Bu)$_3$H.[30b] No reaction was observed with NaBH$_4$ in glyme (75°, 1.5 hr); only low yields of **2** resulted from reactions with Zn(BH$_4$)$_2$ or LiAl(O-*t*-1=)$_3$H. Treatment of ketosilane **5** with triisobutylaluminum (TIBAL)[30c] in pentane gave only 4-octanone and isobutyltrimethylsilane after work-up; when the reaction was quenched with acetic anhydride before aqueous work-up, a mixture of enol acetates was formed, suggesting that an aluminum enolate had been formed.[31]

(30) (a) J. M. Lalancette and A. Freche, *Can. J. Chem.*, **48**, 2366 (1970); (b) H. C. Brown and S. Krishnamurthy, *J. Am. Chem. Soc.*, **94**, 7159 (1972); (c) TIBAL has been shown to be a very selective reducing agent for acyclic α-ketols; see J. A. Katzenellenbogen and S. B. Bowlus, *J. Org. Chem.*, **38**, 627 (1973).

(31) Aluminum enolates have been formed from silyl enol ethers; see L. I. Zakharkin and L. A. Savina, *Izv. Akad. Nauk SSSR*, 378 (1961).

(32) (a) (RO)$_2$B–C–C–Br, D. S. Matteson and J. D. Liedtke, *J. Am. Chem. Soc.*, **87**, 1526 (1965); (b) XHg–C–C–OR, W. Kitching, *Organomet. Chem. Rev.*, **3**, 61 (1968), and references cited therein; (c) Me$_3$Si–C–C–Br, A. W. P. Jarvie, A. Holt, and J. Thompson, *J. Chem. Soc. B*, 852 (1969); see also R. B. Miller and T. Reichenbach, *Tetrahedron Lett.*, 543 (1974); (d) Me$_3$Si–C–C–OMe, see ref 19b; (e) Ph$_3$Sn–C–C–OH, D. D. Davis and C. E. Gray, *J. Org. Chem.*, **35**, 1303 (1970).

(33) C. Trindle, J.-T. Hwang, and F. A. Carey, *J. Org. Chem.*, **38**, 2664 (1973).

(34) In the previous cases where mixtures of cis and trans olefinic products were observed,[8,9,13-15] the intermediate β-hydroxyalkylsilane (usually not isolated) was formed by a similar reaction of an α-silyl organometallic reagent with a carbonyl compound.

(35) D. J. Cram and F. A. Abd Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952). See also J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions," Prentice-Hall, Englewood Cliffs, N.J., 1971.

(36) The dibromides resulting from the addition of bromine to trans vinylboranes undergo elimination reactions which are reported to give either cis or trans vinyl bromides; see H. C. Brown, D. H. Bowman, S. Misumi, and M. K. Unni, *J. Am. Chem. Soc.*, **89**, 4531 (1967).

(37) R. G. Jones and H. Gilman, *Org. React.*, **6**, 339 (1951).

(38) The following columns were used for VPC analysis: (a) 5% SE-30 on Chromosorb W, 5 ft × 0.25 in.; (b) 10% DC-550 on Chromosorb W, 10 ft × 0.25 in.; (c) 3% SE-30 on Varaport 30, 5 ft × 0.25 in.

(39) In the elimination reactions, the ratios and yields of 4-octene were determined by VPC using an internal standard. Authentic samples of *cis*- and *trans*-4-octene for comparison were obtained from Chem Samples, Columbus, Ohio. (a) *n*-Octane was used as the internal standard, using a 20 ft × 0.25 in. column packed with 25% Carbowax 20M on Chromosorb W; typical retention times at 70° were 16.4 min (octane), 20.8 min (*trans*-4-octene), 22.7 min (*cis*-4-octene). (b) *n*-Butylbenzene was used as the internal standard; yields were determined on a 10 ft × 0.25 in. column packed with 10% SE-30 on Chromosorb W [typical retention times at 100°: 3.0 min (octenes), 12.3 min (*n*-butylbenzene)]; cis:trans ratios were determined on a 18 ft × 0.25 in. column packed with 15% Carbowax 20M on GCR [typical retention times at 75°: 10.35 min (*trans*-4-octene), 11.05 min (*cis*-4-octene)].

(40) A crystal of the indicator bipyridyl was present in this solution; in other similar experiments, the bipyridyl was omitted.

(41) This spectrum was taken of material of comparable purity from a separate but similar experiment.

(42) An aliquot taken after 5 min showed the reaction to be only 40% complete.

(43) An aliquot taken after 1 hr showed the reaction to be 79% complete.

Oxides of 1,3-Dithiane and 1,3,5-Trithiane. The Diamagnetic Anisotropy of Carbon–Sulfur Bonds

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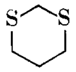
Contribution from the Departments of Chemistry, Northwestern University, Evanston, Illinois 60201, and the University of Virginia, Charlottesville, Virginia 22901. *Received July 15, 1974*

Abstract: The 270-MHz proton spectrum of 1,3-dithiane 1-oxide (**2**) reveals the presence of two isomers, in the ratio 84/16 at −81.5°. Configurational criteria developed in thiane systems confirm that the major isomer is the equatorial oxide. The activation parameters for ring reversal in 1,3-dithiane 1,1-dioxide (**3**) have been measured by the complete line-shape method: E_a = 11.2 kcal/mol, log A = 14.1, $\Delta H^\ddagger$ = 10.6 kcal/mol; $\Delta S^\ddagger$ = 3.8 gibbs, $\Delta G^\ddagger$ (−70.5°) = 9.8 kcal/mol. The proton spectrum of 1,3,5-trithiane 1-oxide (**7**) is invariant with temperature, so that only one isomer, probably with the oxide equatorial, must be present. The 90-MHz spectrum of the 2 protons of 1,3-dithiane *cis*-1,3-dioxide (**5**) changes from an AB quartet at room temperature to a broad singlet at −61°. This reversal of the usual direction of spectral changes is attributed to dimer formation at low temperature in the diequatorial form. Long-range zigzag couplings enable the axial and equatorial nature of the resonances to be identified for the 2 protons in all four of these molecules. The relative order of these resonances can be explained by a model in which the overall diamagnetic anisotropy of the C–S and C–(SO$_2$) bonds has the opposite sign to that of the C–C, C–O, and C–(SO) bonds. This model also explains the order of the axial–equatorial resonances in other thiane and selenane systems.

The conformational analysis of ring systems containing sulfur has been profitable not only because these heterocycles provide an interesting contrast to carbocyclic systems but also because of the widespread occurrence of sulfur heterocycles in nature. The present study is concerned with the conformational properties of the oxides of thiane systems that contain two or three sulfur atoms at alternate ring positions. 1,3-Dithiane (**1**) has one monoxide (**2**) and three dioxides (**3–5**). The monoxide (**2**), furthermore, has axial and equatorial modifications (eq 1). In the parent sulfide, thiane 1-oxide (**6**), the axial oxide form is favored at −90° by 175 cal/mol (62/38).[3] Equilibration methods[4] and comparison with the properties of materials whose configuration has been determined by crystallography[5] have indicated that this conformational preference is reversed in 1,3-dithiane 1-oxide and that the equatorial isomer (**2e**) is favored. The unsubstituted form (**2**), however, has not previously been studied.[6]



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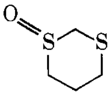

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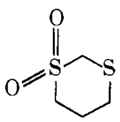

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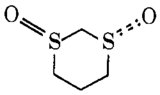

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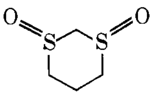

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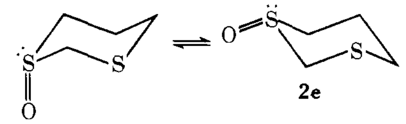
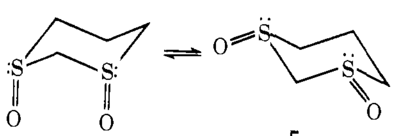


2a **2e** (1)

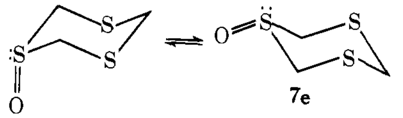
The 1,1-dioxide (**3**) and the *trans*-1,3-dioxide (**4**) of 1,3-dithiane also undergo ring reversal, but by symmetry have an equilibrium constant of unity. The *cis*-1,3-dioxide (**5**)


5a 5e

(2)

again has the choice of two conformations (eq 2). The conformational analysis of all these 1,3-dithianes differs from that of 1,2-dithianes[8] and cyclic sulfites,[9] since the present system lacks ring bonds between two heteroatoms. The 1,4-dithiane oxides, which have been studied briefly,[9,10] also differ from the present system, because of the absence of 1,3-interactions between heteroatoms.

In order to study the conformational preference of the sulfoxide group in the presence of another sulfide or sulfoxide group at the 3 position, we have examined the 270-MHz proton spectra of **2–5** as a function of temperature. The protons at the 2 position in these molecules are nearly isolated by the adjacent sulfur atoms from coupling with the remaining protons in the molecule. The chemical-shift difference and the coupling constant between these geminal atoms offer handles for configurational assignments. A long-range (zigzag) equatorial–equatorial coupling permits unambiguous assignment of the axial or equatorial identity of the 2 protons. The results demonstrate that the "normal" axial preference of sulfoxide, as in thiane 1-oxide, does not survive the introduction of a sulfide or sulfoxide functionality at the 3 position. We have also examined 1,3,5-trithiane 1-oxide (**7**, eq 3) and found that only a single conformation,


7e 7a

(3)

presumably with the oxide equatorial, is present. Examination of the "sense" of the chemical-shift difference between the 2-axial and 2-equatorial protons in **2–5** and **7** gives information concerning the overall diamagnetic anisotropy of the C–S, C–(SO), and C–(SO_2) bonds. The conclusions clarify a number of puzzling chemical-shift observations made in previous studies of sulfur-containing heterocycles.

Results

At room temperature, the 270-MHz proton spectrum of 1,3-dithiane 1-oxide (**2**) consists of an AB quartet centered at δ 3.78 due to the 2 protons, and three multiplets centered at 3.28, 2.60, and 2.24 due to the remaining protons (Figure 1). Ring reversal is slowed as the temperature is lowered. The spectrum passes through coalescence at about −59° and achieves the slow-exchange limit by −81° (Figure 1). The 2-proton resonance at low temperature contains two AB quartets, corresponding to the axial-oxide and equatorial-oxide conformations (eq 1). The high-field halves of the two quartets are superimposed. The higher intensity quartet is assigned to the equatorial conformation (see Discussion). The low-field doublet of the major isomer is assigned to the equatorial 2 proton because of the long-range W coupling to a 4- or 6-equatorial proton. The calculated spectra for the 2 protons at fast and slow exchange are also given in Figure 1. In order to achieve the proper spectral averaging, the low-field doublet of the higher intensity quartet (the equatorial proton of the equatorial-oxide form) must be averaged with the high-field doublet of the lower intensity quartet (the axial proton of the axial-oxide form). Similarly, the high-field doublet of the higher intensity quartet is averaged with the low-field doublet of the lower intensity quartet. This "crossover averaging" is quite common in double-AB spectra of this sort,[3,11] since the axial protons of one form must exchange with the equatorial protons of the other form. The remaining resonances in the slow-exchange spectrum have not been definitely identified. By direct integration the ratio of equatorial-to-axial conformers was found to be 84/16, corresponding to $\Delta G° = 630$ cal/mol at −81.5°.

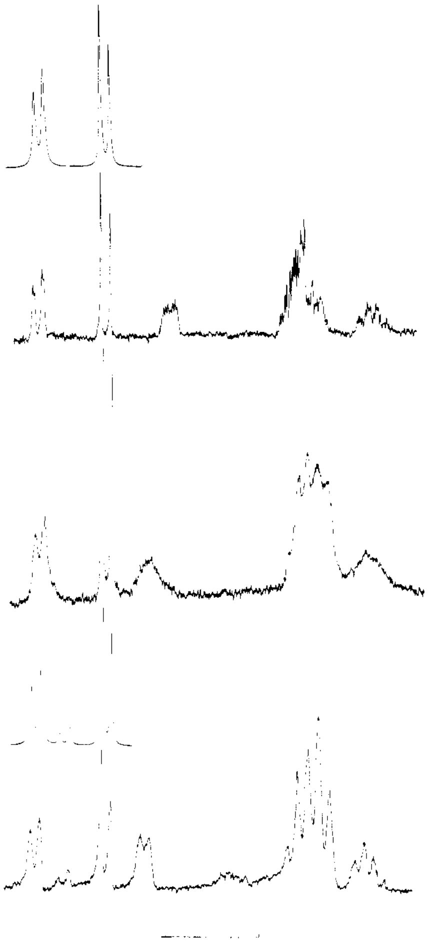


Figure 1. The observed 270-MHz proton spectrum of 1,3-dithiane 1-oxide (**2**) in $CHClF_2$ at +19, −59, and −81.5° (top to bottom). The calculated fast-exchange (top) and slow-exchange (bottom) spectra of the 2-proton resonance are shown as insets. The calibration bar represents 135 Hz.

The 90-MHz proton spectrum of 1,3-dithiane 1,1-dioxide (**3**) displays a singlet at δ 4.1 due to the 2 protons (Figure 2) and two multiplets at 3.3 and 2.6 from the remaining protons. The 2 protons are equivalent at this temperature because of rapid ring reversal. As the temperature is lowered, the 2-proton resonance passes through coalescence (−70.5°) and becomes an AB quartet at the slow-exchange limit (−95°). It is noted that the high-field portion of the quartet is broader in this case. This resonance is therefore assigned to the equatorial 2 proton, because of the expected equatorial–equatorial long-range W coupling. Complete line-shape analysis of the spectral changes, including allowance for the long-range coupling through use of different relaxation times, was carried out at nine temperatures between −55 and −83°. The Arrhenius plot from these kinetic data produced the following activation parameters: $E_a = 11.2$ kcal/mol, $\log A = 14.1$, $\Delta H^\ddagger = 10.6$ kcal/mol, $\Delta S^\ddagger =$ 3.8 gibbs, $\Delta G^\ddagger$ (25°) = 9.5 kcal/mol. The correlation coefficient was 0.997. The rate constant at coalescence (k_c) was computed from eq 4, in which ν_A and ν_B are the respective chemical shifts and J_{AB} is the coupling constant of the AB

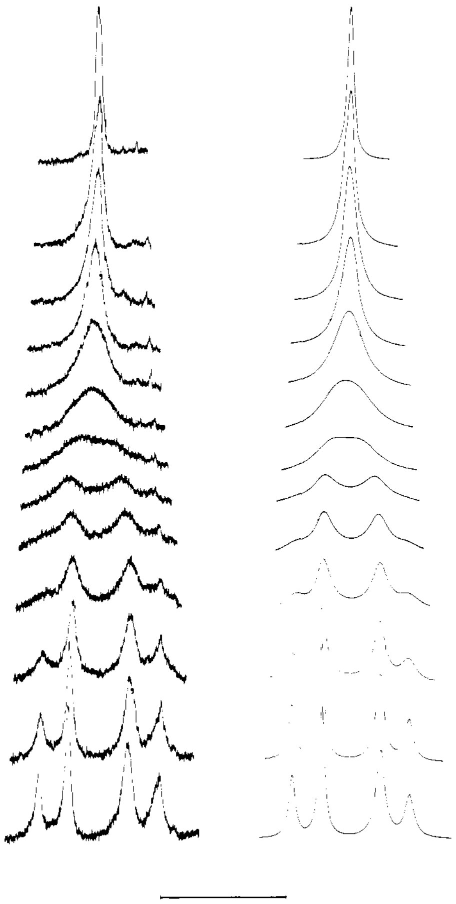


Figure 2. The observed (left) and calculated (right) 90-MHz spectrum of the 2 protons of 1,3-dithiane 1,1-dioxide (3) in CD_3OD as a function of temperature. From top to bottom the temperatures (lifetimes in sec) are +27 (fast-exchange limit), −51 (0.0010), −55 (0.0017), −60 (0.0025), −65 (0.0050), −68 (0.0080), −70.5 (0.010, coalescence), −73.5 (0.020), −77 (0.030), −80 (0.045), −83 (0.10), −89 (0.8), and −95° (slow-exchange limit). The points at −51 and −89° were not included in the Arrhenius plot. A small peak on the upfield side of the quartet is an impurity. The calibration bar represents 60 Hz.

$$k_c = \frac{\pi}{\sqrt{2}}[(\nu_A - \nu_B)^2 + 6J_{AB}^2]^{1/2} \qquad (4)$$

system at the slow-exchange limit. With 39.6 Hz for $\Delta\nu$ and 14.4 Hz for J, k_c was found to be 118 sec^{-1}. From transition-state theory (eq 5), the free energy of activation at co-

$$\Delta G_c^{\ddagger} = RT \ln (kT/k_c h) \qquad (5)$$

alescence (−70.5°) was calculated from k_c to be 9.8 kcal/mol, in good agreement with the value from the complete line-shape analysis.

Of the two configurational isomers of 1,3-dithiane 1,3-dioxide, the trans form (**4**) was found to be too insoluble for low-temperature studies. The cis form (**5**), however, produced good spectra down to −70° in SO_2. The 90-MHz proton spectrum at room temperature exhibited a well-resolved AB quartet centered around δ 4.2 at room temperature, due to the 2 protons, and a complicated multiplet in the 2.5–3.5 range from the remaining protons. The lower field part of the AB quartet was identified as the equatorial resonance by the clean long-range coupling from two protons elsewhere in the molecule to produce a triplet. The cis isomer (**5**) can exist as two nonequivalent conformations (eq 2). If the equilibrium is biased entirely toward one form, however, the spectrum should not change as the temperature is lowered. On the other hand, if both forms are significantly populated, lowering of the temperature should freeze out ring reversal and produce separate resonances at the slow-exchange limit. Neither of these expectations was realized (Figure 3). As the temperature was lowered, the AB quartet slowly collapsed to a singlet, in the reverse of the familiar A_2-to-AB transformation illustrated in Figure 2. We interpret this phenomenon not as a kinetic process of coalescence but simply as a decrease in the AB chemical-shift difference with temperature, as the result of an equilibrium shift (vide infra). There is no evidence for the presence of more than one conformation, and at present we favor the diequatorial form. The spectrum broadens appreciably below −61°, since the solute begins to come out of solution.

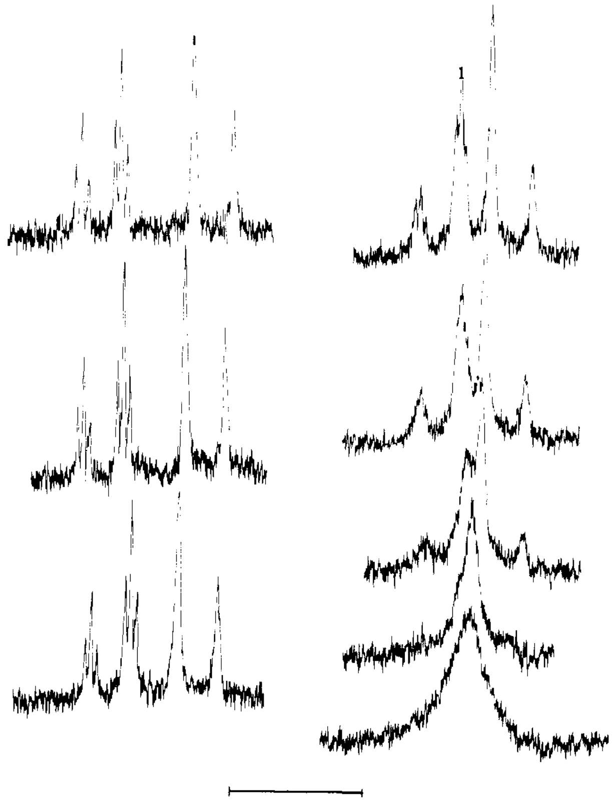


Figure 3. The 90-MHz spectrum of the 2 protons of 1,3-dithiane *cis*-1,3-dioxide (5) in SO_2 as a function of temperature (+27, +9, −11, −30, −42, −51, −61, and −70°, top left to bottom right). The calibration bar represents 40 Hz.

The proton spectrum of 1,3,5-trithiane 1-oxide (**7**), which is almost unintelligible at 90 MHz, proved to be made up of two AB quartets when observed at 270 MHz (Figure 4). The more intense quartet ($\Delta\nu$ = 0.23 ppm, J = 13.6 Hz), from the 2 and 6 protons, is centered at δ 3.8; the less intense quartet ($\Delta\nu$ = 0.55 ppm, J = 14.6 Hz), from the 4 protons, is centered at 3.4. The high-field half of the 4-proton resonance and the low-field half of the 2,6-proton resonance are broader than the other half of their respective quartets and hence must correspond to the equatorial protons. The long-range coupling is resolved as a doublet splitting in the more intense (2,6-proton) quartet. The proton spectrum of **7** remained unchanged down to −70°, the limit of solubility. We therefore conclude that only one conformer, probably with the oxide equatorial, is present.

Discussion

Sulfoxide Configuration. Three criteria have been developed for determining the axial or equatorial nature of the oxygen on sulfur by NMR spectroscopy.[3,11] The protons α to sulfur in an equatorial isomer generally have the larger geminal chemical-shift difference, the smaller coupling constant, and the lower field quartet midpoint. On the other hand, in the axial isomer these protons have the smaller chemical-shift difference, the larger coupling constant, and the higher field midpoint. Thus for thiane 1-oxide, in the axial isomer $\Delta\nu = 0.48$ ppm and $J = 13.7$ Hz, and in the equatorial isomer $\Delta\nu = 0.87$ ppm and $J = 11.7$ Hz. Although the coupling constant criterion has invariably been found to hold, strong local substituent effects can override the chemical-shift criteria.[11] Caution must therefore be exercised in applying the latter criteria to heavily substituted systems. It is also ill advised to attempt a configurational determination unless *both* isomers are observed, since changes of atoms within the ring can have a large effect both on chemical shifts and coupling constants.

The first question we wanted to answer was whether these configurational criteria apply to the 1,3-dithiane system. Previous work[4,5] established that substituted 1,3-dithiane 1-oxides exhibit a preference for the equatorial conformation. It was reasonable to assume, therefore, that the unsubstituted system (**2**) has a similar preference. The more intense AB quartet from the 2 protons in **2** has $\Delta\nu = 0.36$ ppm, $J = 12.6$ Hz, and appears at lower field. The less intense quartet has $\Delta\nu = 0.26$ ppm, $J = 13.5$ Hz,[12] and appears at higher field. All three criteria are in agreement with a favored equatorial form and therefore probably may be applied generally to 1,3-dithiane systems.

Establishment of the configuration of the oxide functionalities in 1,3,5-trithiane 1-oxide (**7**) and 1,3-dithiane *cis*-1,3-dioxide (**5**) is more problematic because in each case the spectra exhibit resonances from only one isomer. For the trithiane oxide, the coupling constant between the protons α to the sulfoxide functionality is 13.6 Hz. Although this value is very close to that of the axial-oxide isomer of 1,3-dithiane 1-oxide (13.5 Hz), such a comparison is dangerous. The coupling constant for the equatorial-oxide isomer of **2**, in fact, is only 0.9 Hz smaller (12.6 Hz). It is likely that other factors can become important when small differences are being compared. Thus, the coupling constant between the 2 protons in 1,3,5-trithiane itself (14.5 Hz)[13] is slightly larger than that of 1,3-dithiane (14.2).[14] Without having both isomers of **7** available, no firm conclusion about the oxide configuration can be drawn from the NMR data. It seems reasonable, however, that the trend of increasing amounts of the equatorial isomer in going from thiane 1-oxide (38%) to 1,3-dithiane 1-oxide (84%) will be continued in 1,3,5-trithiane 1-oxide (>95%). This point cannot be proved by the present data.

Similarly, only one isomer is observed for 1,3-dithiane *cis*-1,3-dioxide (**5**). The geminal coupling constant of this isomer alone (12.5 Hz) is insufficient to base a configurational proof. The large dipole-dipole repulsion expected in the diaxial isomer, however, leads us to favor the diequatorial form for this molecule. The most unusual aspect of the spectrum of **5** is the coalescence of the AB quartet from the 2 protons as the temperature is *lowered* (Figure 3). The coupling constant remains essentially constant. We interpret this observation as resulting from an equilibrium between monomer and dimer, with a larger proportion of dimer at lower temperatures. We originally considered the possibility of dimer formation in the case of thiane 1-oxide itself[3] but were able to exclude it on the basis of molecular weight measurements. Dimers have been found to contribute significantly to the spectra of 2-thiaindan 2-oxide.[15] If the disulfoxide **5** exists as an equilibrium between monomer and dimer, then the observed chemical-shift difference between the α protons is a weighted average. The spectra of **5** indicate that $\Delta\nu$ for the dimer must be almost zero, since the observed value dwindles from 0.35 ppm at room temperature to almost nothing at −61°. If the dimer has the structure given by **8**, the 2-equatorial protons do reside in a much more shielded position than in the monomer. The preference of 1,3-dithiane *cis*-1,3-dioxide (**7**) to exist as a dimer, but of thiane 1-oxide (**6**) to exist as a monomer (see structures III and IV in ref 3), must result from the ability of **7** to form two attractive dipolar interactions in the dimer (**8**), whereas **6** can form only one. The more favorable enthalpy of dimer formation can then overcome the unfavorable entropy of formation. The situation is similar to the preference of organic acids for the dimer in the gas phase (two hydrogen bonds) but of alcohols for the monomer (one hydrogen bond per pair).

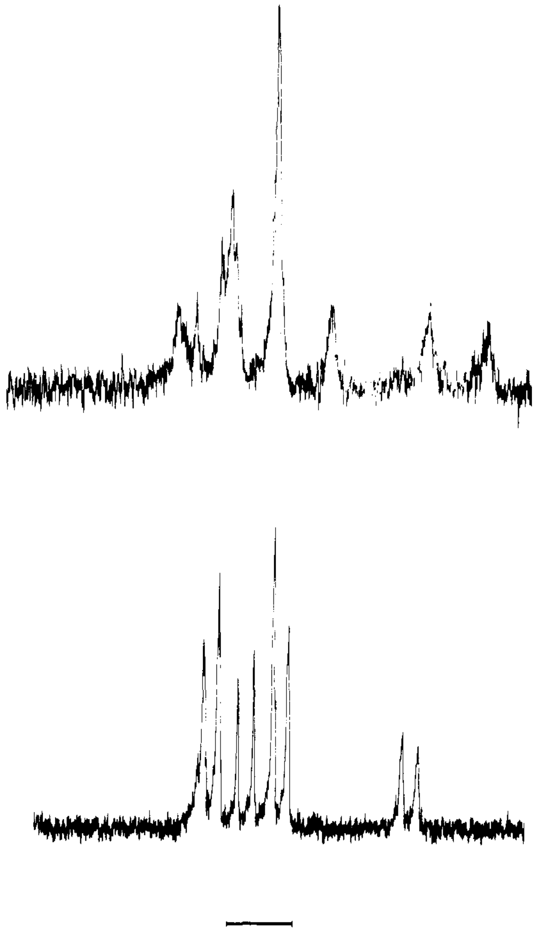
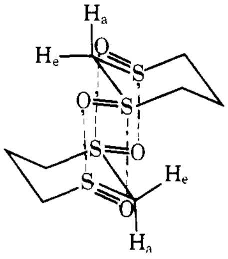


Figure 4. The 90- (top) and 270-MHz (bottom) proton spectra of 1,3,5-trithiane 1-oxide (**7**) in $CHClF_2$. The calibration bar represents 16 Hz for the top spectrum and 60 Hz for the bottom spectrum.



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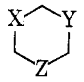
Anisotropy of the Carbon–Sulfur Bond. It has generally been accepted that the major contribution to the chemical-shift difference between geminal axial and equatorial protons is the anisotropy of the ring bonds that are β to the CH_2 group.[16] In the sulfides and selenides that have been studied here and previously,[3,17,18] there is quite a variability in the magnitude and even the sign of the chemical-shift difference. In pentamethylene heterocycles it is sometimes

Table I. Sign and Magnitude of the Geminal Chemical-Shift Difference between Protons α to a Heteroatom



X	Y	Z	$\Delta\nu$,[a] ppm	Source
CH_2	CH_2	CH_2	+0.48	*b*
O	CH_2	CH_2	+0.50	*c*
S	CH_2	CH_2	−0.19[d]	*c*
Se	CH_2	CH_2	−0.30[d]	*c*
Te	CH_2	CH_2	−0.75[d]	*c*
ax-SO	CH_2	CH_2	+0.48	*e*
eq-SO	CH_2	CH_2	+0,87	*e*
SO_2	CH_2	CH_2	<0.1	*f*
ax-SeO	CH_2	CH_2	+0.25	*c*
eq-SeO	CH_2	CH_2	+0.80	*c*
SeO_2	CH_2	CH_2	<0.1	*c*
S	S	CH_2	−0.77	*g*
ax-SO	S	CH_2	+0.26	This work
eq-SO	S	CH_2	+0.36	This work
SO_2	S	CH_2	−0.44	This work
eq-SO	eq-SO	CH_2	+0.35[h]	This work
S	O	CH_2	−0.14	*g*
ax-SO	O	CH_2	+0.38	*i*
eq-SO	O	CH_2	+1.10	*i*
O	O	CH_2	+0.31	*g*
S	S	S	−0.76[d]	*j*
eq-SO	S	S	+0.23[k]	This work
eq-SO	S	S	−0.55[l]	This work

[a] A positive sign indicates that the axial proton is at higher field. [b] F. A. Bovey, F. P. Hood 111, E. W. Anderson, and R. L. Kornegay, *J. Chem. Phys.*, **41**, 2041 (1964). [c] Reference 18. [d] Sign predicted; others determined by W coupling. [e] Reference 3. [f] Reference 17. [g] Reference 14. [h] Variable chemical-shift difference. [i] Reference 7. [j] Reference 13. [k] Protons between SO and S. [l] Protons between S and S.

difficult to determine whether the axial or the equatorial proton resonates at higher field. The 1,3-dithianes are particularly well suited to study this property because the sign of the chemical-shift difference for the 2 protons is not in doubt. There are no vicinal couplings, because of the sulfur atoms on either side, so that any broadening or splittings must be due to long-range couplings to the 4 and 6 protons. The largest such coupling must be the W-pathway coupling between the 2-equatorial and the 4- or 6-equatorial protons. The zigzag five-bond coupling to the 5-equatorial proton may also be significant.[19] The 2-equatorial proton therefore may always be identified as the broader or more widely split half of the AB spectrum at the slow-exchange limit.[20] The largest W coupling in the present study is observed for protons α to a sulfoxide group. Thus the equatorial protons next to $-S-$ or $-SO_2-$ give rise only to broadened resonances, but those next to $-SO-$ have resonances that are well split. An equatorial proton next to one sulfoxide group, as in **2** and **7**, gives rise to a doublet resonance (Figures 1 and 4), whereas an equatorial proton between two sulfoxides, as in **5**, gives rise to a triplet resonance (Figure 3). The sulfoxide group thus shares with the carbonyl group the ability to enhance the W coupling.

For some of the cases in the present study the 2-axial proton resonates at higher field than the 2-equatorial proton, as in **2** and **5**, and for others it is at lower field, as in **3**. We will refer to the former case as a positive (+) chemical-shift difference ($\Delta\nu$), and to the latter as a negative (−) chemical-shift difference. From examination of a large number of group 6 heterocycles (Table I), a pattern emerges that can be interpreted empirically in terms of the sign and magnitude of the overall diamagnetic anisotropy ($\chi_L - \chi_T$) of the β bonds. It has been suggested that the sign of the C–S anisotropy is opposite to that of the C–C anisotropy.[21] The results in Table I can be understood in terms of this assignment, along with the further assignments that the C–O and C–(SO) anisotropies have the same sign and the C–(SO_2) the opposite sign to that of the C–C bond.

From the long-range coupling in 1,3-dithiane[14] it is readily seen that $\Delta\nu$ must have a negative sign, in agreement with the assigned sense of the C–S anisotropy. The chemical-shift difference between the 2 protons in 1,3-dithiane 1-oxide (**2**) has opposing contributions from the C–S and the C–(SO) bonds. That the latter is dominant can be seen from the values of $\Delta\nu$ for thiane and thiane 1-oxide. For thiane, $\Delta\nu$ is small and probably negative, whereas for the oxide it is large and positive for both isomers.[3] The common (positive) sign for the two isomers of **2** (eq 1) follows from the observed crossover averaging of chemical shifts. When interconverting isomers have values of $\Delta\nu$ with the opposite sign, there cannot be crossover averaging. The positive contribution from the C–(SO) bond outweighs the negative contribution from the C–S bond, so that $\Delta\nu$ has the "normal" positive value, and the axial protons are observed at higher field. It is for this reason that the configurational criteria discussed in the previous section hold. Had the C–S contribution outweighed the C–(SO) contribution, the chemical-shift criteria would have been altered.

In 1,3-dithiane 1,1-dioxide (**3**), the contributions from the C–S and C–(SO_2) bonds are reinforcing, so that $\Delta\nu$ is relatively large and negative. The magnitude of the C–(SO_2) anisotropy must, however, be smaller than that of the C–S, since the values of $\Delta\nu$ in 1,3-dithiane and 1,3,5-trithiane are even larger than in **3**. In 1,3-dithiane *cis*-1,3-dioxide (**5**), the two C–(SO) bonds produce a positive $\Delta\nu$, but the absolute magnitude is meaningless because of the monomer-dimer equilibrium. In 1,3,5-trithiane 1-oxide (**7**), the C–(SO) contribution again outweighs the C–S anisotropy, so that $\Delta\nu$ for the 2 protons has a positive sign. The value of $\Delta\nu$ for the 4 protons, on the other hand, is determined by two C–S bonds, so it is large and negative. It is for this reason that the two sets of methylene protons in the molecule have $\Delta\nu$ values of opposite sign (Figure 4).

This approach to an interpretation of the sign and magnitude of chemical-shift differences in group 6 heterocycles clarifies some long-standing, unexplained observations that we made in earlier studies. In the group 6 pentamethylene heterocycles (tetrahydropyran, thiane, selenane, tellurane), $\Delta\nu$ is large for the oxygen heterocycle, achieves a minimum at sulfur, and increases through selenium to quite a large value for tellurium (Table I).[17,18] Comparison of the long-range couplings of the 2 protons in the spectra of 1,3-dioxane and 1,3-dithiane shows that the C–O and C–S anisotropies must be opposite in sign. Thus for the pentamethylene heterocycles, there should be a change of sign between oxygen and sulfur, and a slowly increasing magnitude of the anisotropy for the C–Se and C–Te bonds. The value of $\Delta\nu$ for the 2 protons in thiane 1,1-dioxide[3,17] and selenane 1,1-dioxide[18] was observed to be essentially zero. No splitting was found in the slow-exchange limit. Apparently the anisotropies of the C–C bond and the C–(SO_2) or C–(SeO_2) bonds are nearly equal in magnitude but opposite in sign. The effects of the two bonds therefore cancel each other out. The value of $\Delta\nu$ for the γ protons in these molecules is determined by two C–C bonds, so that a quite normal value of $\Delta\nu$ was observed.[3,17,18]

This qualitative approach unfortunately cannot be extended to a quantitative level. An attempt at developing a least-squares regression analysis proved to be fruitless. The anisotropies in pentamethylene heterocycles cannot be brought over to the 1,3-diheterocycles, because the geometries of these two types of molecules are quite different.[22] Thus the positive value of $\Delta\nu$ in tetrahydropyran is larger than the negative value in thiane, but the negative value in

1,3-dithiane is larger than the positive value in 1,3-dioxane (Table I). In all the systems both the angular portion ($3 \cos^2 \theta - 1$) and the anisotropy ($\chi_L - \chi_T$) are important, so that quantitative correlations based entirely on the latter cannot be made. The geometries, however, are sufficiently similar that we can draw valid qualitative conclusions entirely on the basis of the sign of the anisotropy.

It should be noted that all of the examples listed in Table I refer to methylene groups on the heteroatom end of the C–X bond. Because the X group, with its lone pairs and/or substituents, is expected to have an appreciable direct contribution to what we have called the "overall" diamagnetic anisotropy of the C–X bond, distinct effects may be observed for methylene groups at opposite ends of the bond, i.e., for C–X–CH_2 and CH_2–C–X. Any electric-field effect could increase this distinction. Our conclusions apply only to the C–X–CH_2 case.

Summary

Ring reversal may be frozen out in 1,3-dithiane 1-oxide (**2**) and 1,3-dithiane 1,1-dioxide (**3**) below −81.5 and −95°, respectively. Two isomers are observed in the former case in the ratio 84/16. The major isomer, assigned the equatorial structure, has the larger chemical-shift difference, the smaller coupling constant, and the lower field quartet midpoint. The configurational criteria developed in thiane and selenane systems therefore carry over to these dithianes. 1,3-Dithiane *cis*-1,3-dioxide (**5**) and 1,3,5-trithiane 1-oxide (**7**) exhibit resonances for only one isomer down to −70°. It is suggested that this isomer has the equatorial structure in both cases, although the configurational criteria cannot be applied in the absence of the second isomer. In the case of the 1,3-dioxide, a coalescence of the AB spectrum for the 2 protons as the temperature is decreased is attributed to an equilibrium between monomer and dimer that favors dimer at lower temperatures.

The 2-axial proton resonates at higher field than the 2-equatorial proton for both isomers of 1,3-dithiane 1-oxide (eq 1). For the sulfone (1,3-dithiane 1,1-dioxide, **3**), the 2-axial resonance occurs at lower field, but, for the disulfoxide (1,3-dithiane *cis*-1,3-dithiane, **5**), it occurs at higher field. Finally, for 1,3,5-trithiane 1-oxide (**7**), the 2- and 6-axial resonance (from the protons next to the sulfoxide group) is found at higher field than the geminal equatorial resonance, whereas the 4-axial resonance (from the proton between the two sulfide linkages) is found at lower field. These assignments were made on the basis of the observed long-range equatorial–equatorial W-pathway coupling. All these observations can be explained in terms of a model in which the overall anisotropy of the C–(SO) bond is taken to have the same sign as that of the C–C bond but opposite in sign to the anisotropy of the C–S and the C–(SO_2) bonds. This model also explains some long-standing chemical-shift mysteries in group 6 heterocyclic conformational analysis.

Experimental Section

Preliminary and routine NMR spectra were recorded on Varian Associates T-60 and Hitachi Perkin-Elmer R20B 60-MHz spectrometers. The spectra determined as a function of temperature were obtained either on a Bruker HX-270 operating at 270 MHz[23] or on a Bruker HFX-10 operating at 90 MHz. The MIT program NMRCTL was used for the analysis of the spectra found in Figure 2, and the Northwestern program ABAB was used for calculation of the spectra in Figure 1. The Northwestern program ARRP was used to calculate Arrhenius parameters.

1,3-Dithiane 1-oxide (2) was prepared as described by Carlson.[24]

1,3-Dithiane 1,1-Dioxide (3). To 408 mg (3 mmol) of **2** in 30 ml of H_2O containing 1 g of $MgSO_4$ was slowly added a solution of 316 mg (2 mmol) of $KMnO_4$ in 20 ml of H_2O.[25] Decolorization of the $KMnO_4$ occurred instantly. After 1.5 hr, excess sodium metabisulfite was added and the resulting clear, colorless solution was extracted with $CHCl_3$ and the extracts dried over Na_2SO_4. Evaporation of the $CHCl_3$ afforded 412 mg (91%) of **3**, mp 138–139°. The analytical sample was obtained by recrystallization from dichloromethane–ether, mp 139–140°. Anal. Calcd for $C_4H_8O_2S_2$: C, 31.56; H, 5.30; S, 42.12. Found: C, 31.69; H, 5.16; S, 42.27.

1,3-Dithiane *cis*-1,3-Dioxide (5). *m*-Chloroperoxybenzoic acid (10 mmol) in 30 ml of CH_2Cl_2 was added dropwise to a cooled (0°) solution of **2** (1.36 g, 10 mmol) in 50 ml of CH_2Cl_2. The solution was allowed to stand at 0–5° for 14 hr, warmed to 25°, then allowed to stand a further 48 hr. The solvent was removed and the residue washed with 200 ml of ether to leave 1.19 g of white solid, mp 154–172° dec. The crude product appeared to be a mixture of *trans*-1,3-dioxide (**4**) and *cis*-1,3-dioxide (**5**) by NMR. Three recrystallizations from ethanol gave 236 mg of pure **5**, mp 215–216° dec (sealed capillary). Anal. Calcd for $C_4H_8O_2S_2$: C, 31.56; H, 5.30; S, 42.12. Found: C, 31.63; H, 5.23; S, 42.31.

1,3,5-Trithiane 1-oxide (7) has been prepared previously by oxidation of 1,3,5-trithiane with H_2O_2 in acetone (reported mp 187°).[26] In the present study use of *m*-chloroperoxybenzoic acid in CH_2Cl_2 afforded the same product (mp 186–187°).

References and Notes

(1) (a) Northwestern University; (b) University of Virginia.

(2) (a) UNESCO Fellow, 1970–1974. (b) This work was supported by the National Science Foundation (Grants GP-34259X and GP-35868X) and by the donors of the Petroleum Research Fund, administered by the American Chemical Society.

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