Filtration and removal of solvent gave 34.8 mg (71%) of 8, which was purified by preparative GC. The pure compound so obtained was found to be identical in GC retention time, ^{1}H NMR, IR and mass spectra with that of an authentic sample.[36]

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Conformational Analysis of 1,3-Dioxanes with Sulfide, Sulfoxide, and Sulfone Substitution at C(5). Finding an Eclipsed Conformation in *cis*-2-*tert*-Butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane

Eusebio Juaristi,*[1a] Roberto Martínez,[1a] Rodolfo Méndez,[1a] Rubén A. Toscano,[1b] Manuel Soriano-García,[1b] Ernest L. Eliel,[1c] Amorn Petsom,[1d] and Richard S. Glass*[1d]

Departamento de Química, Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, 07000-México, D.F., México, Instituto de Química, Universidad Nacional Autónoma de México, Ciudad Universitaria, 04510-México, D.F., México, Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514, and Department of Chemistry, University of Arizona, Tucson, Arizona 85721

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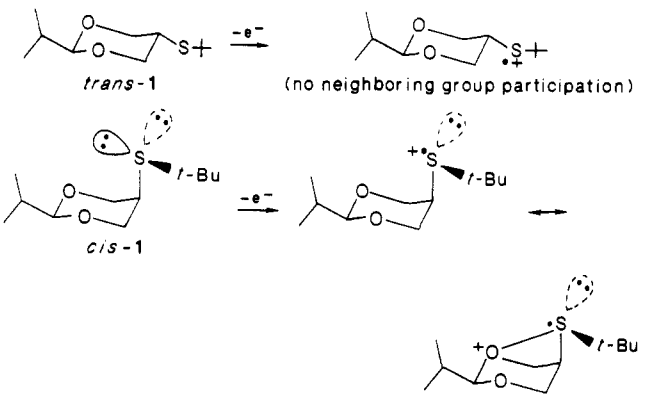
The positions of equilibrium, established by acid catalysis, between diastereomeric *cis*- and *trans*-5-(*tert*-butylthio)- (1), 5-(*tert*-butylsulfinyl)- (2), and 5-(*tert*-butylsulfonyl)-2-isopropyl-1,3-dioxanes (3) are reported and compared with previously published data for the 5-methylthio (4), 5-methylsulfinyl (5), and 5-methylsulfonyl (6) analogues. Although $\Delta G°$ values for the sulfides 1 and 4 are very similar, the difference in conformational behavior for sulfoxides 2 and 5 is significant, and the effect of changing from methyl to *tert*-butyl in the sulfones (6 → 3) is quite dramatic: the large preference of the methyl analogue for the axial position (1.19 kcal/mol) is reversed in 3 where the equatorial isomer is more stable by 1.14 kcal/mol. The conformational behavior in 1–6 is discussed in terms of the rotamer population of the axial isomer, in which steric and electrostatic effects are dominant. X-ray crystallographic data on *cis*-2-*tert*-butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*cis*-9, axial sulfonyl) show that the *S*-*tert*-butyl group is outside the ring, with both sulfonyl oxygens above the dioxane ring and eclipsing the endocyclic C–C bonds. The electrochemical behavior of *cis*-1 and *trans*-1 supports the idea that lone-pair/lone-pair electron repulsion is responsible for the large predominance of the equatorial isomer.

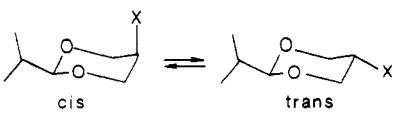
Several years ago, Eliel and Evans reported the conformational equilibrium of 5-(methylthio)-1,3-dioxane,[2] which shows a marked preference for the equatorial conformation ($\Delta G°$ = −1.82 kcal/mol in cyclohexane). Because this value is more negative than the corresponding value for (methylthio)cyclohexane (−1.00 to −1.07 kcal/mol[3]), a repulsive interaction of the m-shell electrons of sulfur with the p electrons of the ring oxygens was proposed.[4] On the other hand, Wilson et al.[5] observed that the electrochemical oxidation of aliphatic thioethers is significantly facilitated by suitably disposed electron-rich neighboring groups that experience lone-pair/lone-pair repulsion.

With this information, it was deemed of interest to measure the oxidation potentials of *cis*- and *trans*-2-isopropyl-5-(*tert*-butylthio)-1,3-dioxanes (*cis*-1 and *trans*-1), the 2-isopropyl group acting as an effective holding group for the 1,3-dioxane ring[6] and the *tert*-butyl group ensuring that at least one electron pair on sulfur in *cis*-1 is pointing into the ring and suitably disposed for lone-pair/lone-pair interaction (Scheme I) such that the electron/electron destabilizing interaction may be replaced by electrostatic attraction, or even bond formation on electron removal.[7]

Scheme I



Scheme II



1, X = S-*t*-Bu
2, X = S(O)-*t*-Bu
3, X = SO_2-*t*-Bu
4, X = SMe
5, X = S(O)Me
6, X = SO_2Me
7, *t*-Bu instead of *i*-Pr, X = S-*t*-Bu
8, *t*-Bu instead of *i*-Pr, X = S(O)-*t*-Bu
9, *t*-Bu instead of *i*-Pr, X = SO_2-*t*-Bu

(1) (a) Instituto Politécnico Nacional. (b) Universidad Nacional Autónoma de México. (c) University of North Carolina. (d) University of Arizona.

(2) Eliel, E. L.; Evans, S. A. *J. Am. Chem. Soc.* **1972**, *94*, 8587–8589.

(3) Jensen, F. R.; Bushweller, C. M.; Beck, B. H. *J. Am. Chem. Soc.* **1969**, *91*, 344–351. Eliel, E. L.; Kandasamy, D. *J. Org. Chem.* **1976**, *41*, 3899–3904.

(4) Called the "repulsive gauche effect": Zefirov, N. S.; Gurvich, L. G.; Shashkov, A. S.; Krimer, M. Z.; Vorob'eva, E. A. *Tetrahedron* **1976**, *32*, 1211–1219. Eliel, E. L.; Juaristi, E. *J. Am. Chem. Soc.* **1978**, *100*, 6114–6119. Juaristi, E. *J. Chem. Educ.* **1979**, *56*, 438–441.

(5) Coleman, B. R.; Glass, R. S.; Setzer, W. N.; Prabhu, U. D. B.; Wilson, G. S. In *Electrochemical and Spectrochemical Studies of Biological Redox Components*; Kadish, K. M., Ed.; Advances in Chemistry 201; American Chemical Society: Washington, DC, 1982; pp 417–441.

(6) Nader, F. W.; Eliel, E. L. *J. Am. Chem. Soc.* **1970**, *92*, 3050–3055.

0022-3263/87/1952-3806$01.50/0

Table I. Conformational Equilibria in 5-Substituted 1,3-Dioxanes 1-6 (Scheme II)

compd	X	$\Delta G°$,[c] kcal/mol	solvent	temp, °C
4	SCH_3[a]	−1.73 ± 0.02	ether	26.5
1	S-*t*-Bu[b]	−1.90 ± 0.11	$CHCl_3$	23.0
5	$SOCH_3$[a]	+0.82 ± 0.11	$CHCl_3$	54.0
2	SO-*t*-Bu[b]	+0.10 ± 0.01	$CHCl_3$	23.0
6	SO_2CH_3[a]	+1.19 ± 0.10	$CHCl_3$	50.0
3	SO_2-*t*-Bu[b]	−1.14 ± 0.01	$CHCl_3$	23.0

[a] References 2 and 8. [b] This work. [c] Positive $\Delta G°$ values indicate axial preference.

In addition, the chemical equilibrations of the 5-(*tert*-butylthio)- (*cis*-1 ⇄ *trans*-1), 5-(*tert*-butylsulfinyl)- (*cis*-2 ⇄ *trans*-2), and 5-(*tert*-butylsulfonyl)-2-isopropyl-1,3-dioxanes (*cis*-3 ⇄ *trans*-3) were carried out and the results examined in light of those obtained earlier for the methyl analogues (4–6)[2,8] which demonstrated the importance of attractive interactions between sulfoxide or sulfone and ether functional groups (Scheme II).

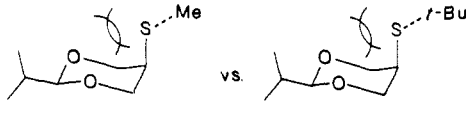
Results and Discussion

A. Electrochemical Oxidation of Sulfides *cis*-1 and *trans*-1. The cyclic voltammetry of these diastereomers was performed in acetonitrile with platinum as the indicating electrode and a Ag/0.1 M Ag^+ in acetonitrile reference electrode. The peak potentials for *cis*-1 and *trans*-1 were 1.36 and 1.54 V, respectively, and appear to support the earlier proposal[2,4] for electron–electron repulsion in *cis*-4, since the cis derivative undergoes a more facile oxidation by 180 mV.

Although the lower oxidation potential for *cis*-1 could also be explained by bridging in the product,[5,7] photoelectron (PE) spectra show that the ionization potential for *cis*-1 is 0.20 eV *less* than that for *trans*-1. Because the PE spectra are recorded on a much faster time scale than the electrochemical experiments, bond formation involving substantial movement of atoms cannot explain the values observed for the anodic oxidation potentials. Therefore, lone-pair/lone-pair repulsion or attractive interaction between $>S^{\bullet+}$ and the lone pairs on O (not involving substantial atomic movement) can account for the results.

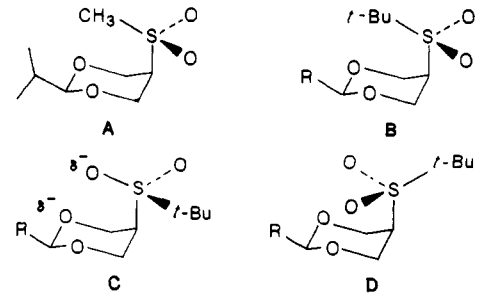
B. Conformational Analyses of 1–3. Equilibration of sulfides (*cis*-1 ⇄ *trans*-1), sulfoxides (cis-2 ⇄ *trans*-2), and sulfones (*cis*-3 ⇄ *trans*-3) was readily performed by means of BF_3.[9] The corresponding free energy differences are summarized in Table I, which includes, for comparison purposes, those for 4–6.[2,8]

In the case of the sulfides 1 and 4, the $\Delta G°$ values are very similar. It is reasonable here that both the methyl and *tert*-butyl groups point outside the dioxane ring, and therefore the effective steric interactions are comparable.

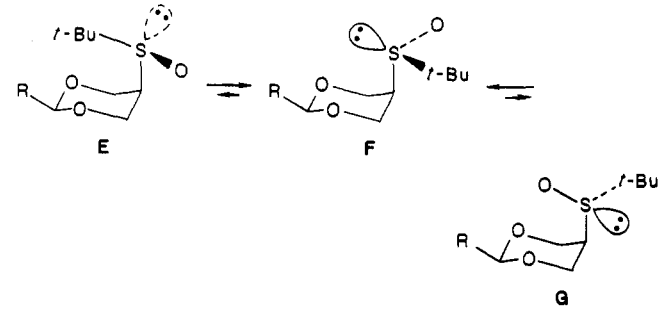


On the other hand, the effect of changing from methyl to *tert*-butyl in the sulfones is quite dramatic; the large preference of the methyl analogue (6) for the axial isomer (1.19 kcal/mol) is reversed in *cis*-3 ⇄ *trans*-3 in which the equatorial isomer is more stable by 1.14 kcal/mol. Thus, the *tert*-butyl ligand on sulfur shifts the equilibrium toward the equatorial conformation by 2.33 kcal/mol. Nevertheless, it is clear that some of the electrostatic, attractive interaction operative in 6-axial is still present in *cis*-3 (axial sulfone), since the equatorial predominance of 1 ($\Delta G°$ = −1.90 kcal/mol) decreases in 3 ($\Delta G°$ = −1.14 kcal/mol) despite the increase in steric bulk.

Scheme III



Scheme IV



The axial preference of the methylsulfonyl group in 6 has been rationalized in terms of an attractive, electrostatic interaction between the positive end of the S^+–O^- dipole and the negative ring oxygen atoms.[2,8] The large long-range (*W*) coupling constant of 1.14 ± 0.02 Hz between the sulfonyl methyl and the hydrogen at C(5) of the dioxane was taken as an indication that *cis*-6 exists with the methyl group pointing into the ring (structure **A**, Scheme III); this in turn was explained by postulating electrostatic repulsion between the (electronegative) ring oxygens and the negative end of the S–O dipole.[2,8]

Two explanations suggested themselves to account for the contrasting behavior of 3 and 6: (1) An axial sulfonyl group with the alkyl ligand still inside the ring (structure **B**, Scheme III) would lead to significant steric congestion, causing the axial isomer to be destabilized. (2) A conformation with the *tert*-butyl group turned outward (structure **C**, Scheme III) places the (negative) ring oxygens close to the (negative) sulfonyl oxygen, leading to an unfavorable electrostatic interaction (see above).

The situation with sulfoxide 2 is intermediate: the axial isomer is favored, but only marginally ($\Delta G°$ = +0.10 kcal/mol), while in the methyl analogue (5) the axial preference is 0.82 kcal/mol. It is likely that the latter material exists at least partly with the methyl inside the ring (conformation analogous to **E**, Scheme IV). This conformation would be congested in the *tert*-butyl analogue; the conformation with oxygen inside (**G**) is presumably disfavorable in both 2 and 5. We shall return to this point below.

The possibility that the Lewis acid BF_3 forces a higher population of one of the two isomers because of enhanced coordination with the lone pairs on the oxygen atoms was

(7) For a recent study of S∴O interactions and more detailed suggestions for this bonding, see: Glass, R. S.; Hojjatie, M.; Wilson, G. S.; Mahling, S.; Göbl, M.; Asmus, K.-D. *J. Am. Chem. Soc.* **1984**, *106*, 5382–5383.

(8) Kaloustian, M. K.; Dennis, N.; Mager, S.; Evans, S. A.; Alcudia, F.; Eliel, E. L. *J. Am. Chem. Soc.* **1976**, *98*, 956–965.

(9) Eliel, E. L.; Knoeber, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 3444–3458.

Table II. 250-MHz ^{1}H NMR Chemical Shifts (ppm) for *cis*- and *trans*-2-Isopropyl-5-(*tert*-butylsulfinyl)- (*cis*- and *trans*-2) and *cis*- and *trans*-2-*tert*-Butyl-5-(*tert*-butylsulfonyl)-1,3-dioxanes (*cis*- and *trans*-9) at Room Temperature in $CDCl_3$[a]

proton	*cis*-2	*trans*-2	*cis*-9	*trans*-9
H(2)	4.32	4.25	4.10	4.04
H(4ax)	3.97	3.99	4.07	3.98
H(4eq)	4.66[b]	4.29	4.65	4.35
H(5)	2.62	3.16	2.91	3.59
H(6ax)	4.21	4.02	4.07	3.98
H(6eq)	4.06	4.11	4.65	4.35
S-*t*-Bu	1.27	1.30	1.48	1.40
$(CH_3)_2CH$	0.95	0.93		
$(CH_3)_2CH$	1.87	1.80		
t-Bu C(2)			0.91	0.88

[a] H(4ax/eq) and H(6ax/eq) may be interchanged. [b] Syn to S=O bond.

discarded when equilibria were run at different BF_3 concentrations (1, 2, 4 equiv): the same diastereomeric ratio was obtained within the experimental error limits ($\Delta G°$ values within ±0.01 kcal/mol).

C. Rotamer Population in Sulfoxides 2 and Sulfones 3. 1. ^{1}H NMR Spectra. Table II lists the chemical shifts observed for the hydrogen atoms in sulfoxides **2** and sulfones **9**, the 2-*tert*-butyl analogues of sulfones **3** (which provide somewhat simpler spectra than **3**), in $CDCl_3$ at 250 mHz and room temperature.

The large chemical shift difference between H(4eq) and H(6eq), 0.60 ppm, supports rotamers **E** and **F** (Scheme IV) for sulfoxide *cis*-**2** in view of the known downfield proton shift induced by a *syn*-S=O group.[10] By contrast, $\Delta\delta$(4ax/6ax) = 0.24 ppm in *cis*-**2**, and $\Delta\delta$(4eq/6eq) = 0.18, $\Delta\delta$(4ax/6ax) = 0.03 ppm in *trans*-**2**. Conformer **G** for *cis*-**2** is ruled out in view of the small shifting effect expected from the *tert*-butyl group as evidenced in related, sterically congested compounds.[11]

On the other hand, the lack of any compression effect on the ^{13}C NMR chemical shifts for the *tert*-butyl-S(O) methyls (Table III) argues for a negligible contribution of rotamer **E**. By contrast, a large difference in chemical shifts was observed for the methyl carbons in the sulfones *cis*-**6** (43.0 ppm; inside methyl group) and *trans*-**6** (40.2 ppm),[12] supporting the idea of a much greater steric difference in this case.

Further evidence in support of a high predominance of conformation **F** (Scheme IV) of *cis*-**2** was obtained from the study of its ^{1}H NMR spectrum after the addition of 0.03 equiv of $Eu(fod)_3$. The lanthanide-induced shifts (LIS) decreased in the order H(4eq) > H(5) > H(4ax) > *t*-Bu > H(2) ~ H(6eq) ~ H(6ax). (It is realized that shift reagents sometimes change conformation, so this argument is less definitive than the previous one.)

Structures **E** and **G** (Scheme IV) seem to be significantly higher in energy relative to **F**, since the proton NMR spectra of *cis*-**2** [particularly $\Delta\delta$(4eq/6eq)] did not vary in the temperature range −40 to +100 °C, suggesting that the rotamer population is not significantly altered by the large change in temperature. The great predominance of conformer **F** explains the but slight predominance for axial over equatorial SO–R seen in **2** (as compared with **5**): the electrostatic $S^+\cdots O$ (ring) attraction in conformer **F** is partly offset by an O/S lone-pair repulsion, similar to that seen in sulfides **1** and **4**.

As for sulfones *cis*-**3** and *cis*-**9**, an NMR spectrum corresponding to a plane of symmetry through C(2) and C(5) was recorded. This is to be expected for structure **B** (Scheme III) or two equally populated, equilibrating (by rotation around the C(5)–S bond) mirror-image conformations corresponding to **C** and its enantiomer (Scheme III). Conformer **D** was initially disregarded in view of the normally expected much higher energy of eclipsed conformations (see, however, below). However, the somewhat anomalous vicinal coupling constants found for *cis*-**9** (J(4,6ax/5) = 4.2 Hz ≫ J(4,6eq/5) = 0.8 Hz) (Table IV) suggested some deformation of the heterocyclic chair, with outward bending of the C–S bond.

2. ^{17}O NMR Spectra. No further information concerning rotamer population in *cis*-**9** could be derived from the ^{13}C NMR spectra (Table III). However, ^{17}O NMR spectra on *cis*-**9** and *trans*-**9** were instructive in light of the recent work by Manoharan and Eliel[12] that shows the manifestation of δ-compression effects as downfield shifts relative to the uncompressed system. Both *cis*-**9** and *trans*-**9** give very good sulfone peaks, the axial one at 139.5 ppm and the equatorial one at 138.0 ppm. By contrast, in the corresponding methyl compounds, the SO_2 resonance of the axial isomer (*cis*-**6**, in which the methyl group is inside the ring; see structure **A**, Scheme III) is at 159.8 ppm and that for the equatorial isomer at 161.5 ppm.[12] Although the differences are slight and possibly within the limits of the experimental error of the ^{17}O measurements, the reversal of the order between the pairs *cis*/*trans*-**3** and *cis*/*trans*-**6** suggests that the downfield signal in *cis*-**3** shows some δ-compression effect and, therefore, lends some support to structure **C** (a pair of rapidly equilibrating enantiomers) and/or **D** (rather than **B**).

3. X-ray Diffraction Data. Definitive evidence for the structure of *cis*-**3** in the solid state was obtained by single-crystal X-ray diffraction of its 2-*tert*-butyl analogue, *cis*-**9**; the crystals of *cis*-2-isopropyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*cis*-**3**) were not of sufficient quality for crystallographic work.

A perspective view of the molecular structure is shown in Figure 1 (supplementary material). Tables V–VIII (supplementary material) present the appropriate bond distances, bond angles, torsional angles, and the Cartesian coordinates. The heterocyclic six-membered ring exists in a chair conformation, with the substituent at C(5) being axial. The sulfonyl *tert*-butyl group is outside the ring, suggesting that the steric congestion that would be present if the alkyl group was inside the ring is more severe than the electrostatic repulsion between the (negative) oxygens. This repulsion is nonetheless manifested as some bending of the C(5)–S bond away from the ring [C(4)–C(5)–S = 112.0°, C(6)–C(5)–S = 112.7°] and by an unusually large torsional angle in the O–C–C–S segments of ca. 78°, which is in accord with the ^{1}H NMR data (vide supra). Also, the C(5)–S bond length (1.829 (9) Å) is longer than normal (1.80 Å).[13]

The most interesting feature of the crystallographic data is, however, that they correspond to structure **D**, not **C** (Scheme III). This result was rather surprising because chemical intuition might have favored the former, with staggered rather than eclipsed S–O/C–C and C-*t*-Bu/C–H bonds. However, the average torsional angles O–S–C–C are 8.25 ± 2.35°, indicating the *nearly eclipsed* nature of

(10) Lambert, J. B.; Keske, R. G. *J. Org. Chem.* **1966**, *31*, 3429–3431. See also: Juaristi, E.; Guzmán, J.; Kane, V. V.; Glass, R. S. *Tetrahedron* **1984**, *40*, 1477–1485.

(11) Compare, for example, *cis*- and *trans*-4,4-dimethyl-2-pentene: the ^{1}H NMR chemical shifts for the allylic protons at 60 MHz are 1.74 and 1.63 ppm, respectively. Sadtler spectra no. 14297M and 14298M (1972).

(12) Manoharan, M.; Eliel, E. L. *Magn. Reson. Chem.* **1985**, *23*, 225–231.

(13) Cf: Sutton, L. E., Ed. *Tables of Interatomic Distances, Supplement*; The Chemical Society: London, 1965.

Table III. ^{13}C NMR Data (ppm) for 2-Isopropyl- and 2-*tert*-Butyl-5-(*tert*-butylsulfinyl)-1,3-dioxanes (*cis*- and *trans*-2, *cis*- and *trans*-8) and 2-Isopropyl- and 2-*tert*-Butyl-5-(*tert*-butylsulfonyl)-1,3-dioxanes (*cis*- and *trans*-3, *cis*- and *trans*-9) in $CDCl_3$

	cis-2	*trans*-2	*cis*-8	*trans*-8	*cis*-3	*trans*-3	*cis*-9	*trans*-9
C(2)	105.99	105.82	107.59	107.70	105.84	105.56	108.09	107.79
C(4)[a]	63.77	65.58[b]	63.82	65.66	64.62	66.04	64.93	66.35
C(5)	49.72	46.32	50.00	46.59	56.25	48.92	56.82	49.32
C(6)	66.70	67.83[b]	66.85	67.94	64.62	66.04	64.93	66.35
$SC(CH_3)_3$	54.31	54.95	54.23	54.77	62.24	61.01	62.28	61.15
$SC(CH_3)_3$	23.04	22.89	23.08	22.97	23.40	23.04	23.40	23.32
$CH(CH_3)_2$	32.63	32.51			32.50	32.23		
$CH(CH_3)_2$	16.74, 16.81[c]	16.91			16.82	16.76		
C(2) $C(CH_3)_3$			35.16	34.83			35.15	34.80
C(2) $C(CH_3)_3$			24.49	24.65			24.66	24.66

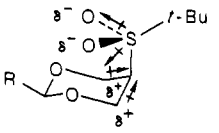
[a] Carbon syn to S=O bond. [b] These values may be interchanged. [c] Diastereotopic carbons show separate signals.

Table IV. Coupling Constants (Hertz) for 2-Isopropyl-5-(*tert*-butylsulfinyl)- (2) and 2-*tert*-Butyl-5-(*tert*-butylsulfonyl)-1,3-dioxanes (9)

cis-2		*trans*-2		*cis*-9		*trans*-9	
nuclei	*J*	nuclei	*J*	nuclei	*J*	nuclei	*J*
4eq/4ax	12.3	4eq/4ax	11.9	4,6eq/4,6ax	13.6	4,6eq/4,6ax	11.9
4eq/5eq	1.4	4eq/6eq	2.2	4,6eq/5eq	0.8	4,6eq/5ax	4.8
4eq/6eq	2.6	4eq/5ax	5.2	4,6eq/5eq	4.5	4,6ax/5ax	11.2
4ax/5eq	2.8	4ax/5ax	11.1				
6eq/6ax	12.9	5ax/6eq	5.3				
6eq/5eq	1.3	5ax/6ax	11.1				
6ax/5eq	2.5	6ax/6eq	11.3				

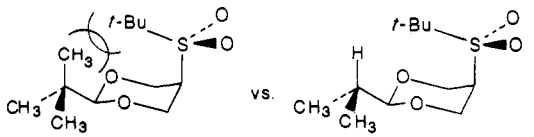
the crystal structure (see Figure 2, supplementary material).

The eclipsing of bonds in **D** may be a necessary evil to minimize the electrostatic repulsion between oxygens and/or to mitigate *t*-Bu/CH_2 steric interactions present in **C**. In addition, conformer **D** may lead to stabilizing attraction between the negatively charged sulfone oxygens and the positively charged methylenes. Finally, it is interesting to note that Wiberg et al.[14] interpret the lower energy of eclipsed *n*-alkyl ketones as resulting from dipole-induced dipole interactions, which in our system might also be important in lowering the energy of the eclipsed sulfones *cis*-3 and *cis*-9.



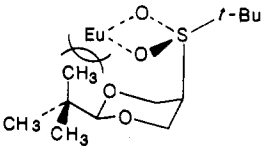
Molecular orbital calculations are presently being carried out in order to test these ideas, and also to predict whether the unusual eclipsed conformation in *cis*-9 observed in the solid state exists also in the gas phase.[15]

4. Isopropyl vs. *tert*-Butyl Substitution at C(2). While the isopropyl and *tert*-butyl groups at C(2) in 1,3-dioxanes are in essence equally effective as conformational anchoring groups,[9] observations of Dreiding models as well as molecular orbital calculations[15] indicate that conformer **B** (Scheme III) may be more unfavorable in *cis*-9 relative to *cis*-3 because of steric interaction between the alkyl moieties. Comparison of the NMR data however, suggests



that the same population of rotamers is present with either substituent at C(2). In particular, the ^{13}C NMR data for the pairs *cis*-2/*cis*-8, *trans*-2/*trans*-8, *cis*-3/cis-9, and *trans*-3/*trans*-9 are practically identical (excepting, of course, C(2) and its substituent; Table III).

Nevertheless, the steric effect of the C(2) *tert*-butyl group was manifested in an experiment with $Eu(fod)_3$ shift reagent and the *cis*-3/*cis*-9 pair: although the relative magnitude of lanthanide-induced shifts (LIS) is the same [H(5) > H(4,6eq) > *t*-Bu > H(4,6ax) > H_2 (effect still significant)], the absolute values of LIS with *cis*-3 are approximately twice as strong relative to those experienced by *cis*-9. This result argues for weaker complexation in the latter due to greater steric hindrance from the C(2) *tert*-butyl group.



Experimental Section

Melting points were obtained in a Mel-Temp and/or Electrothermal melting point apparatus with an open capillary tube.

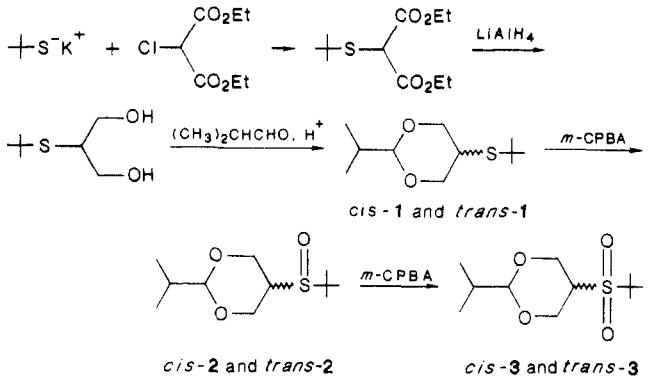
Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN, and by Atlantic Microlab, Inc., Atlanta, GA.

Proton NMR spectra were recorded on Varian EM-360 (60-MHz) or Varian EM-390 (90-MHz) spectrometers. ^{13}C NMR spectra were recorded on Bruker WM-250 (62.9-MHz) or JEOL FX-90Q (22.49-MHz) instruments operated in pulsed Fourier transform mode and locked on solvent deuterium. Samples were prepared as 5–10% solutions in $CDCl_3$ with 2–5% Me_4Si as internal reference in 5- or 10-mm-o.d. tubes. The ^{17}O NMR spectra were recorded on a Bruker spectrospin WM-250 spectrometer equipped with a 10-mm probe at 33.91 MHz in the FT mode without a lock. Samples (natural ^{17}O abundance) were in 1 M solutions in toluene (dried over anhydrous $CaCl_2$) in 10-mm tubes, heated to 100 °C. The spectral settings were as follows: 4–20-kHz spectral width, 128–1000 data points, 90° pulse angle corresponding to a 30-μs pulse width, 5–30-ms acquisition time with a 250-μs acquisition delay, 10^5–10^6 scans. Under these conditions, the observed signals had half-bandwidths in the range 100–200 Hz. Chemical shifts were measured without proton decoupling and are reported relative to external tap water as reference at

(14) Wiberg, K. B.; Martin, E. *J. Am. Chem. Soc.* **1985**, *107*, 5035–5041. Wiberg, K. B. *Ibid.* **1986**, *108*, 5817–5822.

(15) Glass, R. S.; Broeker, J.; Rubio, M. F.; Gordillo, B.; Juaristi, E., work in progress.

Scheme V



100 °C. Although they were read to 0.1 ppm, their reproducibility is probably no better than 2–3 ppm.

Preparation of the 5-Substituted 1,3-Dioxanes. The preparation of *cis*- and *trans*-5-(*tert*-butylthio)- (*cis*-**1** and *trans*-**1**), *cis*- and *trans*-5-(*tert*-butylsulfinyl)- (*cis*-**2** and *trans*-**2**), and *cis*- and *trans*-5-(*tert*-butylsulfonyl)-2-isopropyl-1,3-dioxanes (*cis*-**3** and *trans*-**3**) and their 2-*tert*-butyl analogues (**7**–**9**) was carried out according to the procedure of Eliel et al.[2,8] with *t*-BuSK instead of CH_3SH (Scheme V). Since condensation of the diol and aldehyde affords **1** as a mixture of isomers containing less than 5% of the cis form, *cis*-**2** was prepared by equilibration of *trans*-**2** followed by separation; *cis*- and *trans*-**3** were prepared by oxidation of *cis*- and *trans*-**2**, respectively.

Diethyl (*tert*-Butylthio)malonate. Potassium hydroxide (5.6 g, 100 mmol) was dissolved in 30 mL of absolute ethanol, a solution of *tert*-butyl mercaptide (9.6 g, 106 mmol) in 20 mL of ethanol was added, and the mercaptide solution was poured into a cold solution (ice bath) of diethyl chloromalonate (20.6 g, 106 mmol) in ethanol (20 mL). Potassium chloride precipitated immediately. The suspension was stirred at room temperature for 1.5 h, diluted with water (150 mL), and extracted with ether (3 × 100 mL). The ethereal extracts were combined, dried ($MgSO_4$), and concentrated to dryness (rotary evaporator) to afford a yellow oil, which was distilled to afford a colorless material: 19.0 g, 74.5%; bp 135–7 °C (0.05 mm); ^1H NMR ($CDCl_3$, 90 MHz) 1.30 (t, J = 7.6 Hz, 6 H, CH_3), 1.40 (s, 9 H, *t*-Bu), 4.16 (s, 1 H, CH), 4.22 (q, J = 7.6 Hz, 4 H, CH_2) ppm. Anal. Calcd for $C_{11}H_{20}O_4S$: C, 53.20; H, 8.12. Found: C, 52.65; H, 7.94.

2-(*tert*-Butylthio)-1,3-propanediol. A solution of diethyl (*tert*-butylthio)malonate (15.0 g, 60 mmol) in 50 mL of anhydrous ether was added (1.5 h) to a suspension of lithium aluminum hydride (4.56 g, 120 mmol) in 75 mL of anhydrous ether under a nitrogen atmosphere. The resulting suspension was refluxed for 22 h and then stirred at room temperature for 20 h. It was extracted with water (5 mL), a 15% solution of NaOH (ca. 6 mL), and more water (ca. 15 mL) and then stirred rapidly for 3 h and filtered; the filtrate was concentrated (rotary evaporator) to give 8.0 g (81% yield) of the crude product. Recrystallization (acetone/hexane, 1:2) afforded 7.11 g (72% yield) of white crystals: mp 78–79 °C; ^1H NMR ($CDCl_3$, 90 MHz) 1.38 (s, 9 H, *t*-Bu), 2.82 (t, J = 6.3 Hz, 2 H, OH), 3.0 (quintet, J = 5.8 Hz, 1 H, CH), 3.75 (t, J = 6.0 Hz, 4 H, CH_2) ppm. Anal. Calcd for $C_7H_{16}O_2S$: C, 51.18; H, 9.81. Found: C, 51.42; H, 9.40.

***cis*- and *trans*-2-Isopropyl-5-(*tert*-butylthio)-1,3-dioxanes (1).** A solution of 6.56 g (40 mmol) of 2-(*tert*-butylthio)-1,3-propanediol, 2.88 g (40 mmol) of isobutyraldehyde, and a few crystals of *p*-toluenesulfonic acid in ca. 80 mL of benzene was refluxed until 0.72 mL of water was removed (Dean–Stark trap). The resulting solution was washed with a 10% solution of KOH (30 mL) and 100 mL of water, dried ($MgSO_4$), and concentrated (rotary evaporator) to afford 5.9 g of a yellow oil. This material was shown by vapor-phase chromatography (on a 6 ft × $^1/_8$ in. 10% UC-W98 column on Chromosorb W 80–100 mesh, at 140 °C) to consist of ca. 4% of the cis sulfide (*cis*-**1**) and ca. 96% *trans*-**1**. Separation of this mixture was achieved by flash chromatography[16] (hexane/ethyl acetate, 95:5). Trans isomer: bp 76–77 °C (0.1 mm); ^1H NMR ($CDCl_3$, 90 MHz) 0.92 (d, J = 6.5 Hz, 6 H, $(CH_3)_2CH$), 1.37 (s, 9 H, *t*-Bu), 1.57–2.07 (m, 1 H, $(CH_3)_2CH$), 2.93 (m, 1 H, C_5-H), 3.40 (dd, J_{gem} = −11.2 Hz, J_{anti} = 12 Hz, $C_{4,6}$-H_{ax}), 4.15 (d, J_{vic} = 4.8 Hz, C_2-H), 4.16 (dd, J_{gem} = −11.2 Hz, J_{gauche} = 4.9 Hz, $C_{4,6}$-H_{eq}) ppm. Anal. Calcd for $C_{11}H_{22}O_2S$: C, 60.50; H, 10.15; S, 14.68. Found: C, 60.37; H, 10.05; S, 14.58. Cis isomer: mp 58–60 °C; ^1H NMR ($CDCl_3$, 60 MHz) 0.92 (d, J = 6.6 Hz, 6 H, $(CH_3)_2CH$), 1.33 (s, 9 H, *t*-Bu), 1.5–2.1 (m, 1 H, $(CH_3)_2CH$), 2.59 (q, J = 2.4 Hz, 1 H, C_5-H), 4.02 (d, J = 2.4 Hz, 4 H, $C_{4,6}$-H), 4.17 (d, J = 5.2 Hz, 1 H, C_2-H) ppm. Anal. found C, 60.56; H, 10.20; S, 14.67.

***trans*-2-Isopropyl-5-(*tert*-butylsulfinyl)-1,3-dioxane (*trans*-2).** A solution of 3.92 g (22.7 mmol) of *m*-chloroperoxybenzoic acid in 50 mL of dichloromethane was added dropwise to a cold solution (−20 °C) of *trans*-2-isopropyl-5-(*tert*-butylthio)-1,3-dioxane (4.93 g, 22.6 mmol) in 30 mL of dichloromethane. The reaction mixture was stirred at this temperature for 1 h at room temperature overnight. The solution was then washed with saturated aqueous sodium bicarbonate (50 mL) and water (50 mL), dried ($MgSO_4$), and concentrated (rotary evaporator) to afford a colorless solid. Crystallization of this material from *n*-hexane gave 4.57 g (86% yield) of a crystalline solid: mp 83–85 °C; ^1H NMR in Tables II and IV; ^{13}C NMR in Table III. Anal. Calcd for $C_{11}H_{22}O_3S$: C, 56.38; H, 9.46. Found: C, 56.21; H, 9.44.

***cis*-2-Isopropyl-5-(*tert*-butylsulfinyl)-1,3-dioxane (*cis*-2).** A solution of *trans*-2-isopropyl-5-(*tert*-butylsulfinyl)-1,3-dioxane (1.0 g, 4.27 mmol) was dissolved in 60 mL of chloroform and the resultant mixture treated with 0.572 g (2 mmol) of boron trifluoride etherate. The solution was stirred at room temperature for 5 days, neutralized with 10% aqueous $NaHCO_3$, washed with water, dried ($MgSO_4$), and concentrated. The oil obtained was then separated by flash chromatography[16] (hexane/ethyl acetate, 70:30) into *trans*-**2** (155 mg) and *cis*-**2** (180 mg). The latter is a white, crystalline material: mp 114–116 °C, ^1H NMR in Tables II and IV; ^{13}C NMR in Table III. Anal. Calcd for $C_{11}H_{22}O_3S$: C, 56.38; H, 9.46. Found: C, 56.82; H, 9.69.

***cis*- and *trans*-2-*tert*-Butyl-5-(*tert*-butylthio)-1,3-dioxanes (*cis*- and *trans*-7).** 2-(*tert*-Butylthio)-1,3-propanediol (7.0 g, 42 mmol) and 3.67 g (42.6 mmol) of pivalaldehyde were allowed to react according to the procedure described above for the preparation of **1**. The desired product (as a mixture of cis and trans isomers, ca. 4:96) was formed in 85% yield (8.4 g) and was used without further purification for the preparation of *cis*- and *trans*-2-*tert*-butyl-5-(*tert*-butylsulfinyl)-1,3-dioxane.

***cis*- and *trans*-2-*tert*-Butyl-5-(*tert*-butylsulfinyl)-1,3-dioxane (*cis*- and *trans*-8).** A mixture of *cis*- and *trans*-2-*tert*-butyl-5-(*tert*-butylthio)-1,3-dioxanes (5.6 g, 24 mmol, ca. 4:96) was oxidized with 4.8 g (28 mmol) of *m*-chloroperoxybenzoic acid as described above in the preparation of *trans*-**2**. The mixture of sulfoxides obtained (5.0 g, 84% yield) was equilibrated with boron trifluoride as described above for the preparation of *cis*-**2** and separated by flash chromatography[16] (hexane/ethyl acetate, 60:40) to afford 0.85 g of the trans isomer and 1.15 g of the cis isomer. Trans isomer: mp 129–130 °C; ^1H NMR ($CDCl_3$, 90 MHz) 0.93 (s, 9 H, *t*-Bu-C_2), 1.30 (s, 9 H, *t*-Bu-S), 2.75–3.60 (m, 1 H, C_5-H), 3.85–4.45 (m, 5 H, $C_{2,4,6}$-H) ppm; ^{13}C NMR ($CDCl_3$, 22.49 MHz) 22.99 [$(CH_3)_3C$-S], 24.65 [$(CH_3)_3C$-C_2], 34.83 [$(CH_3)_3C$-C_2], 46.59 (C_5), 54.77 [$(CH_3)_3C$-S], 65.66 (C_4), 67.94 (C_6), 107.70 (C_2) ppm. Cis isomer: mp 158–160 °C; ^1H NMR ($CDCl_3$, 90 MHz) 0.91 (s, 9 H, *t*-Bu-C_2), 1.26 (s, 9 H, *t*-Bu-S), 2.60 (m, 1 H, C_5-H), 3.96 (dd, J_{gem} = −12.3 Hz, J_{gauche} = 3.3 Hz, 1 H, C_4-H_{ax}), 3.92–4.35 (m, 2 H, C_6-H), 4.67 (dm, J_{gem} = −12.3 Hz, 1 H, C_4-H_{eq}) ppm; ^{13}C NMR ($CDCl_3$, 22.49 MHz) 23.08 [$(CH_3)C$-S], 24.49 [$(CH_3)_3C$-C_2], 35.16 [$(CH_3)_3C$-C_2], 50.00 (C_5), 54.23 [$(CH_3)_3C$-S], 63.82 (C_4), 66.85 (C_6), 107.59 (C_2) ppm. Anal. Calcd for $C_{12}H_{24}O_3S$: C, 58.03; H, 9.74. Found for trans isomer: C, 58.11, H, 9.75. Found for cis isomer: C, 58.43; H, 9.86.

***trans*-2-Isopropyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*trans*-3).** A solution of *trans*-2-isopropyl-5-(*tert*-butylsulfinyl)-1,3-dioxane (220 mg, 0.94 mmol) and *m*-chloroperoxybenzoic acid (170 mg, 0.99 mmol) in 25 mL of chloroform was stirred at room temperature overnight. The solution was then washed with saturated aqueous sodium bicarbonate (25 mL) and water (25 mL), dried ($MgSO_4$), and concentrated (rotary evaporator) to give, after recrystallization from hexane/acetone (2:1),

(16) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

235 mg (ca. 100% yield) of colorless needles: mp 134–136 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) 0.92 (d, J = 7.2 Hz, 6 H, $(CH_3)_2CH$), 1.44 (s, 9 H, t-Bu), 1.75 (m, 1 H, $(CH_3)_2CH$), 3.4–4.5 (m, 6 H, $C_{2,4,5,6}$-H) ppm. Anal. Calcd for $C_{11}H_{22}O_4S$: C, 52.77; H, 8.86. Found: C, 52.85; H, 9.00.

***cis*-2-Isopropyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*cis*-3)** was similarly prepared from *cis*-2-isopropyl-5-(*tert*-butylsulfinyl)-1,3-dioxane (220 mg, 0.94 mmol). Recrystallization of the product from hexane/acetone (2:1) gave 315 mg (94% yield) of *cis*-**3**: mp 145–147 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) 0.95 (d, J = 6.6 Hz, 6 H, $(CH_3)_2CH$), 1.50 (s, 9 H, t-Bu), 1.65–2.05 (m, 1 H, $(CH_3)_2CH$), 3.01 (~t, J_{gauche} = 4.2 Hz, 1 H, C_5-H), 4.11 (dd, J_{gem} = −12.5 Hz, J_{gauche} = 4.2 Hz, 2 H, $C_{4,6}$-H_{ax}), 4.32 (d, J = 4.8 Hz, 1 H, C_2-H), 4.67 (~d, J_{gem} = −12.5 Hz, J_{gauche} ~0, 2 H, $C_{4,6}$-H_{eq}) ppm. Anal. Calcd for $C_{11}H_{22}O_4S$: C, 52.77; H, 8.86. Found: C, 52.78; H, 8.88.

***trans*-2-*tert*-Butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*trans*-9)** was similarly prepared from *trans*-2-tert-butyl-5-(tert-butylsulfinyl)-1,3-dioxane (251 mg, 1.0 mmol). Recrystallization of the product from hexane/acetone (2:1) gave 220 mg (82% yield) of the pure product: mp 195–196 °C; ^{1}H NMR in Tables II and IV; ^{13}C NMR in Table III. Anal. Calcd for $C_{12}H_{24}O_4S$: C, 54.52; H, 9.15. Found: C, 54.89; H, 9.16.

***cis*-2-*tert*-Butyl-5-(*tert*-butylsulfonyl)-1,3-dioxane (*cis*-9)** was similarly prepared from *cis*-2-*tert*-butyl-5-(*tert*-butylsulfinyl)-1,3-dioxane (230 mg, 0.92 mmol). Recrystallization of the product from hexane/acetone (2:1) gave 200 mg (82% yield) of the pure product: mp 177–178 °C; ^{1}H NMR in Tables II and IV; ^{13}C NMR in Table III. Anal. Calcd for $C_{12}H_{24}O_4S$: C, 54.52; H, 9.15. Found: C, 54.40; H, 8.85.

Electrochemical Measurements. Cyclic voltammetry was performed on a PAR 362 scanning potentiostat equipped with the Houston 200 XY recorder.

Cyclic voltammetry was carried out in 0.1 M tetramethylammonium tetrafluoroborate in acetonitrile at a scan rate of 200 mV/s. The working electrode was a platinum flag with an area of 0.35 cm^2. The counter electrode was also a platinum flag, and the reference electrode was Ag/0.1 M $AgNO_3$ in CH_3CN throughout the experiments. The platinum electrode was cleaned by burning before each experiment.

Equilibrations and Analysis. Equilibrium was approached from both sides; boron trifluoride etherate was the catalyst: 25–30 mg of the dioxane was placed in a 20-mL ampule and dissolved in 10 mL of chloroform before the addition of two to three drops of boron trifluoride etherate. The ampule was sealed and submerged in a constant-temperature bath until equilibrium was reached. Quenching was effected by pouring the equilibrating solution into aqueous sodium bicarbonate. The dioxanes were then extracted with chloroform, dried, and evaporated, and the progress of the equilibration was conveniently monitored by ^{1}H NMR spectroscopy. Quantitative product analysis was carried out by vapor-phase chromatography (on a 6 ft × $^1/_8$ in. 10% UC-W98 column on Chromosorb W 80–100 mesh, at 140 °C) except in the case of the (involatile) sulfoxides and sulfones where a less accurate analysis was obtained by integration of appropriate peaks in the ^{1}H NMR spectrum (e.g., H_5). In the case of the sulfones, the analysis was effected in the presence of Eu(fod)$_3$ to ensure adequate separation of the *tert*-butyl peaks used in the analysis.

Structural X-ray Analysis. A crystal measuring approximately 0.03 × 0.27 × 0.29 mm was used to collect intensity data on a Nicolet R3m four-circle diffractometer within the angular range $3.0 < 2\theta < 45°$, using monochromatic Mo Kα radiation and ω-scan mode. Least-squares refinement of the setting angles of 25 reflections with a good distribution throughout reciprocal space provided the unit cell dimensions: monoclinic, a = 23.139 (7), b = 6.034 (3), c = 10.553 (4) Å; β = 97.33 (3)°; V = 1461.5 Å^3; F_{000} = 576; μ(Mo Kα) = 2.13 cm^{-1}; Z = 4; d_{calcd} = 1.199 g·cm^{-3}. Systematic absences indicated the monoclinic space group Cc. Of the 963 independent reflections measured, 191 had intensities less than $3\sigma(F_o)$ and were not used in the refinement. The remaining 772 reflections were corrected for Lorentz and polarization effects and used to solve and refine the structure.

Positions of all non-hydrogen atoms were located by using the direct-methods program available as part of the SHELXTL package.[17] Idealized hydrogen positions were calculated and tied to the associated non-hydrogen positions through a riding model. Final refinement of 17 non-hydrogen atoms using anisotropic thermal parameters and 24 hydrogen atoms using fixed isotropic thermal parameters, U = 0.06 Å^2, gave residual values of R_1 = 0.0613 and R_2 = 0.0576, where $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$ and $R_2 = [\sum_w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$.

Acknowledgment. This project was supported in part by the National Science Foundation (Grant INT-8312711) and CONACYT (México, Grant PCCBBEU-020165) as a result of the Cooperative Science Program between U.S. and México and in part by NSF Grant CHE-8314169. R.M. is grateful to Universidad Nacional Autônoma de México for economic support during his stay at Instituto Politécnico Nacional. The ^{17}O spectra were recorded by Dr. David Harris.

Registry No. *cis*-**1**, 109151-25-9; *trans*-**1**, 109151-28-2; *cis*-**2**, 109151-26-0; *trans*-**2**, 109151-29-3; *cis*-**3**, 109151-27-1; *trans*-**3**, 109151-30-6; *cis*-**7**, 109151-34-0; *trans*-**7**, 109151-35-1; *cis*-**8**, 109181-88-6; *trans*-**8**, 109151-36-2; *cis*-**9**, 109151-31-7; *trans*-**9**, 109151-32-8; diethyl (*tert*-butylthio)malonate, 76000-58-3; oxygen-17, 13968-48-4; *tert*-butyl mercaptide, 20733-19-1; diethyl chloromalonate, 14064-10-9; 2-(*tert*-butylthio)-1,3-propanediol, 109151-33-9; isobutyraldehyde, 78-84-2; pivaldehyde, 630-19-3.

Supplementary Material Available: Listings of anisotropic thermal parameters for all non-hydrogen atoms, isotropic thermal parameters for hydrogen atoms, bond distances, bond angles, torsional angles, and the Cartesian coordinates and two ORTEP drawings of **9** (7 pages); observed and calculated structure factors (5 pages). Ordering information is given on any current masthead page.

(17) Sheldrick, G. M. *Nicolet SHELXTL Operations Manual*; Nicolet XRD Corp.: Cupertino, CA, 1981.