Tetrahedron Vol. 40, No. 9, pp. 1477 to 1485, 1984
Printed in Great Britain.

0040-4020/84 $3.00 + .00

CONFORMATIONAL PREFERENCE OF THE S→O BOND. ^{1}H AND ^{13}C NMR STUDIES OF THE MONO-S-OXIDES OF 1,2-, 1,3- and 1,4-DITHIANES.

Eusebio Juaristi* and José Guzmán

Departamento de Química, Centro de Investigación y de Estudios
Avanzados del Instituto Politécnico Nacional, Apartado Postal 140-740,
07000-México, D. F., México

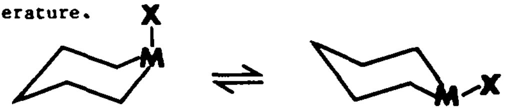
Vinayak V. Kane and Richard S. Glass*

Department of Chemistry, The University of Arizona,
Tucson, Arizona 85721

(*Received in USA* 15 *August* 1983)

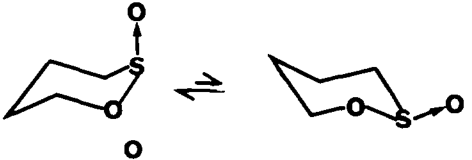
Abstract - The ^{1}H and ^{13}C NMR behavior of the monosulfoxides of 1,2-, 1,3- and 1,4-dithianes (1-3) were studied in order to determine the conformational preference of the S→O bond in these heterocycles. From the results of variable temperature, double irradiation, solvent effects and shift reagent experiments, it is concluded that the axial conformers dominate the conformational equilibria of 1 and 3. On the other hand, 2-equatorial is more stable than 2-axial by 0.64 kcal/mol (ΔG°) at -80°, in CD_3OD. This value is essentially identical with the one determined in $CHClF_2$, and the lack of a solvent effect appears to indicate that dipole/dipole interactions do not control this equilibrium. A $\Delta G_c^{\ddagger} = 11.0$ kcal/mol was determined for the inversion process of 2. Complete ^{1}H and ^{13}C NMR assignments for 1-3 are presented.

Nearly twenty years ago the classical papers of Johnson and Martin showed that the normal equatorial orientation of substituents in the cyclohexane ring (eq. 1, M = CH) was reversed in thiane oxide (eq. 1, M-X = S→O).[1] A generally accepted value for the conformational free energy difference of 0.2 kcal/mol was measured by Lambert and Keske[2] from the proton NMR spectrum below the coalescence temperature.

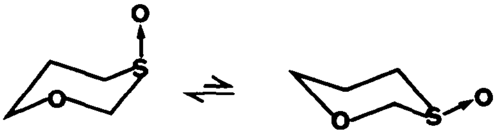


(1)

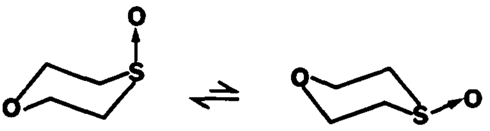
The preference of the S→O bond for the axial orientation was even greater in the oxathiane-S-oxides. Thus, Harpp and Gleason found no evidence for the equatorial conformer in 1,2-oxathiane-2-oxide (eq. 2), and estimated ΔG° to be greater than 2 kcal/mol at -90°C.[3] Anteunis and Cook have independently reported a 0.6-0.7 kcal/mol preference for axial 1,3-oxathiane-3-oxide (eq. 3).[4,5] More recently, Anteunis and Evans determined a 0.5-0.7 kcal/mol free energy difference in favor of the axial 1,4 analog (eq. 4).[6,7]



ΔG° > 2 kcal/mol (2)



ΔG° = 0.6-0.7 kcal/mol (3)



$\Delta G° = 0.5\text{-}0.7$ kcal/mol (4)

The basis for the enhanced predominance of the axial S→O bond observed when a methylene group is substituted by an oxygen atom in pentamethylene sulfoxide remains an open question, although the involvement of dipole-dipole interactions and the anomeric effect in the 1,2-isomer[8] appear inescapable. Further insight into this question should be afforded by conformational analysis of 1,2-, 1,3-, and 1,4-dithiane-mono-S-oxides. Indeed, such detailed studies on 1,3-dithiane-1-oxide have been reported.[9] Preliminary observations on the 1,2- and 1,4-analogs have also been recorded.[10]

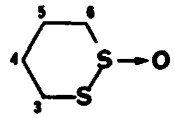
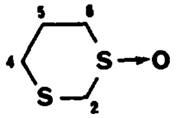
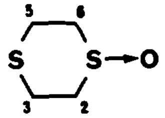
This paper reports the results of high resolution ^1H and ^{13}C NMR studies on the title heterocycles 1-3. Essentially complete assignment of the spectra was possible by the examination of variable temperature, double irradiation, aromatic solvent and lanthanide shift reagent effects.[11] These data not only afforded much of the required structural and stereochemical information, but they also provided a wealth of spectroscopic observations which should be of diagnostic value in the analysis of related systems.

Results and Discussion

A. ^{13}C NMR Spectra.

Table I contains the chemical shifts observed for the carbon atoms present 1-3 at 22°C and -90°C in CD_3OD-CD_3SOCD_3 (3:1).[12] The assignments were based on anticipated shifts due to the inductive and field effects of the sulfur atom and the sulfinyl moiety.[13] The chemical shifts reported in Table I for 1 are all consistently ca. 1.0 ppm downfield relative to the values measured by Oae in $CDCl_3$.[14] In the case of 2 the agreement with values obtained in $CDCl_3$ is better ($\Delta\delta$ < 0.5 ppm).[15]

Table I. ^{13}C NMR Data for the Monosulfoxides 1-3 in CD_3OD-CD_3SOCD_3 at 62.9 MHz

Dithiane 1-Oxide	 1		 2		 3	
T (°C)	22	-90	22	-90	22	-90
C_2	-	-	50.18	a	47.48	44.36
C_3	22.44	24.23	-	-	19.60	17.22
C_4	26.50	26.32	27.70	28.11	-	-
C_5	16.24	16.07	28.60	30.52	19.60	17.22
C_6	52.75	51.78	52.66	53.20	47.48	44.36

[a] Obscured by overlap with residual protiated solvent signal.

Only one set of resonances is observed for the three samples from room temperature to -90°C. Likely explanations for this result are that $\Delta G°$ are too large (>1.0 kcal/mol) or $\Delta G^{\ddagger}$ are too small (<10 kcal/mol) for the axial ⇄ equatorial equilibria in 1-3. Indeed, reduced 1-2 rotational interactions in 1 should lower its barrier to chair-chair interconversion.[3,16] Allinger calculated by the molecular mechanics method[17] a $\Delta G°$ of 1.1 kcal/mol in favor of 3-axial. On the other hand, the fact that the conformational isomers of 2 were not observed at -90° is not readily understandable since $\Delta G°$ and $\Delta G^{\ddagger}$ for this system are 0.6 and 11.0 kcal/mol, respectively (vide infra).

The single most important chemical shift in the ^{13}C NMR spectrum of 1 is that of C(5) at 16.2 ppm (T=22°). This value represents a 11-13 ppm upfield shift relative to the chemical shift of this carbon atom in 1,2-dithiane (δ = 27.8 ppm[13a,14]) which can confidently be ascribed to the γ-effect[18] of the axial S→O bond.[19] There is essentially no change in this chemical shift at -90° (δ = 16.1 ppm) and these observations lend support to the proposal of Bass and Evans that 1 exists exclusively in the axial conformation at ambient temperature.[13a]

The signal for C(3,5) in 3 appears at 19.60 ppm (T=22°) and is again indicative of an axial orientation of the sulfinyl group. Here, however, the apparent upfield shift relative to the unoxidized 1,4-dithiane (δ = 29.1 ppm[20]) is smaller: ca. 9.5 ppm. It appears that 3-axial predominates over 3-equatorial, although not to a great extent. Supporting evidence for this conclusion comes from the 2-3 ppm upfield shifts for C(2,6) and C(3,5) when the temperature was lowered to -90°. It has been shown that both the β and γ carbons experience upfield shifts in going from equatorial to axial S→O,[19] and the temperature effect described above appears to indicate that the 3-axial/3-equatorial ratio increases at lower temperatures.[21]

In the ^{13}C NMR spectrum of 2 at room temperature, the chemical shifts of C(5) and C(6) are the most diagnostic for conformational analysis,[15,22] and clearly suggest a predominance of the equatorial conformer. In particular, from the known β and γ effects of an axial S→O bond,[15,22] values of ca. 15 and ca. 46 ppm are predicted for C(5) and C(6), respectively, for 2-axial and ca. 31 and ca. 54 ppm, respectively for 2-equatorial. The observed chemical shifts of 28.6 and 52.7 ppm are much closer to the predicted values for the equatorial conformer. Downfield shifts are observed when the temperature is lowered to -90° and this may be indicative of an increased preference of 2-equatorial in the equilibrium (vide supra).

B. ^1H NMR Spectra.

Table II contains the chemical shifts observed for the hydrogen atoms in 1 and 3, both in CD_3OD and C_6D_6, at 250 MHz and room temperature. Details of the ^1H NMR spectrum of 2 have been given by others.[9a]

1,2-Dithiane 1-oxide

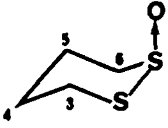
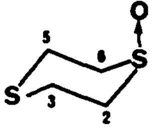
Even at 250 MHz, the proton spectrum of 1 is fairly complex (Figure 1), and the complete assignment of the signals was only possible after double irradiation experiments and by the addition of shift reagents.

Nevertheless, it is known that a syn-diaxial orientation between a proton and a sulfinyl group results in significant (ca. 0.7 ppm) downfield shifts for the proton.[3,6,23,24] Our C-13 data suggested a highly predominant 1-axial conformer (vide supra) and that led to the assignment of the signals at 3.58 (d of d of d) and 2.77 (d of t) to H(3ax) and H(3eq), respectively [$\Delta\delta$ = 0.81 ppm]. Similarly, the signals at 2.54 (d of t of t) and at 1.88 (d of quintets) were ascribed to H(5ax) and H(5eq) [$\Delta\delta$ = 0.66 ppm]. Indeed, irradiation at 3.58 ppm caused the signals at 2.77 ppm to lose their geminal coupling, collapsing into a triplet. Similarly, irradiation at 2.54 ppm modified the signals centered at 1.88 ppm into a single quintet.

By contrast, the axial and equatorial hydrogens at C(6) and C(4) differ by less than 0.1 ppm in chemical shift and appear in the spectrum as partially overlapped signals at ca. 3.2 and ca. 2.1 ppm. When H(5eq) was irradiated (at 1.88 ppm), both H(6ax) and H(6eq) lost one gauche coupling and became doublets of doublets at 3.24 and 3.15 ppm, respectively. Because J_{gem} and J_{anti} for H(6ax) have the same magnitude (13.5 Hz, see Table III), this last signal appears as a triplet.

The signal for H(4eq) could also be assigned with confidence since irradiation at 3.58 ppm [H(3ax)] caused it to lose one gauche coupling, becoming a doublet of quartets centered at 2.12 ppm.

Table II. 250 MHz ^{1}H NMR Chemical Shifts for 1 and 3 at 22°C.

Dithiane 1-Oxide	 1		 3	
Solvent	CD_3OD	C_6D_6	CD_3OD	C_6D_6
H(2ax)	-	-	3.15*	2.04
H(2eq)	-	-	3.15*	2.30
H(3ax)	3.58	3.34	3.47	3.32
H(3eq)	2.77	1.92	2.60	1.69
H(4ax)	2.02*	1.30*	-	-
H(4eq)	2.12	1.30*	-	-
H(5ax)	2.54	2.29*	3.47	3.32
H(5eq)	1.88	1.02	2.60	1.69
H(6ax)	3.15	2.29*	3.15*	2.04
H(6eq)	3.24	2.40*	3.15*	2.30

*This number may be in error by as much as 0.05 ppm, due to partial overlap with other signal(s).

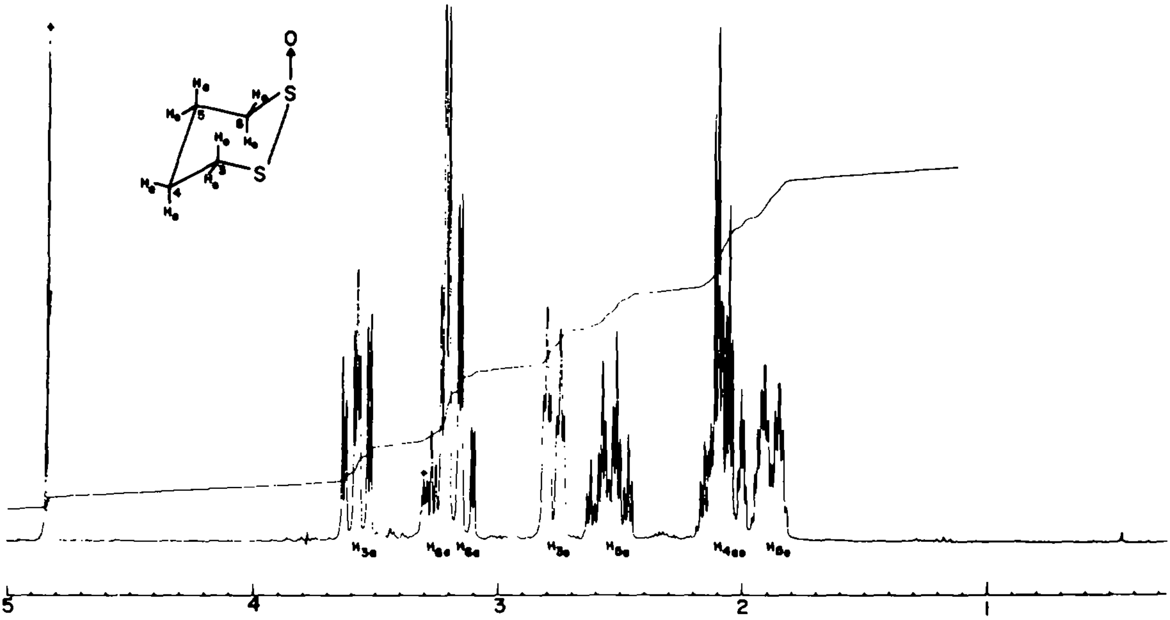
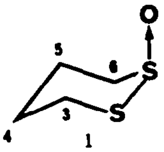


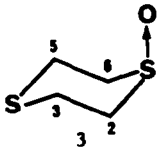
Figure 1. The observed 250-MHz proton spectrum of 1,2-dithiane 1-oxide (1) in CH_3OD at 22°C. Residual protiated solvent signals are indicated by +.

Table III lists the coupling constants extracted from the original spectrum of 1 (Figure 1) and the various double-irradiation experiments (supplementary material).

Table III. Coupling Constants for the Hydrogens in 1 and 3.



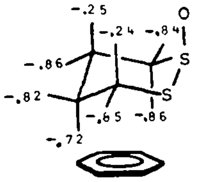
1



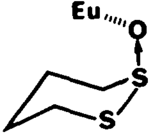
3

Coupled Nuclei	J (Hz)	Coupled Nuclei	J (Hz)
3ax/3eq	14.0	2ax/2eq	13.7
3ax/4ax	11.7	2ax/3ax	11.4
3ax/4eq	3.4	2ax/3eq	2.8
3eq/3ax	14.2	2eq/2ax	13.6
3eq/4	3.5	2eq/3	1.7
4eq/4ax	14.3	3ax/3eq	14.6
4eq/3,5	4.1	3ax/2ax	9.8
5ax/5eq	14.85	3ax/2eq	1.7
5ax/4,6a	12.0	3eq/3ax	15.05
5ax/4,6e	3.8	3eq/2	2.4
5eq/5ax	14.7	3eq/6eq	5.4
5eq/4,6	3.7	6eq/3eq	4.7
6ax/6eq	13.5		
6ax/5ax	13.5		
6ax/5eq	3.05		
6eq/6ax	13.9		
6eq/5	4.3		

It can easily be seen in Table II that, relative to the values obtained in $CDCl_3$, most of the signals in 1 are shifted upfield in C_6D_6 by an average of ca. 0.825 ppm. The only signals that remain relatively unchanged are those due to H(3ax) and H(5ax). These induced shifts (Δ ASIS) clearly indicate the formation of a collision complex[11b,25] between the aromatic solvent and the axial conformer of sulfoxide 1:



Further evidence in support of a high predominance of the axial conformation of 1 was obtained from the study of its ^1H NMR spectrum after the addition of 0.15 equivalents of $Eu(fod)_3$ in CD_2Cl_2. The lanthanide induced shifts (LIS) decreased in the order H(5ax)>H(3ax)>H(6eq)>>H(4ax, 6ax, 5eq, 3eq, 4eq), which strongly suggests the complex as shown below.



Interesting features about this LIS spectrum (supplementary material) are that the 6eq and 6ax resonances which overlap in CD_3OD ($\Delta\delta$ = 0.09 ppm) are now separated by 0.71 ppm; and similarly, $\Delta\delta$(3ax 3eq) and $\Delta\delta$(5ax 5eq) more than double under these conditions.[26] Unfortunately, neither AIS nor LIS effects causes a separation of the signals of 4eq and 4ax.

From the coupling data present in Table III, it is possible to estimate the approximate solution geometry of 1 by means of Lambert's R-value method.[27] The results obtained [R_{34} = 2.20; R_{45} = 2.12; R_{56} = 2.26. ψ_{34} = 58.2°; ψ_{45} = 57.65°; ψ_{56} = 58.6°] suggest a mostly undistorted cyclohexane-like shape for 1, with some slight puckering in the $-CH_2CH_2-$ segments adjacent to sulfur.

In an attempt to observe different signals for the individual conformers in 1-axial $\rightleftarrows$ 1-equatorial, the spectrum was recorded at -80°C in CD_3OD. The spectrum is the same at this temperature and room temperature. This, together with the additional information collected, indicates that the participation of 1-equatorial in the equilibrium is not significant.

1,3-Dithiane 1-oxide.

A complete assignment of the ^1H NMR spectrum of 2 was reported by Cook.[9a] Thus, only the spectroscopic behavior of the low field hydrogens [H(2)], which have been shown to provide pertinent information on the conformational behavior of this system,[9] will be briefly discussed here.

The room temperature (+22°C) spectrum of 2 in CD_3OD shows an AB pattern centered at 3.99 ppm (Figure 2). The lower field half of this quartet is further split by a long-range W coupling (J = 2.6 Hz) to H(4eq) and can be confidently assigned to H(2eq).

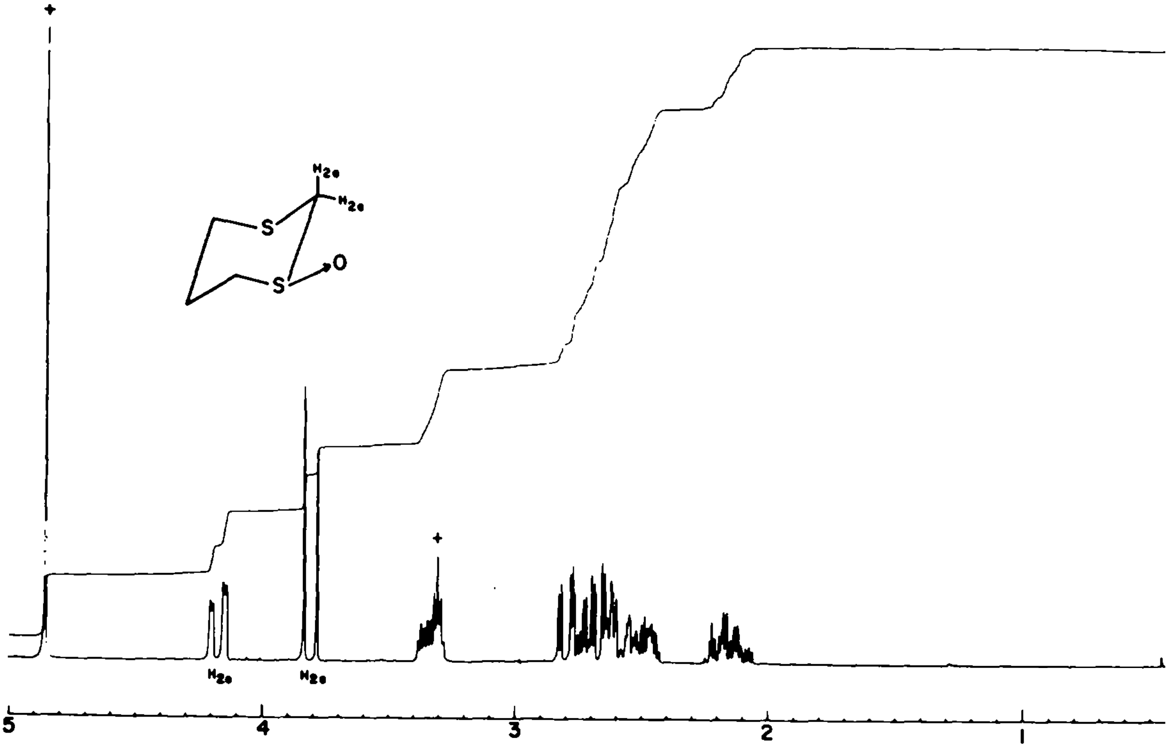
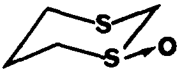


Figure 2. The observed 250-MHz proton spectrum of 1,3-dithiane 1-oxide (2) in CD_3OD at 22°C. Residual protiated solvent signals are indicated by +.

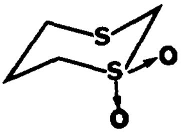
As the temperature of the sample was lowered, a broadening of the signals was observed, with eventual coalescence at -55°. Two AB quartets are recorded at -80°; the more intense centered at 4.13 ppm (J_{AB} = 11.9 Hz) and the less intense at 4.05 ppm (J_{AB} = 14.8 Hz). The ratio of the two AB quartets is 84:16 corresponding to a $\Delta G°_{-80°}$ = 0.64 kcal/mol.

The larger AB system is ascribed to 2-equatorial in view of its lower field position and smaller geminal coupling constant.[2,5,6,9,28] It should be mentioned that the third criterion commonly used for the assignment of sulfoxide configuration, that is larger $\Delta\delta$ ax/eq for a methylene α to an equatorial S→O bond,[2,5,6,9,28] is not applicable here since both AB quartets show approximately the same $\Delta\delta = 0.34$ ppm.[29] Therefore, the equatorial conformer of 2 predominates at equilibrium, and the free energy difference measured in CD_3OD ($\Delta G^\circ_{-80^\circ} = 0.64$ kcal/mol, this work) is essentially identical with that obtained in a Freon ($\Delta G^\circ_{-81.5^\circ} = 0.63$ kcal/mol).[9c] This lack of a solvent effect argues against the importance of a dipole/dipole mechanism for explaining the preference of 2 for the equatorial orientation.[17,30]

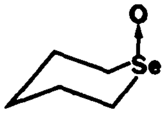
From the coalescence temperature ($T_c = -55^\circ$) and the chemical shift difference for H(2) in 2-axial and 2-equatorial ($\Delta\delta = 19.18$ Hz), a $\Delta G_c^\ddagger = 11.0$ kcal/mol could be estimated. For comparison, the free energy differences of activation for related systems are shown below.



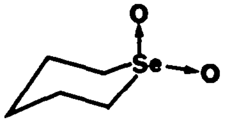
$\Delta G_c^\ddagger = 11.0$ kcal/mol
(this work)



$\Delta G_c^\ddagger = 9.8$ kcal/mol[9c]



$\Delta G_c^\ddagger = 8.3$ kcal/mol[31]



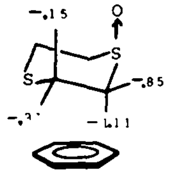
$\Delta G_c^\ddagger = 6.7$ kcal/mol[31]

1-4-Dithiane 1-Oxide.

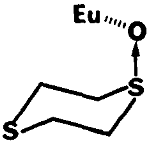
The chemical shifts and coupling contants determined from the spectra of 3 are summarized in Tables II and III. Figure 3 depicts the ^1H NMR spectra of 3 in CD_3OD and C_6D_6.

The signals located at 3.47 and 2.60 ppm in the ^1H NMR spectrum of 3 in CD_3OD were assigned to H(3,5ax) and H(3,5eq), respectively, because ^{13}C NMR evidence (vide supra) suggested the predominance of 3-axial and a deshielding effect of the syn-axial S→O group (ca. 0.7 ppm)[3,6,23,24] was therefore expected.[32] In this solvent, the resonances of 2,6ax and 2,6eq overlap at 3.15 ppm. However, all signals are well separated in C_6D_6. That the assignments given in Table II are correct was confirmed by double irradiation experiments: decoupling of the signal located at 3.32 ppm [d of d of d, H(3,5ax)] caused H(3,5eq) the loss of J_{gem}, H(2,6ax) the loss of J_{anti}, and H(2,6eq) the loss of one J_{gauche}. Similarly, irradiation at 2.04 ppm [d of d of d, H(2,6ax)] caused H(2,6eq) the loss of J_{gem}, H(3,5ax) the loss of J_{anti}, and H(3,5eq) the loss of one J_{gauche}. Finally, when the signal located at 1.69 ppm [d of d of t, H(3,5eq)] was decoupled H(2,6ax) lost J_{gauche}, H(2,6eq) lost ^5J_w and one J_{gauche}, and H(3,5ax) lost J_{gem}.

Relative to the spectrum recorded in CD_3OD, the shifts induced by benzene as solvent (Δ ASIS) clearly indicate the formation of a collision complex[11b,25] involving the axial conformer of sulfoxide 3:



Additional evidence for the predominance of the axial conformer of sulfoxide 3 comes from the CD_2Cl_2 proton spectrum recorded after the addition of 0.15 equiv of $Eu(fod)_3$. All resonances are well separated under these conditions (supplementary material), with observed LIS in the order H(3,5ax)> H(2,6eq)>>H(3,5eq)>H(2,6ax). Complexation of the shift reagent to axial-3 is therefore apparent.



As was the case with sulfoxide 1 (vide supra) attempts to observe the individual conformers of 3 at low temperature failed, even in the presence of shift reagent, which increases the difference in chemical shifts for the individual hydrogens and was expected to raise the coalescence temperature.[33,34] A plausible conclusion at this point is that for sulfoxide 3, the amount of the equatorial isomer is only minor at equilibrium.[6,17]

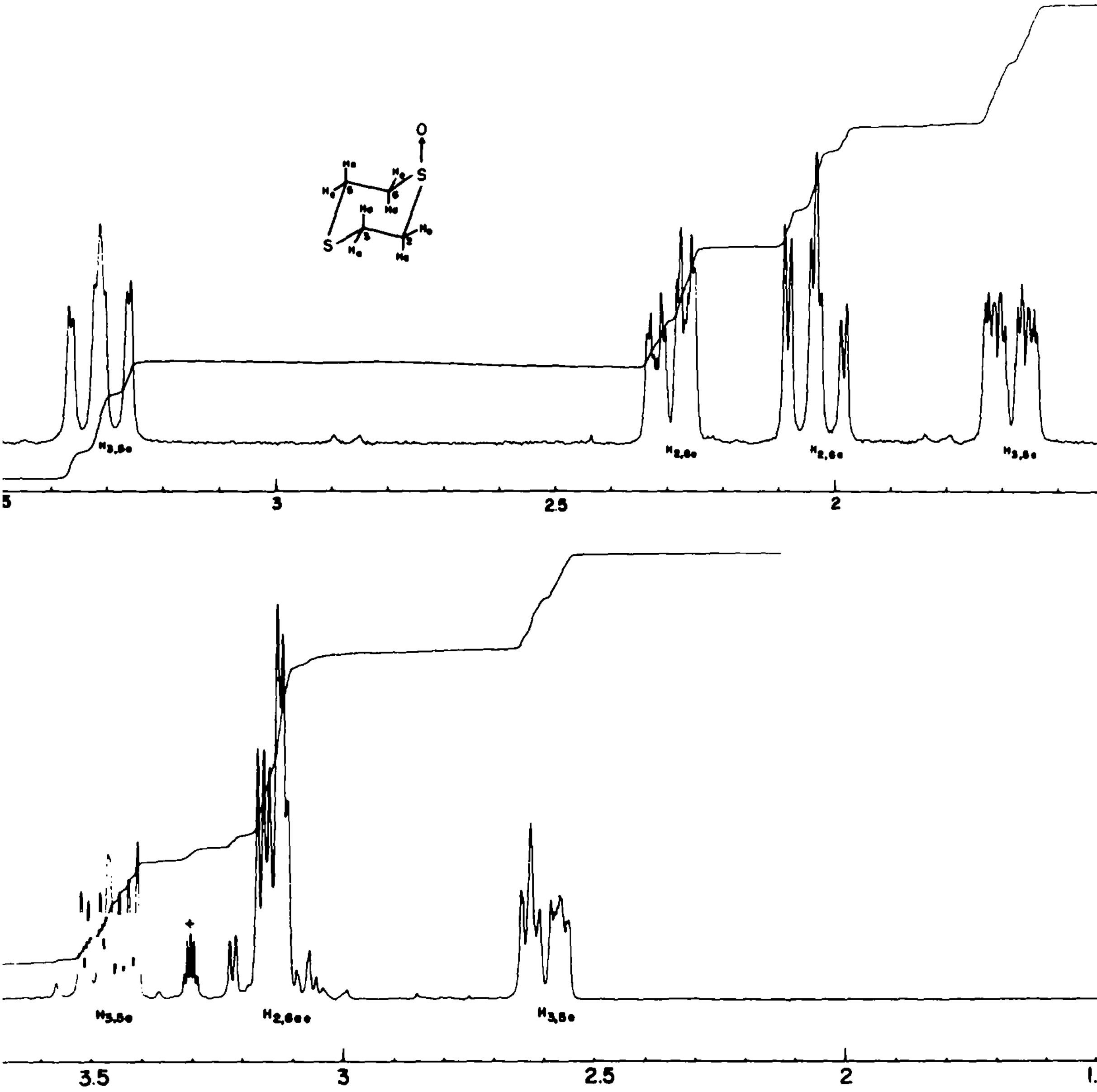


Figure 3. The observed 250-MHz proton spectrum of 1,4-dithiane 1-oxide (3) in C_6D_6 (top) and CD_3OD (bottom) at 22°C. Residual protiated solvent signals are indicated by +.

Experimental Section

The ^1H and ^{13}C NMR spectra were recorded on Bruker WM-250 spectrometer at 250 and 62.9 MHz, respectively, and are reported in ppm from internal tetramethylsilane (TMS) on the δ scale. Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), integration, coupling constants (Hz), assignment.

Preparation of 1,2-Dithiane 1-oxide (1). 1-2-Dithiane was prepared from 1,4-dichlorobutane, sodium sulfide and sulfur according to the method of Eliel et al.[35] Oxidation to 1 was achieved with sodium periodate.[36]

Synthesis of 1,3-Dithiane 1-oxide (2). 1,3-Dithiane was prepared from 1,3-propanedithiol and dimethoxymethane following the procedure of Corey and Seebach.[37] Oxidation to 2 was accomplished with acetyl nitrate.[38]

Preparation of 1,4-Dithiane 1-oxide (3). 1,4-Dithiane was prepared from 1,2-ethanedithiol and 1,2-dibromoethane in the presence of sodium ethoxide.[39] Oxidation to **3** was carried out with hydrogen peroxide.[40]

Supplementary Material Available: Copies of the more pertinent spectra from double irradiation and shift reagent experiments (10 pages). Ordering information is given on any current masthead page.

References and Notes

1. (a) Johnson, C.R.; McCants,D. J. Am. Chem. Soc. 1964, 86, 2935-2936; (b) Martin, J.C.; Uebel, J.J. Ibid. 1964, 86, 2936-2937.
2. Lambert, J.B.; Keske, R.G. J. Org. Chem. 1966, 31, 3429-3431.
3. Harpp, D.N.; Gleason, J.G. Ibid. 1971, 36, 1314-1316.
4. Van Acker, L.; Anteunis, M. Tetrahedron Lett. 1974, 225-228.
5. Bergesen, K.; Cook, M.J.; Tonge, A.P. Org. Magn. Reson. 1974, 6, 127-128.
6. Nachtergaele, W.A.; Anteunis, M. Bull. Soc. Chim. Belg. 1980, 89, 525-535. Van Acker, L. Ph.D. Thesis, R.U.G., Gent, Belgium, 1977.
7. Frieze, D.M.; Evans, S.A. J. Org. Chem. 1975, 40, 2690-2691.
8. (a) Szarek, W.A.; Horton, D., Ed., "Anomeric Effect", ACS Symp. Ser. 87; Am. Chem. Soc.: Washington, D. C., 1979; (b) Kirby, A.J. "The Anomeric Effect and Related Stereoelectronic Effects at Oxygen", Springer-Verlag: Berlin, 1983.
9. (a) Cook, M.J.; Tonge, A.P. Tetrahedron Lett. 1973, 849-850; Cook, M.J.; Tonge, A.P. J. Chem. Soc., Perkin Trans. 2, 1974, 767-772; (b) Van Acker, L.; Anteunis, M. Tetrahedron Lett. 1974, 225-228; (c) Khan, S.A.; Lambert, J.B.; Hernández, O.; Carey, F.A. J. Am. Chem. Soc. 1975, 97, 1468-1473.
10. 1,2-Dithiane-1-oxide: See Ref. 3. 1,4-Dithiane-1-oxide: See Ref. 6. Also, Hayasaki, K. Tokyo Gakugei Daigaku Kenkyu Hokoku, 3-bu, Shizen Kagaku 1961, 12, 25-28. Chem. Abstr. 1964, 60, 6724h.
11. (a) Fraser, R.R.; Wigfield, Y.Y. Chem. Commun. 1970, 1471-1472; (b) Fraser, R.R.: Durst, T.; McClory, M.R.; Viau, R.; Wigfield, Y.Y. Int. J. Sulfur Chem. A 1971, 1, 133-142.
12. Poor solubility of 1-3 in other solvents at -90°C led us to this choice of a polar medium.
13. cf. (a) Bass, S.W.; Evans, S.A. J. Org. Chem. 1980, 45, 710-715; (b) Hirsch, J.A.; Havinga, E. Ibid. 1976, 41, 455-462; (c) Wiseman, J.R.; Krabbenhoft, H.O.; Anderson, B.R., Ibid. 1976, 41, 1518-1521.
14. Takata, T.; Iida, K.; Oae, S. Heterocycles 1981, 15, 847-850.
15. Carey, F.A.: Dailey, O.D.; Hutton, W.C. J. Org. Chem. 1978, 43, 96-101.
16. Wilson, E.B. Adv. Chem. Phys. 1959, 2, 367-393.
17. Allinger, N.L.; Kao, J. Tetrahedron 1976, 32, 529-536.
18. Grant, D.M.; Cheney, B.V. J. Am. Chem. Soc. 1967, 89, 5315-5318.
19. Buchanan, G.W.; Durst, T. Tetrahedron Lett. 1975, 1683-1686.
20. Szarek, W.A.; Vyas, D.M.; Sepulchre, A.M.; Gero, S.D.; Lukacs, G. Can. J. Chem. 1974, 52, 2041-2047.
21. We consider it unlikely that the observed upfield displacements of all carbons in 3 reflect a temperature effect independent of the conformational equilibrium since the magnitude and sign of the temperature induced shifts are so different in 1, 2, and 3 (see text).
22. Koskimies, J.K. Ph.D. Dissertation, University of North Carolina at Chapel Hill, 1976.
23. Cooper, R.D.G.; DeMarco, P.V.; Cheng, J.C.; Jones, M.D. J. Am. Chem. Soc. 1969, 91, 1408-1415.
24. Nachtergaele, W.A.; Tavernier, D.; Anteunis, M. Bull Soc. Chim. Belg. 1980, 89, 33-44.
25. Ronayne, J.; Williams, D.H. J. Chem. Soc., B, 1967, 540-546. Bhacca, N.S.; Williams, D.H. "Application of NMR Spectroscopy in Organic Chemistry", Holden-Day: San Francisco, 1964, Chapter 7.
26. Large downfield shifts for the hydrogen atoms closer to the S→O group in 1,2-oxathiane 2-oxide were observed by Buchanan, et al., upon the addition of 0.5 equiv. of Eu(fod)$_3$: Buchanan, G.W.; Sharma, N.K.; de Reinach-Hirtzbach, F.; Durst, T. Can. J. Chem. 1977, 55, 44-49.
27. Lambert, J.B. Acc. Chem. Res. 1971, 4, 87-94.
28. Lambert, J.B.; Mixan, C.E.; Bailey, D.S. J. Am. Chem. Soc. 1972, 94, 208-214.
29. In contrast, $\Delta\delta$(2ax 2eq) in 2-equatorial equals 0.36 ppm; $\Delta\delta$(2ax 2eq) in 2-axial equals 0.26 ppm, in CHClF$_2$ as solvent.[9c]
30. The lack of a solvent effect is also unexpected in view of the ability of sulfoxides to hydrogen bond with alcohols: Tamres, M.; Searles, S. J. Am. Chem. Soc. 1959, 81, 2100-2104.
31. Lambert, J.D.; Mixan, C.E.; Johnson, D.H. Tetrahedron Lett. 1972, 4335-4338.
32. The ^{1}H NMR spectrum of 1,4-dithiane in CDCl$_3$ consists of a single line at 2.85 ppm: Sadtler spectrum no. 330.
33. Hofer, O. Top. Stereochem. 1976, 9, 111-197.
34. Actually, broadening and coalescence of the signals in the presence of Eu(fod)$_3$ was observed at -50°. However, the spectrum recorded at -85° cannot be readily assigned to any conformer of 3. Further studies are clearly required.
35. Eliel, E.L.; Rao, V.S.; Smith, S.; Hutchins, R.O. J. Org. Chem. 1975, 40, 524-526.
36. Johnson, C.R.; Keiser, J.E. Org. Synth., Coll. Vol. 5, 791-793.
37. Corey, E.J.; Seebach, D. Ibid. 1970, 50, 72-74.
38. Louw, R; Vermeeren, H.P.W.: van Asten, J.J.A.: Ultée, W.J. J. Chem. Soc., Chem. Commun. 1976, 496-497.
39. Gillis, R.G.; Lacey, A.B. Org. Synth., Coll. Vol. 4, 396-398.
40. Kuhn, R.; Neugebauer, F.A. Chem. Ber. 1961, 94, 2629-2644.