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Conformational Analysis of 5-Substituted 1,3-Dioxanes. 5. Bond Eclipsing in *tert*-Butylsulfonyl-Substituted 1,3-Dioxanes and Cyclohexanes. X-ray Diffraction Studies, MMP2 Calculations, and Interpretation[1]

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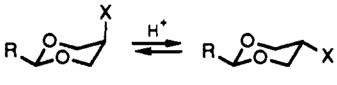
Abstract: Crystal-structure studies of *cis*-4-*tert*-butyl-1-(*tert*-butylsulfonyl)cyclohexane (*cis*-**9**), *cis*-4-*tert*-butyl-1-(methylsulfonyl)cyclohexane (*cis*-**10**), *trans*-4-*tert*-butyl-1-(*tert*-butylsulfonyl)cyclohexane (*trans*-**9**), and *trans*-2-*tert*-butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*trans*-**4**) were performed in order to determine the preferred rotational conformation of these compounds in the solid state. These structures were compared with the most stable conformations predicted by MMP2 calculations. From the results of this study, both steric and stereoelectronic interactions appear to be responsible for the S–O/C–C bond eclipsing found in *cis*-2-*tert*-butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*cis*-**4**) and *cis*-4-*tert*-butyl-1-(*tert*-butylsulfonyl)cyclohexane (*cis*-**9**). During the course of this study, we found that the preferred conformation in 2-(*tert*-butylthio)-1,3-propanediol (**11**) is also an eclipsed one.

Introduction

In the area of conformational analysis, saturated heterocyclic compounds, such as 1,3-dioxanes, are interesting targets for study,[3,4] both because of their advantageous spectroscopic properties[4] and because some of them occur in numerous natural products, such as sugars and alkaloids. Moreover, some of these compounds display unexpected attractions or repulsions, often of electrostatic origin, which have been called "special conformational effects".[5] In this context, relevant information concerning the interaction between polar groups has been deduced from studies of the equilibria in 5-sulfur-substituted 1,3-dioxanes.[6–9]

The results of the chemical equilibration of some 5-sulfur-substituted derivatives and the corresponding $\Delta G°$ values in cyclohexane ("*A* values") are presented in Table I. All $\Delta G°$ values for sulfoxide derivatives in Table I are positive, meaning that the axial isomer is preferred. By contrast, the *A* values (conformational preferences in cyclohexane) for the methylsulfinyl and phenylsulfinyl groups are −1.2 and −1.9 kcal/mol, respectively.[10] Thus, the conformational preferences of polar groups in 1,3-dioxanes cannot simply be explained as the result of steric interactions, but require the consideration of unusual O/S gauche attractive interactions.[6–9,11,12]

Table I. Conformational Equilibria in 5-Sulfur-Substituted 1,3-Dioxanes (Solvent, $CHCl_3$)[a]



R = isopropyl or *tert*-butyl

compd	X	$\Delta G°$ (kcal/mol)	temp (°C)	*A* value[c,d]
1	$S(O)CH_3$	+0.82	26.5	−1.2
2	SO_2CH_3	+1.19	50.0	−2.5
3	$S(O)C(CH_3)_3$	+0.10	23.0	*b*
4	$SO_2C(CH_3)_3$	−1.14	23.0	*b*
5	$S(O)C_6H_5$	+1.59	25.0	−1.9
6	$SO_2C_6H_5$	−0.44	25.0	−2.5
7	$S(O)\text{-c-}C_6H_{11}$	+0.81	25.0	*b*
8	$SO_2\text{-c-}C_6H_{11}$	0.00	25.0	*b*

[a] References 6–9. [b] Not determined. [c] Reference 10. [d] For the origin of this term, see: Winstein, S.; Holness, N. J. *J. Am. Chem. Soc.* **1955**, *77*, 5562.

Substantial differences are observed in the conformational behavior of the corresponding sulfones (Table I). Indeed, while the methylsulfonyl derivative shows a strong preference for axial *cis*-**2** ($\Delta G° = +1.19$ kcal/mol),[6] no conformational bias is exhibited by the cyclohexylsulfonyl analogue **8** ($\Delta G° = 0.0$ kcal/mol).[8] On the other hand, the phenyl- and *tert*-butylsulfonyl derivatives prefer the equatorial orientation by −0.44 and −1.14 kcal/mol, respectively.[7,8]

In this regard, the available evidence[1,6–9] indicates that all axial sulfoxides (*cis*-**1**, *cis*-**3**, *cis*-**5**, and *cis*-**7**) adopt conformation **A** (Figure 1) with the substituents at sulfur oriented outside the dioxane ring. By contrast, the alkyl or aryl group in sulfones *cis*-**2**, *cis*-**6**, and *cis*-**8** are situated above the ring (**B**, Figure 1), presumably for electrostatic reasons. However, the sulfonyl *tert*-butyl

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Table II. X-ray Crystal Data for Compounds *trans*-**4**, **9**, *cis*-**10**, and **11**[a,b]

	trans-**4**	*cis*-**9**	*trans*-**9**	*cis*-**10**	**11**
formula	$C_{12}H_{24}SO_4$	$C_{14}H_{28}SO_2$	$C_{14}H_{28}SO_2$	$C_{11}H_{22}SO_2$	$C_7H_{16}SO_2$
fw	264.38	260.43	260.43	250.35	196.26
crystal system	monoclinic	orthorhombic	monoclinic	orthorhombic	monoclinic
space group	$P2_1/n$	$Pbc2_1$	$P2_1/c$	$Pcab$	$P2_1/n$
crystal size, mm	0.08 × 0.48 × 0.76	0.50 × 0.50 × 0.50	0.40 × 0.20 × 0.20	0.03 × 0.34 × 0.60	0.20 × 0.28 × 0.06
diffractometer	R3m	CAD4	CAD4	R3m	R3m
radiation	Cu Kα	Mo Kα	Mo Kα	Cu Kα	Cu Kα
wavelength, Å	1.5418	0.701 73	0.710 73	1.5418	1.5418
a, Å	5.780 (1)	6.240 (5)	13.216 (4)	6.036 (1)	6.284 (1)
b, Å	24.389 (6)	10.286 (6)	10.833 (2)	10.683 (3)	11.809 (4)
c, Å	10.244 (3)	23.717 (11)	11.809 (4)	37.495 (5)	6.799 (2)
β, deg	98.55 (2)		113.05 (3)		91.89 (2)
V, Å^3	1428.1 (6)	1522.6 (16)	1555.7 (8)	2417.8 (8)	974.4 (3)
Z	4	4	4	8	4
$2\theta_{max}$, deg	110	50	45	110	110
d_{calcd}, Mg m^{-3}	1.23	1.136	1.112	1.07	1.15
μ, mm^{-1}	2.00	0.20	0.19	2.14	2.58
no. of reflections measured	2063	5109	2158	1678	1368
no. of unique reflections	1790	2645	2037	1383	1191
no. of observed reflections	1702	2058	1055	1123	1078
{criterion}	$\|F\| > 3\sigma(F_o)$	$I > 2.5\sigma(I)$	$I > 2.5\sigma(I)$	$\|F\| > 3\sigma(F_o)$	$\|F\| > 3\sigma(F_o)$
R_1 (incl. unobsd) ($\sum\|\|F_o\| - \|F_c\|\|/\sum\|F_o\|$)	0.069 (0.072)	0.051 (0.065)	0.057 (0.115)	0.055 (0.066)	0.040 (0.044)
R_w (inc. unobsd) ($[\sum o(\|F_o\| - \|F_c\|)^2/\sum w\|F_o\|^2]^{1/2}$)	0.079 (0.083)	0.057 (0.059)	0.062 (0.072)	0.063 (0.072)	0.044 (0.048)
GOF ($[\sum 2(\|F_o\| - \|F_c\|)^2$/(no. reflns − no. params]$^{1/2}$)	1.30	1.74	1.84	1.18	1.20
max shift for final cycle of least-squares	0.44	0.24	0.004	0.085	0.004
max peak in final difference synthesis e/Å^3	0.57	0.41	0.21	0.30	0.31

[a] Standard deviations are in parentheses. [b] The X-ray crystallographic data for compounds *cis*-**3**, *cis*-**4**, and *cis*-**12** have been described previously.[1,7]

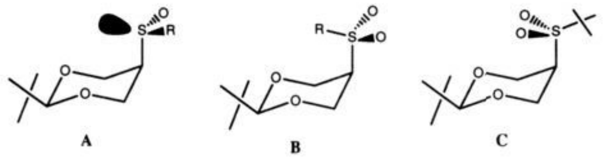


Figure 1. Conformations of *cis*-5-(alkylsulfinyl)- and *cis*-5-(alkylsulfonyl)-2-*tert*-butyl-1,3-dioxanes.

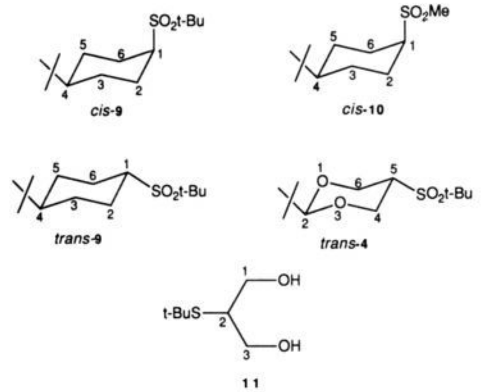


Figure 2. Compounds whose X-ray crystallographic structure was determined in this work.

group is outside the ring in *cis*-**4** (**C**, Figure 1), suggesting that the steric congestion in the corresponding conformation **B** is more severe than the electrostatic repulsion between the (negative) oxygens in **C**. Moreover, X-ray crystallographic data for *cis*-**4** indicate that—at least in the solid state—the *tert*-butylsulfonyl group is nearly eclipsed with the substituents at C(5), thus giving rise to two S–O/C–C and one S–C/C–H eclipsed bond pairs.[7]

In the present work, additional crystallographic data for related compounds are presented and the results examined in the light of molecular mechanics calculations. Our aim was to attempt to pinpoint the effect(s) responsible for the unusual stability of the eclipsed conformation in *cis*-**4**.

Results and Discussion

The compounds studied herein are depicted in Figure 2. Data from the X-ray analyses of these compounds are summarized in Table II.

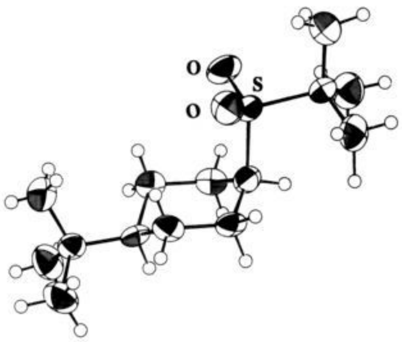
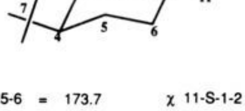


Figure 3. ORTEP perspective of *cis*-4-*tert*-butyl-1-(*tert*-butylsulfonyl)cyclohexane (*cis*-**9**).



χ 7-4-5-6 = 173.7
χ 4-5-6-1 = 53.2
χ 5-6-1-2 = -46.2
χ 6-1-2-3 = 47.3
χ 3-4-5-6 = -58.0
χ 12-S-1-6 = -7.8
χ 11-S-1-2 = -11.0
χ 8-S-1-H = -14.2
χ S-1-6-5 = 80.2
χ S-1-2-3 = -79.4
χ H-1-6-5 = -164.3
χ H-1-2-3 = 170.7

Figure 4. Selected torsion angles (χ, deg) in *cis*-4-*tert*-butyl-1-(*tert*-butylsulfonyl)cyclohexane (*cis*-**9**).

A. Conformation of *cis*-4-*tert*-Butyl-1-(*tert*-butylsulfonyl)cyclohexane (*cis*-9).

The cyclohexane ring has a chair conformation with the *tert*-butylsulfonyl group oriented axially. An ORTEP structure and selected torsion angles are presented in Figures 3 and 4, respectively.

Interestingly, the sulfonyl group turned out to be nearly eclipsed with the ring (χ O–S–C–C = −11.0° and −7.8°, χ C–S–C–H = −14.2°; Figure 4). The similarity of this result with the dioxane analogue (χ O–S–C–C = 5.9° and 10.6°, χ C–S–C–H = 7.6°)[7] indicates that the ring oxygens are not essential for the observed eclipsing.

In order to determine whether the steric crowding between the *t*-BuS and the gauche endocyclic methylenes, in a staggered

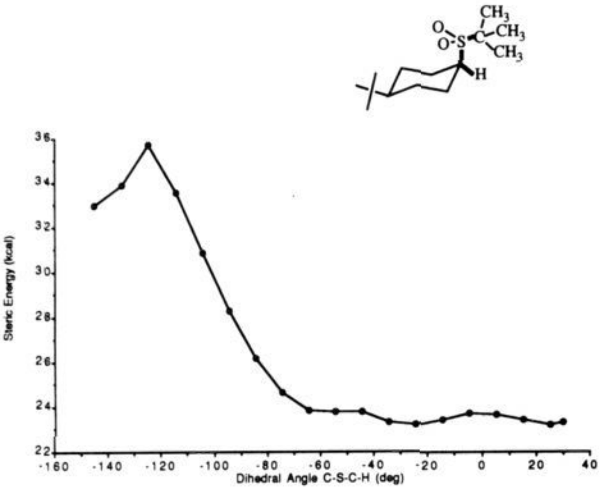
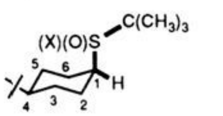
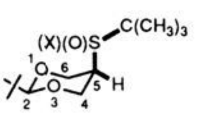


Figure 5. MMP2 conformational potential for *cis*-4-*tert*-butyl-1-(*tert*-butylsulfonyl)cyclohexane (*cis*-**9**).

Table III. Computed Minima (MMP2) and Observed Minima (X-ray Structure) for Cyclohexyl (*cis*-**9**,[a] *cis*-**12**[b]) and 1,3-Dioxanyl (*cis*-**3**,[b] *cis*-**4**[c]) *tert*-Butyl Sulfones and Sulfoxides



cis-**9**, X = O; *cis*-**12**, X = lone pair



cis-**3**, X = lone pair; *cis*-**4**, X = O

compd	ring system	substituent	χ (deg) (X-ray)[d]	χ (deg) (MMP2)[d]	E_{calcd} (kcal/mol)[e]
cis-**9**	cyclohexyl	axial *t*-BuSO$_2$	14.2[f]	25	0.3
cis-**4**	dioxanyl	axial *t*-BuSO$_2$	7.6[g]	30	0.6
cis-**12**	cyclohexyl	axial *t*-BuSO	18.1[h]	20	0.0
cis-**3**	dioxanyl	axial *t*-BuSO	18.8[i]	30	0.1

[a] This work. [b] Reference 1. [c] Reference 7. [d] χ = C–S–C–H torsion angle (deg). [e] Energy calculated as the difference between the minimum calculated by MMP2 and the conformational energy calculated for the experimental (X-ray) structure. [f] χ(mean) O–S–C–C = 9.4°. [g] χ(mean) O–S–C–C = 8.3°. [h] χ O–S–C–C = 27.6°. [i] χ O–S–C–C = 30.4°.

conformation, is serious enough to account for the observed eclipsing, MMP2 force-field calculations[13] were performed for cyclohexanes and 1,3-dioxanes substituted with sulfone and sulfoxide groups. For example, Figure 5 describes the conformational potential of *cis*-**9**. This energy profile (Figure 5) shows a minimum at χ C–S–C–H = 25° with a remarkably shallow potential in the +30° to −40° region, the 0° conformer being only about 0.5 kcal above the minimum.[14] This observation is better evaluated by comparison with the results of MMP2 calculations for various other cyclohexyl and 1,3-dioxanyl *tert*-butyl sulfones and sulfoxides.

Table III summarizes the results of MMP2 calculations for *cis*-**9**, *cis*-**4**, *cis*-4-*tert*-butyl-1-(*tert*-butylsulfinyl)cyclohexane (*cis*-**12**), and *cis*-**3**. For these axial *tert*-butyl sulfones and sulfoxides, the calculation showed potential profiles with shallow minima in the +30° to −30° torsion angle region, with maxima at 120–130°, as shown in Figure 5. The eclipsed conformations were 0.5–1.0 kcal above the minimum.

As can be observed from the data in Table III, the experimental behavior is better reproduced, by MMP2, for sulfoxide than for sulfone substituents, and for cyclohexyl compared to dioxanyl systems.

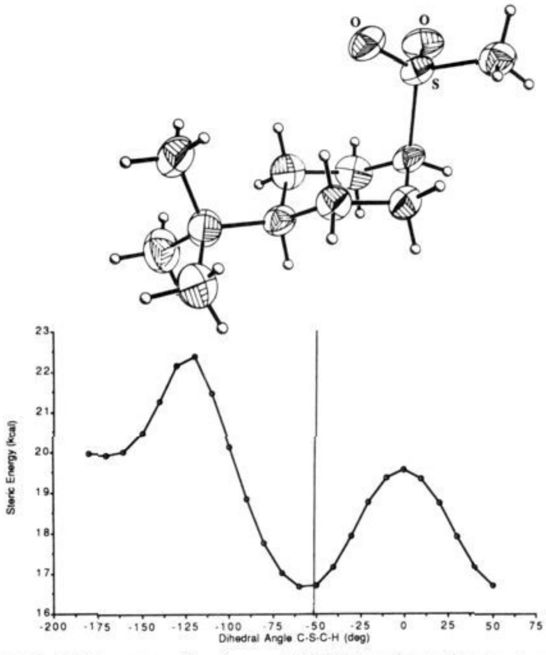


Figure 6. ORTEP perspective view and MMP2 conformational potential for *cis*-4-*tert*-butyl-1-(methylsulfonyl)cyclohexane (*cis*-**10**). The vertical line marks the experimental torsion angle.

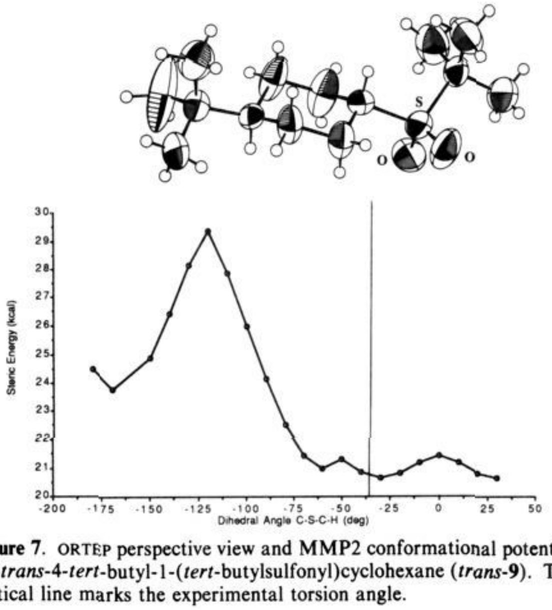


Figure 7. ORTEP perspective view and MMP2 conformational potential for *trans*-4-*tert*-butyl-1-(*tert*-butylsulfonyl)cyclohexane (*trans*-**9**). The vertical line marks the experimental torsion angle.

In the case of the (*tert*-butylsulfonyl)dioxane *cis*-**4**, the fact that force-field calculations predict energy minima at C–S–C–H torsion angles = 20–30° (midway between staggered and eclipsed) indicates that *tert*-butyl crowding is responsible, at least in part, for the eclipsing phenomenon.[15] The difference between the calculated stable rotamer and the experimentally observed one at χ = 8–11° may suggest the involvement of an additional quantum mechanical effect responsible for the stabilization of the observed, nearly eclipsed conformation.

In order to probe this conformational effect, X-ray studies as well as force-field calculations were carried out in a system devoid of steric crowding, the *cis*-4-*tert*-butyl-1-(methylsulfonyl)cyclohexane (*cis*-**10**), and in additional systems presenting *tert*-bu-

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(13) MMP2: Sprague, J. T.; Tai, J. S.; Yuh, Y.; Allinger, N. L. *J. Comput. Chem.* **1987**, *8*, 581. The MM2 program (Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127), available from the Quantum Chemistry Program Exchange, Indiana University, Bloomington, IN 47401, was used to compute the potential energy of diol **11**.

(14) It should be noted that perfect S–O/C–C and S–C/C–H bond eclipsing is not possible because of the differences in pyramidalization at sulfur and carbon, affording bond angles OSO vs $C_2C_1C_6$ of 117.1° vs 112.7°, respectively; see Figure 4. The same situation is present in *cis*-2-*tert*-butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (**C**, Figure 1) with O–S–C and C–C–C bond angles of 119.1° vs 113.3°, respectively.

(15) Cf. Anderson, J. E. *J. Chem. Soc., Perkin Trans. 2* **1991**, 299.

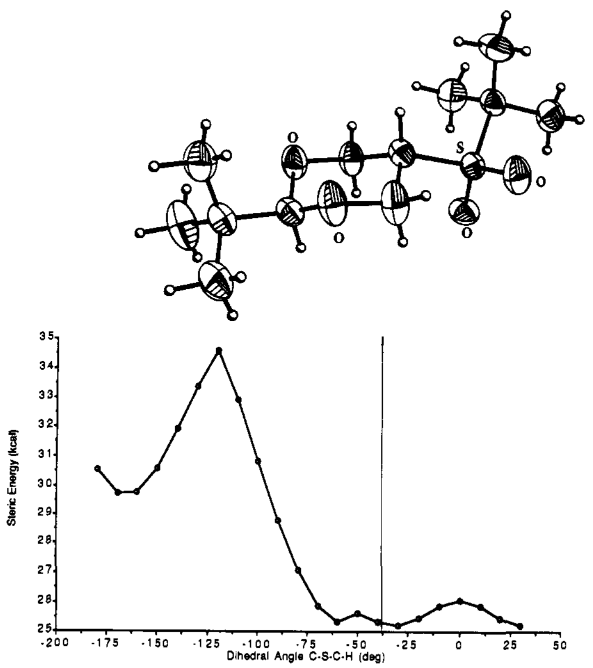
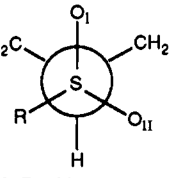


Figure 8. ORTEP perspective view and MMP2 conformational potential for *trans*-2-*tert*-butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*trans*-**4**). The vertical line marks the experimental torsion angle.

Table IV. Torsion Angles χ O–S–C–C and χ C–S–C–H in *cis*-**10**, *trans*-**9**, and *trans*-**4**, as Derived from the X-ray Crystallographic Study[a]



cis-**10**, R = Me
trans-**9** and *trans*-**4**, R = *t*-Bu

compd	χ O_I–S–C–C (deg)	χ O_{II}–S–C–C (deg)	χ C–S–C–H (deg)
cis-**10**	−55.7 (3)	−52.6 (3)	−51.6 (1)
trans-**9**	−33.5 (3)	−36.8 (3)	−36.5 (2)
trans-**4**	−45.1 (2)	−38.8 (2)	−38.6 (1)

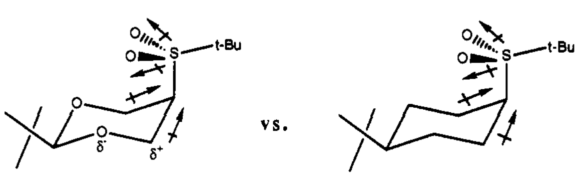
[a] Standard deviations are in parentheses.

tyl/CH_2 gauche interactions but with the *tert*-butylsulfonyl substituent equatorial, as in *trans*-**4** and *trans*-**9**.

B. Conformation of *cis*-4-*tert*-Butyl-1-(methylsulfonyl)cyclohexane (*cis*-10), *trans*-4-*tert*-Butyl-1-(*tert*-butylsulfonyl)cyclohexane (*trans*-9), and *trans*-2-*tert*-Butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*trans*-4). By contrast with axial (*tert*-butylsulfonyl)cyclohexane *cis*-**9**, the X-ray structure of *cis*-**10** indicates an almost perfect alternation of the bonds in the axial methylsulfonyl group and the (chair) cyclohexane C–C bonds. The methyl group and one of the oxygens are both pointing outside the ring; hence, the other oxygen is pointing inside (Figure 6).

On the other hand, X-ray analyses of *trans*-**9** and *trans*-**4** indicate conformations, with the cyclohexane and dioxane rings as chairs and the substituents equatorially oriented, in which the sulfone group is nearly midway between staggered and (S–O/C–C, S–C/C–H, S–O/C–H) eclipsed (Figures 7 and 8). Selected torsion angles for these molecules are summarized in Table IV.

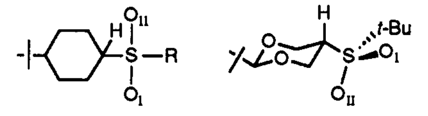
The conformation adopted by *cis*-**10** with one S–O bond pointing inside the ring is in accord with chemical intuition, which suggests that the steric hindrance generated from a methyl-inside rotamer would be greater. The lack of bond eclipsing in this molecule is in line with the force-field calculations, suggesting



cis-**4** *cis*-**9**

Figure 9. Dipole–induced dipole interactions proposed for *cis*-2-*tert*-butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*cis*-**4**) and *cis*-4-*tert*-butyl-1-(*tert*-butylsulfonyl)cyclohexane (*cis*-**9**).

Table V. Selected Bond Lengths and Angles in *cis*-**10**, *trans*-**9**, and *trans*-**4**[a]



cis-**10**, R = Me
trans-**9**, R = *t*-Bu

trans-**4**

	cis-**10**	*trans*-**9**	*trans*-**4**
	Bond Lengths (Å)		
C–C	1.524 (5)	1.499 (9)	1.521 (4)
C–C	1.522 (5)	1.496 (8)	1.522 (4)
C–H	0.960	0.960	0.960
C–S	1.792 (4)	1.802 (5)	1.811 (3)
S–O_I	1.436 (3)	1.432 (5)	1.439 (3)
S–O_{II}	1.437 (3)	1.441 (5)	1.437 (2)
S–C	1.756 (4)	1.826 (5)	1.826 (3)
	Bond Angles (deg)		
C–C–C	112.2 (3)	110.3 (5)	109.8 (2)
C–C–H	108.9 (2)	109.9 (5)	113.8 (2)
C–C–H	105.6 (2)	107.0 (5)	104.9 (1)
O_I–S–O_{II}	117.5 (2)	116.6 (3)	116.7 (1)
O_I–S–C	108.1 (2)	108.5 (3)	107.5 (1)
O_{II}–S–C	107.3 (2)	106.1 (3)	107.8 (1)
C–C–S	111.1 (2)	113.9 (4)	104.9 (2)
C–C–S	114.0 (2)	109.0 (4)	113.8 (2)
H–C–S	105.6 (2)	106.4 (4)	109.9 (1)

[a] Standard deviations are in parentheses.

that the quantum mechanical effect possibly contributing to the eclipsing in *cis*-**4** and *cis*-**9** is weak and becomes evident only when the gauche *t*-Bu/CH_2 crowding produces a flat energy profile, where stabilizing dipole–induced dipole[7,16] or σC–C → σ*S–O stereoelectronic interactions[1] could become dominant. Indeed, MMP2 calculations show a "normal" and rather steep potential profile for *cis*-**10** with minima at ±60° and a maximum at 0° of 2.9 kcal/mol (Figure 6).

Furthermore, the stereoelectronic effect discussed in the previous paragraph does not manifest itself in the equatorial isomers, *trans*-**4** and *trans*-**9**, even though dipole–induced dipole and/or two-electron stabilizing interactions should also be possible in these compounds. Molecular mechanics calculations afford somewhat steeper energy potentials in the +30° to −60° torsional region with the minimum around −30° (Figures 7 and 8). Here again one might suggest that the quantum mechanical effect favoring bond eclipsing is not strong enough to overcome the concomitant increase in steric and torsional energies.

In this regard, the analysis in Table III indicates that the magnitude of the proposed stereoelectronic effect may be worth ca. 0.3 kcal/mol in the cyclohexane system and ca. 0.6 kcal/mol in the dioxanyl framework. This difference—if not due to crystal-packing effects, which are often invoked to explain away such small discrepancies—could be accounted for if, following the dipole–induced dipole proposal, the partial positive charge generated at C(4,6) is better stabilized by the adjacent (negative)

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(16) (a) Wiberg, K. B.; Martin, E. *J. Am. Chem. Soc.* **1985**, *107*, 5035. (b) Wiberg, K. B. *Ibid.* **1986**, *108*, 5817.

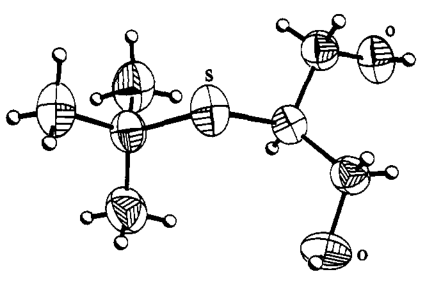
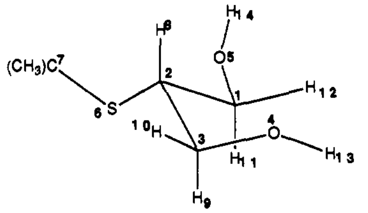


Figure 10. ORTEP perspective of 2-(*tert*-butylthio)-1,3-propanediol (**11**).



χ O_5-C_1-C_2-H_8 = -49.3
χ O_5-C_1-C_2-C_3 = -167.8
χ O_5-C_1-C_2-S_6 = 70.5
χ H_{11}-C_1-C_2-H_8 = -169.8
χ H_{12}-C_1-C_2-S_6 = -169.0
χ C_2-C_3-O_4-H_{13} = -92.5
χ H_{14}-O_5-C_1-C_2 = -98.6
χ S_6-C_2-C_3-H_9 = 58.3
χ S_6-C_2-C_3-H_{10} = -60.9
χ S_8-C_2-C_3-O_4 = 178.8
χ H_8-C_2-C_3-H_9 = 178.1
χ H_8-C_2-S6-C_7 = -12.1
χ C_3-C_2-S_8-C_7 = -106.7
χ C_1-C_2-S_8-C_7 = -129.9

Figure 11. Selected torsion angles (χ, deg) in 2-(*tert*-butylthio)-1,3-propanediol (**11**).

sulfonyl oxygens in the eclipsed conformation (Figure 9). It must be conceded, however, that the calculations may be inaccurate, in as much as the torsional parameters in the available version of the MM2 program[13] used have not been extensively tested and may not be optimal.

Selected bond lengths and angles for *cis*-**10**, *trans*-**9**, and *trans*-**4** are collected in Table V. Most bond lengths seem normal.

C. Conformation of 2-(*tert*-Butylthio)-1,3-propanediol (11). During the course of this work, we discovered by X-ray analysis that the title diol intermediate also adopts a nearly eclipsed conformation. A view of the solid-state conformation is provided in Figure 10. The eclipsing is observed in the C7–S6–C2–H8 segment (torsion angle $\chi = -12.1°$), and presumably the unshared electron pairs at sulfur do eclipse the C(2)–C(1) and C(2)–C(3) bonds[17] (Figure 11).

Molecular mechanics calculations[13] for **11** indicate that, in agreement with the X-ray structure, a nearly eclipsed conformation is the most stable (torsion angle χ C7–S6–C2–H8 = 15.0°), suggesting that the steric crowding of the *tert*-butyl with the methylenes C1 and C3 is as severe as in the cyclic *tert*-butyl sulfones. The gauche conformations (torsion angle χ C7–S6–C2–H8 = 60° and χ C7–S6–C2–H8 = 180°) are 2.1 and 3.2 kcal/mol above the minimum (Figure 12). It is thus reasonable that the staggered conformation is not observed, but it is puzzling why the conformation midway between staggered and eclipsed is not preferred as it was in the case of the axially substituted cyclic *tert*-butyl sulfoxides (*cis*-**3** and *cis*-**12**, Table III) or the equatorially substituted *tert*-butyl sulfones (*trans*-**9**, *trans*-**4**). The remaining structural data for **11** (Figures 13 and 14, supplementary material) seem normal and do not support the involvement of a special stereoelectronic effect; however, it seems clear from the analysis that a repulsive four-electron interaction (σ_{C-C}/n_S) is not dominant in this system.[18] The conformation of **11** may be affected by intermolecular hydrogen bonding in the crystal (H···O distances 195.9 and 198.8 pm).

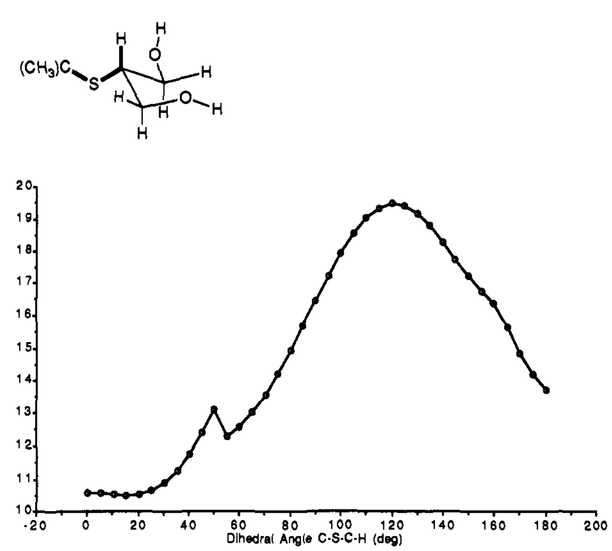


Figure 12. MM2 conformational potential for 2-(*tert*-butylthio)-1,3-propanediol (**11**).

Conclusions

The conformational preference of cyclohexanes and 1,3-dioxanes substituted by sulfur-containing groups (sulfide, sulfoxide, or sulfone) can usually be rationalized in terms of steric and electrostatic effects. For example, the alkyl group and/or oxygen bonded to sulfur is generally oriented outside the ring, so that the less-demanding electron lone pair points into the ring.

In the case of the axial methylsulfonyl group, an O-inside rotamer is preferred over the methyl-inside conformation in the cyclohexane system, reflecting again the relative sizes of oxygen and methyl. Nevertheless, the methyl-inside rotamer is favored in the dioxanyl system as this conformation avoids the electrostatic repulsion between (negative) oxygens. This behavior is reproduced by MMP2 calculations.

A quite different situation is observed for an axial *tert*-butylsulfonyl substituent: a nearly eclipsed conformer is preferred in both cyclohexane and dioxane. The force-field data suggest that interactions between the *tert*-butyl methyls and the endocyclic methylenes afford a shallow energy profile in the staggered to eclipsed region. Probably an additional quantum mechanical effect makes the eclipsed conformation the most stable.

The nature of this conformational effect favoring the eclipsing of S–O/C–C bonds is not obvious from the experimental data. Stereoelectronic dipole–induced dipole or $\sigma_{C-C} \rightarrow \sigma^*_{S-O}$ interactions might be reasonable interpretations. However, the magnitude of such an effect, if real, is not likely to exceed 0.6–0.7 kcal/mol in the most favorable case, the axial dioxane *cis*-**4**.

Bond eclipsing is not observed in the sulfoxide analogues *cis*-**3** and *cis*-**12**, probably because one S–O/C–C attractive interaction is not enough to overcome the concomitant steric and torsional repulsions. Conformations intermediate between staggered and eclipsed are found in the equatorial isomeric sulfones, *trans*-**4** and *trans*-**9**.

The fact that eclipsing is more important in dioxane (*cis*-**4**) than in cyclohexane (*cis*-**9**) is best explained in terms of the dipole–induced dipole mechanism since, in the dioxane, the induced positive charge that develops is further stabilized by the adjacent (negative) oxygen atoms.

Experimental Section

General Information. Melting points were obtained in a Mel-Temp and/or Electrothermal melting point apparatus with an open capillary tube. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Proton NMR spectra were recorded on Varian EM-360 (60 MHz), Varian EM-390 (90 MHz), or Bruker WM-250 (250 MHz) spectrometers. ^{13}C NMR spectra were recorded on Bruker WM-250 (62.9 MHz) or JEOL FX-90Q (22.49 MHz) instruments, all operated

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[17] Assuming sp^3-hybridized electron lone pairs at sulfur; cf. Patterson, C. H.; Messmer, R. P. *J. Am. Chem. Soc.* **1990**, *112*, 4138.

[18] For a pioneering study concerning the availability of the σ^*_{S-O} orbital in two-electron stabilizing interactions and four-electron σ_{C-C}/n_S repulsive interactions, see: Wolfe, S. Sulfur-Containing Carbanions and Related Species. In *Organic Sulfur Chemistry*; Bernardi, F., Czismadia, I. G., Mangini, A., Eds.; Elsevier: Amsterdam, 1985; Chapter 3.

in the pulse Fourier transform mode and locked on solvent deuterium.

***cis*-4-*tert*-Butyl-1-(*tert*-butylsulfonyl)cyclohexane (*cis*-9).** This compound was synthesized by oxidation of *cis*-4-*tert*-butyl-1-(*tert*-butylthio)cyclohexane (obtained according to a published procedure[1] following the sequence *trans*-cyclohexanol → *trans*-mesylate → *cis*-sulfide). A hydrogen peroxide solution (30%) (4 mL) was added to a stirred mixture of (0.91 g, 4.0 mmol) of the *cis*-sulfide and 12 mL of acetic acid/acetic anhydride (1:1). The resulting mixture was stirred for an additional 6 h and then 40 mL of water was added. The organic layer was extracted with a mixture of chloroform/methylene chloride (1:1), washed with sodium bicarbonate solution, and dried over $MgSO_4$. It was filtered, and the solvent was removed in a rotary evaporator to yield a solid which, after recrystallization from hexanes, gave 0.85 g (81.7%) of colorless crystals (mp 142–143 °C) suitable for X-ray diffraction analysis. Data for *cis*-9: ^1H NMR (60 MHz) ($CDCl_3$) δ 0.86 (s, 9 H, *tert*-butyl-C), 1.42 (s, 9 H, *tert*-butyl-S), 1.55–2.12 (m, 7 H), 2.43 (m, 2 H, C2,6-H_e) 3.47 (m, 1 H, C_1-H_e); ^{13}C NMR (22.5 MHz) ($CDCl_3$) δ 23.23 ($C_{3,5}$), 23.71 [$(CH_3)CS$], 27.39 [$(CH_3)C$-C_4], 27.48 ($C_{2,6}$), 32.50 [$(CH_3)C$-C_4], 47.11 (C_4), 50.71 (C_1), 60.98 [$(CH_3)CS$]; IR (KBr) 2960, 2870, 1395, 1365, 1280, 1110 cm^{-1}; MS *m/z* 203 ($M^+ - 57$), 139, 82, 57, 41. Anal. Calcd for $C_{14}H_{28}SO_2$: C, 64.57; H, 10.84. Found: C, 64.84; H, 10.48.

***cis*-4-*tert*-Butyl-1-(methylsulfonyl)cyclohexane (*cis*-10).** This compound was synthesized as described in the literature[19] (mixture of cis/trans mercaptans[20] → cis/trans sulfides → cis sulfone; selective recrystallization from acetic acid). Recrystallization from *n*-pentane[21] afforded colorless crystals, mp 171–172 °C (lit.[19] mp 175.5–176.5 °C), suitable for X-ray diffraction analysis.

***trans*-4-*tert*-Butyl-1-(*tert*-butylsulfonyl)cyclohexane (*trans*-9).** This compound was obtained through epimerization of its cis epimer as previously described[22] for analogous compounds. The cis sulfone (0.265 g) in 20 mL of 8% ethanolic sodium ethoxide gave the product in quantitative yield. Recrystallization from petroleum ether gave colorless crystals: mp 146–147.5 °C (suitable for X-ray diffraction analysis); ^1H NMR (250 MHz) ($CDCl_3$) δ 0.87 (s, 9 H, *tert*-butyl-C), 1.05 (m, 3 H), 1.52 (s, 9 H, *tert*-butyl-S), 1.66 (m, 2 H), 1.97 (m, 2 H), 2.22 (dm, J_{gem} = 12.0 Hz, 2 H, $C_{2,6}$-H_e), 3.06 (tt, J_{anti} = 12.4 Hz, J_{gem} = 3.7 Hz, 1 H, C_1-H_a).

***trans*-2-*tert*-Butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*trans*-4).** This compound was prepared as described.[7] Recrystallization from hexanes afforded colorless crystals, mp 195–196 °C (lit.[7] mp 195–196 °C), suitable for X-ray diffraction analysis.

2-(*tert*-Butylthio)-1,3-propanediol (11). The synthesis of this compound has been previously described.[7]

X-ray Analyses. The structures of *cis*-9,[23] *cis*-10,[24] *trans*-9,[23] *trans*-4,[24] and diol 11[24] were determined by single-crystal X-ray diffraction. Intensity data for suitable crystals were collected on either an Enraf-Nonius CAD4 diffractometer using graphite monochromated MoKα radiation[23] or a Nicolet R3m diffractometer using Ni-filtered CuKα radiation.[24] All of the structures were solved using direct methods techniques and refined by full-matrix least-squares using weights determined from counter statistics. Full experimental details are given in Table II.

The programs used were the SHELXTL[25] package for *cis*-**10**, *trans*-**4**, and diol **11** and the NRCVAX[26] package for *cis*-**9** and *trans*-**9**.

The shortest intermolecular contacts (H···H) in the crystal are 249 pm for *cis*-9 and 239.5 pm for *trans*-9, i.e., outside and barely within the sum of the H···H van der Waals radii of 240 pm. Those for *trans*-4 are 246.7 (H···H) and 266.5 pm (O···H), again outside the van der Waals radii.[27]

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Registry No. *trans*-4, 109151-32-8; *cis*-9, 138432-81-2; *trans*-9, 138432-82-3; *cis*-10, 4943-24-2; 11, 109151-33-9; *cis*-4-*tert*-butyl-1-(*tert*-butylthio)cyclohexane, 123185-94-4.

Supplementary Material Available: Listing of anisotropic thermal parameters for all non-hydrogen atoms, isotropic thermal parameters for hydrogen atoms, bond distances, bond angles, torsional angles, and the fractional coordinates for *cis*-**9**, *cis*-**10**, *trans*-**9**, *trans*-**4**, and diol **11**, and MMP2 curves for *cis*-**3**, *cis*-**4**, and *cis*-**12** (42 pages). Ordering information is given on any current masthead page.

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(24) Structures resolved at UNAM, México, by R. A. Toscano.

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(27) These data are reported to exclude the likelihood of intermolecular interactions being responsible for the conformational behavior of these compounds in the crystalline state.