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CONFIGURATION ASSIGNMENT IN THIETANE 1-OXIDE SYSTEMS (1,2)

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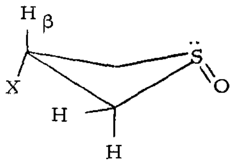
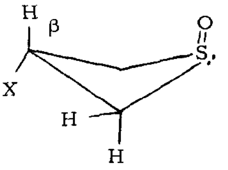
Several recent publications have included reports on the isolation and assignment of stereochemistry to substituted thietane 1-oxides, but the methods for configuration assignment were not applicable to any broad spectrum of substituents. A method of seemingly general utility is reported here, based on the nmr chemical shift values of the ring protons, for the assignment of *cis* or *trans* geometry to 3-substituted thietane 1-oxides.

Allenmark (4) has assigned stereochemistry to *trans*-3-carboxythietane 1-oxide **1**-*t* from a crystallography study and Arbuzov (5) has assigned the *trans* geometry to an isomer of 3-chlorothietane 1-oxide **2**-*t* by a dipole moment study; however, these methods have obvious limitations. Dodson (6) assigned stereochemistry to two of the three isomeric 2,4-diphenylthietane 1-oxides from the nmr spectra but has not yet reported his data. Lautenschlaeger (7) has also employed nmr spectroscopy to assign stereochemistry to sulfoxides **3** and **4** but his assignments are inconsistent with the anisotropic nature of the S=O bond as observed in other ring systems.



cis



trans

1 X= CO_2H
2 X= Cl
5 X= *p*-ClC_6H_4
6 X= $(CH_3)_3C$
7 X= C_6H_5
8 X= $OCOCH_3$
c= cis
t= trans

We recently reported stereochemical assignments for 3-*p*-chlorophenylthietane 1-oxides **5**-*c* and **5**-*t* from a dipole moment study and for 3-*t*-butylthietane 1-oxides **6**-*c* and **6**-*t* from the chemical shift values of the β-proton (8). Examination of the nmr spectra of several pair of *cis* and *trans* 3-substituted thietane 1-oxides shows not only consistent differences in the chemical shift of the β-H (Table I) but also very characteristic absorption patterns for the α-methylene protons of the *cis* or *trans* isomers (Figure I). This now makes possible (a) the assignment of *cis* or *trans* geometry in many cases when only one isomer is available, and (b) a method for checking the isotopic purity of a sample. (In the case where the nmr spectrum is of least utility (X= *t*-butyl) the purity is readily ascertained by gas phase chromatography (8).)

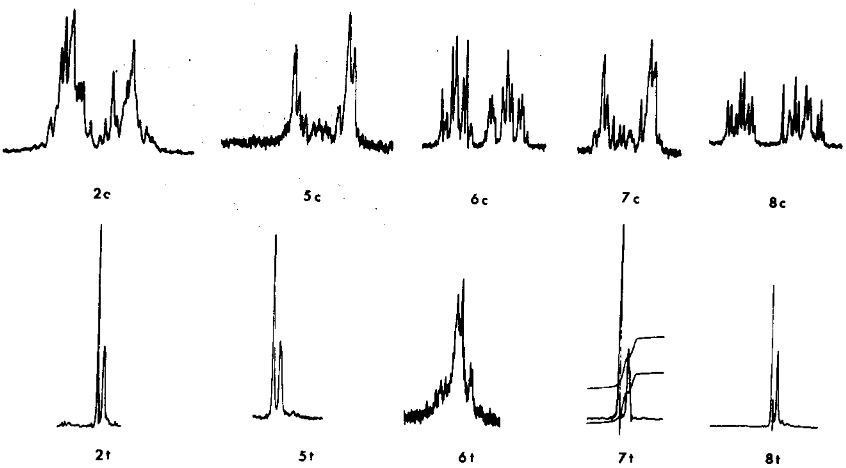


Figure I

α-Methylene proton absorption signals. Recorded in CCl_4 or $CDCl_3$ at 60 MHz.

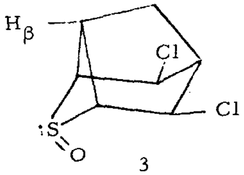
TABLE I

Compound	Solvent	Chemical Shift[a] α-CH_2 Protons	 β-CH Proton	Chemical Shift Difference of β-H Δ [$\delta_{\underline{trans}} - \delta_{\underline{cis}}$][d]
2 (X= Cl) *cis*	$CDCl_3$	195-275(m)	--[b]	---
trans	$CDCl_3$	218+ 224(d)	308-334(m)	
5 (X= *p*-ClC_6H_4) *cis*	$CDCl_3$	182-246(m)	--[b]	
	CCl_4	--	193[c]	
trans	$CDCl_3$	212+ 217(d)	245-271(m)	65
	CCl_4	--	257.5[c]	
6 (X= $(CH_3)_3C$) *cis*	CCl_4	155-85(m); 190-220(m)	100-130(m)	
	CCl_4	--	115[c]	
trans	CCl_4	175-220(m)	--[b]	68
	CCl_4	--	183[c]	
7 (X= C_6H_5) *cis*	CCl_4	187-204(m); 225-240(m)	208-220(m)	
trans	CCl_4	211+ 217(d)	245-278(m)	47
8 (X= $OCOCH_3$) *cis*	CCl_4	179-213(m); 236-257(m)	275-307(m)	
trans	CCl_4	210+ 216(d)	334-356(m)	54

(a) Chemical shift values are reported in Hz downfield from tetramethylsilane, recorded on a Varian A60A spectrometer at room temperature. (b) The β-H is buried under the α-CH_2 multiplet. (c) This value obtained from the α-deuterated sulfoxide (see ref. 8). (d) The center of gravity of a multiplet was employed in determining these values.

The sulfoxides were prepared by oxidation of the corresponding sulfide with sodium metaperiodate or *m*-chloroperbenzoic acid. The sulfides of series 2 (9) and 8 (10) are known and the syntheses for sulfides of 5, 6, and 7 will be reported elsewhere (11). The isomeric sulfoxides were separated by elution chromatography from silica gel (*cis* isomer eluted prior to *trans*). The isomers were characterized from spectral data and elemental analyses and/or mass spectrometry.

The significant deshielding effect of the S=O bond on the *cis* β-hydrogen has been utilized for stereochemical assignment to both 5- and 6-membered ring sulfoxides (12, 13). In this study the β-hydrogen *cis* to the S=O bond (*trans* sulfoxide) appeared downfield 47-68 Hz from the β-hydrogen *cis* to the nonbonded electron pair (*cis* sulfoxide) (Table I).



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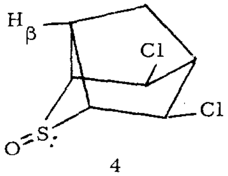

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In hexachlorobutadiene at 100° the chemical shifts assigned to the β-hydrogen in the thietane rings of sulfoxides 3 and 4 were δ 4.26 and δ 2.67 respectively (6), a chemical shift difference of 1.59 ppm (95 Hz). The high value probably reflects the difference in ring puckering between this highly rigid system and the more flexible systems examined in the present investigation. Clearly the original configurational assignments should be reversed.

The nmr signal for the α-methylene protons of thiane 1-oxide (14) and certain oxathiane oxides (13c) is related to the configuration at sulfur. A larger chemical shift difference (axial *vs.* equatorial hydrogen) was observed when the electron pair on sulfur was axial. In the five sulfoxide pairs observed the signal for the α-methylene protons extends over a much larger field for the *cis* isomer (electron pair quasi-axial) than for the *trans* (Figure I). The conformations shown are probably the preferred conformations (8). The similarity of the spectra argues against a significant variation in the conformational equilibrium with a change in the ring substituent. It is difficult to discern the signal of the α-protons for 6-*t* because of overlap with the broad multiplet of the β-hydrogen. Despite this overlap the broad absorption signal for the methylene protons of the *cis* isomer exceeds that of the *trans*. Given this partial exception the pattern for the other *trans* isomers is striking in its similarity.

Keller, Lusebrink, and Sederholm (16) have reported a non-first-order spectrum for 3-chlorothietane and have shown the difficulty associated with a complete analysis of the spectrum. The difference in absorption patterns exhibited by the α-methylene protons of the *cis* and *trans* sulfoxides most likely arises from (a) the difference in dihedral angle between the protons and the anisotropic S=O bond, and (b) the difference in dihedral angle between the vicinal protons (and the angle between protons at C_2 and C_4) which result from a difference in ring puckering for the two isomers (17).

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