

benzenes no satisfactory $pK^*-\sigma$ correlation was found.^{6c}

(8) Procter and Gamble Co. Research Fellow, 1963-1964.

(9) American Cancer Society Research Fellow, 1962-1963.

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RECEIVED MAY 11, 1964

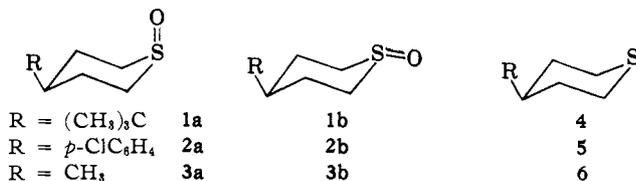
Equilibration of 4-Substituted Thiane 1-Oxides¹

Sir:

There is much current interest in stereochemical aspects of sulfoxides. We have previously reported on a stereoselective method of inversion of configuration of sulfoxides.² Subsequently, Mislow and co-workers³ have described the hydrogen chloride catalyzed racemization of sulfoxides and Henbest and Khan,⁴ the thermal isomerization of sulfoxides.

For 4-*t*-butylthiane 1-oxides (1) thermally-induced equilibrium (190° in decalin) was reported to exist at a *cis:trans* ratio of 20:80, although no arguments were presented for the assigned configurations.⁴ We have also prepared these sulfoxides⁵ and our results indicate that the previous stereochemical assignments are in error. This work further demonstrates that in 4-substituted thiane 1-oxides the isomer bearing the axial oxygen is more stable.

The geometries of the 4-*t*-butylthiane 1-oxides were ascertained by physical and chemical analogies with the corresponding 4-*p*-chlorophenylthiane 1-oxides (2) of known configuration.^{2a} Periodate oxidation of sulfide 5 provides a 70:30 mixture of 2a:2b, whereas peroxide oxidants yield approximately 30:70 mixtures.^{2a} By analogy, the *cis* configuration (1a) is assigned to the predominant product (75%) obtained by periodate oxidation of 4 and *trans* (1b) to the isomer predominating in peroxide oxidations.⁶ In each case, the compound of *cis* assignment is found to predominate under equilibrating conditions (see below). This chemical evidence is corroborated by a correspondence in physical behavior of compounds of like assignment. In each case the compound assigned the *cis* structure had the



higher melting point (1a, m.p. 70-71°, lit.⁴ 49-50°; 1b, m.p. 57-59°, lit.⁴ 68-70°; 2a, m.p. 172.5-173°; 2b, m.p. 120-120.5°); the *cis* compounds are eluted prior to the *trans* isomers in both column and gas

(1) We gratefully acknowledge support by the National Science Foundation (Grant No. GP-1159).

(2) (a) C. R. Johnson, *J. Am. Chem. Soc.*, **85**, 1020 (1963); (b) C. R. Johnson and J. B. Sapp, Abstracts, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963, p. 23Q.

(3) K. Mislow, T. Simmons, J. T. Mellillo, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **86**, 1452 (1964). We are grateful to Professor Mislow for providing us with details of this method prior to publication.

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

(5) Satisfactory analyses have been obtained on compounds herein reported.

(6) A detailed study of the stereochemistry of oxidation at sulfur will be published: C. R. Johnson and D. McCants, Jr. in preparation.

chromatography⁷; there is a striking similarity in the sulfoxide stretching region (1000 to 1100 cm.⁻¹) of the infrared spectra for the compounds of like assignment.

Thermal equilibrations were run in purified decalin at 190° employing a quartz flask and nitrogen atmosphere. Mixtures of the 4-*t*-butylthiane 1-oxides (*cis:trans*, 75:25 and 25:75) rapidly provided an equilibrium composition of 80% *cis* and 20% *trans*. With pure samples of 1a and 1b, approach to equilibrium is very slow and significant side reactions could not be avoided. Thermal equilibration of 2 was also found to be impractical because of partial decomposition.

Treatment of pure 1a, 1b, or mixtures thereof with hydrochloric acid-dioxane^{3,8} for 20 min. is sufficient to provide a *cis:trans* equilibrium mixture of 90:10. Similar equilibrium compositions were obtained for compounds 2 and 3 (Table I).

TABLE I
EQUILIBRATION OF 4-SUBSTITUTED THIANE 1-OXIDES

Com- pounds	Method (°C.)	Equilibrium composition		ΔF , kcal./mole
		<i>cis</i>	<i>trans</i>	
1	HCl (25)	90	10	1.3
2	HCl (25)	80	20	0.8
3	HCl (25)	80	20	0.8
1	Decalin (190)	80	20	1.3
3	Decalin (190)	65	35	0.6
1	N ₂ O ₄ (0)	81	19	0.8
3	N ₂ O ₄ (0)	76	24	0.6

We have found that dinitrogen tetroxide, a useful reagent for the conversion of sulfides to sulfoxides,⁹ is also capable of isomerization of sulfoxides. Treatment of sulfide 4 and sulfoxide 1a or 1b yields a mixture composed of 81% 1a and 19% 1b. Optically active (+)-benzyl *p*-tolyl sulfoxide is rapidly racemized by this reagent.

As can be seen from the data in Table I, there is considerable variation in the equilibrium composition dependent upon conditions and the identity of the 4-substituent; however, there is always a marked preference for the isomer with the axial oxygen. The best value for the conformation free-energy difference for the sulfoxide within the six-membered ring is probably that (1.3 kcal./mole) obtained with the very bulky and nonpolar 4-*t*-butyl group from both thermal and hydrogen chloride catalyzed equilibrations. In the dinitrogen tetroxide reaction, free sulfoxides are probably not involved in the equilibration observed.⁹

The question remains open as to why an axial oxide on sulfur in thianes is energetically favored over the equatorial configuration. One explanation is that this preference simply reflects the relative steric requirements of oxygen vs. the free electron pair. If this were true, it would be unlikely that the electron pair of sulfoxides is located in a 3s orbital as has been proposed.¹⁰ On the other hand, the lone pair could reasonably be

(7) Gas chromatography employing a 6-ft. silicone gum nitrile (GE XE-60) column provided excellent resolution of the sulfide, the two sulfoxides, and the sulfone.

(8) Use of anhydrous hydrogen chloride in benzene (ref. 3) was found to result in a mixture of sulfide, α -chlorosulfide, and sulfoxides.

(9) C. C. Addison and J. C. Sheldon, *J. Chem. Soc.*, 2705 (1956); L. Horner and F. Hubenett, *Ann.*, **579**, 193 (1953).

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

expected to occupy a $3sp^3$ orbital of sulfur.¹¹ 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 the van der Waal's contact radii of hydrogen and oxygen. It is possible that attractive terms outweigh repulsions and create a favorable interaction between the oxygen and the ring. The evidence presented in this report does not allow a conclusion to be made. It is noteworthy that trimethylene sulfite is reported to exist almost exclusively with the oxide in the axial position,¹² that *trans*-1,4-dithiane 1,4-dioxide prefers the form with two axial S=O bonds,¹³ and that both *cis*- and *trans*-4-chlorothiane 1-oxide appear to prefer the conformer bearing an axial oxide.¹⁴

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

(12) D. G. Hellier, J. G. Tillett, H. F. Van Woerden, and R. F. M. White, *Chem. Ind. (London)*, 1956 (1963).

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

(14) J. C. Martin and J. J. Uebel, *J. Am. Chem. Soc.*, 86, 2936 (1964). Our thanks are due to Prof. Martin for a discussion of these results prior to publication.

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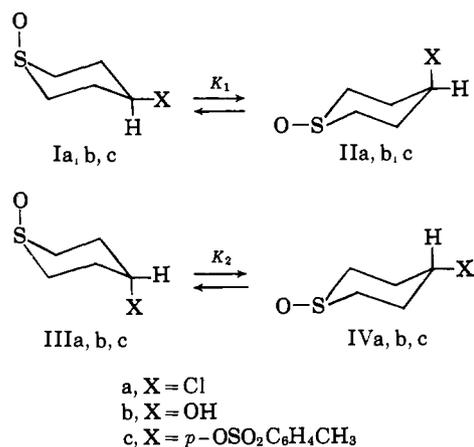
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RECEIVED MAY 25, 1964

Conformational Equilibria and Solvolyses of Six-Membered Ring Sulfoxide Derivatives

Sir:

Structures of the *cis*- and *trans*-4-chlorothiane 1-oxides (Ia and IIIa) have been well established through dipole moment studies and solvolysis rate and product studies. Structures for Ib, Ic, IIb, and IIc may be assigned by analogy.



Spectroscopic evidence (n.m.r., infrared) suggests that these compounds exhibit a surprising conformational preference for forms I and III with sulfoxide oxygen axial. This is to be contrasted with the recent report¹ assigning the *cis* geometry to the less stable (and lower melting) of the isomers of 4-*t*-butylthiane 1-oxide, V. Our data lead to a conclusion parallel to that of Johnson,² who has presented evidence suggesting the opposite assignment for the isomers of V.

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

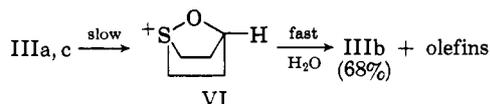
(2) C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, 86, 2935 (1964).

For all of the compounds of our work and those of Johnson the *cis* isomer is higher melting than the *trans* (Ia, m.p. 120–121°, and IIIa, 104–105°; Ic, 136.5–138°, and IIc, 112–113°).

The sulfoxides I and III, prepared by oxidation of the corresponding sulfides with ozone or sodium metaperiodate,³ were separated by column chromatography, the *trans* isomers being eluted first in every case. (In the case of Johnson,² the isomers postulated to have a preponderance of axial sulfoxide oxygen were also eluted first.)

Electric dipole moments for Ia and IIIa were compared with those calculated using thiane, thiane 1-oxide, and cyclohexyl chloride as models. The assumption was made⁴ that the sulfoxide group dipole moment is directed at an angle of 38° out of the C–S–C plane toward the oxygen atom. Dipole moments, measured at 25° in CCl₄, were: for 4-chlorothiane, 1.63 ± 0.13 D. (calcd. 1.8); for Ia–IIa, 4.18 ± 0.22 (calcd. 4.8); and for IIIa–IVa, 2.12 ± 0.15 (calcd. 2.2).

Structural evidence from solvolytic rate studies is based on the large values of the k_{trans}/k_{cis} ratio (about 630 for chlorides Ia and IIIa at 140° in 50% v/v. aqueous ethanol and about 150 for *p*-toluenesulfonates Ic and IIc in 80% v/v. aqueous ethanol at 100°). This is interpreted in terms of oxygen participation in the ionization of the *trans* isomer to give intermediate VI. Attack of water on VI either on S⁵ or on C would be expected to give cleanly the only observed alcohol product, IIb, with over-all retention of configuration. No 4-thianone, from elimination involving the bridgehead proton, could be detected in the reaction mixture.



The proton of the CHX group in these derivatives gives rise to a multiplet in the n.m.r. spectrum which is broader and at lower field for the *cis* than for the *trans* isomer, as would be expected⁶ for a predominantly axial proton. This suggests a conformational preference for the forms (Ia–c or IIIa–c) having sulfoxide oxygen axial over those with sulfoxide oxygen equatorial (IIa–c or IVa–c).

TABLE I
NUCLEAR MAGNETIC RESONANCE DATA FOR THE CHX PROTON
IN 4-SUBSTITUTED THIANE 1-OXIDES

Compound	Chemical shift ^a	Multiplet width (half-height) ^b
Ia	251	14
IIIa	271	9
Ib	227	16
IIIb	242	12
Ic	277	17
IIIc	288	10

^a C.p.s. from tetramethylsilane at 60 Mc. ^b C.p.s.

The absorption intensities at the infrared C–Cl stretching frequencies (748 and 719 cm.⁻¹ for Ia–IIa

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

(4) In a method similar to that described by C. W. N. Cumper and S. Walker, *Trans. Faraday Soc.*, 52, 193 (1956), and C. W. N. Cumper and A. I. Vogel, *J. Chem. Soc.*, 3521 (1959).

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

(6) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Company, Inc., New York, N. Y., 1959, Chapter 14.