is governed by *thermodynamic product control*. Secondly, the product distribution may be controlled by competitive attack from the sterically favored (relatively unhindered equatorial) vs. the hindered (axial) side (*steric approach control*). Lastly, an energetic consideration termed *product development control* which in this case we imply to mean that the same factors influencing the stability of the final products are operative in the transition state though not necessarily to the same extent and, that these products, once formed, are not further equilibrated.

(13) K. Hayasaki, *Tokyo Gakugei Daigaku Kenkyu Hokoku, 3-bu, Shizen Kagaku*, 12, 25 (1961); *Chem. Abstr.*, 60, 6724 (1964).

(14) (a) H. M. M. Shearer, *J. Chem. Soc.*, 1394 (1959); (b) P. B. D. de la Mare, D. J. Millen, J. G. Tillett, and D. Watson, *ibid.*, 1619 (1963); (c) C. Y. Chen and R. J. W. LeFevre, *Australian J. Chem.*, 16, 917 (1963).

(15) D. G. Hellier, J. G. Tillet, H. F. VanWoerden, and R. F. M. White, *Chem. Ind. (London)*, 1956 (1963).

(16) O. Bastiansen and H. Vierwoll, *Acta Chem. Scand.*, 2, 702 (1948).

(17) W. G. Dauben, G. J. Fonken, and D. S. Noyes, *J. Am. Chem. Soc.*, 78, 2579 (1956).

The 4-substituted thianes were oxidized by the majority of the methods outlined in the literature for the sulfide-sulfoxide transformation. Conditions were judiciously chosen to prevent any oxidation to the sulfone stage. Product analysis was made by gas phase chromatography employing a silicone-gum nitrile column capable of excellent resolution of sulfide, sulfoxides, and sulfone. Table II gives the relative percentages of *cis* and *trans* sulfoxides formed under a variety of oxidizing conditions. Examination of this data reveals that the isomer distribution is surprisingly unaffected by the nature of the substituent in the 4-position. It is apparent that these oxidations, at least with respect to orientation, are not subject to significant electrical effects from substituents at position 4. In continuation of our comparison of sulfide oxidation to ketone reduction it is noteworthy that polar substituents in position 4 of cyclohexanones exert marked directive effects on the stereochemistry of hydride reduction.<sup>18</sup>

Of particular interest is the remarkable stereoselectivity of the oxidation of 4-substituted thianes by the method of Skell and Epstein employing *t*-butylhypochlorite.<sup>19</sup> In the procedure employed for the oxidations reported here, *t*-butyl hypochlorite was added to a methanolic solution of the sulfide at -70°. Anhydrous sodium carbonate was added to the mixture when the temperature had reached -40°. The reaction mixture was allowed to continue to warm to room temperature and was filtered, the solvent was removed, and the product was analyzed. Intermediate alkoxy-sulfonium salts are formed in this reaction. Under the reaction conditions these salts are subsequently solvolyzed to provide sulfoxide. Employing these conditions, the sulfoxides obtained from 4-*p*-chlorophenyl, 4-*t*-butyl-, and 4-methylthianes were found to be almost entirely *cis* (98, 100, and 89%, respectively).

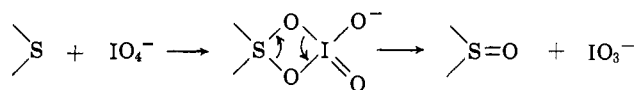
With all of the 4-substituted thianes now studied, sodium metaperiodate<sup>20</sup> has been found to provide a marked predominance of a more stable *cis* sulfoxide. Under the reaction conditions—aqueous solution, 0°—neither periodate nor iodate isomerized sulfoxides.

(18) For example, see H. Kwart and T. Takeshita, *ibid.*, 84, 2833 (1962).

(19) P. S. Skell and M. F. Epstein, Abstracts, 147th National Meeting of the American Chemical Society, New York, N. Y., April 1963, p. 26N.

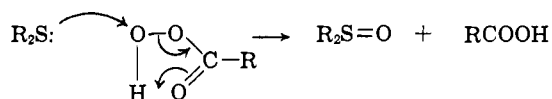
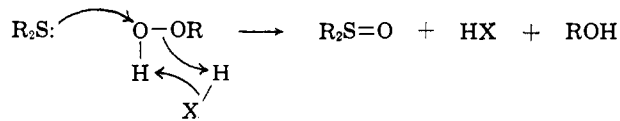
(20) N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, 27, 282 (1962);

It thus appears that in periodate oxidation of sulfides to sulfoxides the geometrical distribution in the product is strongly affected by product development control. In analogy to the oxidation of glycols by periodate a cyclic mechanism<sup>21</sup> can be suggested. Here, in contrast to glycol oxidation, if such an intermediate is involved the oxidation step occurs during formation of the intermediate rather than during its breakdown to products.<sup>21</sup>



As has been noted above, in the oxidation of sulfides to sulfoxides employing dinitrogen tetroxide, thermodynamic product control obtains. Undoubtedly a similar situation occurs with the fuming nitric acid-acetic anhydride oxidations since dinitrogen tetroxide is present in the reaction mixture. However, in this latter case subjection of isolated sulfoxides to reaction conditions results in extensive oxidation to the sulfone stage.

It will be noted that most peroxy agents provide a predominance of the *trans* product. The mechanism generally accepted for such oxidations involves the nucleophilic attack by sulfur on an electrophilic oxygen atom.<sup>2</sup> Several examples are given below. The stereoselectivity of the oxidation with ozone is somewhat surprising even though these reactions are carried out at very low temperatures.<sup>22</sup> It appears, as might be expected from consideration of the mechanisms involved, that steric approach control prevails in the oxidations with these peroxy reagents.



### Experimental<sup>23</sup>

**1-Benzoyl-4-*t*-butylpiperidine.** One mole (125 g.) of 4-*t*-butylpyridine dissolved in 150 ml. of 6 *N* hydrochloric acid was hydrogenated at 4 atm. and 55° employing 3 g. of platinum oxide catalyst. On completion of the hydrogenation, the mixture was filtered and the filtrate was placed in a 2-l., three-necked flask equipped with an electric stirrer and addition funnel. The solution was cooled to 0° with an ice bath, and 170 g. of sodium hydroxide dissolved in 300 ml. of water was added with stirring. After stirring for 30 min., benzoyl chloride (141 g., 1 mole) was added during 1 hr. The mixture was stirred overnight. The white solid was filtered, washed with water, and air dried.

(21) G. J. Binst, C. A. Bunton, and J. H. Miles, *J. Chem. Soc.*, 743 (1959); F. R. Duke, *J. Am. Chem. Soc.*, 69, 3054 (1947); C. C. Price and M. Knell, *ibid.*, 64, 552 (1942).

(22) When stoichiometric quantities of ozone were employed, considerable over-oxidation was experienced. This is in accord with the observations of D. Barnard, *J. Chem. Soc.*, 4547 (1957), and Q. E. Thompson, *J. Am. Chem. Soc.*, 83, 845 (1961); see also E. J. Corey and W. C. Taylor, *ibid.*, 86, 3881 (1964).

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

Purification was accomplished by sublimation at 150° (0.4 mm.) to give 220 g. (90% over-all) of 1-benzoyl-4-*t*-butylpiperidine, m.p. 51–53°,  $\lambda_{\text{max}}^{\text{CHCl}_3}$  1640  $\text{cm}^{-1}$  (C=O).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{23}\text{NO}$ : C, 78.36; H, 9.55. Found: C, 78.63; H, 9.52.

**1,5-Dibromo-3-*t*-butylpentane.**<sup>24</sup> To 1-benzoyl-4-*t*-butylpiperidine (62 g., 0.253 mole) in a 500-ml. distilling flask was added phosphorus tribromide (69 g., 0.255 mole) dropwise over a 45-min. period at room temperature. After stirring at room temperature for 2 hr. the light yellow solution was cooled with an ice bath, and dropwise addition of bromine (63 g., 0.287 mole) was completed over a 45-min. period. The resulting reddish solid was distilled at 20 mm. The distillate was poured onto ice and stirred for 1 hr. The heavy oil was removed and refluxed with 100 ml. of 48% hydrobromic acid for 3 hr., and the mixture was steam distilled. The distillate was extracted three times with 100-ml. portions of petroleum ether; the extracts were combined, washed with saturated sodium hydrogen carbonate, and dried over calcium chloride. Distillation under reduced pressure gave 30 g. (40%) of 1,5-dibromo-3-*t*-butylpentane, b.p. 87–88° (0.7 mm.),  $n_{\text{D}}^{25}$  1.5085.

*Anal.* Calcd. for  $\text{C}_9\text{H}_{18}\text{Br}_2$ : C, 37.76; H, 6.28. Found: C, 38.02; H, 6.20.

**1,5-Dichloro-3-*t*-butylpentane.** A mixture of phosphorus pentachloride (104 g., 0.5 mole) and 1-benzoyl-4-*t*-butylpiperidine was heated at 100° for 2 hr. and distilled at 20 mm. The distillate was worked up in the manner described above. The dichloride was thus obtained in 6% (12 g.) yield, b.p. 83–85° (2.8 mm.),  $n_{\text{D}}^{20}$  1.4698.

*Anal.* Calcd. for  $\text{C}_9\text{H}_{18}\text{Cl}_2$ : C, 54.83; H, 9.14. Found: C, 54.99; H, 9.12.

**1,5-Dibromo-3-methylpentane.** To a stirred solution of 4-methyltetrahydropyran (100 g., 1 mole) in 300 g. of 48% hydrobromic acid was cautiously added 98 g. of concentrated sulfuric acid. The mixture was refluxed for 2 hr. The reaction mixture was cooled, the organic layer was removed, and the aqueous layer was extracted three times with 100-ml. portions of methylene chloride. The combined organic layers were dried, the methylene chloride was distilled, and the residue was fractionated to give 110 g. (46%) of the dibromide, b.p. 59–61° at 0.3 mm. (lit.<sup>25</sup> b.p. 116–117° at 20 mm.,  $n_{\text{D}}^{20}$  1.5084).

**4-*t*-Butylthiane (II).** To a refluxing solution of sodium sulfide nonahydrate (11 g., 0.045 mole) in 150 ml. of 50% aqueous ethanol was added dropwise 0.06 mole of the dihalide and an additional 150 ml. of the sodium sulfide (11 g.) solution at such a rate that the addition of both was completed in 1 hr. After refluxing for 8 hr. the mixture was steam distilled. The distillate was diluted with an equal amount of water and extracted with three 100-ml. portions of methylene chloride. The combined organic extracts were dried over anhydrous magnesium sulfate, the methylene chloride was removed by evaporation, and the residue was distilled, b.p. 47–48° (1 mm.),  $n_{\text{D}}^{27}$  1.4913.

(24) Adapted from a method of J. von Braun, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 428.

(25) E. V. Whitehead, R. A. Dear, and F. A. Fidler, *J. Am. Chem. Soc.*, 73, 3632 (1951).

Cyclization using dibromide provided the 4-*t*-butylthiane in 74% yield whereas the dichloride afforded an 89% yield of thiane.

*Anal.* Calcd. for  $C_9H_{18}S$ : C, 68.36; H, 11.39. Found: C, 68.63; H, 11.26.

The 4-*t*-butylthiane-mercuric chloride complex had m.p. 178–180°.

*Anal.* Calcd. for  $C_9H_{18}Cl_2HgS$ : C, 25.11; H, 4.19. Found: C, 25.30; H, 4.40.

**4-Methylthiane (III).** This compound was prepared from 1,5-dibromo-3-methylpentane in 76% yield, b.p. 53° at 20 mm. (lit.<sup>25</sup> 54° at 22 mm.).

**General Methods of Oxidation. A. Sodium Meta-periodate.**<sup>20</sup> The sulfide (1 mmole) was added to sodium metaperiodate (0.225 g., 1.05 mmoles) in 25 ml. of water, cooled with an ice bath. The mixture was stirred at 0° for 12 hr. and filtered. The filtrate was extracted three times with 10-ml. portions of methylene chloride. The combined extracts were dried over anhydrous magnesium sulfate prior to analysis for sulfoxides.

**B. Dinitrogen Tetroxide.**<sup>10</sup> Excess liquified dinitrogen tetroxide was added to the sulfide (1 mmole) maintained at 0° with an ice bath. After stirring for 30 min. at 0°, the ice bath was removed and the excess dinitrogen tetroxide was allowed to evaporate.

**C. *m*-Chloroperbenzoic Acid.**<sup>26</sup> *m*-Chloroperbenzoic acid (0.9 mmole) in 15 ml. of methylene chloride was added dropwise, with stirring, to a solution of the sulfide (1 mmole) in 10 ml. of methylene chloride at 0°. The solution was stirred at this temperature for 12 hr. followed by filtration. The filtrate was washed three times with 25-ml. portions of saturated sodium hydrogen carbonate, and dried over anhydrous magnesium sulfate.

**D. Ozone.**<sup>22</sup> Ozone (0.5 equiv.) was passed into a solution of the sulfide (1 mmole) in 20 ml. of carbon tetrachloride or methylene chloride at -40°. The solution was then allowed to stand at room temperature for 2 hr.

**E. Hydrogen Peroxide in Acetic Acid.** A solution of 30% hydrogen peroxide (0.75 equiv.) in 2 ml. of acetic acid was added to a solution of the sulfide (1 mmole) in 1 ml. of acetic acid at room temperature. The solution was stirred for 12 hr., neutralized with aqueous sodium hydrogen carbonate, and filtered. The filtrate was extracted three times with 10-ml. portions of methylene chloride. The combined extracts were dried over anhydrous magnesium sulfate.

**F. Hydrogen Peroxide in Acetone.** A similar procedure as that described above employing acetic acid was used. The neutralization step was unnecessary.

**G. Iodosobenzene in Benzene.**<sup>27</sup> The sulfide and iodosobenzene (1 mmole each) in 5 ml. of dry benzene were refluxed on the steam bath for 12 hr. The mixture was filtered and the filtrate was concentrated and analyzed for sulfoxide.

**H. *t*-Butyl Hydroperoxide.**<sup>28</sup> A soft glass tube containing the sulfide (1 mmole) and *t*-butyl hydroperoxide (1 mmole) in 0.5 ml. of dry benzene or methanol was

flushed with nitrogen, sealed, and heated at 50° for 100 hr.

**I. *t*-Butyl Hypochlorite.**<sup>19</sup> To a solution of the sulfide (1 mmole) in 10 ml. of methanol cooled to -70° with an acetone-Dry Ice bath was added 1 equiv. of *t*-butyl hypochlorite. When the temperature of the bath reached -40° anhydrous sodium carbonate was added. The mixture was allowed to come to room temperature and the methanol was removed under reduced pressure. The residue was washed three times with 20-ml. portions of methylene chloride and the washings were combined.

**J. Nitric Acid.**<sup>29</sup> A solution of 0.2 g. (3.1 mmoles) of fuming nitric acid (*d* 1.5) in 1 ml. of acetic anhydride was added dropwise to a stirred solution of the sulfide (1 mmole) in 2 ml. of acetic anhydride, cooled with an ice-salt bath. The resulting green solution was allowed to stand at 0° for 24 hr., poured into ice-water, and neutralized with sodium carbonate, and the mixture was extracted with methylene chloride. The extract was dried over sodium sulfate, the solvent was evaporated, and the resultant sulfoxide mixture was analyzed by gas chromatography.

**K. Chromic Acid.**<sup>30</sup> To a solution of the sulfide (1 mmole) in 2 ml. of pyridine, chromic acid (0.20 g., 2 mmoles) was slowly added. The mixture was allowed to stir for 1 hr. and poured into water and the sulfoxides were extracted with methylene chloride.

**Equilibration Studies. A. Dinitrogen Tetroxide.** Excess liquid dinitrogen tetroxide was added to the sulfoxide (*cis*, *trans*, or a mixture thereof) at 0°. The mixture was stirred for 30 min. at 0° and the ice bath was removed; the dinitrogen tetroxide was allowed to evaporate and the products were analyzed by gas phase chromatography.

**B. Hydrochloric Acid-Dioxane.**<sup>9</sup> The sulfoxide (*cis*, *trans*, or a mixture thereof) was added to a 1:2 (v./v.) mixture of concentrated hydrochloric acid and dioxane and was stirred at room temperature for 20 min. The solution was diluted with 10 ml. of water and extracted with three 10-ml. portions of methylene chloride. The combined extracts were dried over anhydrous magnesium sulfate.

**C. Thermal.**<sup>8</sup> A 1% solution of the sulfoxides in freshly distilled decalin was heated at 190° under a nitrogen atmosphere in a quartz flask for 1 hr. Continued heating did not effect the isomer distribution.

**Vapor Phase Analysis.** Percentage compositions were ascertained by planimetric integration of curves obtained from an F and M Model 720 chromatograph equipped with silicon gum nitrile (GE XE-60) columns. These columns were capable of excellent resolution of sulfide, sulfoxides, 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. Product composition data reported in Table II were obtained from reactions in which no over-oxidation to sulfone occurred. In several of the oxidations excess sulfide was employed.

(26) Available from FMC Corporation, Inorganic Chemicals Division, New York, N. Y.

(27) A. H. Ford-Moore, *J. Chem. Soc.*, 2126 (1949).

(28) D. Barnard, *ibid.*, 489 (1956).

(29) F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, 79, 717 (1957); A. Pollard and R. Robinson, *J. Chem. Soc.*, 3090 (1926).

(30) D. Edwards and J. B. Stenlake, *ibid.*, 3272 (1954).

**Table III.** Dipole Moment Data for 4-*p*-Chlorophenylthiane 1-Oxides

	$\alpha$	$\beta$	$\epsilon_1$	$P_{2\infty}$	$d_1$	$M_D$	$\mu$
<i>cis</i>	22.497	0.806	2.2722	384.3	0.87304	60.014	3.98 ± 0.02
<i>trans</i>	9.813	0.790	2.2727	198.2	0.87320	60.014	2.60 ± 0.02

**Isolation of Pure Isomers.** The separation and isolation of pure *cis*- and *trans*-4-*p*-chlorophenylthiane 1-oxide has been reported.<sup>4</sup> Separation of the isomeric sulfoxides from 4-methyl- and 4-*t*-butylthiane has been accomplished on a small scale by preparative gas chromatography and by generation of sulfoxide from purified O-ethyl fluoroborate salts.<sup>31</sup> Pure *cis*- and *trans*-4-*t*-butylthiane 1-oxides have also been obtained by the method of Henbest and Khan<sup>8</sup> which entails the regeneration of sulfoxides from their purified mercuric chloride adducts employing aqueous potassium cyanide (see below). Separation of the 4-methylthiane 1-oxides could also be effected by this method.<sup>31</sup>

***trans*-4-*t*-Butylthiane 1-Oxide–Mercuric Chloride Complex.** A hot solution of mercuric chloride (0.33 g., 1.22 mmoles) in 3 ml. of 60% aqueous ethanol was added to a solution of pure *trans*-4-*t*-butylthiane 1-oxide (0.082 g., 0.5 mmole) in 1 ml. of ethanol. The mixture was cooled in an ice bath and the precipitate was collected. The adduct, 0.32 g. (90%) was recrystallized from ethanol, m.p. 123–123.5°.

*Anal.* Calcd. for C<sub>9</sub>H<sub>18</sub>Cl<sub>4</sub>Hg<sub>2</sub>OS: C, 15.04; H, 2.51. Found: C, 15.20; H, 2.75.

***cis*-4-*t*-Butylthiane 1-Oxide–Mercuric Chloride Complex.** The complex, prepared in a manner identical with that described above, had m.p. 147–148°.

*Anal.* Calcd. for C<sub>9</sub>H<sub>18</sub>Cl<sub>4</sub>Hg<sub>2</sub>OS: C, 15.04; H, 2.51. Found: C, 15.25; H, 2.66.

**Separation of *cis*- and *trans*-4-*t*-Butylthiane 1-Oxide–Mercuric Chloride Complexes.** Cooling an aqueous alcoholic solution of the isomeric sulfoxides and excess mercuric chloride provided the *trans* adduct, m.p. 122–123°, after recrystallization from ethanol. Concentration of the filtrate followed by cooling afforded the *cis* adduct, m.p. 147–148° after recrystallization from ethanol.

***trans*-4-*t*-Butylthiane 1-Oxide (Vb).** The less soluble *trans* mercuric chloride adduct (2 g.) was treated for 2 hr. with a refluxing 1% potassium cyanide solution in 50% aqueous ethanol. The solution was concentrated at reduced pressure. The resultant solution

(31) C. R. Johnson and D. McCants, Jr., paper in preparation.

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 at 40° (0.1 mm.) gave 0.4 g. (87%) of *trans* sulfoxide,<sup>32</sup> m.p. 57–59° (lit.<sup>8,33</sup> 68–70°).

***cis*-4-*t*-Butylthiane 1-Oxide (Va).** Treatment of the *cis*-4-*t*-butylthiane 1-oxide–mercuric chloride adduct in the manner described above for the *trans* gave the *cis* sulfoxide,<sup>32</sup> m.p. 70–71° (lit.<sup>8,33</sup> 49–50°) after sublimation at 40° (0.1 mm.).

*Anal.* Calcd. for C<sub>9</sub>H<sub>18</sub>OS: C, 62.07; H, 10.34. Found: C, 62.57; H, 10.55.

**4-*t*-Butylthiane 1,1-Dioxide.** Oxidation of the sulfide or *cis* or *trans* sulfoxide with excess *m*-chloroperbenzoic acid gave an excellent yield of sulfone, m.p. 122.5–123°.

*Anal.* Calcd. for C<sub>9</sub>H<sub>18</sub>O<sub>2</sub>S: C, 56.83; H, 9.55. Found: C, 56.63; H, 9.38.

**Dipole Moment Determinations.** The Dipolemeter DM01 manufactured by Wissenschaftlich–Technische Werkstätten was used for the measurements. The dipole moments were measured in benzene solution at 25 ± 0.01°.<sup>34</sup> The moments were calculated by essentially the method of Halverstadt and Kumler<sup>35</sup> utilizing an IBM 7070 computer programmed as described by Allinger.<sup>36</sup> The data are summarized in Table III. The dipole moments calculated<sup>37</sup> for the 4-*p*-chlorophenylthiane 1-oxides from models and model compounds<sup>38</sup> are 4.30 D. for the *cis* and 2.24 D. for the *trans*.

(32) Note that no stereochemical change results from the sequence, sulfoxide → mercuric chloride complex → sulfoxide.

(33) Our assignment of *cis* and *trans* isomers is the reverse of that suggested by Henbest and Kahn.<sup>8</sup>

(34) The dielectric and density measurements were made by Mr. C. L. Neumann.

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

(36) N. L. Allinger and J. Allinger, *J. Org. Chem.*, **24**, 1613 (1959).

(37) For a discussion of calculations of dipole moments of sulfoxides see N. J. Leonard and C. R. Johnson, *J. Am. Chem. Soc.*, **84**, 3701 (1962).

(38) Thiane 1-oxide, 4.19 D. (A. I. Vogel and C. W. N. Cumper, *J. Chem. Soc.*, 3521 (1959)) and *p*-chlorotoluene, 1.95 D. (N. L. Allinger, S. P. Jindal, and M. A. DaRooge, *J. Org. Chem.*, **27**, 4290 (1962)).